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Pain Catastrophizing as a Predictor for Postoperative Opioid Requirements for Breakthrough Pain in Patients Undergoing Elective Surgery admitted in a Private Institution from January 2021 to June 2021
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A Rare Case of Mixed Adult Hepatoblastoma Mimicking as Hepatocellular Carcinoma
Jan Catherine G. Carrera, MD

Neck Circumference – Height Ratio Cut-Off as a Predictor of Obstructive Sleep Apnea Severity among Adult Patients Diagnosed with Obstructive Sleep Apnea at the Lung Center of the Philippines
Ryan Martin K. Denopol MD, Maria Cecilia I. Jocson, M.D., FPCP, FPCCP, FPSSM

Prophylactic Paracetamol for Intraoperative Shivering Prevention for Patients Undergoing Gynecological Procedures under Spinal Anesthesia: A Randomized Clinical Trial
Angeline Bonne P. Regadio, MD

Platelet-Rich Plasma Injection of Skin Graft in a Patient with Squamous Cell Carcinoma and Psoriasis on Prolonged Methotrexate Therapy: A Case Report
Florteresa G. Ollero, MD, Patricia Cleopatra Geluz Guieb, MD, Maria Cristina A. Puyat, MD, Maria Isabel Beatriz Puno-Gomez, MD, Erika Kim Chan, MD

Gastrointestinal Manifestations and Health Outcomes in Patients with COVID-19 Infection in a Tertiary Hospital
Lester Jan Alvarado Olimba, MD, Ashraf Tawasil, MD, Adrian Alick Bonghanoy, MD, Joshua Josef Torres, MD Agnes Evasan, MD, Eric Yasay, MD, Sonia Salamat, MD, Francisco N. Delos Reyes

A Randomized Clinical Trial Application of Honey versus Ketoconazole 2% Shampoo for the Treatment of Seborrheic Dermatitis
Dianne Christine C. Sia, MD, Lillian Lopez-Villafuerte, MD, FPDS, Zharlah Gulmatico-Flores, MD, FPDS

Metachronous Metastasis to the Stomach from a Primary Colon Cancer in a Filipino Patient – A Case Report
John Alfredo Raphael P. Pangilinan, MD, Juliet D. Gapasin, MD

Effectiveness of Pre-Anesthetic Induction Checklist in Improving General Anesthesia Induction Set-Up in a Simulated Setting during the Covid-19 Pandemic
Karla Shayne D. Feliciano, MD

TABLE OF CONTENTS

Journal of the
PHILIPPINE MEDICAL ASSOCIATION
VOLUME 101, NUMBER 1 ▪ June - December 2022

Intravascular Papillary Endothelial Hyperplasia Mimicking Sister Mary Joseph Nodule in a Patient with Ovarian Carcinoma 1
Tina Elaine M. Resuello, MD, Charlene Marie Ang-Tiu, MD, FPDS

Pain Catastrophizing as a Predictor for Postoperative Opioid Requirements for Breakthrough Pain in Patients Undergoing Elective Surgery admitted in a Private Institution from January 2021 to June 2021 6
Jeena Megan T. Tanco, MD

Covid-19 and Mental Health of Healthcare Workers: A Systematic Review 14
Elsie Lynn Baronia-Locson, MD

The Effects of Gadget Use on Sleep Quality among Elementary Students in Grades 4-6 in a Private School in Lucena City, Quezon Province 36
Charlot Joy D. del Rio, MD, Michelle R. Rejano-Octavio, MD, FPPS

A Rare Case of Mixed Adult Hepatoblastoma Mimicking as Hepatocellular Carcinoma 51
Jan Catherine G. Carrera, MD

Neck Circumference – Height Ratio Cut-Off as a Predictor of Obstructive Sleep Apnea Severity among Adult Patients Diagnosed with Obstructive Sleep Apnea at the Lung Center of the Philippines **56**
Ryan Martin K. Denopol MD, Maria Cecilia I. Jocson, M.D., FPCP, FPCCP, FPSSM

Prophylactic Paracetamol for Intraoperative Shivering Prevention for Patients Undergoing Gynecological Procedures under Spinal Anesthesia: A Randomized Clinical Trial **68**
Angeline Bonne P. Regadio, MD

Platelet-Rich Plasma Injection of Skin Graft in a Patient with Squamous Cell Carcinoma and Psoriasis on Prolonged Methotrexate Therapy: A Case Report **79**
Florteresa G. Ollero, MD, Patricia Cleopatra Geluz Guieb, MD, Maria Cristina A. Puyat, MD, Maria Isabel Beatriz Puno-Gomez, MD, Erika Kim Chan, MD

Gastrointestinal Manifestations and Health Outcomes in Patients with COVID-19 Infection in a Tertiary Hospital **84**
Lester Jan Alvarado Olimba, MD, Ashraf Tawasil, MD, Adrian Alick Bonghanoy, MD, Joshua Josef Torres, MD, Agnes Evasan, MD, Eric Yasay, MD, Sonia Salamat, MD, Francisco N. Delos Reyes

A Randomized Clinical Trial Application of Honey versus Ketoconazole 2% Shampoo for the Treatment of Seborrheic Dermatitis **98**
Dianne Christine C. Sia, MD, Lillian Lopez-Villafuerte, MD, FPDS, Zharlah Gulmatico-Flores, MD, FPDS

Metachronous Metastasis to the Stomach from a Primary Colon Cancer in a Filipino Patient – A Case Report **105**
John Alfredo Raphael P. Pangilinan, MD, Juliet D. Gapasin, MD

Effectiveness of Pre-Anesthetic Induction Checklist in Improving General Anesthesia Induction Set-Up in a Simulated Setting during the Covid-19 Pandemic **109**
Karla Shayne D. Feliciano, MD

Journal of the
PHILIPPINE MEDICAL ASSOCIATION
VOLUME 101, NUMBER 1 ▪ June - December 2022

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Journal of the
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Intravascular Papillary Endothelial Hyperplasia Mimicking Sister Mary Joseph Nodule in a Patient with Ovarian Carcinoma

Tina Elaine M. Resuello, MD[1]
Charlene Marie Ang-Tiu, MD, FPDS[2]

Abstract

Intravascular Papillary Endothelial Hyperplasia (IPEH) is a rare benign vascular lesion of the skin and subcutaneous tissues that results from the proliferation of endothelial cells within a blood vessel. In this article, we present the case of an IPEH mimicking a Sister Mary Joseph Nodule on the umbilicus of a 53-year old female patient with ovarian cancer. A diagnostic workup was performed with a computerized tomography of abdominal cavity and pelvis showing an expansive cystic tumor formation with probable ovarian origin. Two separate histopathologic readings were done on the cutaneous lesion which revealed contradicting findings of benign versus malignant tumors. Immunohistochemical stains done showed that the lesion was positive for ERG and negative for epithelial differentiation markers. No surgical intervention was done at the time of consultation as a cutaneous metastasis was primarily considered initially. It is crucial to rule out a diagnosis of Sister Mary Joseph nodule, especially in a background of ovarian carcinoma as it may mimic vascular lesions occurring on the umbilicus. Immunohistochemical staining is a significant tool to precisely diagnose such lesions so that it is neither inadequately nor aggressively managed.

Keywords: Intravascular Papillary Endothelial Hyperplasia, Masson's tumor, Sister Mary Joseph nodule, ovarian cancer, case report

INTRODUCTION

Intravascular Papillary Endothelial Hyperplasia (IPEH), also known as Masson's tumor or Masson's vegetant intravascular hemangioendothelioma (MVH) is a benign tumor that clinically presents as bluish to purplish red cystic masses containing sanguineous material. This case report describes an 53-year-old female diagnosed with an ovarian new growth presenting with umbilical skin lesions grossly resembling what was first thought of as a Sister Mary Joseph's (SMJ) nodule given the patient's background of a pre-existing carcinoma. It was upon further testing with immunohistochemistry that the final diagnosis was confirmed. Cutaneous metastasis like the SMJ nodule, although extremely rare is an important physical finding as it is a sign of advanced stage of malignancy. Hence, it was at the outset, considered in the case. However, it is also of significant to arrive with an accurate diagnosis in this case because it influences the management of the primary tumor and alleviates additional stress to the patient.

CASE REPORT

A 53-year old Filipino female patient presented with a 2-year history of slowly progressing abdominal enlargement with subsequent appearance of multiple, slightly tender papules and nodules on the umbilicus. The appearance of cutaneous lesions started 2 months prior to the referral of the Department of Obstetrics and Gynecology (OB-GYN) to the Department of Dermatology. Review of systems revealed accompanying significant weight loss and abdominal discomfort. The past medical and personal and social

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[2] *Consultant, Department of Dermatology, Rizal Medical Center*

history were unremarkable. She had no history of previous surgeries. The family medical history revealed a history of diabetes mellitus in a sibling and myoma on the paternal side. On physical examination, the patient had evident ascites with a presence of skin-colored and hyperpigmented papules, few nodules and cystic mass on the umbilicus. Dermoscopy of the cutaneous lesions revealed patchy pseudo reticular network with thick brown lines surrounding a s tructureless area and a milky red structureless area some with white veil and multiple shiny white lines and strands (Figure 3). These dermoscopic features points out to a probable vascular lesion.

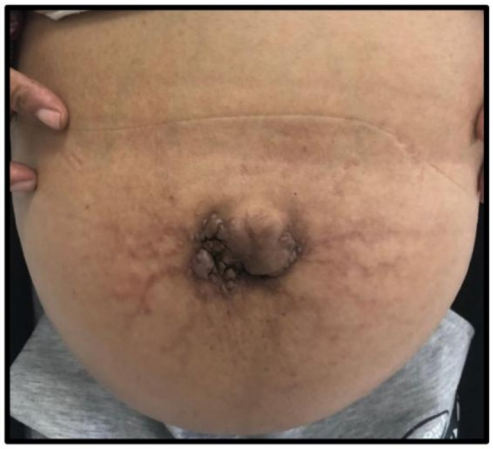

Figure 1. Abdomen distended and tense. Percussion reveals ascites with shifting dullness

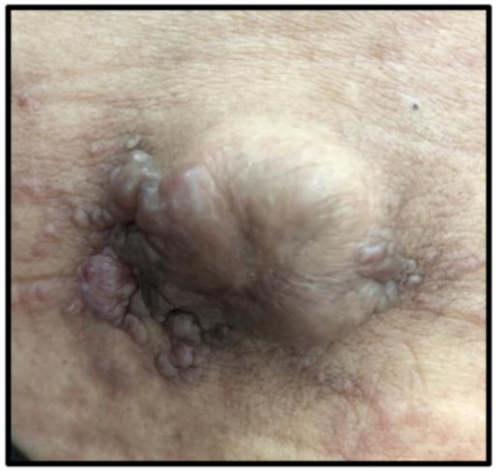

Figure 2. Multiple skin-colored to pinkish papules, few nodules and solitary cystic mass

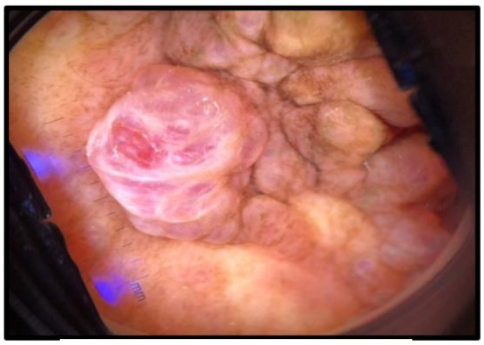

Figure 3. Dermoscopy of the lesion

Previous outpatient diagnostic workup done by the Department of OB-GYN revealed a normal sized anteverted uterus with thick endometrium suggestive of endometrial pathology and a pelvoabdominal mass probably an ovarian new growth with undetermined laterality, malignant by International Ovarian Tumor Analysis. A computerized tomography of the abdominal cavity and pelvis showed a huge complex mass, predominantly cystic, measuring 24.6 x 25.4 x 20.5 cm. Mass effect is seen displacing the surrounding structures peripherally. The uterus is unremarkable. The bowels are not dilated. Free fluid collection is seen in the peritoneal and pelvic cavities (Figure 4,5). Blood test demonstrated mild microcytic, hypochromic anemia, mild hyponatremia and hypocalcemia and increased levels of Cancer antigen 125 at >500 mg/dL. Chest radiograph showed pleural effusion on the bilateral lung. The Department of Dermatology did a 4 mm skin punch biopsy at 2 sites on the umbilicus. The histopathological result of skin biopsy revealed metastatic deposits of tumor cells over the dermis in an Indian file formation. Dilated lymph vessels and thinning of endothelial wall, containing atypical pleomorphic cells spill over the dermal interstitial fibers (Figure 6). These results were indicative of a cutaneous metastasis from a primary source. A separate reading was done by the Department of Pathology which revealed dilated vascular spaces lined by pleomorphic cells exhibiting mild atypia. Their primary consideration was intravascular papillary endothelial hyperplasia arising in a pre-existing lymphagioma or papillary hemangioma. Immunohistochemistry was performed paraffin-embedded tumor tissue. Tissue cells showed positive staining for ERG, which is a specific

immunohistochemical marker for vascular differentiation, including benign and malignant vascular tumors[1] (Figure 7). The cells of interest were negative for CK7, CK20, p63 and Pax8. Histomorphology and immunohistochemical profile supports the diagnosis of intravascular papillary endothelial hyperplasia.

Prior to performing the immunohistochemical staining, the patient was initially referred back to the OB-GYN Department with the apprising of a poor prognosis due to a consideration of a metastasis. Few days after her initial visit to Dermatology Department, patient noted recurrence of bleeding and was given first-aid management. The patient was then lost-to-follow-up due to the ongoing community quarantine in the area because of the COVID-19 pandemic. Until three months later, she was admitted by the primary service, co-managed by the Department of Internal Medicine, for management of worsening pleural effusion. Unfortunately, the patient was not optimized for further treatment of the primary tumor as a result of her deteriorating functional capacity. Meanwhile, the skin lesions have remained the same in size, without development of new lesions. Less than a week after admission, the patient expired due to pulmonary complications.

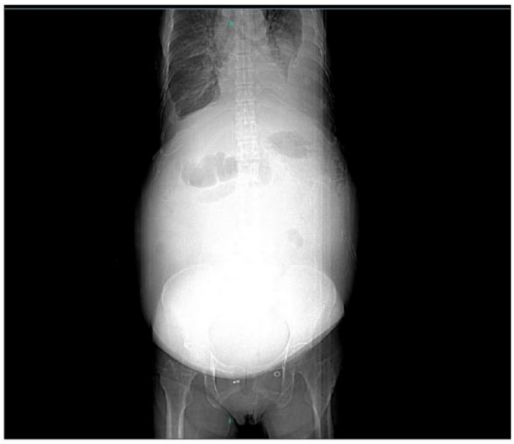

Figure 4. CT of abdominal cavity and pelvis showing an expansive tumor formation

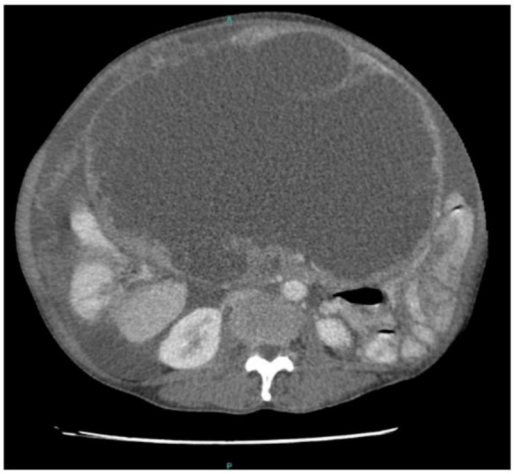

Figure 5. CT of abdominal cavity and pelvis with signs of tumor propagation to the front

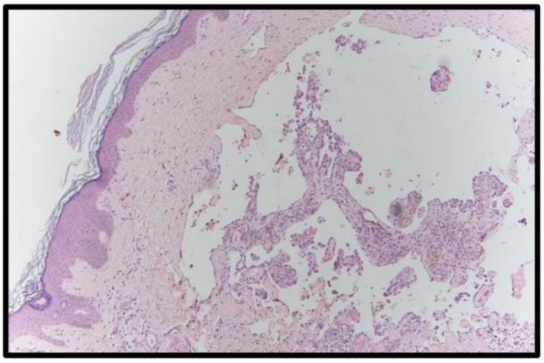

Figure 6. Histopathology showing dermal nests of neoplastic cells underneath intact epidermis (H&E, 40x)

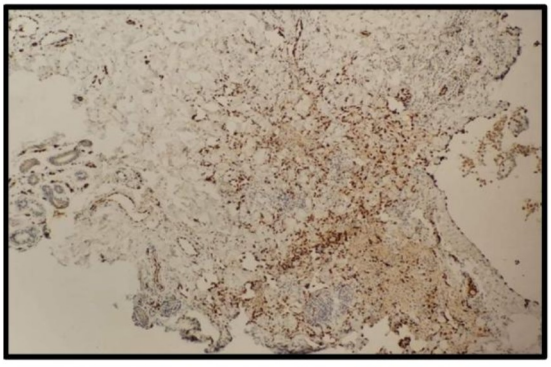

Figure 7. Immunohistostaining showing positivity for ERG in the cells of interest

DISCUSSION

Intravascular Papillary Endothelial Hyperplasia (IPEH), also known by its eponym Masson's tumor was first described by Pierre Masson in 1923 in an inflamed hemorrhoid of a 68-year old patient which he believed was a neoplastic lesion. He first called it Hémangioendothéliome végétant intravasculaire but later it was described as a reactive phenomenon by Henschen[3]. IPEH is a benign vascular lesion comprising around 2% of the vascular tumors of the skin and subcutaneous tissue. The condition is slightly predominant among females with a female to male ratio of 1.2:1[4]. It has a common incidence between the 3rd to 4th decade of life[5].

IPEH presents clinically as a sharply demarcated firm, bluish or purplish-red nodule or mass, measuring 0.5 to 5 cm, commonly seen on the fingers, trunk, head and neck. Based on the author's search, there were no previous reports yet of IPEH occurring on the umbilicus. Three variants have been described: (1) the primary form occurs within a dilated vessel, (2) the secondary or mixed form which occurs in association with a thrombus in the setting of a preexisting lesion, e.g. within a hemangioma, arteriovenous malformation, pyogenic granuloma, or varix and (3) the undermined type found in an extravascular location, in which the lesion develops in the bed of a hematoma and trauma is a prerequisite[2]. Our patient exhibits features of the second type.

The pathogenesis of IPEH is still poorly understood but literature review postulates a benign neoplastic process that involves proliferation of the endothelial cells in a papillary formation into the vascular lumen, which can be followed by obstruction and secondary degeneration. It typically follows a traumatic vascular stasis or thrombus. Basic fibroblast growth factor (FGF) appears to be released by the invading macrophages to the trauma site, initiating proliferation of endothelial cells[4] and activating a positive feedback loop of endothelial proliferation[5].

It is imperative to exclude several differential diagnoses of a patient presenting with an umbilical mass or nodule such as a primary umbilical neoplasm, cutaneous metastasis, umbilical hernia, umbilical endometriosis or epidermal inclusion cysts. In this patient, a diagnosis of cutaneous metastasis was originally considered because of the background of an ovarian carcinoma despite contradicting histopathologic findings on H&E stain. The definitive diagnosis of IPEH is obtained by tissue biopsy of the lesions and histologically, should be differentiated with hemangioma, pyogenic granuloma, and angiosarcoma. On tissue biopsy, the lesions of IPEH display dilated vessels that contains papillary proliferation of plump endothelial cells that are one to two cell thick[3]. It frequently overlies a fibrous tissue[6]. It lacks cellular atypia, although there are reported cases with moderate atypia[7]. Fibrin deposition and thrombi formation may be present without areas of necrosis[8].

Although seldom necessary, immunohistochemistry assists in arriving at the exact diagnosis. The cells of IPEH are differentiated endothelial cells, and thus, express markers such as vimentin, CD31, CD34, von Willebrand factor (vWF, factor VIII–related protein), factor XIIIa, and ULEX europaeus agglutinin (UEA-1)[3]. In our case, immunostaining has been instrumental to rule out the diagnosis of cutaneous metastasis and confirming the diagnosis of IPEH. Thus, the author strongly recommends that immunohistochemistry staining be done when the initial H&E findings are equivocal.

The treatment of IPEH requires complete surgical resection with or without wide margins of excision[9]. Sclerotherapy using sodium tetradecyl sulfate followed by surgery resulted in good aesthetic results and minimal intra-operative bleeding in a few reported cases. Recurrence of lesions is uncommon[3].

CONCLUSION

Sister Mary Joseph nodule, especially in a background of Ovarian carcinoma should still be considered as a valuable differential diagnosis as it may mimic vascular lesions occurring on the umbilicus. Although histopathology remains the gold standard in the diagnosis of intravascular papillary endothelial hyperplasia, immunohistochemical staining is vital to precisely diagnose this lesion so that it is neither

inadequately nor aggressively managed. It helps direct treatment options especially in patients with a consideration a cutaneous metastasis from a primary malignancy. It also crucial to prevent recurrence and morbidity.

Compliance with Ethical Standard

Conflict of interest. The authors declare that they have no conflict of interest.

Informed Consent. Informed consent was obtained from the patient and from her next of kin

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Pain Catastrophizing as a Predictor for Postoperative Opioid Requirements for Breakthrough Pain in Patients Undergoing Elective Surgery admitted in a Private Institution from January 2021 to June 2021

Jeena Megan T. Tanco, MD

Abstract

Background: Post-operative pain management is a major challenge encountered by anesthesiologists. Opioids remain to be the most frequently administered analgesic for acute pain despite its many untoward side effects. Little is known about pre-operative pain perception and the psychophysiologic aspects of pain control and response, such as Pain Catastrophizing. The observer aims to identify if pain catastrophizing could be a good predictor for post-operative opioid requirement for breakthrough pain.

Methods: Patients scheduled for elective surgery were stratified pre-operatively as Catastrophizers and Non-Catastrophizers using the Pain Catastrophizing Scale (PCS). Their patient profile, and total opioid consumption in the following stages of surgery: intra-operatively, recovery room admission, and the first post-operative day, were recorded and converted to morphine equivalent doses.

Results: The comparative analysis of the morphine equivalent doses between catastrophizers and non-catastrophizers show that it is significantly different between the two groups of patients for opioid consumption for breakthrough pain in the recovery room and on the first post-operative day. The values suggest that there are significantly higher doses in catastrophizers than in the non-catastrophizers.

Conclusion: Pain Catastrophizers were shown to require a significantly higher amount of opioids for breakthrough pain during recovery room admission and first post-operative day versus Non-Catastrophizers. This finding is consistent with the existing literature suggesting that pain catastrophizing is a predictor of post-operative opioid consumption in patients undergoing various elective surgeries.

Keywords: pain catastrophizing, pain perception, opioids

INTRODUCTION

Postoperative pain management continues to be a major challenge to physicians. A study conducted by Gan reported that more than 80% of patients complained of moderate-to- severe postoperative pain. Across facilities, opioids are the most frequently administered analgesic for acute and chronic pain. Despite considerable investment, no new drugs have surpassed opioids as the preeminent analgesics for treating severe pain, particularly in the acute setting.[3] This does not go without consequence as up to 79% of patients receiving opioids experience at least one adverse effect of the drug. The most frequently reported adverse effects being: drowsiness, constipation, and nausea.[1] To this day, postoperative pain is common and remains undertreated, and the distribution and quality of perceived pain has remained largely unchanged.[2]

Pain management guidelines appear to have had little impact on practice patterns or improvement in pain control for patients. Researchers have begun to shift focus to investigating preoperative aspects and psychophysiologic explanations for insufficient pain relief. Type of surgery, age, and psychological distress have been found to be significant predictors for analgesic consumption.[4]

*1st Place, 2023 Philippine Society of Anesthesiologists Inc. Research Forum Contest
[1]from Chong Hua Hospital, Cebu City

Among psychological factors, pain catastrophizing, broadly defined as a tendency to focus excessively on pain and exaggerate its threat value, has increasingly been recognized as a strong psychological predictor of postoperative pain.[5,6] Anesthesiologists may find it helpful and beneficial to target the psychologic aspect of pain and possibly intervene even from the preoperative period. This study aims to identify patients with a catastrophized perception of pain, and to validate the association between preoperative pain perception and postoperative opioid requirement, particularly for the treatment of breakthrough pain.

GENERAL OBJECTIVE

To determine the relationship of pain catastrophizing, as determined by the Pain Catastrophizing Scale (PCS), and postoperative opioid analgesic requirement for breakthrough pain in patients undergoing elective surgical procedures

Specific Objectives

1. To determine the incidence of "Catastrophizers" and "Non-Catastrophizers" with the use of the preoperative Pain Catastrophizing Scale (PCS) in patients undergoing elective surgery.

2. To determine the patient profile of patients stratified as "Catastrophizers" and "Non-Catastrophizers" as to their age, gender, type of surgery, and diagnosis.

3. To determine the total opioid consumption in morphine equivalent doses of patients stratified as "Catastrophizers" and "Non-Catastrophizers" intra- operatively, during recovery room admission (as part of their pain regimen and for breakthrough pain), and the first post-operative day (as part of their pain regimen and for breakthrough pain).

4. To determine the relationship between pre-operative Pain Catastrophizing Scale Scores and the postoperative requirement for opioid analgesia for breakthrough pain.

Definition of Terms

1. Pain Catastrophizing - a psychological perception of pain that refers to the tendency to focus excessively on pain and exaggerate its threat value

2. Pain Catastrophizers - patients who score 30 points or above on the Pain Catastrophizing Scale

3. Non-Catastrophizers - patients who score 29 points or below on the Pain Catastrophizing Scale

4. Pain Regimen - analgesics prescribed to the patient by their attending anesthesiologist that are administered regardless of pain score

5. Breakthrough Pain - severe pain that erupts while the patient is already being medicated with analgesics

LIMITATIONS OF THE STUDY

This study has the following limitations:

Patients with history of previous surgeries already have experience with pain, thereby possibly affecting their PCS score in either a negative or positive way. However, this study is focused on pain management in the acute setting, which is an issue regardless of the presence of previous surgical history. This study will therefore not exclude those subjects who have had previous surgeries, but in order to eliminate other factors that can affect preoperative PCS score, this study will exclude patients who present with pain preoperatively.

Another limitation is that the patients included in the study will be undergoing different surgical procedures, thus there may be a difference in postoperative pain due to differences in size of postoperative site or predicted pain intensity that is unique to each surgical procedure. However, studies have shown that pain catastrophizing affects postoperative pain management regardless of the type of procedure, so it may be beneficial to study the outcomes of patients across different surgical procedures.

A third limitation is that patients receive opioids intra-operatively, within their recovery room admission, and during the first post-operative day, ordered as a pain regimen by their respective attending anesthesiologists. These medications were not withheld in the study population, and therefore may have affected the incidence of breakthrough pain in the subjects. However, in order to partially correct this variable, the total amount of opioids given as pain regimen was also compared across subjects.

REVIEW OF RELATED LITERATURE

Pain is fundamentally a psychophysiological phenomenon that goes beyond mere nociception. Pain, whether linked with tissue injury, inflammation, or functional impairment, is mediated by processing in the nervous system. Yet, regardless of its source, pain may result in hypervigilance, threat appraisals, emotional reactions, and avoidant behavior. In this sense, pain is psychological.[7] Several studies have found that certain psychological factors, such as anxiety, depression, and pain catastrophizing, play a significant role in the development of postoperative pain.[8] Whereas anxiety and depression are more indicative of underlying clinical conditions, pain catastrophizing is a measure of one's tendency to focus excessively on pain and exaggerate its threat value.[6] Currently, patients are being screened with the use of the Pain Catastrophizing Scale (PCS), which is a 13-item instrument wherein patients are asked to indicate the degree to which they have certain thoughts and feelings when they are experiencing pain. [9,10]

A study conducted on the predictive value of pain catastrophizing for pain intensity was done on patients undergoing cardiac surgery, which revealed that there was a strong positive correlation between preoperative PCS score and postoperative pain intensity.[11] This supports the notion that pain catastophizing may have an effect on one's perception of pain postoperatively, across patients who underwent the same procedures. However, all of the subjects in this study were managed postoperatively with the same pain regimen: intravenous morphine infusion and paracetamol boluses. They received subsequent doses of morphine and tramadol for breakthrough pain. The study did not indicate if pain catastrophizers received higher doses of opioids in comparison to non-catastrophizers, and while the study does predict pain intensity, it does not directly correlate with a higher requirement for opioid usage. Another study conducted on patients who underwent total joint arthroplasty controlled for post-operative opioid consumption between catastrophizers and non-catastrophizers.[5] The study actually yielded no statistically significant difference between opioid consumption by catastrophizers compared to non-catastrophizers during their first 2 days postoperatively. However, the data collected showed a positive correlation between catastrophizers and length of hospital stay, as catastrophizers were shown to be twice as likely to require longer than 2 days of stay in the hospital postoperatively, consequently causing these patients to have a higher opioid consumption compared to their counterparts who were discharged earlier. The researchers suggested that catastrophizers may be higher utilizers of hospital resources, perhaps out of fear of inadequate pain control upon hospital discharge. This knowledge supports our hypothesis that pain catastrophizing can lead to higher opioid consumption postoperatively. The study, however, did not indicate whether opioids were used in their facility routinely in patients undergoing total joint arthroplasty, which brings us to the salient issue that opioids, despite their varying well-known major and minor side effects, still play a large role in postoperative pain control.

For decades, physicians have been reliant on opioid analgesics as the mainstay for peri-operative pain management.[12] They have gained popular use because they are highly effective for relieving moderate-to-severe postoperative pain, do not have a ceiling effect and are available in a wide variety of formulations. However, they are not without some serious dose-limiting side effects that range from bothersome to life-threatening, including nausea and vomiting, constipation, oversedation, somnolence and respiratory depression.[2] Opioids bind to u-receptors expressed at key locations within the pain pathway, and their activation suppresses both the reflexive and affective components of pain. However, the respiratory centers in the brainstem, gut, and chemotrigger zone also contain u-receptors. Their activation results in the various side effects one may

experience with opioid use.[3] One retrospective study on patients who underwent surgery within the past 5 years reported that 70% of patients experienced drowsiness, 47% experienced constipation, and 31% experienced nausea during their in-patient stay related to opioid use.[1] Opioids have additional detrimental effects, including tolerance, hyperalgesia, dependence, and addiction. This may lead to the long-term inevitable growth of prescription opioid dispensing, linked to opioid misuse and abuse. [2,13]

On the other hand, recent work has found that patients in some countries frequently receive opioids either unnecessarily or in excess of their requirements for surgical pain control.[15] This could be attributed to the fact that no new drugs have usurped opioids as the preeminent analgesics for treating severe pain. Opioids have now gained popular use as routine postoperative pain management. Furthermore, early postoperative opioid use has been linked as a strong patient risk factor for prolonged opioid use after surgery.[14]

These alarming numbers point that it is logical to look for alternative approaches to treat severe pain. It may be of immeasurable value to place efforts into studying methods that can intervene at a preoperative level. Screening tools that can identify a patient's likelihood to have an increased analgesic requirement allows for anesthesiologists to prepare for an effective multimodal approach to postoperative pain management and to prevent the unnecessary use of harmful analgesics to those who may not require it.

METHODOLOGY

Study Design

The study conducted is a prospective cross-sectional study.

Study Setting

This study was conducted at a tertiary level private institution located in Cebu City.

Study Population

Between January 2021 and June 2021, the researcher approached adult patients, aged 18 and above, admitted and scheduled for elective surgeries and presented with no symptoms of pain preoperatively. This group was selected because the presence of pain preoperatively would affect the outcome of the Pain Catastrophizing Scale. All eligible patients were tracked from the operating room schedule noted on the day prior to the surgery.

Inclusion criteria

a. 18 years of age or older
b. Scheduled for an elective surgery
c. Eligible admitted patients identified from the operating room schedule on the day prior to the surgery

Exclusion criteria

a. Presence of pain preoperatively
b. Patients requiring intensive care admission post-operatively
c. Patients receiving epidural morphine post-operatively

Data Collection

The conduct of the study was implemented upon approval of the protocol by the Institutional Review Board and the Office of the Medical Director, and after obtaining a written informed consent. Patients were stratified preoperatively as "Catastrophizers" or "Non- Catastrophizers" using the Pain Catastrophizing Scale (PCS). Their patient information was collected using the existing Chong Hua Hospital Pre-anesthesia Assessment form. The Pain Catastrophizing Scale involves a 13-item questionnaire wherein patients are asked to indicate the degree to which they have the thoughts and feelings when they are experiencing pain using the 0 (not at all) to 4 (all the time) scale. A total score is yielded (ranging from 0 to 52), and a total of 30 and above represents clinically relevant level of pain catastrophizing.

The following data elements were identified and recorded in each patient: PCS Score, patient profile with regards to age, gender, type of surgery and diagnosis, and opioid use intra-operatively, during recovery room admission, as part of pain regimen and for breakthrough pain, and on the first post-operative day, as part of pain regimen and for breakthrough pain. The total dose of each opioid used was converted to their respective morphine equivalent doses. All data was collected and tallied under total enumeration with a patient data sheet.

Data Analysis

Qualitative data such as patient demographics, and stratification based on the PCS were summarized as frequencies. Multivariate regression analysis was used to examine the relationship between pain catastrophizing and the primary outcome of opioid analgesic use postoperatively.

RESULTS

Table 1. The Incidence of Catastrophizers and Non-Catastrophizers across Subjects, n=32

	Frequency	Percentage
Catastrophizers	7	22%
Non-Catastrophizers	25	78%

The following table (Table 2) shows the demographic and clinical characteristics of the study subjects. Patients have a mean age of 43 years. Thus, in average, they are middle aged persons. The comparative analysis results tell us that the ages are statistically the same between the two groups of patients. The proportions of male and female patients, types of surgery, and diagnoses between the two groups of patients are observed to comparable.

Table 2. The Patient Profile of Subjects, n=32

Characteristics	All Patients n = 32	Patients who are:		P-Value
		Catastrophizer n = 7	Non-Catastrophizer n = 25	
Age, *in mean (SD)*	43.00 (11.32)	44.71 (8.99)	42.52 (12.01)	[A]0.608
Gender				
Male	15 (46.88)	4 (57.14)	11 (44.00)	[B]0.678
Female	17 (53.13)	3 (42.86)	14 (56.00)	
Surgery				
Completion Thyroidectomy	1 (3.13)	0 (0.00)	1 (4.00)	[B]0.630
Excision of Bilateral Breast Masses	1 (3.13)	0 (0.00)	1 (4.00)	
Laparoscopic Cholecystectomy	15 (46.88)	5 (71.43)	10 (40.00)	
Laparoscopic Hernia Repair	2 (6.25)	1 (14.29)	1 (4.00)	
Loop Colostomy	1 (3.13)	0 (0.00)	1 (4.00)	
Modified Radical Mastectomy, Left	1 (3.13)	0 (.00)	1 (4.00)	
Modified Radical Mastectomy, Right	2 (6.25)	0 (0.00)	2 (8.00)	
Open Cholecystectomy	2 (6.25)	1 (14.29)	1 (4.00)	
Simple Mastectomy	1 (3.13)	0 (0.00)	1 (4.00)	
Total Thyroidectomy	6 (18.75)	0 (0.00)	6 (24.00)	

Loop Colostomy	1 (3.13)	0 (0.00)	1 (4.00)	
Modified Radical Mastectomy, Left	1 (3.13)	0 (.00)	1 (4.00)	
Modified Radical Mastectomy, Right	2 (6.25)	0 (0.00)	2 (8.00)	
Open Cholecystectomy	2 (6.25)	1 (14.29)	1 (4.00)	
Simple Mastectomy	1 (3.13)	0 (0.00)	1 (4.00)	
Total Thyroidectomy	6 (18.75)	0 (0.00)	6 (24.00)	
Diagnosis				
Bilateral Breast Masses	1 (3.13)	0 (0.00)	1 (4.00)	[B]0.966
Breast CA, Right	2 (6.25)	0 (0.00)	2 (8.00)	
Breast Mass, Left	1 (3.13)	0 (0.00)	1 (4.00)	
Chronic Calculous Cholecystitis	15 (46.88)	6 (85.71)	9 (36.00)	
Colon Adenocarcinoma	1 (3.13)	0 (0.00)	1 (4.00)	
Follicular Thyroid Carcinoma	1 (3.13)	0 (0.00)	1 (4.00)	
Hurthle Cell Follicular Neoplasm	1 (3.13)	0 (0.00)	1 (4.00)	
Hydrops of the Gallbladder	2 (6.25)	0 (0.00)	2 (8.00)	
Multinodular Non-toxic Goiter	1 (3.13)	0 (0.00)	1 (4.00)	
Multinodular Toxic Goiter	1 (3.13)	0 (0.00)	1 (4.00)	
Non-toxic Goiter	1 (3.13)	0 (0.00)	1 (4.00)	
Papillary Thyroid Carcinoma	2 (6.25)	0 (0.00)	2 (8.00)	
Phyllodes Tumor	1 (3.13)	0 (0.00)	1 (4.00)	
Umbilical Hernia	2 (6.25)	1 (14.29)	1 (4.00)	

Note: Values are presented in Frequency (Proportion) unless otherwise stated; SD means Standard Deviation, *Significant at 0.05 using [A]T-Test for two independent samples and [B]Fisher's Exact test

The following table (Table 3) shows the comparative analysis of the morphine equivalent doses between catastrophizers and non-catastrophizers. The results show that the morphine equivalent doses are significantly different between the two groups of patients in *recovery room – breakthrough* and in *first post-operative day–breakthrough*. The values suggest that there are significantly higher doses in catastrophizers than in the non- catastrophizers.

The morphine equivalent doses in *intra-operative*, in *recovery room – regimen*, and in *first post-operative day - regimen* show no statistically significant difference between the two groups of patients.

Table 3. The Comparative Analysis of the Morphine Equivalent Doses between Catastrophizers and Non-Catastrophizers, n=32

Morphine Equivalent Dose in milligrams	**Patients who are:**		**Test Statistic (P-Value)**
	Catastrophizer n = 7	Non-Catastrophizer n = 25	
Intra-operative	14.36 (2.50)	15.40 (4.49)	-0.80 (0.434)
Recovery Room - Regimen	6.43 (4.76)	3.40 (2.78)	1.61 (0.152)
Recovery Room - Breakthrough	7.14 (3.93)	1.40 (2.71)	3.63 (0.008) *
First post-operative day - Regimen	7.14 (7.56)	2.80 (3.84)	1.47 (0.193)
First post-operative day - Breakthrough	4.29 (1.89)	0.40 (1.38)	5.07 (0.001) *

Note: Values are presented in Mean (Standard Deviation), * Significant at 0.05 using T-Test for two independent samples. All opioids have been converted to their respective morphine equivalent doses before analysis.

DISCUSSION

This study investigates the association between pain catastrophizing and post- operative opioid requirement for breakthrough pain in patients undergoing elective surgery. The results show that there is a positive correlation between patients who were stratified as Catastrophizers and an increased post-operative opioid requirement. The predictive value of pain catastrophizing was independent of intra-operative and regimented opioid use.

The study adds to the literature that suggests that pain catastrophizing can be a good predictor of psychophysiologic factors affecting pain perception and control in surgical patients.[4,6] Some authors have proposed that catastrophizing interrupts the descending pain inhibition signals to the spinal cord, where it favors neuroplastic changes in response to painful stimuli, causing pain sensitization.[11] This may explain why the patients stratified as Catastrophizers utilized significantly higher amounts of opioids for breakthrough pain post- operatively, even if their intra-operative and pre-existing pain regimen opioid analgesia was comparable to their Non-Catastrophizer counterparts.

The results of the present study have the following important clinical implications: first, the findings suggest that using validated measuring instruments, such as the Pain Catastrophizing Scale, allow clinicians to identify patients who are likely to experience more severe post-operative pain and related complications. Secondly, the possibility of designing interventions that aim to intervene at the pre-operative level, considering that pain catastrophizing is a psychophysiologic factor, should be further explored. It's importance in the clinical practice of anesthesiologists is immeasurable, in that it can possibly contribute to decreased incidence of hospital stay, chronic pain, and unsatisfactory patient pain control, ultimately leading to suboptimal post-operative recovery.

CONCLUSION

In this study, the author sought to determine whether pain catastrophizing could be used as a predictor of post-operative opioid requirement for breakthrough pain in patients undergoing elective surgery. Pain Catastrophizers were shown to require a significantly higher amount of opioids for breakthrough pain during recovery room admission and first post-operative day versus Non-Catastrophizers. There was no significant difference between the two groups in total opioid administered intraoperatively, and as part of their pain regimen during recovery room admission and first post-operative day. This finding is consistent with the existing literature suggesting that pain catastrophizing I a predictor of post-operative opioid consumption in patients undergoing various elective surgeries.

RECOMMENDATIONS

The author recommends the use of Pain Catastrophizing Scale in the pre-operative setting to identify patients who are more likely to require greater amounts of opioids for breakthrough pain post-operatively. The early identification of these patients allows anesthesiologists to adequately plan an effective post-operative pain regimen to achieve optimal patient comfort. The author also recommends that further studies be conducted using the Pain Catastrophizing Scale, while including other variables such as emergency and urgent surgery, as well as the use of other analgesic medications such as non-steroidal anti-inflammatory drugs, local anesthetics, and adjunctive epidural analgesia, which is beyond the scope of this study.

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Covid-19 and Mental Health of Healthcare Workers: A Systematic Review*

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Abstract

Background: The novel coronavirus 2019, or COVID-19, has gripped all corners of the world and has created a crisis that significantly affected people's mental health around the globe, including healthcare workers (HCWs).

Purpose: This study aimed to bring the results to the attention of healthcare systems' policymakers and managers so as to fully recognize the severity of the situation and set the groundwork for appropriate interventions to address the condition of HCWs.

Methods: This systematic review searched PubMed, Google, Google Scholar, and Scopus for literature relevant to mental health conditions among healthcare workers during this pandemic. This review includes the searches from March to October 2020.

Results: The main findings were symptoms of anxiety, depression, stress, psychological trauma, insomnia and sleep problems, burnout and fatigue, and distress. Most studies suggest that social and family support, hygiene measures, and physical activity are safeguards for mental health and are among the recommended protective interventions for promoting mental health.

Limitations: The researcher has reservations about the findings' generalizability as the samples may not represent the population.

Conclusion: This review highlights the existing burden of mental health conditions reported by HCWs during the COVID-19 pandemic. It revealed consistent reports of stress, anxiety, and depressive symptoms resulting from COVID-19.

Implications: Longitudinal data will be helpful through surveys of representative samples of the general population. More relevant and recent data in Asian countries could inform understanding of challenges concerning COVID-19 and the impacts on healthcare workers' mental health and well-being, particularly those in the Philippines.

Keywords: COVID-19 pandemic, mental health, healthcare workers

BACKGROUND

Due to the massive spread of the much-dreaded novel coronavirus (COVID-19), the World Health Organization (WHO) declared an international public health emergency in March 2020. The associated morbidity and mortality affected the world's populations and challenged global healthcare systems. Our HCWs have been placed in the direct care of patients before. They are again called upon to play a vital role in responding to the COVID-19 pandemic.

Some aspects of the COVID-19 pandemic intensified its potential to cause mental health issues among healthcare workers. For one, there is fear of the notion that “no one is safe” due to the astronomic rise in the number of cases reported and countries affected. Media reports compounded its spread in the hospital community and other healthcare facilities with increased death rates among HCWs. Due to the sudden spike in infections, much medical staff was reassigned to higher-risk frontline jobs causing disruptions in standard workplace practices. The WHO called for a collective effort to alleviate the impact on healthcare workers (WHO, 2020).

Maunder et al. (2006) mentioned that HCWs found severe acute respiratory syndrome (SARS) to be stressful. Years later, the 2015 Middle East respiratory syndrome (MERS) put our healthcare professionals in a

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similar predicament. They experienced depression and stress. Post- traumatic stress disorder (PTSD) also persisted among these frontliners even after an absence from work (Lee et al., 2018). Other studies reported on mental health implications for healthcare workers involved during epidemics. Stuijfzand et al. (2020) also suggest that HCWs exposed to patients during an epidemic/pandemic become vulnerable. The HCSw are likely to suffer from mental health problems such as psychological distress, insomnia, alcohol/drug misuse, and symptoms of post-traumatic stress disorder (PTSD), depression, anxiety, burnout, anger, and higher perceived stress. There were heightened anxiety, stress symptoms, and PTSD (Kang et al., 2020; Huang et al., 2020) even after some time had transpired since the end of the emergency (Li et al., 2020). The studies indicate that these mental health problems might compromise the quality of patient care.

Amidst the outbreak of this infectious disease in more than 200 countries, HCWs continue to be indispensable in screening and treating this condition. They are the world's frontliners in health service delivery. While COVID-19 has placed everyone in a constant state of stress, grief, and anxiety, healthcare providers should remain calm so as not to pass the stress on to the patients (WHO, May 2020). As such, HCWs have become highly vulnerable to developing severe psychological consequences. The high number of cases, growing death tolls, limited safety equipment and vaccines, increased workload, inadequate support, and widespread media coverage have resulted in adverse consequences such as HCWs' unwillingness to work, stress, anxiety, and other long-term psychological implications.

The WHO (2020) reported the complexity of HCWs' psychological response to the epidemic of infectious diseases. This observation is secondary to a myriad of factors, such as feelings of vulnerability, loss of control, concerns about one's health, possible infection of colleagues and family, fear of death, and isolation. The economic aspect must also be considered, like employment uncertainty and financial woes. Also, the surge of cases and shortages of PPEs and other supplies further exacerbate the health workers' pressures and concerns.

HCWs, as a result, are highly susceptible to experiencing psychological and mental problems. The preceding suggests that psychological support and interventions should be made accessible to healthcare providers to help ensure the effective execution of their job. Mental health issues like stress, anxiety, and emotional exhaustion affect staff morale adversely, resulting in absenteeism, high turnover rates, and reduced work satisfaction and quality of care.

In this critical situation, the medical staff's mental health should be considered an urgent public health concern. It is, therefore, necessary to prioritize the mental health of our HCWs and support the mitigation of the adverse psychological impact of the COVID-19 pandemic.

Understanding the risks and impacts on healthcare workers' mental health during this COVID-19 pandemic cannot be ignored. This review will investigate the articles addressing HCWs' mental health status during the SARS-CoV-2 outbreak. It aimed to identify, assess, and summarize current evidence on COVID-19 and its impact on healthcare workers' mental health. It focuses on their mental health issues and will, hopefully, contribute to informing where interventions and organizational efforts can support their mental health. Moreover, this initiative needs immediate attention and action, particularly in countries like the Philippines, where healthcare workers struggle against violence and discrimination, on top of the delay in compensation and release of their hazard pay (Philippine Star, January 31, 2021).

This review attempted to address the following questions: 1) After a few months into the pandemic, what is the current status of the COVID-19 research on healthcare workers? 2) Among these types of workers, how impactful is the COVID-19 pandemic in worsening their mental health?

The secondary data gathered was saved in a secured google folder accessed by the researcher only and sharing of secondary data was not allowed. The study was submitted to the Fe del Mundo Medical Center Institutional Review Board (FMMDC IRB) and was approved for exempt from review. Any leak of

information will be reported to FDMMC IRB. Actions in accordance to Philippine Health Research Ethics Board (PHREB) and institutional IRB guidelines will be applied if there is any leak of information.

METHODS

The literature review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The researcher performed a structured literature search to identify studies that reported mental health issues among healthcare workers during the COVID-19 pandemic in the following databases in English: PubMed, Cochrane Library, Scopus, Google Scholar, Center for Diseases Control, World Health Organization (WHO), and local databases like the Philippine National Institute of Health.

Information about these databases was gathered from the internet and recommendations of colleagues who have done similar research. Scopus is a good resource for scholarly literature from almost any discipline. PubMed covers literature in medicine or biological sciences and makes available full-text links to the publisher sites and links to the free PDF. The Cochrane Library's collection is described as high-quality, independent evidence to inform healthcare decision-making. Google Scholar offers a simple way to broadly search the world of scholarly research in many disciplines and sources: articles, theses, books, abstracts, and court opinions, from academic publishers, professional societies, online repositories, universities, and other websites. Search in web-based resources was undertaken on Google and through searching specific websites (WHO, https://www.who.int and Centers for Disease Control and Prevention, https://www.cdc.gov). The researcher also reviewed selected articles and references from local databases like the Philippine National Institute of Health for additional literature.

INCLUSION CRITERIA

The researcher included any study about healthcare workers during the covid-19 pandemic, with outcomes relating to their mental health. The researcher did not place any restrictions related to the study design or research locale. The search located studies on which to assess the mental health or psychological impact of the COVID-19 pandemic among healthcare workers and find out what factors protect or prevent adverse consequences of the crisis on their mental health.

The search results were screened based on the pre-set selection criteria. After the individual titles and abstracts were assessed, the following inclusion criteria were applied: primary studies, written in the English language, related to COVID-19 and the mental health of healthcare workers, mental health or mental well-being, or psychological outcomes.

The exclusion criteria were duplicated articles, publication outside the period between March and October 2020, no access to the full article, and no prevalence or absence of mental health issues among healthcare personnel.

LITERATURE SEARCH AND ARTICLE SELECTION

The search covered all types of articles published in March 2020–October 2020 like reviews, commentary, correspondence, letters to the editor, original research articles, full papers, abstracts, interim reports, official documents, and published and unpublished studies that are relevant to the subject of the review. Also included were studies that evaluated the presence of depression, stress, and anxiety among healthcare workers during this pandemic and reports of videoconferences. However, the researcher excluded reviews, theses, position papers, protocol papers, and studies not published in English.

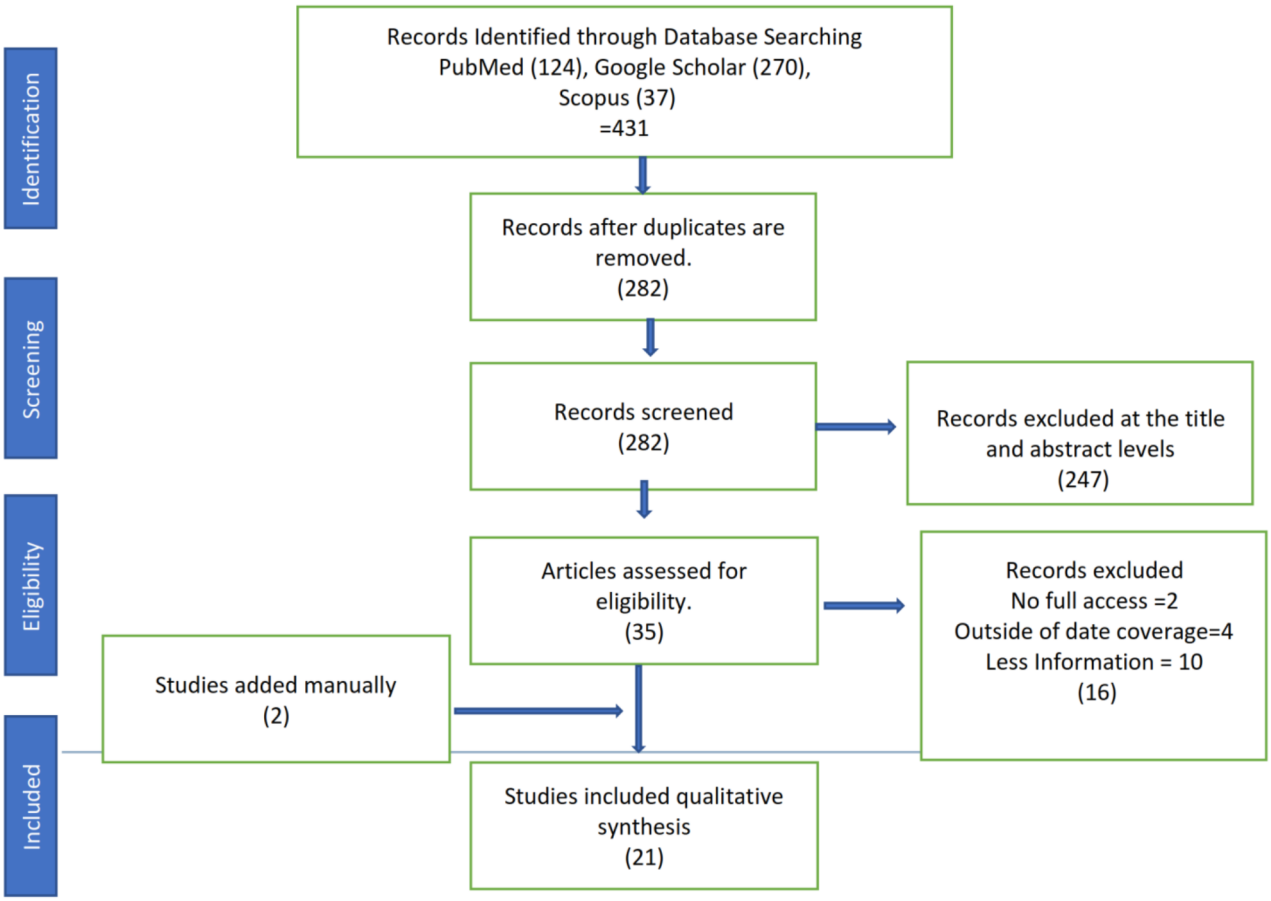
The search was conducted in early 2021 at a time when COVID-19 had taken hold of most of the world. COVID-19 is not the first strain of the coronavirus we have experienced. Therefore, SARS, Ebola, H1N1, and MERS (Middle East respiratory syndrome) were also included.

The researcher set a date range criterion within the search parameters of the literature review due to the constraints she faced. Her time was mostly confined to their hospital's demands when it was declared a covid-19 only accepting facility from March 2020 until October 2021.

In retrieving the studies, the researcher used the following terms in her search: COVID-19 or COVID-19-2019 or COVID-192019 or coronavirus disease 2019 or SARS-CoV-2 or SARS2 or 2019 novel coronavirus infection or coronavirus disease-19 or novel coronavirus or SARS-CoV-2019 or sars-COVID-19 or sars-COVID-192019 or sars-COVID-19 2019 or Wuhan virus or coronavirus, or psychological, or stress, or depression, or anxiety, or mental health, or psychiatric issues, and COVID-19, corona, SARS, SARS-CoV, MERS, MERS-CoV, Middle East respiratory syndrome, novel coronavirus, and HCW, or doctors, or medical staff, or health care professionals, or health care workers, or frontliners, or medical frontliners.

The following data were extracted from the results in a structured table: author/s, date of publication, sample and study location, study design, main findings, mental health issues, and the number of references. The descriptive analyses helped determine the prevalence of mental health issues and risk factors in the covered literature and the strategies to resolve these mental health concerns. Table 1 presents an overview of the articles included in the review.

Table 1. PRISMA



DATA EXTRACTION AND QUALITY ASSESSMENT

An associate researcher assisted the author in conducting the literature search. They participated in the data extraction by screening the acquired studies simultaneously. In order to reconcile the screening process results, Brainstorming and resolution of differences in views were made through private discussions via Zoom.

HCWs do not form a homogeneous population. However, in this review, they were treated as a single group, as evidence suggests that this group may be at risk of experiencing poor mental health due to the COVID-19 pandemic. The reasons for such adverse psychological outcomes include excessive workload, long work hours, inadequate personal protective equipment, over-enthusiastic media news, and inadequate support. The infection rate among medical staff triggers fears and is crucial for such a psychological impact. Also, the role reversal from a healthcare worker to a patient might result in frustration, helplessness, adjustment issues, stigma, and fear of discrimination.

The researcher understands that there is no one-size-fits-all practical approach to supporting HCWs. She stresses the importance of identifying groups within the larger population and appropriately targeting personalized interventions to be made available to support them.

This systematic review incorporated a critique or appraisal of the research evidence. The appraisal assessed the methodological quality of the included studies and ascertained if the possibility of bias in its design, conduct, and analysis has been addressed. The included papers in the review were subjected to the appraisal of the researcher and her colleague. The evaluation data were used as the basis for the synthesis and interpretation of the study's results.

The JBI (Joanna Briggs Institute) Quality Assessment tool was used to assess the quality of the included studies. The summary of the appraisal is shown in Table 2 in the appendix. Most of the studies met the sampling criteria based on the assessment tool, and the authors clearly defined the inclusion and exclusion guidelines. The participants' demographics, research setting, and time frame were also indicated. Appropriate measurement methods and analytical techniques were used.

There are, however, some limitations. Some samples in the studies were small and limited; thus, they may not represent the populations. Also, other studies were confined to specific groups; hence the generalizability of the application of the results may also be restricted. Because of the cross-sectional design, the researcher could not account for or comment on potential changes in the levels of psychological impact over time. Recruitment for most of the studies occurred shortly after WHO announced COVID-19 as a Public Health Emergency of International Concern and for only seven months, through October 2020. Also, the researcher recognizes that the widespread COVID-19 media coverage and information may have triggered changes in the healthcare workers' perceptions during data collection. Most instruments were self-reported and not confirmed by medical records or other unique evaluations.

The studies used online questionnaires and selected populations with access to the internet, which might have affected their samples' representativeness. Some selection bias may have been present. Health workers without internet access, older healthcare workers, and those who might have been busy with their work duties might have opted not to participate and could not share the pandemic's impact on their mental health. Because results were mainly self- reported and taken from subjected scales, respondent bias should be eliminated.

DATA PRESENTATION AND ANALYSES

The studies included in our review are about healthcare workers during the covid-19 pandemic, with outcomes focusing on their mental health. We also unearthed information on interventions that prevent or reduce adverse mental health impacts on healthcare workers. We also did not restrict our literature review regarding study design and methodology.

In order to delineate content specific to COVID-19, the concepts that were considered relevant to the search criteria were the following: the COVID-19 virus, the classification of COVID-19 as a pandemic, the healthcare workers regardless of classification, and the mental health or psychological impact of the COVID-19 pandemic among healthcare workers.

RESULTS

Search results

The entire text of potentially relevant papers was retrieved for a more intent examination. The 431 records of interest were found from the single search. After 149 duplicates were removed, 282 records were screened. Of these, 35 potentially relevant studies were assessed for eligibility. Twenty-one (21) published studies met the inclusion criteria for the review shown in Table 3 in the appendix. Five of the studies were from China. The rest were from Egypt (1), Italy (2), KSA (2), Nepal (1), Oman (2), Pakistan (1), Philippines (1), Poland (1), Singapore (1), Spain (1), Turkey (2), and Global (1) covering 31 countries from the Western Pacific Region and Eastern Mediterranean. Several validated tools assessed anxiety, depression, insomnia, stress, post-traumatic stress (PTS), and burnout.

The twenty-one (21) studies focused on the psychological impact of the COVID-19 crisis. Validated instruments were used to assess the psychological symptoms as outlined in Table 1 - the summary of included studies. The most common outcomes assessed were stress, fear, anxiety, and depression. Given the unprecedented challenges and effects of COVID-19, exploration of stress, fear, anxiety, and symptoms of depression among healthcare workers was prevalent in the included studies. These studies showed that various factors were associated with mental pressures experienced by healthcare workers. Working in areas with a high incidence of infection was significantly associated with higher stress and psychological disturbance.

The COVID-19 pandemic is more than a medical phenomenon (Shah, 2020; Javed et al., 2020). Its impact extends beyond being a disease. It has affected the entire world and continues to cause disruption, anxiety, stress, stigma, and xenophobia. Its rapid transmission led nations and governments to institute health protocols to stem the spread of this disease. People have to observe isolation, social distancing, closure of offices and workplaces, and other restrictive measures that undoubtedly have adversely affected individual's mental health, including those of the healthcare workers who attend to the treatment and care of those infected.

This review reports and examines the psychological impact of the disease among healthcare workers. The results of the studies were categorized according to the psychological impact of COVID-19 on healthcare workers and presented by geographic location.

1. Mental Health Issues by geographic location

1.1 Asia (China, Nepal, Pakistan, Philippines, Singapore)

In China, participants reported having experienced anxiety, depression, insomnia, and other psychological issues like somatization and obsessive-compulsive and post-traumatic stress symptoms. A significant proportion of those who participated in the Lai et al. (2020) study admitted having anxiety, depression, and insomnia symptoms, and more than 70% reported psychological distress. Among physicians and nurses in hospitals with fever clinics or wards for patients with COVID-19 and healthcare workers responding to the spread of COVID-19, high rates of symptoms of depression, anxiety, insomnia, and distress were reported. Lu et al. (2020) disclosed that the medical staff had more significant psychological distress than the administrative staff. The medical front-liners were twice more likely to suffer anxiety and depression than those having close contact with infected patients. Those in critical departments showed higher scores on the fear scale. Que et al. (2020) reported that in general, healthcare workers reported anxiety, depression, or insomnia, with the nurses observed to have the highest prevalence of anxiety symptoms (51.44%); the public health professionals(48.80%) and medical residents (40.53%) revealed depressive symptoms. In Zhang et al. (2020) study, medical health workers had higher prevalence rates of severe insomnia, anxiety,

depression, somatization, and obsessive-compulsive symptoms than nonmedical health workers. Post-traumatic stress (PTS) symptoms were prevalent in this sample of Chinese healthcare professionals (Si et al., 2020), and 40.2% had significant post-traumatic stress disorder symptoms. Perceived threat and passive coping strategies were positively correlated to PTS and DASS (depression, anxiety, stress) scores. Among medical care workers, nurses were the more likely to be anxious during this pandemic.

From a total of 475 Nepali health workers (Khanal et al., 2020), it was reported that 41.9% had anxiety, while some showed symptoms of depression (37.5%) and insomnia (33.9%). High symptom levels of anxiety, depression, and insomnia among the health workers were observed during the beginning of the outbreak. They also admitted to experiencing stigma, as reported by more than half of the participants.

In the study of Sandesh et al. (2020), many Pakistani participants admitted having experienced anxiety, stress, and depression. Around 89% of healthcare workers feared for their families, and 80% feared being infected.

Labrague et al. (2020) reported that of the 325 Filipino nurses who participated in their survey, 123 (37.8%) revealed dysfunctional anxiety levels. Moreover, more than 90% of frontline nurses admitted not being fully prepared to manage COVID-19 patients, and only 20.3% expressed absolute willingness to care for COVID-19 patients.

In Singapore, Tan et al. (2020) study revealed the prevalence of depression, stress, anxiety, and post-traumatic stress disorder (PTSD) among healthcare workers.

1.2 Middle East (Oman, Saudi Arabia, Turkey)

Healthcare workers revealed depression, anxiety, insomnia, and distress symptoms in the Middle East. In Oman, the study of Alshekaili et al. (2020) involving 1139 frontline and non-front-line healthcare workers appeared to conform with other studies suggesting that the COVID-19 pandemic has resulted in a higher rate of depressive symptoms, anxiety, and insomnia. Findings in another Omani study (Badahdah et al., 2020) revealed a pessimistic portrait of healthcare workers' mental health. Based on the GAD-7, one in four (26%) healthcare workers suffered either from moderate or severe anxiety. In the combined mild, moderate, and severe anxiety categories, two-thirds (65%) of the sample had some degree of anxiety. In this study, female and young healthcare workers were more likely to experience moderate to severe anxiety than males and older ones. The stress level was high, especially among female participants.

Of the healthcare workers in Saudi Arabia (Al-Hanawi, 2020), the proportion of respondents as a percentage of the total sample increased from average (28.9%), through mild (33.7%), to severe (39.9%) distress. The preliminary evidence shows that health workers are at greater risk of psychological distress than non-health workers. There is also a significant trend among frontline health workers, with the percentage growing from normal (13.4%), through mild (15.5%), to severe (24.3%) distress. The evidence showed that 40% of the Saudi sample are distressed due to COVID-19, approximately 33% are mildly distressed, and 7% are severely distressed. The high distress levels are of the young, females, private sector employees, and health workers, especially those working on the frontline. The Temsah et al. (2020) study showed Saudi staff feeling more anxious about family members contracting the virus than getting infected. Forty-one percent (41%) of staff are more stressed about COVID-19 than from MERS-CoV, and a similar percentage shared that they have similar stress to both infectious diseases. The findings further disclosed the following: On a scale of 0–10 for anxiety, the respondents scored higher anxiety to COVID-19 and MERS-CoV than seasonal influenza. Many healthcare workers reported experiencing mild anxiety 397 (68.25%), followed by moderate anxiety 121(20.8%). In comparison, few had high moderate 47 (8.1%), and the least had very high anxiety 17 (2.9%).

In Turkey, Sahin et al. (2020) reported that female healthcare workers exhibit higher depression, anxiety, insomnia, and distress symptoms. While nurses were found to experience more insomnia and distress symptoms, both nurses nor physicians did not report

any difference in symptoms of depression or anxiety. Depressive symptoms were more prevalent among frontline workers than among second-line workers. Those with a history of psychiatric ailment and receiving psychiatric support revealed depression, anxiety, insomnia, and distress symptoms.

1.3 Europe (Italy, Poland, Spain)

European healthcare workers reported high depressive and post-traumatic stress symptoms (PTSS, anxiety and depressive symptoms, burnout, or psychological conditions. In Piedmont, Italy, Di Tella et al. (2020) presented that healthcare professionals involved in COVID-19 management have high depressive and post-traumatic stress symptoms (PTSS). Depressive and post-traumatic stress symptoms were high among healthcare professionals assigned to the COVID-19 wards. Giusti et al. (2020) reported that health professionals have a high risk of experiencing burnout or psychological conditions due to the COVID-19 pandemic.

In their study, there were two hundred and thirty-five health professionals (71.2%) with scores of state anxiety above the clinical cutoff. There were 88 (26.8%) who had clinical levels of depression, 103 (31.3%) with anxiety, 113 (34.3%) with stress, and 121 (36.7%) with post- traumatic stress. With burnout, 107 (35.7%) had moderate and 105 (31.9%) have severe levels of emotional exhaustion; 46 (14.0%) had moderate, and 40 (12.1%) have severe levels of depersonalization; 132 (40.1%) had moderate and 113 (34.3%) severe levels of reduced personal accomplishment. The findings further revealed that 60% of the population had reduced personal accomplishment together with moderate to severe levels of emotional exhaustion. 25% of the participants exhibited moderate to severe levels of depersonalization.

In Spain, tertiary hospital workers and those working in ambulance services had a higher stress level (Romero et al., 2020). As expected, there was a spike in distress levels in the geographical areas with the highest incidence of COVID-19. Those who felt the need for psychological therapy but failed to receive it were more stressed than those who did not need it.

In the study of Szylińska et al. (2020), participants who had direct contact with COVID-infected patients in the emergency and infectious wards and ICUs were more vulnerable to showing anxiety and depressive symptoms. A significant proportion of these 441 healthcare workers in the Western Pomerania region in Poland had bouts of anxiety, depression, and insomnia. Over 90% of these symptoms were prevalent among those who had direct exposure to persons infected or suspected of having COVID-19.

1.4 Africa (Egypt)

In Egypt, many healthcare workers dealing with COVID-19 in 20 hospitals admitted to having anxiety, depression, insomnia, and stress symptoms (Elkholy et al., 2020).

1.5 Global

With 2097 participants from 31 countries worldwide, the study (Htay et al., 2020) reported that healthcare workers have a substantial burden on mental health and warranted effective mental health support interventions. The data provide evidence of a high prevalence of anxiety (60%) and depression symptoms (53%) among healthcare workers covering the Eastern Mediterranean Region (EMRO) and the Western Pacific Region.

2. Risk Factors and adverse mental health outcomes

This review identified the risk factors linked to adverse mental health outcomes during the COVID-19 pandemic. The author researcher grouped them into the following categories:

2.1 Virus/Medical Concerns

Chinese healthcare workers directly involved with the diagnosis, treatment, and care of patients with COVID-19 are most likely to experience psychological burdens (Lai et al., 2020). Predictors of unfavorable psychological outcomes include exposure to the virus. Lu et al. (2020) mentioned that worrying about being infected and the epidemic would never be controlled as

contributing to their psychological pressure. Si et al. (2020) reported that adverse psychological symptoms were prevalent. Medical care workers admitted to having experienced stigma, fear, risk of infection and transmission to others, and lack of necessary medical supplies. Zhang et al. (2020) mentioned common risk factors for insomnia, anxiety, depression, and obsessive- compulsive symptoms among medical health workers, i.e., currently having organic disease, living in rural areas, and being at risk of contact with COVID-19 patients in hospitals.

In Nepal, medication history for mental health problems was heavily linked to their study's mental health outcomes (Khanal et al., 2020). Also, inadequate precautionary measures were associated with higher anxiety and depression symptoms. The study (Sandesh et al., 2020) found that the most common reason for stress and anxiety among healthcare workers treating COVID-19-positive patients in Pakistan was the fear that they might infect their family members (89.2%), followed by the fear of getting infected themselves (80.3%). Another reason was the lack of PPE (62.5%).

The overall psychological well-being of healthcare workers in Oman (Badhadha et al., 2020) revealed that working closely with COVID-19 patients is worrying and detrimental to psychological health. Temsah's (2020) study was conducted at a tertiary care teaching hospital in Saudi Arabia. The authors initiated and administered a pilot-validated self-reported questionnaire to the healthcare workers. They assessed their concerns, worries, and knowledge regarding COVID-19, past exposure to MERS-COV (proven or suspected patients), intended behavior during the pending pandemic, and whether these factors were associated with psychological stress. These were considered some risk factors --the possible transmission to a family member, virulence, and lack of effective treatment.

Meanwhile, the findings in the Al-Hanawi et al. (2020) study hinted that health workers in Saudi Arabia working in close contact with infected people, not only for fear of infection, were more likely to experience mild and severe distress.

Sahin et al. (2020) in Turkey reported that a history of psychiatric illness is a factor that predicts chances of depression, anxiety, insomnia, and distress symptoms. Another risk factor for insomnia and distress symptoms is being tested for COVID-19. The findings in another study in Turkey (Yalcin et al.,2020) revealed that the COVID-19 pandemic affected the mental health of hospital workers, but the difference is observed among work areas. According to those who stated that the infection measures taken in the hospital were insufficient, depression, anxiety, and stress rates were significantly higher than those who claimed they were sufficient. Those with a history of psychiatric illness are also more inclined to experience depression, anxiety, and stress.

In Italy, Di Tella et al. (2020) reported factors closely linked to the prevalence of acute mental health conditions among healthcare workers in Italy, including the harsh, unyielding spread of the virus, the threat of being infected, limited supply of medical protective equipment. Giusti et al. (2020) reported that psychological comorbidities and fear of infection were risk factors. For emotional exhaustion and depersonalization, the predictor was contact with COVID-19 patients.

2.2 Work-related Issues

Working as front liners is a predictor of unfavorable psychological outcomes among Chinese health workers (Lai et al., 2020). Other possible risk factors linked to psychological problems are the nature of work, e.g., working in the isolation ward (Lu et al., 2020; Que et al., 2020), exposure to pandemic-related information, receipt of negative feedback from front liners, and uncertainty or unwillingness to join frontline work (Que et al., 2020). Medical care workers in China admitted to having experienced too much workload (Si et al., 2020). Medical health workers in rural areas might worry about being infected with the same COVID-19 during the fight against the epidemic due to a different workplace involving different medical skills and medical conditions. Zhang et al. (2020)

On the other hand, inadequate precautionary measures were associated with higher anxiety and

depression symptoms. Compared with other health workers in Nepal, nurses had higher odds of developing anxiety (Khanal et al., 2020). In Pakistan, the most common reason for stress and anxiety among 64.2% of healthcare workers treating COVID-19-positive patients was increased workload (Sandesh et al., 2020).

In Oman, those who attended to COVID-19 patients experienced lower well-being. They confirmed that working closely with COVID-19 patients is worrying and detrimental to psychological health. As expected, those who cared for COVID-19 patients had a higher level of stress and poorer psychological well-being (Badhadha et al., 2020).

A study (Al-Hanawi et al., 2020) showed that being a frontline health worker is related to distress in KSA. They also hinted that health workers are more likely to experience mild and severe distress due to increased workload and long working hours, considering the growing number of COVID-19 cases.

In Turkey, another risk factor for insomnia and distress symptoms resulting in depression is being assigned as front-liners. Also, working in a rural area is more likely to cause anxiety, while the occupation is a risk factor for insomnia and distress (Sahin et al., 2020). The COVID-19 pandemic affected the mental health of hospital workers, but the difference is observed among work areas in Turkey (Yalcin et al., 2020). Stress is more likely to occur in those assigned to emergency services. Emergency room workers revealed a higher level of Post-traumatic stress disorder symptoms.

Di Tella et al. (2020) identified factors, i.e., lack of sufficient rest, workload, and if exposed for a longer time to events like the death of patients and colleagues, and other traumatic events as closely linked to the prevalence of acute mental health conditions in Italy's healthcare workers. For emotional exhaustion and depersonalization, the predictors were working in the hospital and being in contact with COVID-19 patients. The reduced personal accomplishment was also predicted by age (Giusti et al., 2020).

In this Polish study (Szylińska et al., 2020), healthcare workers who work with patients with COVID-19 in emergency and infectious wards and ICUs are more likely to develop anxiety and depressive symptoms and experience sleep disorders.

In a global study in Eastern Mediterranean Region (EMRO) (52.0%) and Western Pacific Region (WPRO) (25.4%), those respondents working in a hospital were at a higher risk of anxiety than those working in the laboratory and other workplaces (Htay et al., 2020).

2.3 Personal and Other Factors

Adverse psychological symptoms were prevalent among medical care workers in China during the COVID-19 epidemic. As expected, several factors contributed to the expansion of psychological pressure, including a shortage of protective equipment and feeling lonely due to isolation from loved ones (Lu et al., 2020). Lack of social support and maladaptive coping were risk factors for healthcare workers' adverse psychological outcomes (Si et al., 2020). Zhang et al. (2020) mentioned that being female is a common risk factor for insomnia, anxiety, depression, and obsessive-compulsive symptoms among medical health workers.

Among healthcare workers treating COVID-19-positive patients, the most common reasons for stress and anxiety were the lack of security (62.5%) and lack of awareness about COVID-19 among the general population (46.4%) (Sandesh et al., 2020). Stigma and being female nurses were heavily linked to all the mental health outcomes in Khanal et al.'s (2020) study.

Meanwhile, in the study of Al-Hanawi et al. (2020) in Saudi Arabia, the findings showed that being a young person, a female, and a private sector employee is related to distress.

In Oman, poor psychological well-being was found among female healthcare workers and those who attended to COVID-19 patients. Female healthcare workers fared worse than males and showed elevated anxiety and stress levels and poor psychological well-being. Moreover, older healthcare workers seemed to have developed better coping skills, faring well than young healthcare workers (Badhadha et al., 2020).

Sahin et al. (2020) reported that being female is a factor that predicts chances of depression, anxiety, insomnia, and distress symptoms in Turkey. Also, Yalcin et al. (2020) revealed that stress is more likely to occur among female health workers. Higher levels of post-traumatic stress, depression, anxiety, and stress were observable among women.

Di Tella et al. (2020) described factors closely linked to the prevalence of acute mental health conditions among healthcare workers. These include frequent isolation from family and other traumatic events. Certain predisposing factors among healthcare professionals working in COVID-19 wards are being female and not in a relationship for depressive symptoms and being female and older for PTSS. Perceived support from friends was the predictor of burnout, and for emotional exhaustion and depersonalization, the predictor was a female nurse (Giusti et al., 2020). Moreover, healthcare workers are less likely to experience anxiety if they are staying with family and friends (Htay et al., 2020).

3. Interventions recommended addressing the adverse mental health outcomes

Mental health (WHO, 2005) is described as a state of well-being in which the individual realizes his or her abilities, can cope with the everyday stresses of life, can work productively and fruitfully, and can contribute to his or her community. In this positive sense, mental health is the foundation for well-being and effective functioning for an individual in a community. As has been consistently pointed out, the mental health of our healthcare workers needs to be promoted, particularly during the pandemic.

While there is no consistent evidence found in the literature to support any one particular approach, studies suggest that implementing a mental health program has great potential to improve the mental health of our healthcare workers. Since mental health issues vary and people differ, staffing issues, personality traits, other demographics, and other conditions need to be looked into for interventions to be effective.

Lai et al. (2020) stressed in their study that a significant portion of public health measures for addressing the current pandemic is the protection of healthcare workers. They contended that interventions to promote the mental well-being of healthcare workers exposed to COVID-19, particularly women, nurses, and front liners, must be implemented without delay. Lu et al. (2020) stressed that effective strategies for improving mental health should be provided to healthcare workers. Que et al. (2020) stated that healthcare workers' knowledge and skills must be improved to cope adequately and competently with infectious diseases. They suggested that steps should be taken to provide the necessary support to reduce the risk of infection and improve the work environment. The study by Si et al. (2020) bared the prevalence of adverse psychological symptoms among medical care workers in China during this epidemic. The authors argued that screening for adverse psychological outcomes and developing corresponding preventive measures would be beneficial in decreasing adverse psychological outcomes. They also pointed to the importance of providing tailored mental health support and including observing the trajectory changes of the post-pandemic mental health situation and establishing a nationwide psychological support group to curb the potential spike in psychiatric cases before it develops into social and economic burdens. In addition, they favor appropriate intervention measures based on the psychological assessment in each stage of the pandemic (present and future, if any) to include counseling and screening, development of positive coping strategies, and a more friendly social environment and mass media network. For Zhang et al. (2020), adequate working conditions and recovery programs seem necessary to ensure the health workers' best physical, mental, and social conditions for optimal health. Some recommendations to support medical staff have been raised to include reduced job demands and workload.

To improve the healthcare workers' mental well-being, Khanal et al. (2020) recommended focusing on stigma reduction, equipping health workers with protective measures, and ensuring personal and family support for those with a history of mental health issues. Sandesh et al. (2020) affirmed that the government and healthcare agencies should take responsibility. Both

should ensure a healthy work environment. The high prevalence of anxiety, depression, and stress among healthcare workers treating COVID-19 patients necessitates investing resources to promote their mental health; this should be given priority.

Even in the Philippines, the need to design and implement interventions to address the adverse effects of the pandemic on healthcare workers' mental health is highly recognized. Labrague et al. (2020) opined that providing adequate mental and psychological support should be prioritized in addressing the dysfunctional levels of COVID-19 anxiety, as this may adversely affect nurses' mental health and well-being. The nurse managers looked up to in terms of being responsible for instituting evidence-based strategies to promote the mental health of nurses should ensure that they have extended access to psychological treatment or psychotherapy, including materials and resources to support mental health. The authors affirm that nurse managers should prioritize and promote self-care among nurses. These initiatives may include flexible or shorter duty hours, adequate breaks, and time scheduling to assuage the negative impact of the crisis and alleviate nurses' anxiety.

Al-Hanawi et al. (2020) argue that increased efforts in raising public awareness of COVID-19 and providing supportive psychological programs and verified social networks, in both the immediate and long term, remain vital in mitigating the psychological distress among the affected Saudis. The authors are hopeful that the results may be shared and applied in KSA and even in Arabian Gulf countries with their shared backgrounds, culture, religion, and challenges.

In Oman, Badhadha et al. (2020) noted that support for healthcare workers, especially those who display signs of trauma and stress, is critical, particularly during this pandemic. They also mentioned the factors that can endanger healthcare workers' mental health. These include fear of infection, stress, anxiety, and concern for their well-being and significant others. If not addressed soon, many psychological problems might result in maladaptive coping behaviors, such as substance abuse and suicide. These problems have been observed in previous disease outbreaks. The authors underscore the urgency and importance of extending administrative and psychological support and educating and providing healthcare workers with up-to-date and accurate information about the COVID-19 virus.

Sahin et al. (2020) noted the high levels of depression, anxiety, insomnia, and distress symptoms experienced by healthcare workers. While the Turkish Health Ministry and several other associations and institutions have already established units, helplines, and other support measures, it was observed that healthcare workers generally had not applied to receive such support. There should be programs to promote these services and amplify interventions, and other simple, practical interventions like electronic devices may be initiated.

Yalcin et al. (2020) describe several factors to promote mental well-being in healthcare workers: adequate working conditions, especially for women, nurses, and frontline workers; necessary and adequate medical protective equipment; adequate resting periods; and multidisciplinary programs such as psychological support. They insist that these should be provided and immediately put into practice. They also noted that providing scientific and regular information to healthcare workers during the pandemic management prevents psychological stress levels from escalating. In addition to all these measures and interventions, they acknowledge the importance of psychological support in enhancing and improving the quality of medical services.

Giusti et al. (2020) claimed that health professionals in Italy had high levels of burnout and psychological symptoms during the COVID-19 emergency. Therefore, they advocate the monitoring and timely treatment of these conditions to preserve the professionals' health and enhance the healthcare systems' preparedness to face the medium- and long-term consequences of the COVID-19 pandemic.

In Poland, Szylińska et al. (2020) hold that an essential public health task in the fight against the COVID-19 pandemic is to protect health professionals, especially the front liners.

Elkholy et al. (2020) stressed the importance of protecting healthcare workers in Egypt during this pandemic. They agreed on the immediate implementation of particular interventions to promote the healthcare workers' mental well-being and mitigate the pandemic's effects on their current mental health. Interventions may include raising awareness of the early symptoms of depression, anxiety, and stress, initiating individual coping strategies (acceptance, behavioral activation, and mindfulness), resilience building, social interactions, and peer-support programs.

DISCUSSION

This systematic review identified studies about healthcare workers' mental health during the covid-19 pandemic. The total of 21478 participants included frontline nurses, doctors, and other healthcare workers who provided clinical care, administration, or other clinical tasks. The studies reported various outcomes and situations, including implementing interventions to prevent or reduce mental health problems, other resources, and strategies utilized by healthcare workers.

The sampled healthcare workers in the included studies reported anxiety, depression, fear, distress, and sleep problems. The incidence of stress, regardless of culture and background, was higher in situations involving healthcare workers on the front lines. The main risk factors and conditions that worsen or trigger mental health issues include age, direct contact with infected patients, not being knowledgeable enough about COVID-19, prolonged work hours, and limited PPEs and supplies. In general, hospital safety and preparedness, reliable and updated education on the disease's transmission and prevention, adequate PPEs and supplies, and self- care activities may work positively to curtail "coronophobia" and other adverse psychological reactions among healthcare workers. The crucial and massive front liner role of healthcare workers during pandemics makes them anxious and stressed out due to a long list of factors (Lai et al., 2020; Si et al., 2020; Zhang et al., 2020; Sandesh et al., 2020; Badhadha et al., 2020; Temsah, 2020; Al-Hanawi et al., 2020; Di Tella et al., 2020; Giusti et al., 2020). The working conditions during pandemics adversely affect healthcare workers' mental health. The workload and work-related pressure vis-à-vis the rising cases may have contributed to the mental health concerns reported in the studies. Exposure to patients with covid-19, a lack of personal protective equipment, and subsequent fear of getting infected or infecting colleagues and loved ones contribute to the healthcare workers' distress.

Healthcare workers are generally recognized for their emotional resilience, even before the COVID-19 pandemic. While trained to be robust and constant exposure to infected patients makes them susceptible to distress and fear. Also, they are faced with additional responsibilities, physical hardships, and tough mental and psychological challenges this time. Reports confirmed their anxiety over patient care, the threat of getting infected, and the possible infection of family members. With the continued mutation of the virus, we need clarification and clarity about how to combat this virus and stem its transmission effectively.

In the prior period of viral outbreaks, there was also the prevalence of anxiety, depression, distress, and insomnia among healthcare workers. Various infectious diseases hounded the world in the past, i.e., SARS-CoV-1, H1N1 influenza, and Ebola virus, and were triggers of mental health issues that impacted healthcare workers (Lee, S. M. et al., 2018; E.Y. Kim et al., 2016: H. Jeong, *et al.,2016;* J.S. Ro et al., 2017). What complicates people's perceptions and exacerbates their fear originates from the comprehensive media coverage of the COVID-19 pandemic. Information spreads faster than the previous SARS outbreaks, H1N1 flu, MERS-CoV, or even Ebola, owing to massive public fear, panic, and stress. During the first few months, we saw many infected healthcare workers; some even died. Health workers get affected as they are not exempt from emotional reactions and psychological distress. Hospitals are encouraged to conduct educational campaigns targeting healthcare workers to improve their knowledge and awareness about COVID-19 before the pending pandemic hits the actual facility. This action is crucial to minimize staff stress and prepare them for the COVID-19 pandemic (Temsah, M. H, 2020).

More interventions towards improving the knowledge and skills of HCWs, as well as reassuring them of the efficiency of proper infection prevention and

control measures, and providing a safe environment, are needed (Temsah, M. H, 2020). The authors further argued that this high degree of stress came out since COVID-19 is a newly emerging virus with uncertain contagiousness, high transmission rate, and degree of information associated with it (Temsah, M. H, 2020). The same observation of stress and anxiety has been noticed during the H1N1 Influenza pandemic. Healthcare workers reported significant concerns about acquiring COVID-19 and transmitting it to a family member. This finding is expected and reproduced from previous similar studies (Temsah, M. H, 2020).

When SARS broke out, there was an unprecedented threat and a great challenge to health professionals in Hong Kong. In this study, many participants reported a high-stress level, with about 57% having experienced psychological distress. Their psychological morbidity was better understood in terms of personal vulnerability, stress, and support in the workplace (Tam et al.(,2003). During the SARS epidemic, healthcare workers were anxious and scared; some even resorted to leaving their jobs (Chen et al., 2006).

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The studies in this review reported that isolation and high-risk workplaces and contact with infected people caused much stress and trauma—the fact of human-to-human transmission and the presence of infected but asymptomatic persons triggered anxiety and fear among healthcare workers. Similarly found, in the study of Maunder et al. (2004), distress in response to the severe acute respiratory syndrome outbreak is more significant in nurses and those who care for patients with the severe acute respiratory syndrome. Even years after epidemics, healthcare workers on the frontline still experienced psychological distress. The Ebola and SARS outbreaks disclosed these outcomes (Khalid et al., 2016).

Health fear becomes real due to the inevitability of providing care to patients with contagious diseases, including SARS, MERS, and SARS-CoV-2. They are responsible for their patients and are concerned about becoming infected and transmitting the disease to their family members (Chen et al., 2006). Quarantined healthcare workers reported fear, stigma, and frustration during the SARS outbreak. The authors contend that advice on coping and stress management techniques for healthcare workers are needed in preparation for potential future outbreaks of infectious diseases.

During the COVID-19 outbreak, healthcare workers find themselves in a dilemma trying to find justifiable answers to questions about their duty to provide care to patients, their obligations to protect their families, and even their right to look after and protect their health. In the Philippines alone, healthcare workers, due to too much workload, a rising number of patients to attend to, and resource challenges, have been experiencing psychological and emotional issues. As reported in the study of Labrague et al. (2020), nonmedical front liners are more overwhelmed with mental health status disorders (e.g., fear, anxiety, and panic). Therefore, strategies on the individual and organizational levels must be designed for the healthcare workers' mental health and overall wellness. With optimism, we remain steadfast that the patient's safety is not compromised.

The studies in the review also described possible risk and protective/resilience factors. Health care workers reported their junior status, exposure, health fear, infected family member, lack of practical and social support, stigma, and younger age as risk factors. On the other hand, they identified protective factors such as access to adequate personal protective equipment, adequate rest, and family and psychological support.

Some studies have recommended improving the psychological health and well-being of healthcare workers faced with COVID-19 challenges. With more research on what works or hat may work given the

circumstances, we can provide our modern-day heroes the support they most direly need. From the researcher's perspective, comparing mental health outcomes among countries may not be the priority consideration. The enemy cannot be seen. That alone makes it scary. With an undisclosed enemy, the researcher thinks it is customary to exhibit these symptoms mentioned in all the studies included in the review.

During this COVID-19 pandemic, healthcare systems face unprecedented challenges in whatever part of the globe. Easing the psychological burden among healthcare workers is one. Thus, strategic interventions for their mental health should be available and accessible. Many other initiatives mentioned in the studies would help build healthcare workers' resilience by reinforcing positive coping strategies and self-efficacy and enhancing social support. While the psychological aspect is taken care of, the implementation of a safe work environment, provision of adequate PPEs and supplies, and information updates about the disease, including relevant training programs, can lead to improved healthcare workers' morale and overall state of health. As the pandemic continues, essential clinical and policy strategies are needed to support healthcare workers.

Adequately placed intervention strategies and resources are necessary for promoting mental health during pandemics like COVID-19. The studies, generally cross-sectional, presented a variety of healthcare workers' mental health responses and outcomes. They also include interventions recommended to prevent or reduce mental health problems and other resources and strategies healthcare workers utilize to cope with the COVID-19 pandemic. Several patterns were shown, e.g., healthcare workers were for social support to relieve mental health impacts, feared virus transmission to the families, were overwhelmed by the workload and believed the healthcare systems/organizations should address healthcare workers' mental health concerns.

Strengths and limitations

The strength of this review is that it was systematically conducted, and the studies were conducted in Asia and from other continents. This review provides an essential reference for future studies on healthcare workers worldwide. The results are consistent with reports from other studies on the impacts of COVID-19 on healthcare workers' mental health. While we see some value, the present study acknowledges some limitations. The study only covered data from March to October 2020; thus, the mental health outcomes might reflect conditions different from recent events. The present review was limited by search strategies designed to retrieve publications focusing on healthcare workers' mental health during the COVID-19 pandemic; thus, studies exclusively about the physical protection, infection, and transmission rates in populations were not retrieved. Also, the search was conducted in a few databases, and the reviewer, with her associate researcher, undertook the screening. Other studies with the same theme could have skipped our attention and analyses. However, we did our best to adopt a comprehensive search strategy and cover a broad range of evidence beyond Asia. Finally, as the current review's searches were carried out early in the pandemic, it will be valuable to consider emerging research from the global arena in light of this review's findings.

Moreover, this review uses descriptive analysis rather than meta-analysis because the data collected were limited, particularly in the Philippines. The period covered is for seven months before the surge of cases. It lacks a longitudinal analysis of data. The review is focused on the impact on the healthcare workers' mental health in general and does not compare the symptoms according to the types of healthcare workers. This shows the need for longitudinal, multi-center studies with more respondents. Also, the number of participants in some studies was small, limiting the generalizability of findings. Most results were based on self-reported questionnaires that investigated psychological problems, which may differ from clinical diagnostic interview findings.

Most papers utilized non-probability sampling methods, with participant numbers between 112 and 3109. The number of respondents seems incomparable, and sample procedures must confirm representativeness to the general population. It relied on convenience samples and may not, therefore, be representative of all healthcare workers. While there may have been well- defined sampling criteria, the lack of

information on samples due to the nature of online surveys is an acknowledged limitation. This results in profound implications as to the applicability to healthcare workers in other settings. Caution in interpretation should be exercised since the findings cannot be generalized and may not apply to other healthcare workers.

The 21 studies were mainly cross-sectional and survey-based, prohibiting us from concluding causality. However, more longitudinal research may identify the causes of mental health problems among healthcare workers. There is a broad stream of literature about the COVID-19 pandemic, but mostly rapidly published. While the researcher tried to qualify the symptoms prevalent in the countries of the included studies, similarities were more evident than differences. The sample distribution is heavy on single-country representations except for China, with five studies, thus restricting a fair comparison of results.

This review has synthesized and discussed the current literature on the psychological impact of the COVID-19 pandemic on healthcare workers' mental health. The researcher sees this as a strength because this pandemic is unique, unprecedented, and, therefore, worth assessing in its own right. It has affected every country and disrupted every person's life across the globe.

The role of the pandemic in the rise of mental health issues needs to be evaluated using a longitudinal study design. Selection bias might be present in most studies. There might be health workers with no or limited internet access, older ones, and those preoccupied with work due to busy schedules who might have opted to pass participation in the studies. Respondent bias may not have been eliminated as the findings were self-reported primarily by health workers and based on a subjective scale. Also, the tools used in the studies should be taken into consideration.

Despite its limitations, this review provides early evidence of the mental health status among health workers during the COVID-19 pandemic in different areas. There is valuable data on risk factors and suggestions to resolve mental health issues during pandemics. Again, particularly in the Philippines, where there is growing discontent among healthcare workers, studies on this subject are scant. The publications, media, and other fora have long stressed the interventions needed by the general public during this pandemic. We should not forget our healthcare workers, who also need extended support regarding their psychological, emotional, and spiritual well-being. One case in point is our country's healthcare workers. Not only is there a lack of personal protective equipment, but our front liners are underpaid. They also experience pressure, stress, insomnia, denial, anger, and fear, despite constant exposure to the COVID-19 virus. WHO head Tedros Adhanom Ghebreyesus has noted, "Even if we do everything else right, if we do not prioritize protecting health workers, many people will die because the health worker who could have saved their lives is sick." (Wilson & Parra, 2020).

Salvation et al.(2017) argued that burnout is associated with increased risks of both physical and psychological long-term detrimental consequences and can increase sick leave, absenteeism, job withdrawal, and poor work efficiency. The pandemic is unprecedented, and its duration is uncertain. We, thus, have to brace for its potentially worse impact. The virus's mutations have caused cases to balloon, and without a doubt, the pandemic is now viewed as a political, social, and biological phenomenon (Bloomberg, September 13, 2021). There is no single approach to the pandemic. Actions should be multi-layered as it has become messy, complicated, and elusive to manage now and probably in the years to come.

Research about the impact of the COVID-19 pandemic on the mental health of healthcare workers, and physician wellness in general, continues to evolve just as the definite profile of the virus remains elusive and challenging to understand fully. Therefore, updated reviews will be necessary for the coming months. Or years. Psychologically, health workers face the same fear and experience similar symptoms wherever they may be deployed. The coronavirus is an emerging novel, and its outbreak surprised the world. On the other hand, access to PPEs and other safety resources and strict observance of health protocols provide them with a semblance of safety. They feel protected from infection

and somehow reduce the fear and anxiety of infecting families and loved ones. Despite reports of their complaints about disturbed sleeping patterns and feelings of isolation, anxiety, and helplessness, healthcare workers remain heroes during this pandemic. This inner strength may be attributed to their sense of meaning and purpose -- the profound resolve to serve humanity.

Implications

Individuals engaged in the fight against the COVID-19 pandemic have grown in number. Among them are healthcare workers who have worked extremely long hours in high-pressure environments and continue to be commissioned to work under highly challenging conditions. COVID-19 places a unique challenge on our healthcare workforce. These healthcare workers might have been directly exposed to the formidable challenges of high-quality care delivery, the limitation posed by limited experience or lack of resources, and even the problem of understaffing. Also, those caring for patients with COVID-19 are at high risk of infection, and as a result, they fear the transmission, that is, the risk of infecting their families. While healthcare workers can thrive in stressful circumstances, protecting their mental health and identifying those who experience psychological injuries is imperative to provide them with appropriate evidence-based support or care.

Our healthcare workers will likely continue to face tough challenges now and in the future. This review confirms that the impact of COVID-19 on healthcare workers' mental health is considerable, with significant levels of anxiety, depression, insomnia, and distress.

The studies included in this review were focused on hospital settings. This is a big concern since, in reality, deaths happen in the community and even in nursing and care homes. Therefore, future studies may tap into other workplaces where other healthcare workers may have been deployed. This suggests that different contexts and cultures may reveal different findings.

Several risk factors emerged in the review of the studies. Those with the most substantial evidence were inadequate PPE, fear of infection, and heavy workload. Some studies suggest that being younger or female may be a risk factor. Another observation is that many of the studies measured adverse mental health outcomes. Future studies may also focus on our healthcare workers' protective factors or coping mechanisms.

Although the current evidence is scarce concerning the direct effects of COVID-19 on mental health, there are indications of increased PTSS and depression following the COVID-19 infection. Regarding the indirect effects of COVID-19 on general mental health, there seems to be evidence of an increase in depressive and anxiety symptoms and a negative impact on general mental health, particularly among healthcare workers. We must welcome research that evaluates the direct psychological consequences and indirect effects on mental health to improve treatment, health care planning, and preventive measures during potential subsequent pandemics.

CONCLUSION

HCWs in varying circumstances have been reporting problems such as anxiety, depression, distress, and sleep deprivation during the covid-19 pandemic. For those in the immediate, the lack of adequate rest and sleep is strongly related to the pressures and burdens of work. This is often exacerbated by inadequate personal protective equipment or insufficient training. Over time, many more HCWs may struggle with mental health and somatic complaints. The studies in the review recommended mental health interventions, and these should be proactive organizational approaches as these are seen to be more effective and less stigmatizing. Furthermore, incorporating high-quality research in pandemic-preparedness planning must also be on the priority list.

This review confirmed that the COVID-19 pandemic adversely affects HCWs' mental health. The studies showed that the healthcare workforce experiences anxiety, depression, insomnia, and distress amid the pandemic. However, it must be pointed out that most studies draw only from the hospital setting, and it is highly possible that other contextual

circumstances may yield different results. In this regard, the researcher recommends conducting more research in primary and social care settings and keeping abreast with rapidly emerging evidence in different parts of the world. This also calls for broader societal and risk factors analysis, including gender, socio-economic disparities, age, and types/categories of HCWs. Although this is not part of the researcher's current review and analysis, these may have the ability to influence the state of mental health in a particular setting.

Given the adverse impact on psychological well-being, there has been a clamor across the globe for more research to identify action points to address mental health issues, particularly during pandemics. A call to action for individual interventions to strengthen psychological resistance and protection against adverse mental health outcomes is essential. The researcher proposes that boosting psychological resilience in an approach that considers both personalized and holistic aspects may effectively protect our healthcare workers from adverse mental health outcomes. It will include significant structural changes to create a healthy, safe, and supportive work environment. Because of the virus' profile that prevents face-to-interventions, digitally-based measures and programs are more likely to be preferred.

Lastly, supporting and protecting healthcare workers' mental health is morally justified. If done well, this should reduce the risk of mental health issues and provide optimum opportunity for staff to experience psychological growth from overcoming the formidable challenges during this trying time. Much could be done to support and protect healthcare workers' physical and mental health as they willingly put themselves in the line of fire to protect and save other people's lives.

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APPENDIX

Table 1. PRISMA

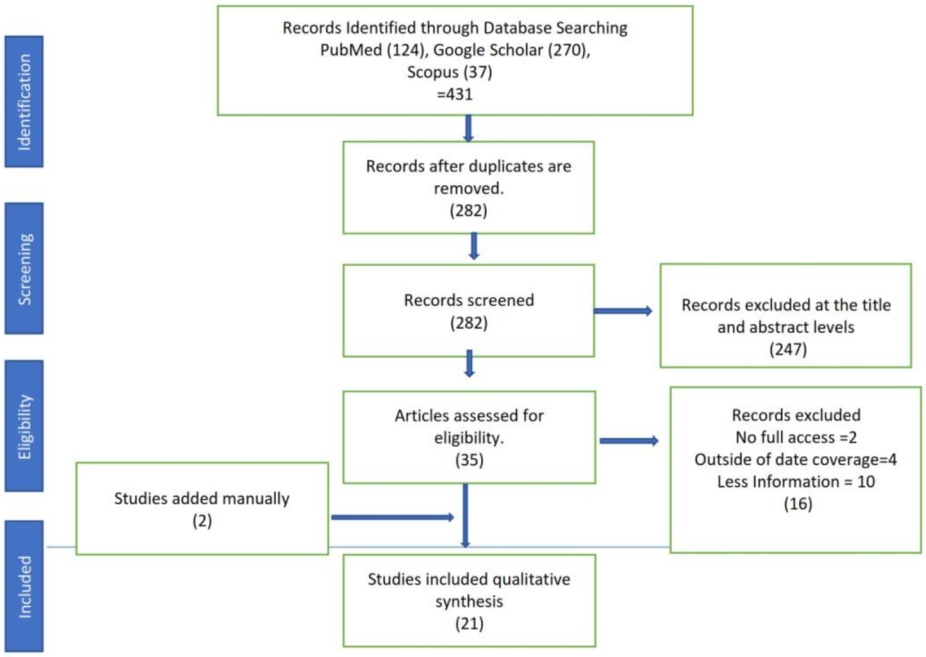

Table 2. Quality assessment of 21 studies including the Joanna Briggs Institute quality assessment tool

	1	2	3	4	5	6
1. Were the criteria for inclusion in the sample clearly defined?	YES	YES	YES	YES	YES	YES
2. Were the study subjects and the setting described in detail?	YES	YES	YES	YES	YES	YES
3. Was the exposure measured in a valid and reliable way?	YES	YES	YES	YES	YES	UC
4. Were objective, standard criteria used for measurement of the condition?	YES	YES	YES	YES	YES	UC
5. Were confounding factors identified?	YES	YES	YES	NA	YES	YES
6. Were strategies to deal with confounding factors stated?	YES	YES	UC	NA	UC	UC
7. Were the outcomes measured in a valid and reliable way?	YES	YES	YES	YES	YES	UC
8. Was appropriate statistical analysis used?	YES	YES	YES	YES	YES	YES

JBI Critical appraisal checklist for analytical cross-sectional studies

Yes / No / Unclear (UC) / Not applicable (NA)

	7	8	9	10	11	12
1. Were the criteria for inclusion in the sample clearly defined?	NO	YES	YES	YES	YES	YES
2. Were the study subjects and the setting described in detail?	YES	YES	YES	YES	YES	YES
3. Was the exposure measured in a valid and reliable way?	YES	YES	YES	YES	YES	YES
4. Were objective, standard criteria used for measurement of the condition?	YES	YES	YES	YES	YES	YES
5. Were confounding factors identified?	YES	YES	YES	YES	YES	YES
6. Were strategies to deal with confounding factors stated?	YES	UC	UC	YES	YES	YES
7. Were the outcomes measured in a valid and reliable way?	YES	YES	YES	YES	YES	YES
8. Was appropriate statistical analysis used?	YES	YES	YES	YES	YES	YES

	13	14	15	16	17	18
1. Were the criteria for inclusion in the sample clearly defined?	NO	YES	YES	YES	YES	YES
2. Were the study subjects and the setting described in detail?	NO	YES	YES	YES	YES	YES
3. Was the exposure measured in a valid and reliable way?	YES	YES	YES	YES	YES	YES
4. Were objective, standard criteria used for measurement of the condition?	YES	YES	YES	YES	YES	YES
5. Were confounding factors identified?	YES	YES	YES	YES	YES	YES
6. Were strategies to deal with confounding factors stated?	YES	YES	YES	YES	YES	YES
7. Were the outcomes measured in a valid and reliable way?	YES	YES	YES	YES	YES	YES
8. Was appropriate statistical analysis used?	YES	YES	YES	YES	YES	YES

	19	20	21
1. Were the criteria for inclusion in the sample clearly defined?	NO	YES	YES
2. Were the study subjects and the setting described in detail?	YES	YES	NO
3. Was the exposure measured in a valid and reliable way?	YES	YES	YES
4. Were objective, standard criteria used for measurement of the condition?	YES	YES	YES
5. Were confounding factors identified?	YES	YES	YES
6. Were strategies to deal with confounding factors stated?	YES	UC	UC
7. Were the outcomes measured in a valid and reliable way?	YES	YES	YES
8. Was appropriate statistical analysis used?	YES	YES	YES

The Effects of Gadget Use on Sleep Quality among Elementary Students in Grades 4-6 in a Private School in Lucena City, Quezon Province*

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Abstract

OBJECTIVE: The study aimed to determine whether prolonged gadget use will have an effect in the child's sleep quality. The study also aimed to ascertain if there is a significant relationship between the parameters of CSHQ and the average length of sleep, average length of gadget use, and frequency of gadget use.

DESIGN: Descriptive research design was used, particularly the survey method. Simple random sampling was used.

SETTING: Private school in Lucena City, Quezon Province

PARTICIPANTS: Parents of Grades 4-6 students in a private school in Lucena City. Sample size was computed at n=131.

RESULTS: 53.4% of the respondents were males, 29.8% of which are 11 year-old, grade 6 students (35.9%). The average length of sleep of most children was at 6-8 hours (57.3%), with an average length of gadget use at 5-10 hours daily (58%), 5-7x a week (61.8%). Weighted means computation showed that parents agreed to the positive statements of the CSHQ but key problems based on the CSHQ statements were identified upon further analysis.

CONCLUSIONS: With an $\alpha = 0.05$, significant relationships were established between the parameters of the CSHQ and the average length of gadget use ($p = 0.012615 < 0.05$), as well as the frequency of gadget use ($p = 0.000116 < 0.05$). Generalization should be made with caution due to the small sample size and non-diversity of the samples. Recommendations are due to improve generalizability by increasing sample size and diversity of the samples.

Keywords: Quality of Sleep, Children's Sleep Habits Questionnaire, CSHQ

INTRODUCTION

The World Health Organization (WHO) declared COVID-19 a global pandemic in March 2020, necessitating temporary school closures as part of efforts to contain the virus's spread among the general population. Globally, the peak of school closures occurred in April 2020, when 199 countries closed schools (World Food Program, 2020). Each country has prepared contingency plans in response to the worldwide school closures to ensure that affected students receive an education.

Individual countries and teachers were forced to adapt to the online learning system across all educational levels, where a variety of methodologies and skill assessments were used to determine whether a student has mastered the topics being taught. To ensure learning continuity given the online learning set-up brought by the COVID-19 pandemic, the Philippine Department of Education developed a series of Modular Distance Learning (MDL) programs in which students utilize Self-learning Modules (SLM) based on the Department of Education's Most Essential Learning Competencies (MELCS) (Gonzales, 2021).

Gadgets (e.g., mobile phones, tablets, personal computers, and laptops) have emerged as one of the most important instruments for schools to use in order to deliver ongoing education to displaced students. They have indeed emerged as the principal channel through which teachers instruct the pupils. Gadgets

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and other devices, whether used for synchronous (live discussion of courses) or asynchronous (modules, pre-recorded videos, worksheets) instruction, have become essential tools for students to get critical information, lessons, and research to cope with the demands of online learning. Likewise, our current generation of students is preoccupied with the use of electronic devices. They frequently want to get the most recent release of these gadgets,in order to satisfy their cravings for amusement and be the first to own the newest and greatest devices. As a result, pupils are more likely to incorporate technological devices into their daily routines.

Researchers have identified several key alarming concepts that may stem from excessive gadget use: (1) language problems and delays (Hinkley et al., 2021); (2) mental and emotional problems, as well as social behavioural concerns, and cognitive and socio-emotional development concerns (Wahyuni et al., 2019; Frashini et al., 2018; & Zahid, 2021); (3) visual acuity problems and computer vision syndrome (Wahyuni et al., 2018; Ahmad et al., 2021); (4) poor sleep quality and shorter sleep duration (Jaisawal et al., 2020; Mak et al., 2014; Brambilla et al., 2017; LeBourgeoiset al., 2017; Xi et al., 2018; Falbe et al., 2015; Hale et al., 2018; Gradisar et al., 2013; Magee et al., 2014; &Merinelli, 2015); and (5) body mass index problems (Fulleret al., 2017).

While there is a wide breadth of researches on the effects of gadget use on a child's sleep quality, there is still a dearth of knowledge and research in the local setting. With this in mind, the researcher aimed to determine the effects of gadget use on the quality of sleep among grades 4-6 elementary school students undergoing online education in a private school in Lucena City, Quezon Province.

Statement of the Problem and Objectives

At the outset, the study aimed to determine the effects of gadget use on the quality of sleep among grades 4-6 elementary school students undergoing online education in a private school in Lucena City, Quezon Province. Subsequently, the study also sought to answer the following specific questions:

1. What is the profile of the respondents in terms of the following:
    a. Age
    b. Gender
    c. Average length of sleep
    d. Length of time of gadget use
    e. Frequency of Gadget use

2. Using the Children's Sleep Habits Questionnaire, what are the sleeping habits of the grades 4-6 students based on the following parameters:
    a. Bedtime behaviors
    b. Sleep behaviors
    c. Waking up during the night
    d. Morning wake up

3. Is there a significant relationship between the respondents' quality of sleep based on the parameters of CSHQ and the average length of sleep, length of time of gadget use, and frequency of gadget use?

Statement of the Hypothesis

With an $\alpha = 0.05$ (95% confidence), the following hypotheses were formulated:

H_o: There is no significant relationship between the respondents' quality of sleep based on the parameters of CSHQ and the average length of sleep, length of time of gadget use, and frequency of gadget use.

H_a: There is a significant relationship between the respondents' quality of sleep based on the parameters of CSHQ and the average length of sleep, length of time of gadget use, and frequency of gadget use.

Significance of the Study

At its inception, the study served to benefit the following groups of people:

General Population – This study can serve as a reminder that, though the perceived "norm" nowadays is that gadgets are an integral part of the children's lives, it is emphasized that there are adverse effects that may result from excessive gadget use, especially in children.

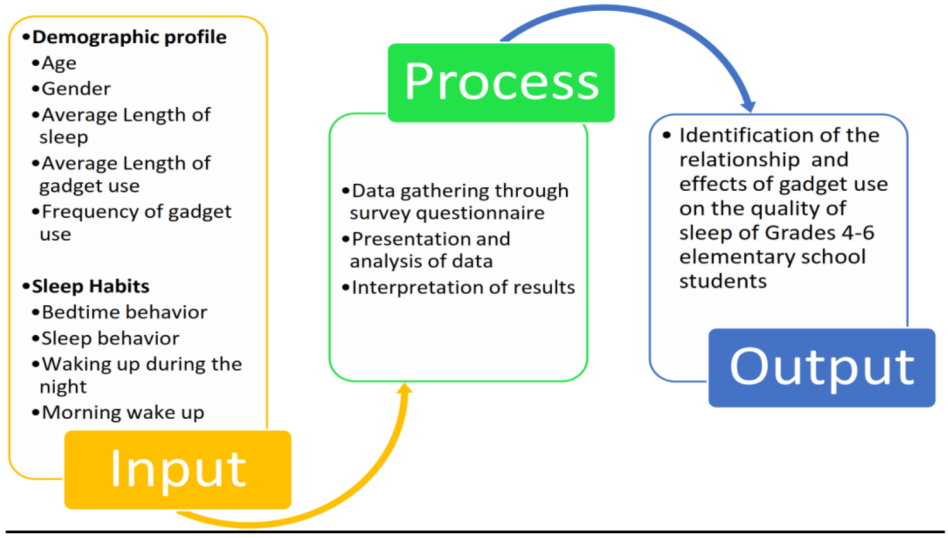
Parents – The study will give the parents the necessary information to help them understand that, although gadgets are necessary asthey are used to provide a continuum in the child's education, there should still be a limit as to the number of hours of screen time to avoid unnecessary problems brought about by gadget usage.
Medical Doctors – This study can be a benchmark through which they can advise their clients regarding the adverse effects of gadget use in the children's quality of sleep. Moreover, this study will also provide them with more concrete evidence on other possible side effects of excessive gadget use, which can greatly help them in clinical decision making.

Prospective Researchers – The study can serve as a springboard for future local setting research on the effects of gadget use in the different aspects of the child's well-being. Additionally, this study will be of great benefit to future researchers who may wish to conduct follow-up studies with larger populations by providing insights about the possible areas that need to be studied in terms of the effects of gadgets in children.

Scope and Limitations of the Study

The study was limited to determining the effects of gadget use on the quality of sleep of Grades 4-6 elementary school students in a private school in Lucena City, Quezon Province. Likewise, the study was limited to a smallsample size so generalization of data may be complex. Furthermore, the study did not take into consideration other effects of gadget use aside from the child's quality of sleep, as perceived by their parents based on the parameters set by the CSHQ. Moreover, the study did not attempt to determine statistical within-group relationships of the parameters as stated in the Children's Sleep Habits Questionnaire, nor did it attempt to consider possible co-morbidities (Autism, ADHD, history of mental health issues, seizure disorder/epilepsy, significant physical illnesses, and diagnosed sleep disorders), whether the children were under medications (melatonin and other medications to address co-morbidities), and the lower grade level of other students. The study also did not consider the distribution of respondents according to grade level.

Conceptual Framework



Definition of Terms

Terms	Definition
Online learning	Online education is education done via the internet. It is also known as "e-learning". However, online learning is merely one sort of "distance learning," which is any learning that occurs outside of a regular classroom and may include self-paced materials (modules), instructional videos, research activities, and the like.
Modular Distance Learning Program	Modular Distance Learning offers personalised teaching and self-learning modules (SLMs) in print or digital format/electronic copy. The teacher is in charge of monitoring the students' progress.
Self-learning Modules	Self-learning modules allow learners to choose what, how, when, and where to learn. Lessons can be completed at the learner's own speed.
Most Essential Learning Competencies	This refers to a set of competencies that students must exhibit in every class and learning activity as set by the Department of Education.
Gadgets	Mobile phones, tablets, laptops, and the like are all examples of small mechanical or electronic devices that have a useful purpose yet are typically viewed as a novelty. Gadget use refers to the amount of time the gadget is being used inan entire day.
Synchronous instruction	The term "synchronous learning" refers to online or remote learning that is both interactive and two-way with a teacher in real time.
Asynchronous instruction	It is a type of learning without real-time teacher-led engagement. Asynchronous learning takes place over the internet and via premade resources.
Language delay	A child is said to be experiencing a language delay if he or she has difficulty comprehending or expressing themselves verbally in everyday situations. Atypical for the child's age, these issues are troubling. Learning new words or saying one's first words might be a challenge for some people, more so creating sentences by combining words.
Socio-emotional development	An important part of the child's social-emotional development includes his or her ability to express his or her feelings and form pleasant and rewarding interactions with other people.
Visual acuity	Visual acuity is one's ability to detect characters or numerals at a certain distance according to a fixed standard.
Computer vision syndrome	Extended computer use can create a group of associated eye and vision disorders. Eye discomfort and weariness, dry eye, impaired vision, and headaches are all symptoms of computer vision syndrome.
Sleep quality	The quality of your sleep is measured by how restful and restorative your sleep is—in other words, how well you're sleeping. It is distinct from sleep satisfaction, which relates to a more subjective evaluation of how you feel about the sleep you are experiencing.
Sleep duration	The overnight or 24-hour sleep duration is commonly used to describe how much sleep a person gets.
Blue Light	Blue light is emitted by your mobile device's screen, which can disrupt your sleep during the daytime, but it's safe to use throughout the day. Using your phone or tablet before night can keep you awake because blue light can stimulate your brain and deceive it into believing it is daytime, keeping you awake if you do so.

REVIEW OF RELATED LITERATURE

Many parents worry about their kids' sleep habits. Sleep deprivation is one of the prevalent plagues of modern cultures, according to Oginska and Pokorski (2006), and Yu et al. (2007). However, such issues aren't new and have existed for over a century. Accordingly, these long-standing worries led to early attempts to suggest sleep durations for children and adolescents, dating back to 1897. According to Holden (1993), the same message rings true today, with groups like the National Commission on Sleep Disorders Research pushing for a “radical transformation in how society interacts with sleep.”

Insufficient sleep has been linked to poor physical and mental health, including reduced concentration and memory, mood problems, motor skill impairment, and overall health and immunological function. Inadequate sleep in children has been linked to poor academic performance, obesity, accidents, suicidal thoughts, and drug and alcohol usage. Adequate sleep for kids has thus become a health problem (Matricciani et al., 2012). Loureiro (2011) also connected sleep to optimal physical, cognitive, and behavioral development in children. In the study of Bonuck et al., (2017), they explicitly stated that when young children do not get enough sleep or have poor quality sleep, it has a negative impact on their behavior and cognitive function. Preschool age (3-5 years) is a critical period for sleep problems, with around 25% of children experiencing behavioral sleep problems (BSPs) during this period. BSPs are classified by the International Classification of Sleep Disorders as difficulties falling asleep or remaining asleep, such as bedtime resistance and night-waking; they correlate to the insomnia diagnosis under the 2014 classification of sleep disorders (Sateia, 2014). Healthy sleep practices (e.g., normal bedtime, nighttime routine) and behavioral therapies (e.g., extinction), on the other hand, promote healthy sleep and addresssleep issues, respectively. In fact, the majority of BSPs in young children do not necessitate specialized care (Bonuck et al., 2017). Turnbull et al. (2013) stated in their study that behavioral sleep issues are the most common sleep difficulties experienced by children in the general population, and they occur most frequently in boys. From their research, they quoted that, according to the National Sleep Foundation, between 15% and 30% of 2- to 5-year-old children have regular difficulties falling asleep (also known as bedtime troubles) or sleeping through the night (i.e., night waking). When compared to preschool children, fewer school-aged children suffer from behavioral sleep disorders, but these issues still affect 11 percent to 15 percent of school-age children (6-12 years).

Due to the withdrawal of approximately 1.5 billion children from school since April 2020, many of these students are spending more time using electronic devices to complete school assignments as part of learning from home, communicate with peers, and play video games to recall activities. Because of the lockdown, people are unable to go outside (Pratiwi et al., 2020). Continual use of gadgets will have a negative impact on children's daily behavior patterns; children who have a tendency to use gadgets constantly will become very reliant on them and will routinely incorporate it in their daily activities, playing gadgets more often than learning and interacting with their surroundings (Moh, 2017).

In accordance with the American Academy of Pediatrics and the Canadian Children's Society, children between the ages of 0 and 2 should not be exposed to any form of technology. Children aged 3-5 years are only allowed to use technology for one hour per day, while children aged 6-18 years are only allowed to use technology for two hours per day. It is possible for children to suffer from sleep deprivation and a lack of concentration, which can result in potentially unhealthy sleep cycles since youngsters are sleepier during the day and sleep less at night. If a child uses a gadget every 15 minutes, this equates to a loss of 60 minutes of sleep time per night. As reported by the American Academy of Children, sleep deprivation affects 75 percent of children aged 9-10 years who are exposed to technology without adult supervision (Pratiwiet al., 2020).Children's biopsychosocial development is greatly aided by their ability to sleep well. As a result of the shortage of sleep time experienced by a child who has difficulties sleeping, the youngster gets overly hyperactive and acts inappropriately approaching bedtime. Drowsiness, difficulty waking up in the

morning, and irritability during the day are all signs that a child is suffering from a sleep deficiency in young children (Moh, 2017).

Based on the findings of some studies, the more time youngsters spend on smart phones, tablets, electronic games, and other handheld devices, the greater the likelihood that the child would experience delays in expressive speech. Interactions with other people will help children develop their ability to talk and communicate. This is the only way they will learn to communicate effectively; if they are not communicating, they will not be learning anything. Every one minute that your youngster spends in front of a screen is one minute that he or she could be conversing or learning with other people. Screen time refers to the amount of time your child spends in front of a screen, whether it is a television or any other gadget. Screen time deprives a youngster of time that he or she could be spending conversing and communicating with other children or adults (Sundus, 2018).Orji et al., (2017) stated that every child is entitled to proper sleep hygiene because it is a necessary and important indicator of overall health. The lack of proper sleep hygiene does not only predispose children to behavioral and cognitive impairment, but it also has a negative impact on their physical health, which may further predispose them to sleep troubles. Accordingly, an examination of sleeping patterns such as the bedtime routine and the sleeping environment may identify elements that are contributing to the sleep impairment. These factors may include the use of technological devices in the bedroom, such as televisions and computers, having a large meal immediately before bedtime, and drinking stimulants before bedtime (such as sodas, chocolate, tea, and coffee).

Hale and associates (2015) also did a systematic review of screen time and sleep among school-aged children and adolescents. In this study, they conducted a comprehensive review and update of the scientific literature on the relationship between screen time (e.g., television viewing, computers, video games, and mobile devices) and sleep outcomes among school-aged children and adolescents. They looked at 67 papers that were published between 1999 and the beginning of 2014. It was discovered that screen usage is connected with negative sleep outcomes (mainly shorter length and delayed timing) in 90 percent of the research they looked at. Additionally, some of the findings differed depending on the type of screen exposure, the age of the participants, their gender, and the day of the week. The study of Rashidet al., (2021) revealed that among all the technologies they checked, cell phones were the most frequently reported to be used daily by the participants (67.11 percent). Because of the current COVID-19 epidemic, 24.48 percent of those who answered the survey used electronic devices to participate in online classes. According to the participants, they use electronics much more in 2020 as compared to the year 2019. Children demonstrated a lower proclivity to participate in outside activities. More than half of those who took part in the study spent less than one hour each day participating in outdoor activities. In their research, they discovered a link between the usage of electronic devices and health concerns such as headaches, backaches, visual disturbances, and sleeping disturbances. However, the study of Brambilla et al. (2017) found out the use of video devices to be a negative predictor of sleep duration.

Children's health and well-being are widely recognized to be dependent on their ability to sleep, and that inadequate sleep is connected with a wide range of unfavorable health effects. This is underscored by the fact that, due to the current educational situation in our country, children spend more time in front of their gadgets most of the time. Additionally, with the advent of different social media platforms and the prevalence of online games, children spend less and less time interacting on a face-to-face basis, while some get lesser sleep duration in effect. A sequela of events is being predicted because of these factors, which is why this study is of paramount importance as a stepping-stone through which the general public will recognize the connection between sleep and gadget time in children. It is hoped that the parents will recognize the importance of sleep and limiting the screen time of their children in an “as needed” basis only instead of allowing them to spend longer periods tinkering with their gadgets.

METHODOLOGY

Study Design

The researcher used a Descriptive Research Design, more precisely a survey method, to determine the effects of gadget use on sleep quality of Grades 4-6 elementary school students in a private school in Lucena City, Quezon Province. This research design was chosen because the researcher focused on the how, what, when, and where of the research problem, rather than on the why, in order to adequately describe the population, situation, or phenomenon under study.

Locale of the Study and Sampling Method

The study was conducted at a private school in Lucena City, Quezon Province. Similarly, the researcher established the following criteria for determining whether a respondent should be included in the study:

1. Grades 4-6 students.
2. Must be undergoing online learning.
3. Can use gadgets for online learning and/or other miscellaneous activities (social media, research, entertainment, etc.)

In order to determine the participants of the study, the researcher utilized the simple random sampling method. The school administrator provided the roster and the total number of students in grades 4-6 (N=198), after which, the sample size was computed via Raosoft Sample Size Calculator, where the sample size of n=131 was determined. After determining the sample size, the researcher assigned a number to each student and then the fishbowl technique was used to determine who will be the participants.

Methodology and Data Gathering Procedures

Throughout the study's conduct, the following procedures were followed:

1. For this research, the researcher opted to use the Short Form of the CSHQ (22 items). Additionally, to maintain the questionnaire's integrity and validity, no additions or revisions were made. However, in order to establish relationships, weighted means and other statistical tools were used.
2. As indicated in the scope and sampling section of the research, the study included grades 4-6 students in a private school in Lucena City, Quezon Province.
3. Through simple random sampling, a total of n=131 samples were chosen. Each student was assigned a number, after which, the fishbowl technique was used to determine who will be able to participate in the study.
4. The parents of the chosen children were given a survey consent form to read and sign if they chose to participate in the study.
5. Questionnaires were subsequently distributed to the respondents by giving them the link to the survey tool's Google Forms.
6. After participants have completed the questionnaire, the researcher collated, checked, made sure that the responses were complete, scored, and tallied the results.

Ethical Considerations

The study was approved by the Research Committee of the De Los Santos Medical Center's Department of Pediatrics. Participants gave a written consent to participate in the study. At all times, confidentiality and privacy were maintained. Patient identifiers such as names were not included on the data collection forms. Rather than that, a unique study code was assigned to each patient. Only the researcher had access to the completed data collection forms. The encrypted data were stored on a password-protected laptop and were available for analysis only to the biostatistician. Completed data collection forms and encoded data will be retained for up to five (5) years after the study concludes. There is no risk or benefit to study participants directly; however, the study's findings may benefit the aforementioned medical institution as well as residents and attending physicians in the Pediatrics department of the same medical institution. The researcher may then present the findings of the study at conferences/symposia and publish in a scientific journal.

The researcher was responsible for all study-related expenses, including funding and other incidentals. To date, no conflict of interest has been declared.

Statistical Treatment of the Data

Encryption and processing of the data collected were performed using Microsoft Excel and Stata. The data were then tallied to calculate the frequency and percentage distribution of responses. After tallying, the data were treated using weighted means for each response. Additional statistical tools, such as the Analysis of Variance (ANOVA), was used to determine the statistical relationships of the parameters of CSHQ and the (1) average length of sleep, (2) average length of gadget use, and (3) frequency of gadget use. Verbal interpretations of the aggregated weighted means were as follows:

1.00 – 1.79	Disagree
1.80 – 2.59	Slightly Disagree
2.60 – 3.39	Neutral
3.40 – 4.19	Agree
4.20 – 5.00	Totally Agree

Additionally, since the abbreviated version of the CSHQ does not have a set cut-off score in determining problem areas and that this particular abbreviated form of the questionnaire uses a Likert-type scale, arbitrary interpretations were done instead to determine statistical significances.

Table 1: Frequency and Percentage Distribution of the Child's Demographic Profile

Gender	Frequency (f)	Percentage (%)
Male	70	53.4%
Female	61	46.6%
Total	n = 131	100%
Age	Frequency (f)	Percentage (%)
9 years old	28	21.4%
10 years old	27	20.6%
11 years old	39	29.8%
12 years old	37	28.2%
Total	n = 131	100%
Grade Level	Frequency (f)	Percentage (%)
Grade 4	42	32.1%
Grade 5	42	32.1%
Grade 6	47	35.9%
Total	n = 131	100%

Interpretation: The demographic profile of the child is depicted in Table 1, which shows the frequency and percentage distribution of the child's characteristics. The information provided was supplied by the parents, who were the primary respondents to the questionnaire. As indicated by the data, 53.4 percent of the respondents were males, while 46.6 percent of the respondents were females. Additionally, 29.8 percent of the respondents were 11 years of age, along with 28.2 percent at 12 years old, 21.4 percent at 9 years old, and 20.6 percent at 10 years old. Furthermore, 35.9 percent of parent/student respondents are currently in Grade 6, while 32.1 percent are currently in Grade 4 and the last 32.1 percent in Grade 5.

Table 2: Frequency and Percentage Distribution of Child's Average Length of Sleep

Average Length of Sleep	Frequency (f)	Percentage (%)
less than 4 hours everyday	0	0.0%
4 hours to 6 hours daily	13	9.9%
6 hours to 8 hours daily	75	57.3%
More than 8 hours daily	43	32.8%
Total	n = 131	100%

Interpretation: Table 2 shows the frequency and percentage distribution of the child's average daily sleep duration. As the data shows, the majority of children (57.3 percent) were able to get at least 6-8 hours of sleep per day, with 32.8 percent getting more than 8 hours of sleep per day and only 9.9 percent getting at least 4-6 hours of sleep per day. There were no responses recorded for those who slept less than 4 hours per day.

Table 3: Frequency and Percentage Distribution of Length of Time of Gadget Use

Length of Time of Gadget Use	Frequency (f)	Percentage (%)
1-5 hours a day	39	29.8%
6-10 hours a day	76	58.0%
11-15 hours a day	15	11.5%
15 hours of more a day	1	0.8%
Total	n = 131	100%

Interpretation: According to the amount of time spent using the gadget, the frequency and percentage distributions of responses are shown in Table 3. On average, 58 percent of children use their gadgets between 6 and 10 hours per day, with 29.8 percent using their gadgets between 1 and 5 hours per day. In addition, 11.5 percent of the children use their gadgets on a daily average of 11-15 hours, with 0.8 percent using their gadgets for 15 hours or more, according to the study.

Table 4: Frequency and Percentage Distribution of Frequency of Gadget Use per Week

Frequency of Use Per Week	Frequency (f)	Percentage (%)
Less than 1x a week	4	3.1%
1-3x a week	10	7.6%
3-5x a week	36	27.5%
5-7x a week	81	61.8%
Total	n = 131	100%

Interpretation: Table 4 shows the frequency and percentage distribution of responses based on the frequency with which the children use their gadgets on a weekly basis. Children use their gadgets 5 – 7 times per week, according to the majority of responses (61.8 percent); with 27.5 percent using their gadgets 3 – 5 times per week, according to the majority of responses. Aside from that, 7.6 percent of those surveyed use their gadgets once to three times per week, with only 3.1 percent using their gadgets less than once per week. As a result of the withdrawal of approximately 1.5 billion children from school since April 2020, many of these students have been increasingly reliant on electronic devices to complete school assignments as part of learning from home, communicating with peers, and playing video games to recall activities from their childhood (Pratiwi et al., 2020).

Table 5: Frequency and Weighted Mean Distribution of Responses Based on the "Bedtime" parameter of CSHQ

Probing Statements for "Bedtime"	Frequency (f)					Weighted Mean	Rank
	5	4	3	2	1		
Child goes to bed at the same time at night.	27	68	33	3	0	3.91	1
Child falls asleep within 20 minutes after going to bed.	15	70	37	8	1	3.69	2
Child falls asleep alone in own bed.	26	49	36	9	11	3.53	4
Child falls asleep in parent's or sibling's bed.	33	44	34	18	2	3.67	3
Child falls asleep with rocking or rhythmic move-ments.	8	18	40	37	28	2.55	9
Child needs special object to fall asleep (doll, special blanket, stuffed animal, etc.).	23	54	28	10	16	3.44	5
Child needs parent in the room to fall asleep.	20	31	39	20	21	3.07	8
Child resists going to bed at bedtime.	12	42	46	14	17	3.14	7
Child is afraid of sleeping in the dark.	9	62	29	15	16	3.25	6
TOTAL	n= 131		Grand Weighted Mean			3.36	

Interpretation: According to the "Bedtime" parameter included in the CSHQ survey questionnaire, the weighted means of the responses are shown in Table 5. The majority of parents believe their children go to bed at the same time every night (WM 3.91), and that they fall asleep within 20 minutes of going to bed (WM 3.69). Also, it was reported that some of parent respondents agree that their child falls asleep in their bed or in the bed of one of their siblings (WM 3.67), although some children do fall asleep alone in their own bed (WM 3.53). Parent respondents also mentioned that their child required special objects to fall asleep (WM 3.44), which may be indicative of anxiety or difficulty calming down.

Some parents reported that their child is afraid of the dark (WM 3.25), and that at times, he or she resists going to bed (WM 3.14) or requires the presence of a parent in the room in order to fall asleep (WM 3.07). Others have reported that rocking or other rhythmic movements helped them fall asleep (WM2.55). Furthermore, it should be noted that children's biopsychosocial development is significantly aided by their ability to sleep soundly on a consistent basis (Moh, 2017). When it comes to a child's development, sleep is critical because it contributes to their ability to reach their full physical, cognitive, and behavioral potential (Loureiro, 2011). International Classification of Sleep Disorders classifies BSPs such as the ones listed above as difficulties falling asleep or remaining asleep, such as bedtime resistance and night-waking; they correlate to the diagnosis of insomnia in accordance with the 2014 International Classification of Sleep Disorders classification (Sateia, 2014). Moh (2017) went on to say that because of the lack of sleep time experienced by children who have difficulty sleeping, the youngster becomes overly hyperactive and behaves inappropriately as the time for bed approaches. When a child is suffering from a sleep deficiency, they may exhibit symptoms such as drowsiness, difficulty getting out of bed in the morning, and irritability throughout the day.

Table 6: Frequency and Weighted Mean Distribution of Responses Based on the "Sleep Behavior" Parameter of CSHQ

Probing Statements for "Sleep Behavior"	Frequency (f)					Weighted Mean	Rank
	5	4	3	2	1		
Child sleeps about the same amount each day.	23	82	24	2	0	3.96	1
Child is restless and moves a lot during sleep.	11	28	56	33	3	3.08	2
Child moves to someone else's bed during the night (parent, sibling, etc.).	10	24	45	32	20	2.79	4
Child grinds teeth during sleep (your dentist may have told you this).	3	19	25	45	39	2.25	6
Child snores loudly.	7	20	47	30	27	2.62	5
Child awakens during the night and is sweating, screaming, and inconsolable.	2	12	41	37	39	2.24	7
Child naps during the day.	6	28	60	23	14	2.92	3
TOTAL	n= 131		Grand Weighted Mean			2.84	

Interpretation: On the basis of the CSHQ parameter "Sleep Behavior," the weighted means of the responses are presented in Table 6. Parent respondents believe that their child sleeps approximately the same amount every day, according to data collected (WM 3.96). Their child is restless and moves a lot during sleep (WM 3.08), and they have also noticed that the child takes naps during the day (WM 2.92). The child has been reported to move to a different bed during the night (WM 2.79), while others have been found to snore loudly (WM 2.62), which would be indicative of either tiredness or other medically-related conditions such as sleep apnea, among other things. Teeth grinding, also known as bruxism, was observed (WM 2.25), and the child awakens in the middle of the night, sweating, screaming, and inconsolable. According to the 2014 International Classification of Sleep Disorders classification, BSPs are classified as difficulties falling asleep or remaining asleep, such as bedtime resistance and night-waking; they are associated with the diagnosis of insomnia (Sateia, 2014).

Table 7: Frequency and Weighted Mean Distribution of Responses Based on the "Waking During the Night" Parameter of CSHQ

Probing Statements for "Waking during the night"	Frequency (f)					Weighted Mean	Rank
	5	4	3	2	1		
Child wakes up once during the night.	7	47	44	25	8	3.15	1
Child wakes up more than once during the night.	4	18	25	59	25	2.37	2
TOTAL	n= 131		Grand Weighted Mean			2.76	

Interpretation: According to the CSHQ parameter "waking during the night," the weighted means of the responses are presented in Table 7. The data presented

shows that the majority of parents have observed their child wake up once during the night (WM 3.15), with a minority of parents reporting that their child wakes up more than once during the night (WM 2.37). Young children can suffer from sleep deprivation and a lack of concentration, which can result in potentially unhealthy sleep cycles because they are sleepier during the day and sleep less at night than their older counterparts when exposed to gadgets for longer periods of time than what was recommended (Pratiwi, et al, 2020).

Table 8: Frequency and Weighted Mean Distribution of Responses Based on the "Morning Wake Up" Parameter of CSHQ

Probing Statements for "Morning wake up"	Frequency (f)					Weighted Mean	Rank
	5	4	3	2	1		
Child wakes up by him/herself.	21	70	39	1	0	3.85	1
Child wakes up very early in the morning (or, earlier than necessary or desired).	14	51	57	9	0	3.53	2
Child seems tired during the daytime.	5	27	60	29	10	2.91	3
Child falls asleep while involved in activities.	7	26	29	47	22	2.61	4
TOTAL	n= 131		Grand Weighted Mean			3.23	

Interpretation: On the basis of the "Morning Wake Up" parameter of CSHQ, the weighted means of responses are presented in Table 8. The majority of parents have reported that their child wakes up on his or her own (WM 3.85), and that he or she wakes up much earlier in the morning than is desired or necessary (WM 3.53). In addition, the respondents stated that the child appears tired during the day (WM 2.91), and that they fall asleep while participating in activities (WM 2.61). It has been noted by both the American Academy of Pediatricians and the Canadian Children's Society that children can suffer from sleep deprivation and lack of concentration, which can result in potentially unhealthy sleep cycles because children are sleepier during the day and less sleepy at night. Furthermore, according to Moh (2017), drowsiness, difficulty waking up in the morning and irritability during the day are all signs that a child is suffering from a sleep deficiency in young children, as well as other symptoms.

Table 9: Summary Statistics of Children's Sleep Habits Questionnaire Responses

Parameters	Grand Weighted Mean	Rank	Interpretation
Bedtime	3.36	1	Neutral
Sleep Behavior	2.84	3	Neutral
Waking During the Night	2.76	4	Neutral
Morning Wake Up	3.23	2	Neutral

Interpretation: The summary statistics for the CSHQ questionnaire parameters are presented in Table 9. Based on the information provided in the preceding table, the majority of parent respondents agreed with the entries made under the "Bedtime" parameter (GWM 3.36), with the child going to bed at the same time every night and falling asleep within 20 minutes of going to bed, but at times falling asleep in their own bed or in the bed of their parents or siblings instead. Morning wake up is the second most important parameter (GWM 3.23), which refers to whether the child wakes up on his or her own or wakes up earlier than necessary in the morning. Another issue that has been identified is that the child appears tired throughout the day and may inadvertently fall asleep during the course of normal activities. Furthermore, respondents to the third-ranked parameter "Sleep behavior" (GWM 2.84) and the fourth-ranked parameter "Waking during the night" (GWM 2.76) reported that their child slept for the same amount of time every day. However, it was also noted that some respondents reported that their child sleeps listlessly, appears tired and naps during the day, and exhibits some signs of sleep disturbance, such as bruxism, requiring "comfort items" to fall asleep. As well, sleep has been proven to be extremely important in the development of a child's overall well-being, according to numerous studies. Because of the use of technology, some people have reported sleeping disturbances, which may have resulted from inadvertently causing them to lose sleep. While the vast majority of respondents stated that their child's sleep quality was not affected by gadget use, a small number of respondents reported sleep disturbances that should be investigated further.

Table 10: ANOVA Test Results and Relationships Between the CSHQ Parameters and the Average Length of Sleep, Length of Gadget Use and Frequency of Gadget Use per Week

Parameters	F-Value	P-Value	Remarks
Ave. Length of Sleep	0.067196	0.976295	Fail to reject H_o
Ave. Length of Gadget Use	5.556949	0.012615	Reject H_o
Freq. of Gadget Use	17.34608	0.000116	Reject H_o

Legend: If computed P-value is <0.05, reject H_0; if computed P-value is >0.05, fail to reject H_0

Interpretation: To determine whether there are any significant relationships between CSHQ parameters and the child's average length of sleep, average length of gadget use, and frequency of gadget use, the ANOVA computation was performed on the data presented in Table 10. Using the data by Average Length of Sleep (F = 0.067196, p = 0.976295), it was impossible to reject the null, confirming that there is no significant relationship between the child's average length of sleep and his or her CSHQ responses. In contrast, when the data were analyzed for the Average Length of Gadget Use (F = 5.556949, p = 0.012615), and the Frequency of Gadget Use (F = 17.34608, p = 0.000116), the computed p values were less than 0.05, prompting the researcher to reject the Ho, indicating that there is a statistically significant relationship between the average length of gadget use, and the frequency of gadget use, to the quality of the child's sleep. These findings were corroborated by a systematic review of the literature conducted by Hale and colleagues (2015), who discovered that screen usage is associated with negative sleep outcomes (primarily shorter sleep duration and delayed timing) in 90 percent of the research they reviewed. When Rashid and colleagues (2021) conducted their research, they discovered that, among the technology examined, cell phones were the most frequently reported to be used on a daily basis by those who took part in the study (67.11 percent). Possibly as a result of the current COVID-19 epidemic, 24.48 percent of those who responded to the survey of the above-mentioned study said they used electronic devices to participate in online classes. According to the survey participants of Rashid et al.'s study, they would use electronic devices significantly more in 2020 than they will in 2019. Children showed a lower proclivity to participate in outdoor activities than adults in the study. More than half of those who took part in that particular study spent less than one hour per day participating in outdoor activities, according to the findings. When they conducted their research, they discovered a link between the use of electronic devices and health problems such as headaches, backaches, visual disturbances, and sleeping disorders (among others).

SUMMARY

This study aimed to determine the effects of gadget use on the quality of sleep among grades 4-6 elementary school students undergoing online education in a private school in Lucena City, Quezon Province. The study tried to determine whether there is a relationship between the parameters of the abbreviated CSHQ and the average length of sleep, average length of gadget use, and frequency of gadget use. The researcher used a descriptive research design, specifically the survey method to gather data. The population of grades 4-6 students in the private school located in Lucena city is 198, and upon computation of the sample size, an n=131 was figured. Simple random sampling was used wherein after getting the roster of students in grades 4-6, they were assigned numbers from which lots were drawn to determine who the participants will be. After the sampling was done and the final roster of respondents was randomly selected, the link to the Google forms was subsequently sent to the selected participants. After the sample size target was reached, the data were tallied and analyzed, and frequencies and percentages were computed, along with the weighted means for the responses. Relationships between the variables were determined through computation of ANOVA.

DISCUSSION

Parents agreed with the "Bedtime" entries, with the child going to bed at the same time every night and falling asleep within 20 minutes, but sometimes in their own or their parents' or siblings' beds instead. The second most critical metric, “morning wake up”, relates to whether the youngster wakes up on his or her own or gets up sooner than necessary. The child also appears

fatigued throughout the day and may unknowingly fall asleep during normal activities. The third-ranked parameter "Sleep behavior" and the fourth-ranked parameter "Waking during the night" both reported that the child slept for the same amount of time every day, but that some respondents reported that their child sleeps listlessly, appears tired, naps during the day, and has signs of sleep disturbance such as bruxism and requiring "comfort items" to fall asleep. Numerous studies have also shown the importance of sleep in a child's overall development. Some people have reported sleep difficulties due to technology use, maybe due to unwittingly losing sleep. While most respondents said their child's sleep quality was not harmed by gadget use, a few indicated sleep difficulties that warranted additional investigation.

The null hypothesis for Average Length of Sleep data results could not be rejected, demonstrating there is no significant link between average length of sleep and CSHQ replies. Consequently, the researcher rejected the null hypothesis for Average Length of Gadget Use and Frequency of Gadget Use because the computed p-values were less than 0.05. According to the perceptions of the parent respondents, while there were some evidences that point to the relationship of length and frequency of gadget use, it was not enough to establish a direct relationship with the results of the CSHQ. Moreover, the data sets denoted that the average length of sleep of children have contributed more to the BSPs that the parents were able to identify in the CSHQ. The study of Hale and colleagues (2015) stated screen use is associated with unfavorable sleep outcomes (mainly lower sleep duration and delayed timing) in 90% of the research they reviewed. As well, Rashid and colleagues (2021) discovered that of all technologies tested, cell phones were the most commonly reported to be used daily by participants (67.11 percent). Perhaps due to the current COVID-19 outbreak, 24.48 percent of individuals surveyed claimed they used electronic devices to participate in online classes. While the studies have supported that increased length of screen and gadget time in children can affect, data gathered from the respondents have not proven that. The survey also found that kids were less likely to go outside compared to adults. According to the data, more than half of the study's participants spent less than an hour every day outside. They observed a correlation between electronic device use and health issues such headaches, backaches, vision impairments, and sleep disorders (among others).

At the outset, the data gathered were able to yield significant results. While most of the weighted means were verbally interpreted as “neutral”, the parents were able to identify key problems that they were able to observe during their child’s sleep time. Relationships were also established between the parameters of the CSHQ and the average length of gadget use, as well as the frequency of gadget use. This was corroborated by various studies stated in the literature review, that prolonged exposure or use of gadgets can adversely affect the different areas of the child’s growth, along with the child’s quality of sleep. Due to the small sample size, generalizability of the data should be taken with a grain of salt; however, the study can serve as the baseline through which a wide-based study can take off, with further analysis of relationships between other factors that were excluded from this study, as stated in the scope and limitations.

CONCLUSIONS

The following conclusions were drawn after data computations and interpretations:

1. Out of a sample size of 131, 35.9 percent were from grade 6, with 53.4 percent being males, and majority were 11 years of age at 29.8 percent.

2. On the average, 57.3 percent of the respondents sleep for 6 to 8 hours daily. They also use gadgets on an average of 6 to 10 hours daily at 58 percent, on a 5 to 7 times a week basis at 61.8 percent.

3. Collectively, most of the responses of the parent respondents were verbally interpreted as “neutral” based on the interpretation matrix. However, the computed grand weighted means yielded that the parent respondents mostly agreed to the positive aspects of the “Bedtime” parameters (GWM 3.36), followed by “Morning wake up” parameter (GWM 3.23), “Sleep behaviors” parameter (GWM 2.84), and finally, “Waking during the night” parameter (GWM 2.76). While most of the parents respondents agreed to the positive statements of the CSHQ

questionnaire, they were able to identify key problems, such as: (1) failing to fall asleep in their own bed or falling asleep in the parents' or siblings' bed; (2) needing a special object to lull them to sleep; (3) being afraid of sleeping in the dark and resisting going to bed; (4) rocking self to sleep, restlessness, snoring, and bruxism; (5) waking up more than once during the night; (6) waking up earlier than was necessary; and (7) seemingly tired during the daytime, and falling asleep during activity performance.

4. ANOVA results yielded statistically significant relationships were established between the average length of gadget use ($p = 0.012615$), and frequency of gadget use ($p = 0.000116$) with the parameters of the CSHQ, wherein the researcher rejected the null hypothesis on the premise that the computed p-value is less than 0.05. However, the study failed to establish a relationship between the average length of sleep and the parameters of the CSHQ ($p = 0.976295$).

RECOMMENDATIONS

1. Establish a more generalizable data set by getting more samples within a set population of students that use gadgets for online learning or other social media and entertainment activities.

2. Create an opportunity to include the respondents' demographic profiles in data analysis of relationships with the parameters of the CSHQ.

3. Facilitate baseline scores using the abbreviated CSHQ and compare it with the original CSHQ manuscript to determine possible problem areas in the child's quality of sleep.

4. While the educational situation in our country today necessitates gadget use, parents should be made aware of the possible adverse effects of prolonged use of gadgets in their child's health and well-being. Limiting the gadget exposure of the children post-online classes should be recommended in order to prevent these adverse effects from taking place.

5. Medical, educational, and other government professionals and officials should take into consideration educating the masses regarding the effects of gadget use in the quality of sleep of the children, as well as its effects in the other aspects of the child's health.

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A Rare Case of Mixed Adult Hepatoblastoma Mimicking as Hepatocellular Carcinoma*

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Abstract

Hepatoblastoma (HB) is a rare pediatric malignant tumor of the liver. Most of these tumors arise in the embryo and this is usually discernible in the first 3 years of life; thus, its occurrence in the adult population seems to be unusual. We present this case due to its rarity and its potential to mimic other primary liver tumors in adults such as HCC. To the best of our knowledge with literature review, there are only 40 cases of adult HB reported worldwide.

In this paper, we report a case of a 49-year-old female, diagnosed with Chronic Hepatitis B, admitted due to abdominal pain. Physical examination revealed hepatomegaly. Liver function test was unremarkable. AFP was elevated at >50,000ng/ml. Triphasic CT scan revealed a hypodense mass in the right lobe of the liver measuring approximately 11 x 11 x 13cm suggestive of HCC. Subsequently, patient underwent right hepatectomy. Pathological examination, however, demonstrated that the tumor showed a malignant neoplasm with epithelial and mesenchymal components consistent with adult HB, mixed type. Since treatment of adult HB is not yet established, studies have suggested that it is logical to follow the treatment protocol for childhood HB. Hence, this patient underwent chemotherapy with Cisplatin, Vincristine and 5-Fluorouracil.

The low incidence of HB in adults presents a diagnostic challenge, requiring a high index of suspicion and a thorough evaluation. Since prognosis could be improved with early detection and treatment, it is important for clinicians not to overlook HB.

Keywords: hepatoblastoma, HCC, liver tumor, hepatomegaly

INTRODUCTION

Hepatoblastoma (HB) is a primary malignant hepatic tumor in children. This accounts for approximately 1% of all pediatric malignancies. Most of these tumors arise in the embryo and is usually discernible in the first three years of life [1].

Conversely, the occurrence of hepatoblastoma in adults seems to be extremely unusual, thus it is considered as a rare cause of primary malignant liver tumor in adults. Due to this, patient may be diagnosed at late stages of the disease leading to poor prognosis in this group with a mean survival time of two months and one-year survival of 24 %. Most of the cases are asymptomatic and may be diagnosed at late stages of the disease. With regards to treatment, no therapeutic strategies have yet been established because of the rarity of the disease. [2].

In this paper, we report a case of a 49 year-old female with chronic hepatitis B, initially diagnosed with hepatocellular carcinoma but was found to have mixed adult hepatoblastoma on histopathology.

OBJECTIVES

General Objective:

To report a rare case of mixed adult hepatoblastoma mimicking as hepatocellular carcinoma in the setting of liver cirrhosis in a 49-year-old, Chinese female.

Specific Objective:

- To briefly discuss the epidemiology, incidence of Adult Hepatoblastoma based on published literature

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- To discuss the diagnostic modalities and work up of Adult Hepatoblastoma

- To review the therapeutic strategies of the management of Adult Hepatoblastoma

THE CASE

A 49 -year old Chinese female was referred to our institution due to a 10 day history of right upper quadrant pain associated with anorexia and weight loss. The patient is known to have liver cirrhosis due to chronic hepatitis B infection without previous episodes of liver decompensation. She is maintained on Tenofovir 300mg tablet once a day. She denied use of alcohol, drugs and contraceptive pills. There was no family history of liver disease, cancer, or autoimmune diseases.

Physical examination was notable for significant hepatomegaly-12 cm below the right midclavicular line with direct tenderness over the involved area. No jaundice, edema and ascites were noted.

Laboratory data showed the following values: alpha-fetoprotein >50,000ng/ml, alanine aminotransferase (ALT) 25IU/L, total bilirubin 0.8mg/dl, alkaline phosphatase 136mg/dl and INR 1.35. Complete blood count was unremarkable. Test for HBV viral load showed 122, 984 IU/ml. Chest Xray was unremarkable. Triphasic CT scan (Figure A) revealed enlarged liver and a hypodense mass was with a small punctate calcification in the right lobe of the liver extending from segments 6, 7 and 8 with characteristic arterial hyperenhancement and subsequent hypoenhancement in the portal venous and delayed phases ("washout") suggestive of hepatocellular carcinoma. This measures approximately 11x11x13cm. Margins were well circumscribed with a pseudocapsule. Splenomegaly was also noted on CT scan.

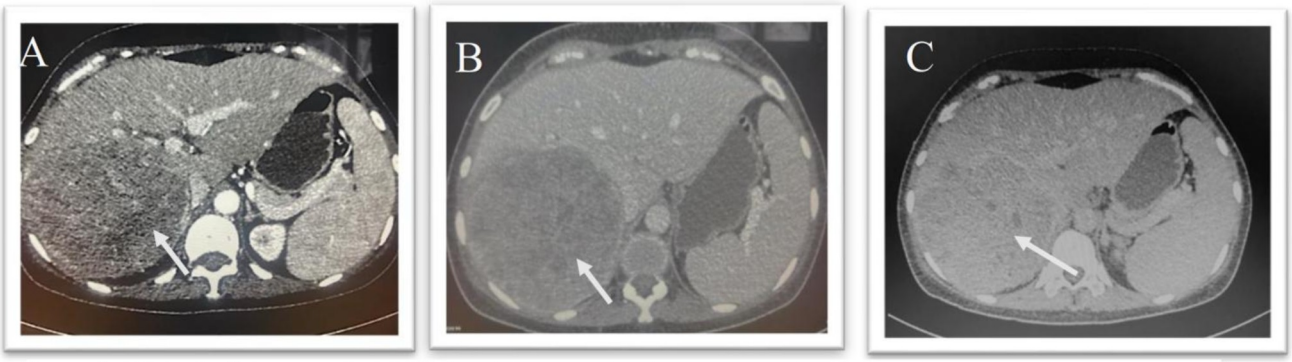

Figure 1. Triphasic CT scan: arterial (A) Arterial phase showing encapsulated mass with heterogenous enhancement. (B) Washout appearance in the portal venous phase (C) Delayed phase showing an isodense area of the mass

Subsequently, patient underwent right hepatectomy. At surgical exploration, a large mass measuring 12 x 13cm was occupying the right lobe of the liver (Figure 2A). On serial sectioning, a largely necrotic, white tan mass with well-defined borders was noted (Figure 2B).

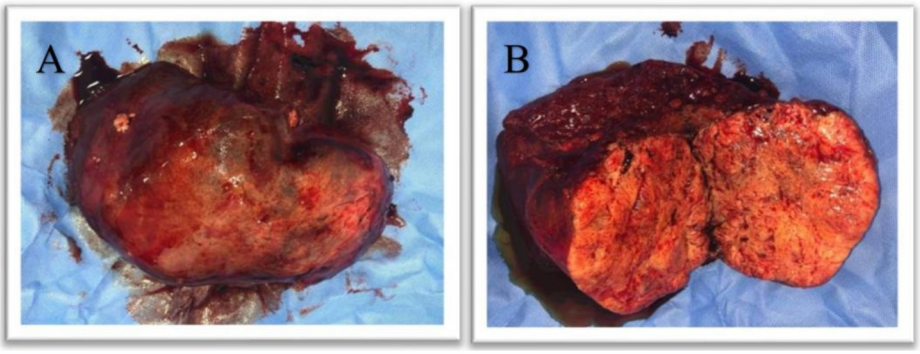

Figure 2. A. Right lobe of the liver showing a well-defined tumor mass. B. Necrotic mass on serial sectioning

Pathological examination, however, demonstrated that the tumor showed a malignant neoplasm with epithelial and mesenchymal components. The epithelial component exhibited embryonal cells arranged in solid sheets with prominent glandular morphology and pseudorosettes. The mesenchymal component displayed an enlarged, elongated bizarre nuclei with prominent nucleoli. This was consistent with adult hepatoblastoma, mixed type. Hepatoblastoma was also confirmed by histologic examination with immunohistochemistry stains using glypican and cytokeratin 19 as shown in the images below.

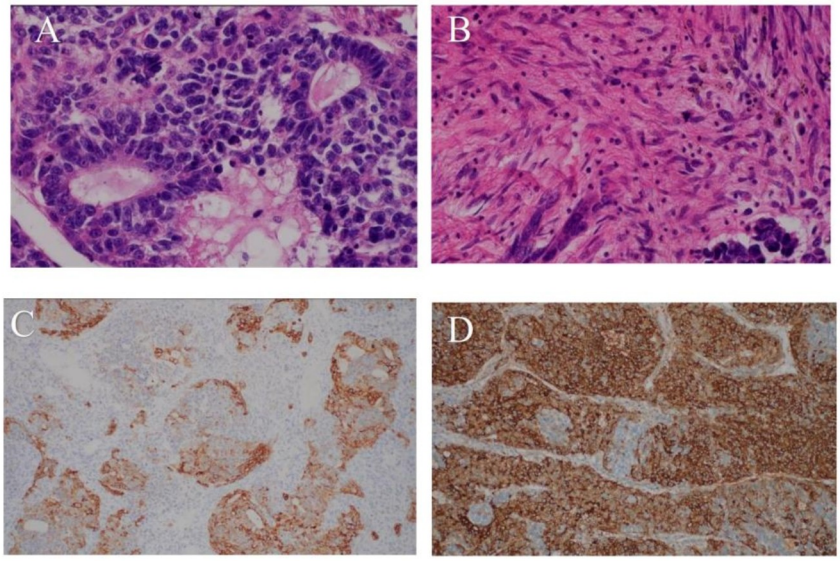

Figure 3 . A. HPO, B. HPO C. CK19 D. Glypican Stain. Microscopic examination shows a malignant neoplasm mainly composed of embryonal cells arranged in solid sheets, nests, with prominent glandular/acinar morphology and pseudorosettes. These are interspersed with areas of necrosis, cyst formation, and mesenchymal elements with variable pleomorphism.

Postoperatively, the patient's hospital course was uneventful, and the patient was discharged 5 days after surgery. Since treatment of adult HB is not yet established, studies have suggested that it is logical to follow the treatment protocol for childhood hepatoblastoma. Hence, this patient had combination chemotherapy with Cisplatin, Vincristine and 5-Fluorouracil. A good response to the treatment was observed with a repeat AFP of 869 ng/ml and a repeat CT scan imaging showed no tumor recurrence.

DISCUSSION

Hepatoblastoma (HB) is the most common primary malignant liver tumor in children.

This accounts for 0.2-5.8% of total malignancies of the liver and for 25%-45% of primary hepatic tumors in children [3]. Their annual incidence is only 0.5-1.5 per 1,000,000 people [4]. Most of the cases occur in patients under 5 years of age.

In this case, we report a Chinese female diagnosed with mixed adult hepatoblastoma. The exact incidence of adult HB in the literature is unknown; however, according to the study of Wang and Liu, only 40 cases of HB has been reported worldwide, one of which was from China. [5]. Hence, the occurrence of HB in adults is extremely rare and the prognosis is poor because they are usually diagnosed late.

A variety of synonyms have been used to describe HB such as hepatic embryonic mixed tumor, mixed tumor of the liver, adult hepatoblastoma, and mixed adult hepatoblastoma. The latter is the most commonly accepted term today [5].

HB originate from the primitive hepatic stem cells that give rise to epithelial cells of the liver. It has two anatomical variants: the epithelial

type and the mixed epithelial and mesenchymal type. The mixed type contains foci of mesenchymal differentiation consisting of primitive mesenchyme, osteoid, cartilage, and striated muscle [6].

The pathologic mechanism of HB has been elusive. It may occur sporadically or in association with hereditary syndromes such as familial adenomatous polyposis (FAP) and Beckwith- Wiedemann syndrome. It should also be mentioned that in 25% of cases, HB is associated with liver disease such as liver cirrhosis, hepatitis B and hepatitis C [7]. Due to the presence of hepatitis B in our case, we initially thought that the tumor was HCC but it turned out to be an adult hepatoblastoma.

The initial diagnosis of HB is mainly based on imaging such as ultrasound (US), computed tomography (CT) or magnetic resonance imaging (MRI). These imaging modalities are used to define the extent of tumor involvement and aid in pre-surgical planning [9]. However, the final diagnosis of adult hepatoblastoma relies on histopathology. Our patient's biopsy report confirmed the diagnosis.

Surgical resection is the cornerstone treatment of hepatoblastoma . Approximately 60% of tumors are unresectable at presentation [10]. If the tumor is unresectable and resistant to chemotherapy, a liver transplant should be offered because this has a good long-term survival rate [10]. Since, there is no standardized chemotherapy for adult hepatoblastoma, studies have suggested to follow the pediatric treatment protocol. The cisplatin/5-fluorouracil (5-FU)/vincristine (VCR) combination is regarded as the accepted chemotherapeutic treatment in hepatoblastoma. In addition, a-fetoprotein (AFP) levels are used as a guide to determine response to therapy [11].

The prognosis of adult hepatoblastoma is generally poor especially if surgery is not possible or tumor recurs after surgery. In adults, the reported cases survived for only 2 weeks to 38months (mean survival duration, 6 months) [12].

CONCLUSION

The low incidence of HB in adults presents a diagnostic challenge, requiring a high index of suspicion and a thorough evaluation. Since prognosis could be improved with early detection and treatment, it is important for clinicians not to overlook HB.

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Neck Circumference – Height Ratio Cut-Off as a Predictor of Obstructive Sleep Apnea Severity among Adult Patients Diagnosed with Obstructive Sleep Apnea at the Lung Center of the Philippines

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Abstract

INTRODUCTION: Obstructive sleep apnea (OSA) is the most common breathing-related sleep disorder. OSA is mainly characterized by a set of symptoms resulting from apnea events that have negative outcomes on health, such as excessive daytime sleepiness, cardiovascular impairment, and increased morbidity and mortality. It is important to develop simple, reliable, cost-effective methods to predict obstructive sleep apnea. Neck circumference - height ratio has limited studies in its relation to obstructive sleep apnea compared to neck circumference.

METHOD: This is a retrospective cross-sectional study using chart review of all patients who had been diagnosed with obstructive sleep apnea by polysomnogram at the Lung Center of the Philippines from January 2019 to December 2019. Demographic characteristics like age, gender, weight, height, neck circumference, BMI, neck circumference – height ratio [NHR], and apnea-hypopnea index were determined. Accuracy of the neck circumference – height ratio cut-off had been determined in predicting obstructive sleep apnea and its severity by comparing neck – circumference – height ratio cut-off with a polysomnogram.

RESULTS: Among the 384 charts collected and reviewed, this study had a total of 194 participants were included. Most participants were male (72.68%) and the age range was between 35 to 60 years old. There were 12 (6%) participants in the Mild OSA group, 19 (10%) in the Moderate OSA group, and 163 (84%) were categorized as Severe. Median Neck Circumference – Height Ratio was 0.23 to 0.26. A cutoff of > 0.23 NHR was used to predict Mild OSA showed PPV of 46.15% (24.47 to 65.98), NPV was 66.67% (50.78 to 79.49), AUC of 0.5307 (0.30 to 0.76), and accuracy of 58.06% (39.08 to 75.45). A cutoff of > 0.23 NHR was used to predict Moderate OSA showed positive predictive value (PPV) was 15.94% (10.91 to 22.7), NPV of 93.6% (89.52 to 96.16), AUC of 0.6421 (0.52 to 0.77), and accuracy of 65.98% (58.85 to 72.61). A cutoff of > 0.23 NHR was used to predict Severe OSA showed PPV of 15.94% (10.91 to 22.7), NPV of 93.6% (89.52 to 96.16), AUC of 0.6421 (0.52 to 0.77), and accuracy of 65.98% (58.85 to 72.61).

CONCLUSION: The NHR cut-off demonstrated a moderate positive correlation with OSA, and NHR increases as the apnea-hypopnea index are increased. NHR cut-off of 0.23 is sufficient to predict severe OSA but has poor diagnostic accuracy for mild and moderate OSA. Moreover, the NHR cut-off may also be an integral tool to predict severe OSA.

Keywords: *Neck Circumference-height ratio, obstructive sleep apnea*

INTRODUCTION

BACKGROUND

Obstructive sleep apnea (OSA) is the most common breathing-related sleep disorder.The disease causes changes in respiratory patterns leading to intermittent hypoxia, hypercapnia, and increased frequency of awakenings. OSA is mainly characterized by a set of symptoms resulting from apnea events that

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have negative outcomes on health, such as excessive daytime sleepiness, cardiovascular impairment, and increased morbidity and mortality. Obesity, gender, genetic, and hormonal factors mediate risk for OSA and interact in a multifaceted manner in the pathogenesis of this disease. Obesity is the most established and primary risk factor for OSA [1]. There is a linear correlation between obesity and OSA [2]. Not only in adults, but also the pediatric obesity has caused serious concern all over the world as the prevalence has increased alarmingly over time in developed and developing countries [3]. The prevalence of OSA in the general population is 3 to 7 % for men and 2 to 5 % for women [2]. Mallampati score, age, and neck circumference (NC) are important factors in predicting moderate OSA. Meanwhile, Mallampati score, body mass index (BMI), age, abdominal circumference (AC), and gender are more predictive for severe OSA [4]. In obese people, fat deposits in the upper respiratory tract narrow the airway; there is a decrease in muscle activity in this region, leading to hypoxic and apneic episodes, ultimately resulting in sleep apnea. Those with the greatest weight gain had a more severe apnea-hypopnea index (AHI) [Error! Bookmark not defined.]. In addition, OSA and Obesity share common mechanisms such as inflammatory activation, oxidative stress, and increased sympathetic activity [5].

It is important to develop simple, reliable, cost-effective methods to predict obstructive sleep apnea. One option is to use anthropometric variables relating to obesity. Anthropometric measures are essential tools used for health evaluation, especially in relation to obesity. The BMI, waist-to-height ratio, neck and waist circumference arethe most widely used. Neck circumference (NC) is a variable tool often considered in sleep medicine due to its capability to predict sleep events [1].

Another way to approach the distribution of fat in the human body is to analyze its relative distribution. If one imagines the neck as more or less a cylinder, then the “thickness” or circumference of the neck will be mathematically proportional to its length for any given neck mass. Further, since neck length is difficult to accurately and reproducibly measure, under an assumption of proportionality of the normal human body, neck length should be proportional to overall height, even under circumstances of obesity. Neck circumference -height ratio (NHR) can be a useful additional aid to predict obstructive sleep apnea [6].

Neck circumference - height ratio has limited studies in its relation to obstructive sleep apnea compared to neck circumference. However, developing evidence suggests that the neck-to-height ratio (NHR) is an innovative index for the evaluation of upper body adipose distribution in patients with a sleep-related breathing disorder [6**Error! Bookmark not defined.**].

Locally, no studies have been published yet looking into the correlation between the NHR cut-off and OSA severity and the predictive value of NHR cut-off in determining the OSA severity. This study aims to contribute to the limited existing body of knowledge in setting cut-off points for the neck circumference – height ratio in the presumptive diagnosis of obstructive sleep apnea and its severity. Once the cut-off values have been determined to be of significant diagnostic accuracy and good predictive value, future studies are recommended on comparing our cut-offs derived from this study with other anthropometric measurements like neck circumference and waist-to-hip ratio in determining obstructive sleep apnea severity.

GENERAL OBJECTIVES

To determine the predictive value of the neck circumference-height ratio cut-off in determining the obstructive sleep apnea severity among adult patients diagnosed with obstructive sleep apnea at the Lung Center of the Philippines from January 2019 to December 2019

SPECIFIC OBJECTIVES

1. To determine demographic profile., anthropometric measurements and neck circumference – height ratio (NHR) cut-off among the different severity of obstructive sleep apnea (Mild OSA, Moderate OSA, and Severe OSA) according to:
    a. Age
    b. Gender
    c. Weight

d. Height
e. Body mass index
f. Neck circumference
g. Apnea – hypopnea index

2. To determine the correlation of neck circumference – height ratio (NHR) cut-off among the different severities of obstructive sleep apnea (Mild OSA, Moderate OSA, and Severe OSA)

3. To evaluate the diagnostic accuracy of the neck circumference – height ratio (NHR) cut-off in predicting the different severities of obstructive sleep apnea (Mild OSA, Moderate OSA, and Severe OSA)
    a. Sensitivity
    b. Specificity
    c. Negative predictive value
    d. Positive predictive value
    e. Negative Likelihood ratio
    f. Positive Likelihood ratio
    g. Area under the Receiver operating characteristics curve

METHODOLOGY

This was a retrospective cross-sectional study conducted at the Lung Center of the Philippines, a tertiary, specialty medical center. This study involved a chart review of all patients who had been diagnosed with obstructive sleep apnea by polysomnogram at the Lung Center of the Philippines from January 2019 to December 2019.

Patients included in the study have the following inclusion criteria: age 18 years old and above, diagnosed with obstructive sleep apnea (AHI of equal or more than 5 events/hour) via type 1 or in-hospital polysomnogram at Lung Center of the Philippines, and full night diagnostic or split night polysomnogram had been performed on the patient.

Patients excluded in the study have the following exclusion criteria: patients with genetic syndromes (Down syndrome, Prader-Willi syndrome), patients with tracheostomy, patients with enlarged thyroid gland (hyper or hypothyroidism), patients with incomplete data in the chart, patients with normal polysomnogram results (AHI of less than 5 events/hour), and full night therapeutic polysomnogram had been performed on the patient.

ETHICAL CONSIDERATION

We conducted this study in compliance with the ethical principle set in the Declaration of Helsinki and RA10173 or Data Privacy Act of 2012. A review of the clinical protocol was completed by the Research Review Committee of the Department of Pulmonary Medicine, and Institutional Ethics Review Board, Lung Center of the Philippines. Informed consent was waived due to the retrospective nature of the study.

Anthropometric indices measurement:

As per protocol of the sleep laboratory in the Lung Center of the Philippines; age and gender are routinely taken. Height (cm) is measured with the use of the stadiometer component of the DETECTO measuring scale by letting the participant stand upright on the stadiometer without shoes, facing forwards as tall andstraight as possible with their arms hanging loosely at their sides, their feet should be flat on the base plate of the stadiometer and positioned slightly apart, and knees should be straight. The sleep personnel standing at the side should then bring the head plate of the stadiometer down onto the head, ensuring it rests on the crown of the head ,and read the level with counter/pointer and measurement read to the nearest 1mm. Weight (kg) is taken using the balance beam scale component of the DETECTO measuring scale, with street clothes without extra outerwear by letting the patient stand straight upright at the base plate of the measuring scale, face facing forward, and remain still as possible. The sleep personnel will adjust the sliding weights to determine the weight of the patient. Both the height and the weight were taken by using the DETECTO measuring scale located near the sleep laboratory (Ward 3A of the Lung Center of the Philippines). Neck circumference (cm) was measured by placing the measuring tape at the point just above the cricoid cartilage to the nearest 0.5 cm, while the patient is

sitting upright on a chair facing forward. BMI was calculated as weight in kilograms divided by the square of height in meters (kg/m^2). All measurements were taken at the sleep laboratory by the sleep technologists or sleep fellows in training. The neck circumference-height ratio will be calculated as neck circumference in centimeters divided by height in centimeters.

Obstructive sleep apnea diagnosis and severity classification in adults:

The diagnosis of sleep apnea should be confirmed objectively by sleep testing. The "gold standard" test is Polysomnogram. Scoring of the sleep study was performed according to the American Academy of Sleep Medicine (AASM) 2018 (version 2.5) guidelines, which was current for that time period. The AHI and other variables were derived from polysomnography (PSG) report and archived for later potential retrieval within the sleep laboratory at the Lung Center of the Philippines database. The diagnosis of OSA is confirmed if the number of obstructive events on PSG is greater than 15 events/hour with the absence of sleep-related symptoms (sleepiness, non-restorative sleep, fatigue, or insomnia, wakes up with breath-holding, gasping, or choking, habitual loud snoring, breathing interruptions, or both during the patient's sleep) or greater than 5 events/hour with sleep-related symptoms. OSA severity is classified as **mild** for AHI 5-14/hour, **moderate** for AHI 15-30/hour, and **severe** for AHI > 30/hour.

Data Collection

Data had been collected by chart review from all the patients at the Lung Center of the Philippines with obstructive sleep apnea by type 1 polysomnogram from January to December 2019. After the collection of the charts, they were segregated whether they can be included or not. Demographic characteristics like age, gender, weight, height, neck circumference, BMI, neck circumference – height ratio, and apnea-hypopnea index were determined. Accuracy of the neck circumference – height ratio cut-off had been determined in predicting obstructive sleep apnea and its severity by comparing neck – circumference – height ratio cut-off with a polysomnogram.

STATISTICAL ANALYSIS

Descriptive statistics wereused to summarize the demographic and clinical characteristics of the patients. Frequency and proportion were used for categorical variables and median and interquartile range for non-normally distributed continuous variables. Kruskal-Wallis test and Fisher's exact test wereused to determine the difference of rank and frequency, respectively, within different Obstructive Sleep Apnea severity. The area under the receiver operating characteristics curve, as well as its diagnostic parameters, wereused to determine the diagnostic accuracy of the Neck Circumference – Height ratio in predicting different levels of Obstructive Sleep Apnea severity. Pearson product-moment correlation was used to determine the linear correlation between Neck Circumference – Height ratio and Apnea-Hypopnea Index. Shapiro-Wilk was used to test the normality of the continuous variables. Null hypotheses were rejected at 0.05α-level of significance. STATA 13.1 was used for data analysis.

RESULTS AND DISCUSSION

DEMOGRAPHICS

Table 1. Demographic profile, anthropometric measurements, and neck circumference - height ratio (NHR) of obstructive sleep apnea patients (n=194)

	Frequency (%); Median (IQR)
Age	46 (35 to 60)
Gender	
Male	141 (72.68)
Female	53 (27.32)
Weight	83.55 (71.5 to 97.5)
Height	165 (156.5 to 170)
BMI	30.84 (26.81 to 36)
Neck Circumference	40 (37 to 43)
Neck Circumference – Height ratio	0.25 (0.23 to 0.26)
Apnea-Hypopnea Index	75.2 (43.9 to 98.6)

Among the 384 charts collected and reviewed, this study had a total of 194 participants who met the inclusion criteria. One hundred ninety charts were excluded due to incomplete data, normal results, and a full therapeutic sleep study was performed on the patient. The demographic profile of the participants included Age, Gender, Weight, Height, BMI, Neck Circumference, Neck Circumference-Height Ratio, and the Apnea-Hypopnea Index (Table 1). Most participants were male (72.68%) and females comprised the remainder (27.32%) of the study population. Frequency (%) and median (IQR) values were calculated for each domain. The age range was between 35 to 60 years old. The median weight was 71.5 to 97.5 kg. The median height was 156.5 to 170 cm. Median BMI was categorized as Overweight up to Obese Class II (26.81 to 36 kg/m^2). Median Neck Circumference was 37 to 43 cm. Median Neck Circumference – Height Ratio was 0.23 to 0.26. Median Apnea-Hypopnea Index was 43.9 to 98.6.

Table 2. Demographic profile, anthropometric measurements, and neck circumference – height ratio (NHR) among the different severity of obstructive sleep apnea

	Obstructive Sleep Apnea			P-value
	Mild (n=12, 6%)	Moderate (n=19, 10%)	Severe (n=163, 84%)	
	Frequency (%); Median (IQR)			
Age	34 (24.5 to 46.5)	56 (45 to 69)	45 (36 to 69)	0.009
Gender				0.020
Male	5 (41.67)	12 (63.16)	124 (76.07)	
Female	7 (58.33)	7 (36.84)	39 (23.93)	
Weight	66.2 (59 to 75.4)	69.6 (64.5 to 81)	87.4 (75 to 101.3)	<0.001
Height	156 (152 to 165)	164 (156 to 168)	165 (160 to 170)	0.060
BMI	26.3 (23.7 to 30)	26.5 (23.7 to 33.1)	31.4 (27.8 to 37)	<0.001
Neck Circumference	36.5 (34 to 39.8)	37 (36 to 39)	41 (37 to 43.7)	<0.001
Neck Circumference – Height ratio	0.23 (0.2 to 0.26)	0.23 (0.22 to 0.25)	0.25 (0.23 to 0.26)	0.021
Apnea-Hypopnea Index	9.3 (7.55 to 10.4)	20.7 (18.3 to 28)	81.7 (63.2 to 104)	<0.001

The severity of OSA according to three categories (Mild, Moderate, Severe) were correlated with the demographic profile (Table 2). There were 12 (6%) participants in the Mild OSA group, 19 (10%) in the Moderate OSA group, and 163 (84%) were categorized as Severe. Frequency (%) and Median (IQR) were calculated per domain.

In the Mild OSA group, the median age range was 24.5 to 46.5 years old. Most were female (58.33%) and the rest were male (41.67%). Median weight was 59 to 75.4 kg and median height was 152 to 165 cm. Median BMI was 23.7 to 30 kg/m^2. Median Neck Circumference was 34 to 39.8 cm, and the median Neck Circumference-Height Ratio was 0.2 to 0.26. The median Apnea-Hypopnea Index was 7.55 to 10.4.

In the moderate OSA group, the median age range was 45 to 69 years old. Most were male (63.16%) and the rest were female (36.84%). Median weight was 64.5 to 81 kg and median height was 156 to 168 cm. Median BMI was 23.7 to 33.1 kg/m^2. Median Neck Circumference was 36 to 39 cm, and the median Neck Circumference-Height Ratio was 0.22 to 0.25. The median Apnea-Hypopnea Index was 18.3 to 28.

In the severe OSA group, the median age range was 36 to 69 years old. Most were male (76.07%) and the rest were female (23.93%). Median weight was 75 to 101.3 kg and median height was 160 to 170 cm. Median BMI was 27.8 to 37 kg/m^2. Median Neck Circumference was 37 to 43.7 cm, and the median Neck Circumference-Height Ratio was 0.23 to 0.26. The median Apnea-Hypopnea Index was 63.2 to 104.

A p-value less than 0.05 denoted statistical significance. OSA category (Mild, Moderate, Severe) was statistically significant for the following variables: age (p=0.009); gender (p=0.020); Neck Circumference-Height Ratio (p=0.021); weight, BMI, Neck Circumference, and the Apnea-Hypopnea Index were all p<0.001. Most of the associations were statistically significant except for height (p=0.060).

Anthropometric indices of obesity (e.g., BMI, waist circumference, and neck circumference) are associated with poor long-term cardiovascular outcomes [2-4]. Previous research has found a link between neck circumference and central body adiposity [2-5]. Thus, an association between upper body fat and cardiovascular risk heightens interest in neck fat. The neck is a well-defined cylindrical compartment that may be assessed and measured by relatively simple means. Due to its ability to predict sleep apnea events, neck circumference is a variable frequently considered in sleep medicine [7]. Fat accumulation in the cervical region has been shown to significantly reduce upper airway diameter. In addition, the neck circumference demonstrated a moderate correlation with cardiovascular risk factors compared with BMI and visceral adipose tissue [1]. Additionally, the large neck circumference is associated with insulin resistance and dyslipidemia, thus clarifying the connection between this metric and cardiovascular outcome [8]. In a clinical study performed by Polesel et al. (2019) involving 1,042 participants who underwent complete full-night PSG, screening methods such as anthropometric measures and effectiveness were utilized to diagnose OSA in both treatment groups [1]. Determining the waist circumference and waist-to-hip ratio (WHR) in the women's treatment arm was an ideal assessment to measure sleep-disordered breathing (SDB). Nonetheless, waist-to-height ratio and neck circumference were the best measures in the men with mild OSA; however, BMI was found to be more closely associated with severe OSA. An increase in neck circumference and the waist-to-height ratio of one unit may increase the probability of OSA by 15% and 13%, respectively [1]. According to asleep cohort study conducted by Young et al. (2009) involving 6,050 patients with sleep issues, incidence rates on having SDB with an AHI >5 was lower at 9% for women compared to 24% for the men. Meanwhile, AHI>15 was reported in 4% of women and 9% for men [9].

OSA prevalence was found to increase progressively with age in a probability sample from two Pennsylvania counties. OSA (AHI>10 events/hour) was reported in 3.2% of men aged 20 to 44 years, 11.3% of men aged 45 to 64 years, and 18.1% of men aged 61 to 100 years. Concurrently, the prevalence of OSA (AHI > 15 events/hour) in women was 0.6%, 2.0%, and 7.0%, respectively, for the 20 to 44year, 45 to 64years, and 61-to-100-year age groups [10,11,12].Similar results have been demonstrated in a community-based Sleep Heart Health Study, wherein the disease prevalence increases steadily with age and reaches a plateau after the age of 60 [10,13]. Furthermore, an epidemiologic study investigated the prevalence of OSA in adults; it was reported that men have higher rates of OSA with a lower male-to-female ratio in the range 2 to 3:1 [10]. The male predisposition to the disorder has been attributed to gender differences in upper airway anatomical and functional properties, as well as the ventilatory response to sleep arousals [10].

The modest to strong correlation between these inter-related measures poses a challenge in determining whether such factors of central obesity can better predict disease risks or severity (i.e., BMI, waist girth, neck circumference). Nonetheless, cross-sectional analyses of the Sleep Heart Health Study data revealed that moderate to severe OSA, as defined as an AHI > 15 events/hour, is independently associated with BMI, neck circumference, and waist circumference in middle-aged and elderly [10,13].

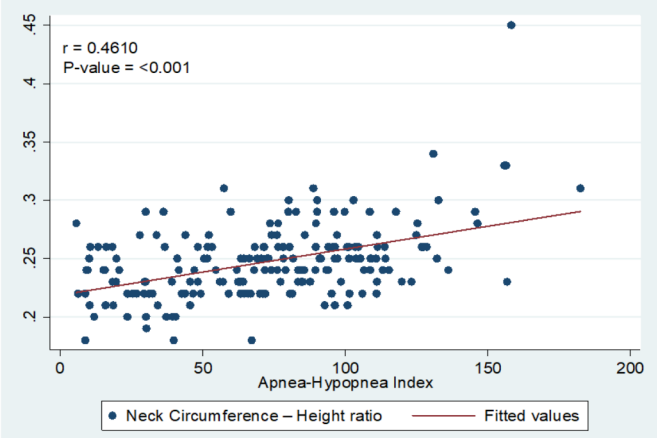
Numerous evidences have consistently identified bodyweight as the strongest risk factor to exhibit OSA. This was assessed and confirmed by the

Wisconsin Sleep Cohort study, which found that a one standard deviation difference in BMI was associated with a fourfold increase in disease prevalence [10]. Given that the pathophysiology of OSA is completely linked with obesity, with an estimated 58% of moderate to severe cases being attributable to a BMI ≥ 25 kg/m^2 [10,15].

Another factor associated with OSA was neck circumference. This was investigated in a retrospective, case-control observational study conducted by Si Eun Kim et al. (2015) with 147 snoring patients. The authors concluded that neck circumference assessment may predict the presence and severity of OSA [16]. Results revealed that a significant correlation between AHI and neck circumference was observed (P<0.0001). Moreover, there was more association between the neck circumference and OSA rather than BMI and age [16]. The results were further evaluated by an observational, cross-sectional pilot study by Ang et al. (2011) [17].Neck circumference cut-off levels of 40cm for males and 33.8cm for females demonstrated low sensitivity and moderately high specificity for identifying patients with abdominal obesity (n=425); 62.07% and 90.09% for males, 67.59% and 85.6% for females, respectively [17]. Except for hypertriglyceridemia, patients with obese neck circumference cut-off levels had asignificant association with component risk factors of metabolic syndrome (MetS) (P<0.001). Hence, potential risk of cardiovascular disease [17].

NHR CUT-OFF

Figure 1: NHR cut-off versus AHI



***Pearson's r interpretation: ≥ 0.7 (strong relationship), 0.4-0.69 (moderate relationship), 0.1- 0.39 (weak relationship), 0 (no or negligible relationship). Adapted from: Dancey C, Reidy J. 2004. Statistics without maths for psychology: using SPSS for windows. London, England: Prentice-Hall**

Table 3.1 Diagnostic accuracy of Neck Circumference – Height ratio to predict Mild OSA

		Obstructive Sleep Apnea		Total
		Mild	Moderate	
NHR	≤ 0.23	6	7	13
	> 0.23	6	12	18
	Total	12	19	31

Sensitivity	50% (21.09 to 78.91)	Positive LR	1.36 (0.60 to 3.07)
Specificity	63.16% (38.36 to 83.71)	Negative LR	0.79 (0.41 to 1.53)
PPV	46.15% (24.47 to 65.98)	AUC	0.5307 (0.30 to 0.76)
NPV	66.67% (50.78 to 79.49)	Accuracy	58.06% (39.08 to 75.45)

PPV, positive predictive value; NPV, negative predicted value; LR, likelihood ratio.

The diagnostic accuracy of Neck Circumference-Height Ratio using Moderate OSA as its reference outcome to predict Mild OSA is shown in Table 3.1. A cutoff of ≥ 0.23 NHR was used to predict Mild OSA using Moderate as the reference (sensitivity: 50% (21.09 to 78.91); specificity: 63.16% (38.36 to 83.71). The PPV was 46.15% (24.47 to 65.98) and the NPV was 66.67% (50.78 to 79.49). The positive likelihood ratio was 1.36 (0.60 to 3.07) and the negative likelihood ratio was 0.79 (0.41 to 1.53). The AUC was determined as 0.5307 (0.30 to 0.76) and the accuracy yielded from the cutoff was 58.06% (39.08 to 75.45).

Table 3.2 Diagnostic accuracy of Neck Circumference – Height ratio to predict Mild OSA

		Obstructive Sleep Apnea		Total
		Mild	Moderate and Severe	
NHR	≤ 0.22	6	40	46
	> 0.22	6	142	148
	Total	12	182	194

Sensitivity	50% (21.09 to 78.91)	Positive LR	2.27 (1.21 to 4.27)
Specificity	78.02% (71.30 to 83.81)	Negative LR	0.64 (0.36 to 1.13)
PPV	13.04% (7.41% to 21.95)	AUC	0.6465 (0.47 to 0.82)
NPV	95.95% (93.04 to 97.67)	Accuracy	76.29% (69.67 to 82.09)

PPV, positive predictive value; NPV, negative predicted value; LR, likelihood ratio.

The diagnostic accuracy of Neck Circumference-Height Ratio using Moderate and Severe OSA as reference outcomes to predict Mild OSA is shown in Table 3.2. A cutoff of ≥ 0.22 NHR was used to predict Mild OSA using Moderate and Severe as reference outcomes (sensitivity: 50% (21.09 to 78.91); specificity: 78.02% (71.30 to 83.81). The PPV was 13.04% (7.41% to 21.95) and the NPV was 95.95% (93.04 to 97.67). The positive likelihood ratio was 2.27 (1.21 to 4.27) and the negative likelihood ratio was 0.64 (0.36 to 1.13). The AUC was determined as 0.6465 (0.47 to 0.82) and the accuracy yielded from the cutoff was 76.29% (69.67 to 82.09).

Table 4.1 Diagnostic accuracy of Neck Circumference – Height ratio to predict Moderate OSA

		Obstructive Sleep Apnea		Total
		Moderate	Mild	
NHR	≥ 0.23	12	6	18
	< 0.23	7	6	13
	Total	19	12	31

Sensitivity	63.16% (38.36 to 83.71)	Positive LR	1.26 (0.65 to 2.45)
Specificity	50% (21.09 to 78.91)	Negative LR	0.74 (0.33 to 1.67)
PPV	66.67% (50.78 to 79.49)	AUC	0.5307 (0.30 to 0.76)
NPV	46.15% (27.47 to 65.98)	Accuracy	58.06% (39.08 to 75.45)

PPV, positive predictive value; NPV, negative predicted value; LR, likelihood ratio.

The diagnostic accuracy of Neck Circumference-Height Ratio using Mild OSA as its reference outcome to predict Moderate OSA is shown in Table 4.1. A cutoff of ≥ 0.23 NHR was used to predict Moderate OSA using Mild as its reference (sensitivity: 63.16% (38.36 to 83.71); specificity: 50% (21.09 to 78.91). The positive predictive value (PPV) was 66.67% (50.78 to 79.49) and the negative predictive value (NPV) was 46.15%27.47 to 65.98). The AUC was determined as 0.5307 (0.30 to 0.76) and the accuracy yielded from the cutoff was 58.06% (39.08 to 75.45).

Table 4.2 Diagnostic accuracy of Neck Circumference – Height ratio to predict Moderate OSA

		Obstructive Sleep Apnea		Total
		Moderate	Mild and Severe	
NHR	≤ 0.23	11	58	69
	> 0.23	8	117	125
	Total	19	175	194

Sensitivity	57.89% (33.5 to 79.75)	Positive LR	1.75 (1.13 to 2.71)
Specificity	66.86% (59.36 to 73.78)	Negative LR	0.63 (0.37 to 1.08)
PPV	15.94% (10.91 to 22.7)	AUC	0.6421 (0.52 to 0.77)
NPV	93.6% (89.52 to 96.16)	Accuracy	65.98% (58.85 to 72.61)

PPV, positive predictive value; NPV, negative predicted value; LR, likelihood ratio.

The diagnostic accuracy of Neck Circumference-Height Ratio using Mild and Severe OSA as reference outcomes to predict Moderate OSA is shown in Table 4.2. A cutoff of ≥ 0.23 NHR was used to predict Moderate OSA using Mild and Severe as the reference outcomes (sensitivity: 57.89% (33.5 to 79.75); specificity: 66.86% (59.36 to 73.78). The positive predictive value (PPV) was 15.94% (10.91 to 22.7) and the negative predictive value (NPV) was 93.6% (89.52 to 96.16). The positive likelihood ratio was 1.75 (1.13 to 2.71) and the negative likelihood ratio was 0.63 (0.37 to 1.08). The AUC was determined as 0.6421 (0.52 to 0.77) and the accuracy yielded from the cutoff was 65.98% (58.85 to 72.61).

NHR CUT-OFF AND SEVERE OSA

Table 5.1 Diagnostic accuracy of Neck Circumference – Height ratio to predict Severe OSA

		Obstructive Sleep Apnea		Total
		Severe	Mild	
NHR	≥ 0.23	130	6	136
	< 0.23	33	6	39
	Total	163	12	175

Sensitivity	79.75% (72.76 to 85.64)	Positive LR	1.60 (0.90 to 2.82)
Specificity	50% (21.09 to 78.91)	Negative LR	0.40 (0.21 to 0.77)
PPV	95.59% (92.45 to 97.46)	AUC	0.6600 (0.49 to 0.83)
NPV	15.38% (8.73 to 25.69)	Accuracy	77.71% (70.82 to 83.65)

PPV, positive predictive value; NPV, negative predicted value; LR, likelihood ratio

The diagnostic accuracy of Neck Circumference-Height Ratio using Mild OSA as reference outcomes to predict Severe OSA is shown in Table 5.1. A cutoff of ≥ 0.23 NHR was used to predict Severe OSA using Mild as the reference outcomes (sensitivity: 57.89% (33.5 to 79.75); specificity: 66.86% (59.36 to 73.78). The PPV was 15.94% (10.91 to 22.7) and the NPV was 93.6% (89.52 to 96.16). The positive likelihood ratio was 1.60 (0.90 to 2.82) and the negative likelihood ratio was 0.40 (0.21 to 0.77). AUC was determined as 0.6421 (0.52 to 0.77) and the accuracy yielded from the cutoff was 65.98% (58.85 to 72.61).

Table 5.2 Diagnostic accuracy of Neck Circumference – Height ratio to predict Severe OSA

		Obstructive Sleep Apnea		Total
		Severe	Mild and Moderate	
NHR	≥ 0.24	111	14	125
	< 0.24	52	17	69
	Total	163	31	194

Sensitivity	68.10% (60.35 to 75.17)	Positive LR	1.51 (1.01 to 2.25)
Specificity	54.84% (36.03 to 72.68)	Negative LR	0.58 (0.39 to 0.86)
PPV	88.80% (84.14 to 92.22)	AUC	0.6568 (0.55 to 0.76)
NPV	24.64% (18.12 to 32.57)	Accuracy	65.98% (58.85 to 72.61)

PPV, positive predictive value; NPV, negative predicted value; LR, likelihood ratio

The diagnostic accuracy of Neck Circumference-Height Ratio using Mild and Moderate OSA as reference outcomes to predict Severe OSA is shown in Table 5.2. A cutoff of > 0.24 NHR was used to predict Severe OSA using Mild and Moderate as the reference outcomes (sensitivity: 68.10% (60.35 to 75.17); specificity: 54.84% (36.03 to 72.68). The PPV was 88.80% (84.14 to 92.22) and the NPV was 24.64% (18.12 to 32.57). The positive likelihood ratio was 1.51 (1.01 to 2.25) and the negative likelihood ratio was 0.58 (0.39 to 0.86). The AUC was determined as 0.6568 (0.55 to 0.76) and the accuracy yielded from the cutoff was 65.98% (58.85 to 72.61).

Likewise, all evidence pointed to a positive relationship between NHR and OSA, which is consistent with our findings. In a retrospective study on 1,939 patients, Ho et al. (2016) utilized a baseline logistic regression model with a cut-off AHI of 5 events/hour for OSA to determine if BMI scores were predictive of OSA [6]. This baseline model includes an NHR cut-off. A later model has been utilized to assess the interaction between BMI score and AHI [6]. Similarly, linear models were then used to examine whether BMI score and NHR cut-off were predictive of AHI. The odds ratio and both positive and negative predictive values of having AHI >5, if NHR cut-off> 0.25 were calculated based on the X^2 table of the99 adult subjects. A significant NHR cut-off effect (P=0.012) was observed in the adult population using an NHR cut-off of 0.25 and an AHI cut-off of 5, with an odds ratio estimated in 18 patients with OSA with an NHR cut-off > 0.25. Although the odds ratio in adults was higher than in children (18 vs 3.47), the positive predictive value was only 25%, but the negative predictive value was elevated at 96%.The authors concluded that determining the NHR cut-off can be used as a simple screening method for OSA in children and adults, and when combined with other predictors, it may improve clinicians' ability to triage children and adults at risk for OSA for further evaluation with PSG [6]. These findings were also observed in another retrospective study conducted by Veeravigrom et al. (2017) determining OSA severity in a pediatric population with a sleep efficiency of < 80% [18]. Polysomnographic and anthropometric data were collected from 98 children (69 Male and 29 Female) aged 5–15 years who presented between September 2013 and August 2016.Results demonstrated that there was an insignificant cut-off point of NHR from the receiver operating characteristic (ROC) curve to predict OSA (OAHI ≥1.5/hour). The cut-off point 0.22 of NHR was selected from the ROC curve with AUC at 0.637 to predict moderate to severe OSA (OAHI ≥ 5/hour) at a sensitivity of 72.3% and specificity of 51%. NHR was found to be more predictive at 0.22 in children > 8 years of age with a sensitivity of 78.3% and specificity of 62%. The odds ratios of OAHI ≥ 5 and children over 8 years of age were 1.67 and 5.85, respectively, for NHR≥ 0.22 [18].

Unfortunately, there was limited evidence in the literature regarding an association between NHR cut-off and OSA.

CONCLUSION

The NHR cut-off demonstrated a moderate positive correlation with OSA, and NHR increases as the apnea-hypopnea index are increased (r=0.4610; p-value<0.001).

NHR cut-off of 0.23 is sufficient to predict severe OSA with a PPV of 95.59% and AUC of 0.66, but has poor diagnostic accuracy for mild and moderate OSA.

Moreover, the NHR cut-off may also be an integral tool to predict severe OSA.

LIMITATION OF THE STUDY

This is a retrospective study involving only patients who have been diagnosed with obstructive sleep apnea using a polysomnogram. Based on the clinical profile of each patient, a polysomnogram was only indicated and requested for patients who were highly suspected of having obstructive sleep apnea.

All of the patient's anthropometric measurements were taken by the patient's on-duty sleep technologists or sleep fellows in training, who alternated between shifts.

RECOMMENDATIONS

We propose conducting a comparative study to determine the diagnostic accuracy of the neck-circumference-height ratio and neck circumference in obstructive sleep apnea. A study to determine the diagnostic accuracy of the neck-circumference-height ratio in determining obesity hypoventilation syndrome (OHS).

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Prophylactic Paracetamol for Intraoperative Shivering Prevention for Patients Undergoing Gynecological Procedures under Spinal Anesthesia: A Randomized Clinical Trial*

Angeline Bonne P. Regadio, MD[1]

Abstract

Introduction: Shivering is defined as an involuntary, repetitive activity of skeletal muscles. Mechanisms of shivering for patients undergoing surgical operation include intraoperative heat loss, increase sympathetic tone, pain, and systemic release of pyrogens. Regional anesthesia, particularly spinal anesthesia causes redistribution of core heat to the peripheral tissues this in turn predisposes patient to shivering and hypothermia. The median incidence of shivering related to regional anesthesia observed in a review of 21 studies is 55%. Paracetamol is one of the most commonly used analgesic and antipyretic drugs around the world, available without a prescription, it has analgesic and antipyretic property similar to NSAIDs it also affects core body temperature through the hypothalamus. Though different modalities have been established for shivering prevention, the search for a cost-effective drug with lesser side effects and improvement of patient satisfaction still continues.

Objective: The aim of this study was to evaluate the effect of prophylactic dose of Paracetamol on postanesthesia shivering on patients undergoing gynecological procedures under spinal anesthesia as compared to patients not given Paracetamol.

Methodology: This is a Double blind, Randomized, Placebo Controlled conducted in patients scheduled for benign gynecological procedures such as Hysterectomy with or without adnexectomy. Using simple random sampling through fishbowl method and a sample size of 42, all patients who consented to participate in the study was randomly assigned to receive Paracetamol 900 mg IV or Placebo 0.9% Saline intravenously 30 minutes prior to induction of spinal anesthesia. Incidence and severity of Shivering was documented using shivering five point scale outlined by Crossley and Mahajan, while patient satisfaction was also evaluated using the Likert Scale, possible side effects was also assessed.

Keywords: Shivering, paracetamol, prophylaxis, spinal anesthesia

INTRODUCTION

Shivering is a common postanesthetic complication, it creates an uncomfortable experience for patients affecting them psychologically and physically[1]. Shivering is also believed to increase oxygen consumption, lactic acidosis, carbon dioxide production, metabolic rate up to 400%, risk of hypoxemia, and to some extent postoperative complications[2]. In addition to anxiety for patients undergoing surgical procedure, shivering may also increase patient's discomfort and lower patient's satisfaction post operatively. The patient's perception of pain postoperatively may also increase due to shivering. Shivering is usually triggered by hypothermia but it can also occur even in normothermic patients during the perioperative period, the etiology of shivering has not been fully understood but even if cold induced thermoregulatory shivering remains an obvious etiology, it has also been attributed to numerous other causes such as pain, disinhibited spine reflexes, decreased sympathetic activity and as well respiratory alkalosis.[2] According to the American Society of Anesthesiologists (ASA) guideline forced-air

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[1]from Baguio General Hospital and Medical Center, Baguio Benguet

warming devices and meperidine are recommended in the control of shivering.[2] In our Institution, Since Meperidine is not available, we used Tramadol as an alternative, however has also undesirable effects such as nausea and vomiting. We only have two (2) units of forced air warmer available in the operating room, however it's use for pediatric patients are prioritized and there is an additional charge for the patient when used. We therefore look for solutions to address shivering by using an affordable medication with lesser side effects and may also aid as an additional Pain reliever, also for patient's comfort and satisfaction improving overall well-being of the patient.

Neuraxial anesthesia is one of the most common surgical procedure done in our institution and prompt treatment and prevention of shivering should be part of overall perioperative management. Neuraxial anesthesia induces shivering due to redistribution of core body heat to the peripheral tissues. Neuraxial block results in impairment of autonomic thermoregulation below the level of the block. The vasodilatation is responsible for this redistribution of heat.[18] Antipyretic agents like paracetamol block endogenous pyrogens by inhibiting cyclooxygenase-mediated prostaglandin synthesis in the brain, the substances responsible for elevating the hypothalamic set point leading to peripheral vasodilation and sweating. Paracetamol has been used in some studies for shivering but has not been established as a standard treatment. Current use of Intravenous Paracetamol for post-operative analgesia and reduction in opioid consumption is also increasing.[28] While several published studies has been made regarding the use of Paracetamol for shivering, only four studies done internationally was done while none was published locally, two of the studies done used prophylactic paracetamol for shivering for patients under general anesthesia, one study of paracetamol for shivering using logistic regression and only one study of paracetamol for prophylactic shivering under regional(spinal) anesthesia. Results of these studies revealed that Paracetamol is an effective anti-shivering medication though none emphasized patient's satisfaction post-operatively.

The aim of this study was to evaluate the effect of Prophylactic Paracetamol on intraoperative shivering on patients undergoing gynecological procedures under spinal anesthesia. Also to demonstrate that there would be a significant difference between the effect of prophylactic paracetamol on shivering compared to Placebo.

METHODS OF RESEARCH

Research Design

This is a Double Blind, Randomized Control trial. Included participants was randomly assigned to two groups by fishbowl method where Group A received Paracetamol 900 mg IV (experimental) and Group B received PLACEBO (control).

POPULATION

Patients scheduled for benign gynecological procedures such as Hysterectomy with or without adnexectomy was recruited to participate in the study and included once surgical, anesthetic and consent for the study has been secured.

Inclusion criteria

- Neuraxial Anesthesia
- Female
- Ages 19 to 65 years old
- ASA Physical status Class I and II
- Benign Gynecological procedures such as hysterectomy with or without adnexectomy

Exclusion criteria

- Contraindications to neuraxial anesthesia
  - Patients refusal
  - Spinal Injuries
  - Localized infection
  - Hypovolemia
  - Coagulopathies
- History of stroke or myocardial infarction
- Known Liver and renal diseases
- Hypersensitivity reaction with previous Paracetamol administration

SAMPLE SIZE

Using OPEN-EPI v 3.01 software, the sample size was computed using the confidence level of 95%. The computed sample size using Fleiss formula with continuity correction is 42. The sample size for each group would be 21 with a computed power at 80%. Sixty four percent (64%) of unexposed with outcome and eighteen percent (18%) of exposed with outcome was based on the study of Gholami, et al (2016). [13] According to the Anesthesia operating room monthly census and Management information system, for the last 6 months we had a to tal of 585 Hysterectomy cases and 1021 exploratory laparotomy involving uterus and fallopian tube, thus the number of target population of the study would be feasible.

Sample Size:X-Sectional, Cohort, & Randomized Clinical Trials

Two-sided significance level(1-alpha):	95
Power(1-beta, % chance of detecting):	80
Ratio of sample size, Unexposed/Exposed:	1
Percent of Unexposed with Outcome:	64
Percent of Exposed with Outcome:	18
Odds Ratio:	0.12
Risk/Prevalence Ratio:	0.28
Risk/Prevalence difference:	-46

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Sample Size - Exposed	18	17	21
Sample Size-Nonexposed	18	17	21
Total sample size:	36	34	42

SAMPLING DESIGN

The sampling design used was simple random sampling. Using the fish bowl method, 42 small rolled piece of paper was equally divided into two groups, each was written with either “Group A” or “Group B” and placed in an opaque envelope. Group A received Prophylactic Paracetamol while Group B received placebo. All eligible participants were asked to pick from the opaque envelope and was allocated to either group A or group B accordingly. A third person, not involved in the study was able to see the result and administer the medications. The results of randomization was concealed from the patient and researcher until all participants have completed the study.

MATERIALS AND METHODS

Participants included in this study are patients who had Elective benign Gynecological Procedures under neuraxial anesthesia either with single shot spinal anesthesia or combined spinal and epidural anesthesia. After eligibility, preoperative evaluation was done by the anesthesia resident-in-charge and researcher, including a detailed history and physical examination. Procedure and medication was explained to the patient. After fulfillment of the inclusion criteria, 42 participants was recruited into study. Eligible participants was recruited during the pre-operative evaluation and Informed consent was secured by the researcher at the patient’s room or ward a day before the procedure. For the randomization, before the procedure, the participants was randomly assigned to receive Prophylactic Paracetamol 900 mg IV (Group A) or Placebo (Group B) using fishbowl method. A senior anesthesia resident not involved in the study prepared the medications, labelled and randomized. There was 42 small rolled piece of paper that was labeled and equally divided into two groups; “Group A” or “Group B” placed in an opaque envelope. Group A received Prophylactic Paracetamol while Group B received the placebo. A 900 mg Iv (6 ml) Paracetamol was aspirated in a 10 ml sterile syringe and was labeled as “A” and another 6 ml of Saline 0.9% was aspirated in a 10 cc sterile syringe and was labeled as “B”. A nurse not involved in the study asked the patient to pick from the prepared opaque envelope with labels of either group A or group B. Depending on the result, to ensure blinding of the patient and anesthesiologist the

nurse saw the result of randomization and administered the medication as labelled accordingly. The Paracetamol is a clear solution so it is impossible to distinguish from a 0.9% saline which is the placebo. Intraoperatively, the anesthesiology resident- in-charge of the patient after administering neuraxial anesthesia observed the patient using the shivering scale. For Group A, Paracetamol 900 mg IV was administered to the patient 30 minutes prior to induction of anesthesia. Group B received 6ml of 0.9% saline intravenously and has also received standard anesthesia care and a similar data collection form was used to document both Group A and Group B. Data Collection form indicated patient's Age and weight and variables to be measured such as shivering scale, side effects, and patients satisfaction rating.

Upon entering the Operating room, monitors was hooked to the patient such as Cardiac monitor, blood pressure and pulse oximeter. Patient was given oxygenation at 2-3lpm via nasal cannula. After recording of basic vital signs, preloading of 10 mL/kg Ringer's solution was infused and then Paracetamol 900 mg IV was given. After 30 minutes, patient was placed in a left lateral decubitus position and aseptic technique was done, spinal anesthesia was performed at L3 –L4 or L4 – L5 intervertebral space with Quincke needle - 25 gauge or with a combined spinal and epidural anesthesia using touhy needle gauge 18, proper placement was ensured and Bupivacaine heavy was administered. Adequate blockade of anesthesia was assessed using Pin prick and Bromage scoring. Patients who experienced failure of SAB or low block level was excluded in the study since the anesthesia may be converted into a general anesthesia for the procedure to continue and is already not in the scope of the study.

During surgery, vital signs was measured every 5 minutes until the end of the surgery. In case of the incidence of hypotension (reduction in systolic pressure below 100 mmHg or 25% decrease in systolic pressure to base pressure of patient), it was treated by 10 cc/kg Lactate Ringer and 5 mg intravenous ephedrine and if PR reduced below 55 beats, 0.01 mg/kg intravenous Atropine was injected to the patient and if it was necessary, it is repeated with the maximum of 0.04 mg/kg.[10]

For the severity of shivering, the anesthesia resident-in-charge recorded and observed severity of shivering using Mahjon and Crossely Shivering Scale (0 = without shivering; 1 = presence of one or more symptoms including vasoconstriction, cold extremities, hair sting, peripheral cyanosis without specific reason; 2= movements in one muscle group; 3= movements in more than one muscles group; 4= severe movements in whole body). For Grades 3-4, Tramadol 50mg IV slow IV push was administered. The anesthesia resident-in-charge also documented possible side effects such as bradycardia, hypotension, headache, nausea and vomiting intraoperatively. At the Post Anesthesia care Unit (PACU), patient's satisfaction was done by asking the patient to answer the question, "How would you rate your experience after the surgery?" using a 7-point Likert verbal rating scale and acceptable satisfaction score of the patient being 5-7.

After the proper documentation and observation and the patient transferred to the ward from PACU, the anesthesia resident-in-charge relayed all the results to the researcher. The researcher was not allowed to collect data directly from the patient, instead relied on the data collected by the anesthesia resident-in-charge.

Prior to Induction of the anesthesia, ASA recommended standard monitors such as cardiac monitor, non-invasive blood pressure monitor and pulse oximeter was used to measure patient's heart rate, electrocardiogram tracing, blood pressure and oxygen saturation. Patient wasbe monitored for changes in vital signs. Sudden incidence of desaturations, hypotension, difficulty of breathing, extreme bradycardia and tachycardia was promptly dealt with.

Patient's safety and comfort was considered at all times. Adequate analgesia, oxygenation, and hydration was ensured. Any unwanted incidences has been reflected in the report.

SAFETY CONSIDERATIONS

Prior to Induction of the anesthesia, ASA recommended standard monitors such as cardiac monitor, non- invasive blood pressure monitor and pulse oximeter was used to measure patient's heart rate, electrocardiogram tracing, blood pressure and oxygen saturation. Patient was monitored for changes in vital signs. Sudden incidence of desaturations,

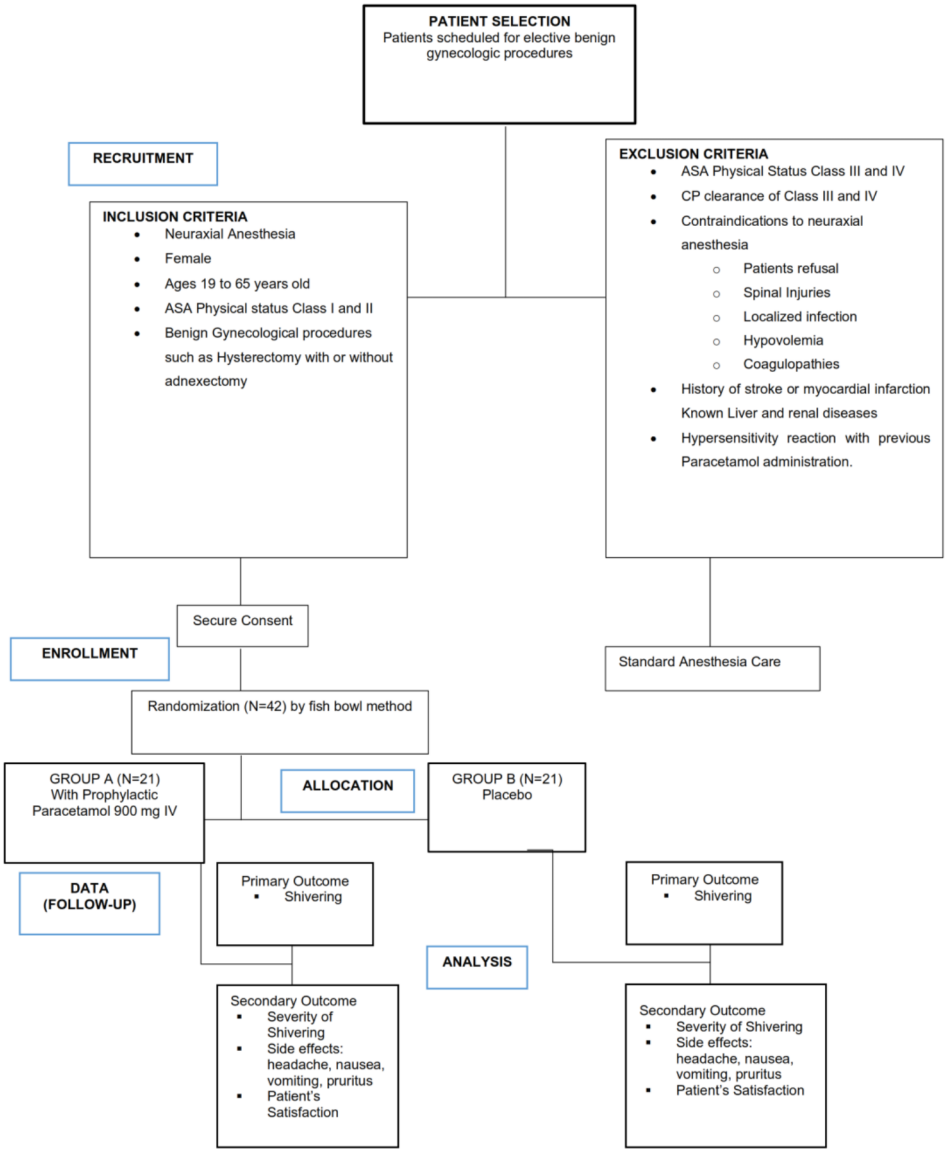
hypotension, difficulty of breathing, extreme bradycardia and tachycardia was promptly dealt with. To avoid toxicity, therapeutic doses of Paracetamol was administered and has not exceeded the recommended daily dose. Although in therapeutic doses there were no reported adverse reactions in humans, possible adverse reactions would be watched out for such as nausea, vomiting, pruritus and headache. Patient's safety and comfort will be considered at all times. Adequate analgesia, oxygenation, and hydration will be ensured. Any unwanted incidences will be reflected in the report.

For patients who had hypothermia, warm blankets was provided, cold fluid infusion was avoided and aircon was turned off during the procedure.

Participation in this study was voluntary and participant was allowed to withdraw at any given time during the study without any penalty for whatever reason the participant may have and was not questioned.

EFFICACY

Several studies on Paracetamol claimed its effectiveness in reducing the incidence on post anesthesia shivering. The study aims to evaluate the effect of Prophylactic Paracetamol in shivering (primary outcome) and as well as it's severity of shivering, possible side effects side effects: headache, nausea, vomiting, pruritus and Patient's Satisfaction (secondary outcome).[9,10,13,14]



STATISTICAL ANALYSIS

All data was recorded using a workbook and encoded to Microsoft Excel worksheet. Statistical Data was analyzed using Statistical Package for Social Sciences Software V.25 (SPSS). The main statistical analysis used was frequency, percentages, mean and odds ratio. Chi-square test of homogeneity to compare between Group A and Group B. Median Test for the statistical analysis of occurrence of Shivering, severity, side effects and patient satisfaction. P value of less than .05 was considered statistically significant. Odds ratio was also used for odds of exposure for shivering and patient satisfaction between Group A and Group B, odds ratio that are greater than 1 indicate that the event (belonging to experimental group) is more likely to occur as the predictor increases. Odds ratios that are less than 1 indicate that the event (belonging to experimental group) is less likely to occur as the predictor increases.

STATEMENT OF HYPOTHESIS

Null Hypothesis

There is no significant difference between the effectiveness of Prophylactic Paracetamol compared to Placebo in the incidence of Shivering among patients undergoing benign gynecological procedures under neuraxial anesthesia.

Alternative Hypothesis

There is a significant difference between the effectiveness of Prophylactic Paracetamol compared to Placebo in the incidence of Shivering among patients undergoing benign gynecological procedures under neuraxial anesthesia.

ETHICAL CONSIDERATIONS

Prior to enrolment from this study, an informed consent was obtained. Confidentiality of information was maintained. All patients scheduled for elective gynecologic surgery and met the inclusion criteria was asked and subjected to informed consent prior to enrollment of the study. The anesthesia resident-in-charge explained and fully disclosed the procedure and its possible risks and complications in their native language if necessary to make sure that the participant have fully understood the procedure. The participant was free to ask questions and clarifications. The identifying data included was the age and weight. Only the researchers have access to the data collected.

After data summary and analysis, the data acquired was stored in a password protected USB drive and was kept in the Department of Anesthesiology for future purposes. Results and findings was disseminated to the Department of Anesthesiology and other care providers involved in anesthetic management.

Participation in this study was voluntary and participants were free to withdraw from the study anytime without penalty. Participants did not receive any form of payment. No participant was forced or coerced to join this research.

The researcher only used Paracetamol that is available in the institution and did not use any other brands. There was no conflict of interest and the researcher does not intend to promote the use, sale of Paracetamol of any brand. The researcher also shouldered all expenses not shouldered by PhilHealth and did not promote or patronize the drug used nor company or distributor involved.

RESULTS & DISCUSSION

A total of 42 adult patients were enrolled in this study: 21 patients in the prophylactic paracetamol group and 21 in the placebo group. Patient characteristics are shown in Table 1.

Table 1: Clinico-Demographic Characteristics of Subjects between Prophylactic Paracetamol group and with no Prophylactic Paracetamol group who underwent benign gynecologic procedures under Neuraxial anesthesia

Table 1: Clinico-Demographic Characteristics of Subjects between Prophylactic Paracetamol group and with no Prophylactic Paracetamol group who underwent benign gynecologic procedures under Neuraxial anesthesia

Clinico-Demographic Characteristics		Prophylactic Paracetamol Group n (%)	Placebo Group n (%)	Total
A. Age (years)	19-27	4 (19.05%)	6 (28.57%)	10 (23.81%)
	28-36	3 (14.29%)	4 (19.05%)	7 (16.67%)
	37-45	4 (19.05%)	5 (23.81%)	9 (21.43%)
	46-54	4 (19.05%)	3 (14.29%)	7 (16.67%)
	55-65	6 (28.57%)	3 (14.29%)	9 (21.43%)
B. Weight (kg)	41-50	4 (19.05%)	7 (33.33%)	11 (26.19%)
	51-60	11 (52.38%)	8 (38.10%)	19 (45.24%)
	61-70	4 (19.05%)	4 (19.05%)	8 (19.05%)
	71-80	1 (4.76%)	2 (9.52%)	3 (7.14%)

The age group with the greatest number of participants (n =10; total of 23.81%) is 19 -27 years old, with 4 people receiving Paracetamol and 6 persons receiving Placebo. Majority of the participants (45.24%) weighed 51-60 kilograms. Both age and weight were analyzed using frequency and percentages.

Table 2: Incidence and Severity of Shivering who underwent benign gynecologic procedures under Neuraxial anesthesia

Severity of Shivering	Prophylactic Paracetamol Group n (%)	Placebo Group n (%)	p-value	Odds Ratio	90% CI for Odds Ratio
Grade 0	15 (71.43%)	6 (28.57%)	0.062*	0.561	(0.337, 0.936)
Grade 1	2 (9.52%)	5 (23.81%)			
Grade 2	0	2 (9.52%)			
Grade 3	4 (19.05%)	7 (33.33%)			
Grade 4	0	1 (4.76%)			

*Significant at 0.10 level of significance but not significant at 0.05 level

Following benign gynecologic procedures under neuraxial anesthesia, the incidence and severity of shivering among the participants were determined in Table 2. Majority of the patients who used Paracetamol (71%) had a Grade 0 or did not experience shivering. The placebo group, on the other hand, had a variety of outcomes: most of the participants in the placebo group (33%) had a grade of 3, 28% are Grade 0, 23% were Grade 1, 9% were Grade 2 while there was 1 patient who has Grade 4 shivering using frequency and proportions.

The Chi square test was used to determine whether there was a relationship between Paracetamol and the severity of shivering. Based on the computed p-value of 0.062, there is no statistically significant

difference in the proportions of patients between the two groups in terms of the severity of shivering at the 0.05 level of significance. At the 0.10 level of significance, however, there is a borderline statistical difference in the percentage of patients in the two groups, supporting the evidence of Rasoli in 2019. Despite having weak evidence, the Paracetamol group has a significantly larger number of patients with Grade 0. The placebo group had a significantly larger number of patients who have at least Grade 1 shivering compared to the control group.

Among the total number of patients, 19% had a grading of $\geq$ 3 in paracetamol (4 out of 21) while 38% with a grade of $\geq$ 3 was noted (8 out of 21 participants) in the placebo group.

In the context of the study, the odds ratio of 0.561 indicates that being part of the experimental group (Prophylactic Paracetamol Group), it is less likely that the patients will experience higher degree of severity of shivering.

Table 3: Possible Adverse Reaction between Prophylactic Paracetamol group and with no Prophylactic Paracetamol group

Side effects	Prophylactic Paracetamol Group n (%)	Placebo Group n (%)
Hypotension	0	2 (9.52%)
Headache	3 (14.29%)	1 (4.76%)
Nausea	0	4 (19.05%)
Vomiting	0	1 (4.76%)

In the following table, we present the differences in Adverse Reaction between the groups receiving prophylactic paracetamol and those who did not (placebo group). Only 3 patients in the paracetamol group (14%) suffered from side effects (headache), whereas 8 patients in the placebo group suffered from nausea (19%), hypotension (9%), vomiting (4%), and headache (4%). In this study, the cause of postoperative headache among the participants is difficult to rule out since it can be a side effect of administering spinal anesthesia in both groups. This is evidenced in Table 3 where there are more participants in the Paracetamol group who experienced headaches (n =3) versus the placebo group (n=1) despite Paracetamol being a common drug to treat headaches. The “medication overuse headache” due to excessive use of Paracetamol for chronic pain, including tension-type headache and migraine was not assessed in the study.

Table 4: Patient Satisfaction between Prophylactic Paracetamol group and with no Prophylactic Paracetamol group

Patient Satisfaction	Prophylactic Paracetamol Group n (%)	Placebo Group n (%)	p-value	Odds Ratio	95% CI for Odds Ratio
Extremely Dissatisfied	0	0	0.501	1.408	(0.922, 2.152)
Dissatisfied	0	0			
Somewhat Dissatisfied	2 (9.52%)	2 (9.52%)			
Undecided	1 (4.76%)	4 (19.05%)			
Somewhat satisfied	5 (23.81%)	7 (33.33%)			
Satisfied	7 (33.33%)	4 (19.05%)			
Satisfied Extremely	6 (28.57%)	4 (19.05%)			
Mean	**5.71**	**5.19**	**0.186**	**-**	**-**

Table 4 shows Patient Satisfaction between Prophylactic Paracetamol group and with no Prophylactic Paracetamol group. It is highlighted in this table that there are more patients satisfied in the paracetamol group compared to the placebo group, as demonstrated by higher mean ratings (Paracetamol = 5.71 vs Placebo = 5.19) and that majority of patients in the paracetamol group (33%) are satisfied. In the placebo group, on the other hand, 7 participants (33%) are somewhat satisfied; 4 participants are undecided and 2 are somewhat dissatisfied.

Using independent-samples t-test to compare the mean ratings of patient satisfaction and chi square test to compare proportions and percentages between both groups, results have found that the distribution was statistically the same in both groups, indicating that there was no statistically significant association between satisfaction and use of prophylactic paracetamol for shivering at 0.05 level of significance.

In the context of the study, the odds ratio of 1.408 indicates that being part of the experimental group (Prophylactic Paracetamol Group), it is more likely that the patients will have a higher degree of patient satisfaction.

DISCUSSION

Shivering is a common complication among patients who have undergone anesthesia. Physical modalities such as intravenous infusion of warm fluids and forced air warmers can help control hypothermia, but they are not always readily available. Forced air warmers are typically administered postoperatively, whereas infusing prewarmed fluids to prevent shivering is not routinely performed in our institution. The mainstay treatment for shivering remains pharmacological due to inadequate control of central hypothermia caused by anesthesia. As a result, it makes sense to prevent shivering rather than treat it once it occurs. The findings of our study indicate that Paracetamol has the potential to reduce the incidence of shivering, as 71% of those in the paracetamol group did not experience shivering. Esmat published a study in 2021 that found Paracetamol and Dexamethasone to be effective in preventing shivering in patients undergoing lower abdominal and limb surgeries under neuraxial anesthesia.[32] Given the role of Paracetamol in inhibiting prostaglandin synthesis as well as its effect on the descending serotonergic pathways in the central nervous system, the fact that it is both an anti-shivering and analgesic agent is a strong point to consider. Furthermore, the second point to consider is its wide safety profile, as Paracetamol is safe to use in pregnant patients and children. Third, in addition to the benefits mentioned previously, it was also evident in the study that, while not statistically significant, Paracetamol leads to greater satisfaction as evidenced by higher satisfaction mean scores among participants due to fewer side effects experienced. Finally, Paracetamol is easily accessible in the operating room, making it more convenient to use. This drug makes it a cost-effective shivering management protocol that could be easily implemented in our institution as well as in resource-limited areas.

LIMITATIONS

There were several limitations to this study. The present study was conducted in a ve ry short period and was carried out at one institution; hence it lacks representation of the general population. The investigators, on the other hand, believed that the randomized, double-blind design and effect size estimation reduced the possibility of bias. Another limitation was the absence of meperidine as a control group due to its unavailability. Lastly, there was a failure to identify the sources of dissatisfaction, both from Paracetamol and placebo groups.[39]

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Platelet-Rich Plasma Injection of Skin Graft in a Patient with Squamous Cell Carcinoma and Psoriasis on Prolonged Methotrexate Therapy: A Case Report

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Abstract

Introduction: Psoriasis and some of its treatments such as methotrexate have been linked to the development of non-melanoma skin cancers including cutaneous squamous cell carcinoma (cSCC). Chronic plaque psoriasis, Koebnerization, and prolonged methotrexate therapy are some of the concerns that may impact wound healing and graft uptake when treating these patients.

Case Report: We report a case of a 64-year-old male with a 32-year history of moderate to severe psoriasis continuously self-medicating with methotrexate for 30 years who presented with a solitary indurated tumor with ulceration on the right anterior leg. Histopathology result revealed acantholytic cSCC. The patient concomitantly has generalized psoriatic plaques that complicated the selection of donor site for the skin graft, and raised concerns on wound healing and graft uptake. He underwent wide excision surgery with gastrocnemius (medial head) flap and split thickness skin graft. Platelet-rich plasma (PRP) injections were utilized post-operatively to increase graft survival and donor site regeneration.

Discussion: The main risk factors for the development of cSCC for this patient are the history of chronic plaque psoriasis and chronic methotrexate therapy. These two can also complicate the success of grafting and wound healing for this patient. PRP was utilized to for better graft survival, faster wound healing, and prevention of Koebnerization.

Keywords: *Platelet-rich plasma, squamous cell cancer, psoriasis, methotrexate*

INTRODUCTION

Psoriasis is a chronic disease characterized by skin inflammation and epidermal hyperplasia. It has multisystemic involvement, and is associated with increased risk of developing arthritis, cardiovascular morbidity, metabolic syndrome, psychosocial challenges (1), and less commonly, nonmelanoma skin cancer (NMSC) (2). Although systemic therapies have resulted in a significant reduction in disease burden for these patients, concerns regarding their association with malignancy persist (3). One of the most highly effective treatment for chronic plaque psoriasis is methotrexate, which has been found to have a 2.8-fold increased risk for NMSC (4). The most common NMSC in immunosuppressed patients is cutaneous squamous cell carcinoma (cSCC) (1). The prevalence of cSCC in patients with psoriasis is not known.

Standard treatment of cSCC is wide excision (5). In patients with active skin inflammation such as psoriasis, concerns on wound healing and successful graft uptake arise. Koebnerization may also occur in the donor site (6). Furthermore, there are uncertainties on the effects of methotrexate on wound healing and successful graft uptake (7).

We report a case of a 64-year-old male with chronic plaque psoriasis who developed cSCC. The patient underwent wide excision with flap and skin graft, and platelet-rich plasma was utilized to ensure good wound healing and successful graft uptake.

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CASE REPORT

A 64-year-old male with a 32-year history of chronic plaque psoriasis, on chronic methotrexate therapy with a cumulative dose of 4,000 mg, presented with a 10-month history of slow growing tumor on the right anterior leg. The lesion started as a yellow to brown, tender plaque, which was unresponsive to initial treatment with antibiotics. In the interim, there was a gradual increase in size, evolving into a brownish, ulcerated tumor. Notably, the patient had 40- pack year history of smoking, and no history of chronic UV exposure, though he underwent 30 sessions of narrowband UVB phototherapy 26 years prior. Progression prompted referral to our institution for further evaluation.

Cutaneous examination revealed a solitary, well-defined, brownish tumor with an overlying ulceration, measuring 3x3 cm on the right anterior leg (Figure 1). His psoriasis was also in flare, presenting as multiple, well-defined erythematous plaques with white adherent scales all over the body, onychodystrophy, and palmoplantar keratoderma (Figure 2.). Incisional biopsy of the tumor revealed neoplastic squamous cells invading into the underlying dermis, mild to moderate nuclear pleomorphism, enlarged round to oval hyperchromatic to vesicular nuclei, prominent nucleoli, detached neoplastic keratinocytes, and occasional keratin pearls (Figure 3). The clinical and histopathologic findings were consistent with acantholytic squamous cell carcinoma, well-differentiated. The patient was then referred to General Surgery for wide excision with skin graft.

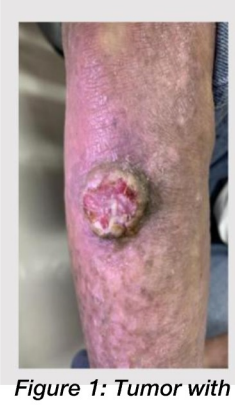

Figure 1: Tumor with ulceration on the right pretibial area

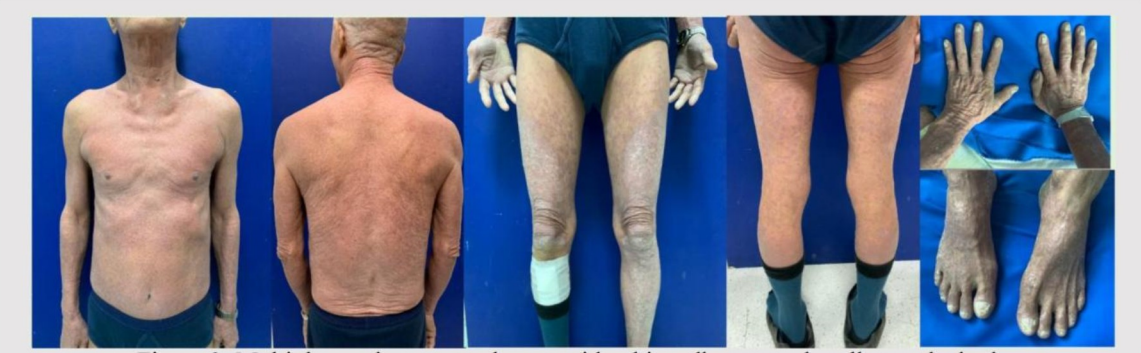

Figure 2: Multiple, erythematous plaques with white adherent scales all over the body

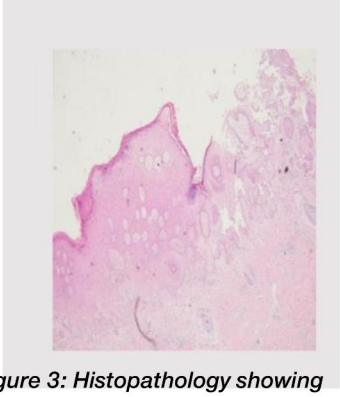

Figure 3: Histopathology showing acantholytic squamous cell carcinoma

Selection of the donor site for the skin graft was complicated by the patient's ongoing psoriasis flare. The right anterior thigh was selected as the donor site as it had less erythematous plaques compared with his trunk and upper extremities. Methotrexate 10 mg/week was continued, and clobetasol propionate 0.05% cream was applied on the area twice daily for 2 weeks prior to surgery to further decrease the inflammation. Wide excision with frozen section was done leaving a skin defect of 7 x 7 cm. Lazy S incision was done on the posterior part of the right leg, and a gastrocnemius (medial head) flap was created, which was applied on the wound bed. Split thickness of 0.6 cm graft was harvested from the right medial thigh, and was apposed to the wound bed (Figure 4).

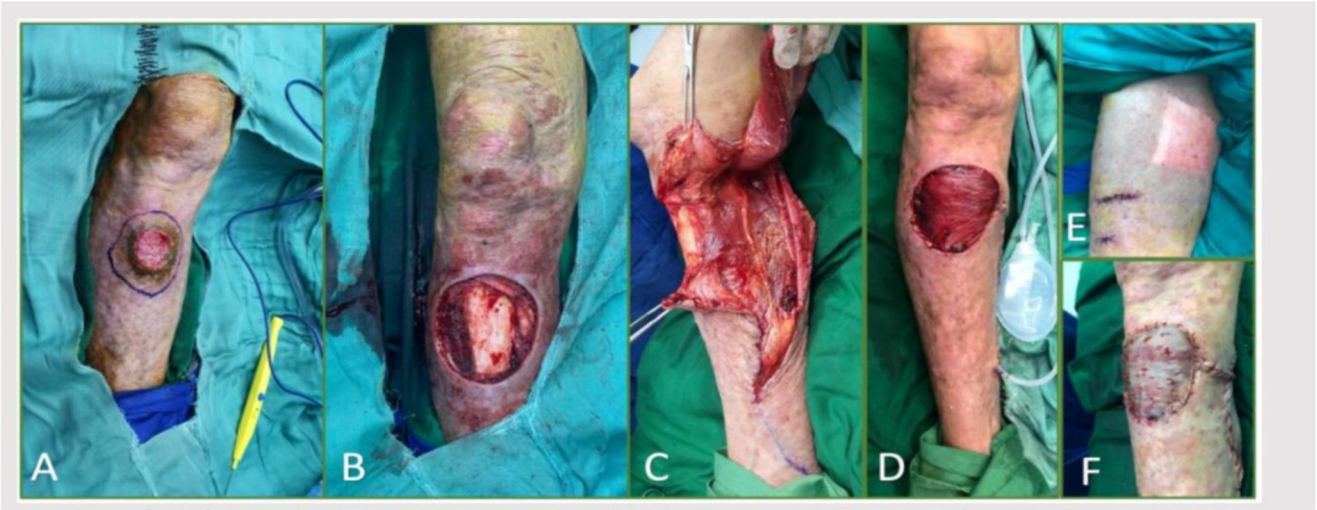

Figure 4: (A) 3.5 cm wide fungating tumor with marking of nearest excision margin at 1 cm. (B) 7x7 cm skin defect. (C & D) Gastrocnemius (medial head) flap. (E) 0.6 cm split thickness skin graft. (F) Skin graft apposed to the wound bed

On the 12th postoperative day, the recipient site showed partial separation of the edges of the incision site and yellow devitalized tissue were noted on the medial part of right leg (Figure 5) although there was no evidence of infection and graft failure. On the other hand, the donor site showed no evidence of extension or flare-up. To facilitate wound healing and increase graft survival, debridement of the yellow devitalized tissue was done, and platelet-rich plasma (PRP) was then injected intradermally on both the donor and recipient sites. He was monitored and treated with PRP every week. On his 33rd postoperative day and after his 4th PRP injection, the recipient site showed better graft survival, wound healing, and almost complete coaptation of the graft and surrounding normal skin. There was decrease in the size of previously dehisced wound with less edema and erythema. The donor site showed re-epithelialization (Figure 6).

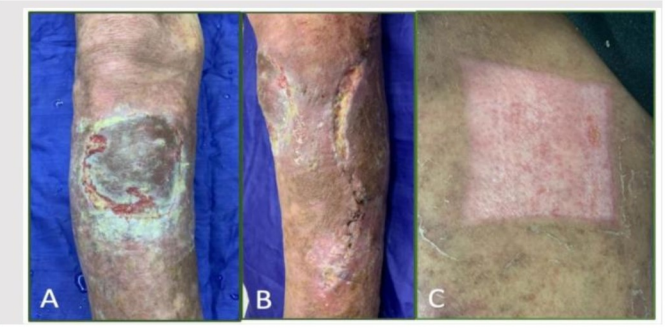

Figure 5. (A&B) Pre-PRP injection of recipient site (C) Pre-PRP injection of donor site

On follow-up, the patient had intermittent flares of psoriasis for which he was treated with methotrexate and topical steroids. The grafted site continued to heal which showed less hyperpigmentation and better texture (Figure 7). Additionally, the psoriasis lesions eventually showed improvement.

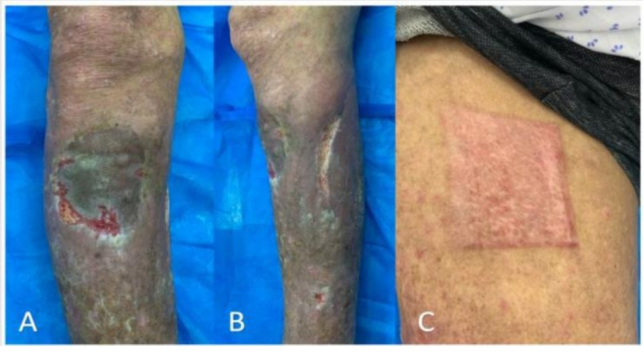

Figure 6. 33 days postoperative and after 4th PRP injection. (A&B) recipient site (C) Donor site

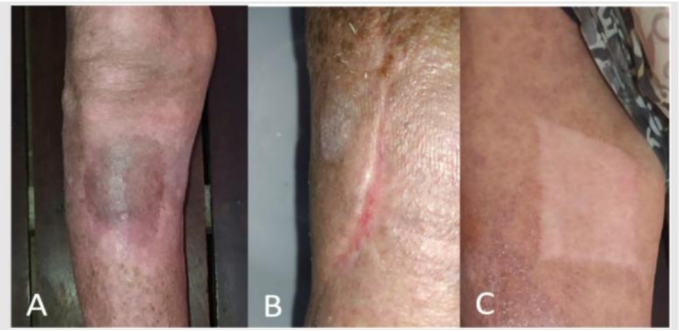

Figure 7. 104 days postoperative and 69th day from the 4th PRP injection. (A&B) recipient site (C) donor site (photos sent by the patient via teledermatology)

DISCUSSION

cSCC is the second most common skin cancer in immunocompetent individuals but the most common skin cancer in the immunosuppressed. Although the main environmental risk factor for cSCC is UV exposure, other risk factors include light skin complexion, exposure to arsenic or environmental carcinogens, immunosuppression, chronic use of photosensitizing drugs, long-term therapy with psoralen plus UVA radiation, HPV infection, and chronic inflammation of the skin (1).

For our patient, it appears that the main risk factors for the development of cSCC are the history of chronic plaque psoriasis and chronic methotrexate therapy. The link between psoriasis and the risk of NMSC is still unknown although one study by Wang et al. found out that patients with psoriasis had 1.72 times higher risk of developing NMSC (2). Aside from phototherapy, several therapeutic options for psoriasis, such as methotrexate, cyclosporine, and tumor necrosis factor-a inhibitors, have also been associated with increased malignancy risk (3). However, studies on methotrexate show conflicting findings. A study by Filippos et al. found that the use of methotrexate was linked to an elevated incidence of cSCC in patients with psoriasis. (8). Lang et al similarly found that both psoriasis and the use of methotrexate are associated with an increased risk of NMSC (4). However, a more recent study by Geller et al. showed that there was no increased risk for malignancy with low-dose methotrexate monotherapy of <30 mg/week orally, or 17.5–22.5 mg/week subcutaneously (3).

The primary therapeutic option for cSCC is wide excision (5). Skin graft transplantation is recommended for larger defects to improve cosmetic outcomes, as was the case for our patient. There is limited evidence on performing skin grafting in the background of chronic inflammatory diseases such as psoriasis. Due to the active psoriatic lesions on the donor site, there were several concerns regarding the success of skin grafting in active skin inflammation, including delay in wound healing, the possibility of Koebner phenomenon, and the risk of developing of psoriatic plaques on the graft. (6) Furthermore, there were uncertainties on the effects of methotrexate on wound healing and graft uptake (7).

The potential for poor wound healing may be explained by the pathophysiology of psoriasis with inappropriate activation of cutaneous cellular immunity inducing hyperplasia of keratinocytes with rapid and incomplete differentiation (6). However, Young et al. revealed no significant differences in the healing of traumatic wounds between psoriasis patients and non-psoriasis patients (6). In addition, in vitro and experimental studies suggest that methotrexate adversely affects wound healing. There was one report of graft failure possibly due to methotrexate therapy (7). In contrast, another study showed that low-dose methotrexate is safe and does not affect the incidence of postoperative wound complication (9).

Although current evidence is limited, platelet-rich plasma (PRP) injection has been shown to increase graft take. Several studies have been done PRP for diabetic foot ulcers, venous leg ulcers and burns (10). However, data regarding the use of PRP as an adjunct treatment for skin graft in the context of cSCC and psoriasis is lacking. PRP is an autologous blood-derived biomaterial that has 2- to 6- fold concentration of platelets, multiple growth factors (PFGF, EGR) and anti-inflammatory components. It promotes wound closure, stable adhesion of skin graft and increase oxygen diffusion. In addition, they may play a significant role in inhibiting infection (10). These could contribute to better

graft survival and faster healing of the wound. After several sessions of PRP in our patient, we noted graft take, contraction of the previously dehisced wound, faster regeneration of the donor site, and prevention of Koebnerization.

After treatment for cSCC, the National Comprehensive Cancer Network (NCCN) advises regular follow up, sun-protective measures, and frequent self-examination of the skin. Patients with a history of cSCC have a higher risk of developing new cSCC. Regular follow up every 3-12 months for 2 years is essential for early detection of new lesions (11). Our patient is regularly monitored and had no recurrent or new cSCC after 4 months post-operation.

CONCLUSION

Several studies have linked psoriasis and methotrexate to the development of cSCC. As such, it is important to conduct regular full body examination of the skin on psoriasis patients with a risk for developing cSCC. Surgical management is the treatment of choice for cSCC. Due to limited evidence, there are no guidelines for the treatment of psoriasis patients with concomitant cSCC despite concerns of poor wound healing and poor graft uptake. Though further studies are needed to strengthen the evidence, PRP injection appears to be a promising adjunct treatment to improve wound healing and graft survival in these patients.

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Gastrointestinal Manifestations and Health Outcomes in Patients with COVID-19 Infection in a Tertiary Hospital

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Abstract

Objectives: to determine the frequencies of gastrointestinal manifestations and identify associations with outcomes among COVID-19 patients admitted in a tertiary hospital. Furthermore, it sought to determine conditions and risk factors that can be attributed to the development of these gastrointestinal symptoms.

Materials and Methods: This was a retrospective cohort of 1212 adult patients admitted at the Philippine General Hospital from April to September 2020 for COVID-19 infection. Data were gathered from an established database and chart review. Frequencies of observations were tabulated and expressed in percentages. Analytical statistics via the Fisher's Exact test was used to determine associations.

Results: A total of 597 observations of gastrointestinal symptoms was noted: diarrhea (16.4%), anorexia (13.3%), ageusia/dysgeusia/hypogeusia (7.7%), vomiting (4.5%), abdominal discomfort (4.7%), nausea (1.7%), and gastrointestinal bleeding (0.7% - [melena 0.5%, hematochezia 0.16%, hematemesis 0.08%]). Most of these patients had moderate COVID infection (38.37%). Gastrointestinal bleeding was significantly associated with the need for oxygen support (p = 0.009), invasive ventilation (p = 0.002), invasive ventilation (p= 0.001), ICU admission (p = 0.006) and mortality (p= 0.006). Anorexia was significantly associated with the need for oxygen support (p = <0.001), invasive ventilation (p= <0.001), renal replacement therapy (p = 0.003), ICU admission (p = <0.001) and mortality (p = <0.001). Vomiting was significantly associated with need for invasive ventilation (p = 0.023) and renal replacement therapy (p = 0.003).

Conclusion: Gastrointestinal manifestations can present among patients with COVID-19 infection and can affect overall prognosis.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) is an infectious disease caused by a new strain of coronavirus (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]) and was unknown before an outbreak was documented in Wuhan, China last December 2019.[1] Since its inception, many countries had been affected, crippling economic machineries and taking away lives. During the time of this writing, across 5 continents, at least a 103 million confirmed cases with at least 2.2 million deaths had already been documented.[2] The Philippines has not been spared and as of January 27, 2021, a total of at least 524 thousand cases with 10 thousand deaths had been recorded.[3] These figures are still continuing to grow.

It has been widely reported that respiratory symptoms, such as fever, dry cough and dyspnea, are the most frequent manifestations of COVID-19 infection. However, the incidence of less common features like diarrhea, nausea, vomiting, ageusia/dysgeusia/ hypogeusia, abdominal discomfort and gastrointestinal bleeding have as well been documented; these varies significantly among different study populations, presenting frequently with early and mild onset followed by the typical respiratory symptoms.[4]

Gastrointestinal Manifestations of COVID-19

Emerging data suggest that the gastrointestinal tract and the liver might also be affected by SARS-CoV-2, on the basis that gastrointestinal epithelial cells and

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liver cells express angiotensin-converting enzyme 2 (ACE2), the major receptor of SARS-CoV-2.[5] Furthermore, patients can present with a multitude of gastrointestinal manifestations such as anorexia, vomiting and abdominal pain as a systemic viral response. Diarrhea can also be present, which was the most common symptom in both adults and children. Although the specific mechanisms involved in diarrhea pathogenesis are not entirely known, viral infection is likely to cause an alteration of intestinal permeability, resulting in enterocyte malabsorption.[6]

Data on Frequency of Gastrointestinal Manifestations of COVID-19

Two systematic reviews and meta-analysis were published showing data on the frequency of gastrointestinal manifestations of COVID-19.

A study done by Cheung, et. al.[7] reviewing 60 studies with data on GI symptoms (4243 patients) had shown that the pooled prevalence of GI manifestations was 18%. The most common symptom was anorexia (27%), followed by diarrhea (12%), nausea and vomiting (10%), and abdominal pain (9%). Prevalence of GI symptoms was 17% in patients with severe disease compared with 12% in those with non-severe disease and was similar among adults, children, and pregnant women.

In a much earlier systematic review and meta-analysis published in The Lancet Gastroenterology & Hepatology Journal, Ren Mao and colleagues[8] analyzed data from 35 studies that included 6686 patients with COVID-19. In 29 studies (6064 cases) reporting gastrointestinal symptoms in patients with COVID-19, the pooled prevalence of digestive symptoms was 15% (95% CI 10–21), the most common of which were nausea or vomiting, diarrhea, and anorexia. Of note, the authors report that around 10% of patients presented only with gastrointestinal symptoms and without respiratory features.

Among studies involving cohorts of patients with COVID-19 infection, the latest study looking into the same interest was done by Lijing, et.al.,[9] which included 204 patients with confirmed COVID-19 cases. They found out that 103 of these individuals presented with digestive symptoms, such as lack of appetite (79%), diarrhea (34%), vomiting (4%), and abdominal pain (2%). They reported of six patients with only digestive manifestations present during the whole course of the disease.

Presently, no data has been published in the local settings regarding the frequency and characteristics of gastrointestinal manifestations among Filipino COVID-19 patients.

Clinical Implications of Gastrointestinal Manifestations of COVID-19

There are contradictory results among studies in terms of association of presence of gastrointestinal symptoms with more severe COVID-19 illness.[10] A systematic review of four studies by Gul, et. al.[11] showed that the presence of gastrointestinal symptoms were equivocally related with mortality (pooled OR 0.91, 95% CI 0.49-1.68) and shows a trend to the development of ARDS (pooled OR 2.94, 95% CI 1.17-7.40). Additional studies are needed to clarify this.

RESEARCH QUESTION

Among adult patients diagnosed with COVID-19 infection, how frequent are gastrointestinal manifestations and how do the presence of these manifestations affect the over- all prognosis and health outcomes of infected patients?

OBJECTIVES

General Objectives:

To determine the frequency of gastrointestinal manifestations among COVID-19 patients and correlate these with health outcomes among patients admitted in the Philippine General Hospital from April 1, 2020 to September 30, 2020

Specific Objectives:

1. To determine the frequency and characteristics of the gastrointestinal symptoms of patients with COVID-19 infection, specifically:
    a. Nausea and Vomiting

b. Anorexia
c. Dygeusia/Ageusia/Hypogeusia
d. Diarrhea
e. Abdominal pain/discomfort
f. Gastrointestinal bleeding presenting as coffee-ground vomiting, melena, hematochezia or hematemesis

2. To determine prior conditions and risk factors that can be attributed and correlated to the development of gastrointestinal symptoms among these patients, specifically:
    a. Comorbidities: heart disease, hypertension, diabetes, chronic lung diseases, (asthma and COPD), chronic liver disease, active tuberculosis, chronic kidney disease, HIV infection, prior stroke/neurologic diseases and malignancies.
    b. Smoking, alcohol intake and illicit drug use

3. To determine association between the presence of gastrointestinal manifestations and health outcomes among these patients, specifically:
    a. Need for Oxygen Support
    b. Need for Invasive ventilation/Intubation c. Need for ICU admission
    c. Need for Renal Replacement Therapy e. Mortality

METHODOLOGY

Study Design and Setting

This was a retrospective cohort study of patients admitted at the COVID wards of the Philippine General Hospital admitted from April 1, 2020 to September 30, 2020.

Data were gathered through an established database and chart review of medical records of adult patients with laboratory-confirmed COVID-19 infection admitted at the designated COVID wards of the Philippine General Hospital.

Study Population and Sampling

A total of 1212 patients were included in this study. Purposive sampling was utilized for the inclusion of patients in this study. Eligibility of the included patients was guided by the following criteria:

Inclusion criteria: Adult patients aged ≥ 18 years old with laboratory – confirmed COVID-19 positive test admitted at the Philippine General Hospital form April 1, 2020 to September 30, 2020

Exclusion criteria: pediatric patients

Definition of Terms

a. Previous Classification of Disease Severity use by Chinese Center for Disease Control and Prevention[12]

    Mild to moderate – patients with mild symptoms up to mild pneumonia
    Severe – patients with dyspnea, hypoxia, or >50% lung involvement on imaging
    Critical – patients with respiratory failure, shock, or multiorgan system dysfunction

DATA COLLECTION AND STATISTICAL ANALYSIS

Data Collection and Monitoring

a. Data Collection Instruments – The data were collected by handpicking data by the principal investigator and co-investigators from an existing COVID-19 database collated and anonymized by the Department of Medicine, Division of Infectious diseases. In case there was no data or the data is incomplete on the signs/symptoms and laboratories in the database, the patients' charts were retrieved for review upon request for de-anonymization of the database from the department. Other laboratory tests which may not be available on the chart will be retrieved via OpenMRS™ software that is provided readily by the hospital to all authorized physicians.

b. Data Management – Data were encoded by the principal investigator through the use of the data collection forms and the dummy tables. Appropriate patient code were assigned to each individual patient to ensure anonymity.

c. Data Protection Plan – In the event that de-anonymization of the database were needed for further data collection, all records retrieved that link an individual patient to a specific information were kept in confidence and were not released. Only the investigators of this study had access to the data. In case of breach in privacy and confidentiality, reports were forwarded to the PGH Data Privacy Officer for mitigation.

d. Data Archiving – Data were kept under lock and key by the principal investigators and co-investigators. Data will be stored for at least 1 year from the publication of this paper. Data were encoded in word and excel formats. These are encrypted and stored in dedicated hard drives only accessible by the principal investigator of this study.

Statistical Analysis

Frequencies of observations were tabulated and expressed in percentages. To determine associations, the Fisher exact test was used for statistical analysis given that the data were not normally distributed. All statistical analyses were performed using SPSS 22.0. The significance level recognized was at a P value of < 0.05.

ETHICAL CONSIDERATIONS

The study was conducted upon the approval of the Technical Review Board (TRB) of Department of Internal Medicine and PGH-Expanded Health Research Office (EHRO).

Informed Consent

Since the research presented no more than minimal risk due to its nature being only a retrospective review, informed consent for this study was waived for the chart review part. This was approved by the UP-Medicine Research Ethical Board (UPMREB) after application and assessment by the said board.

A request for a waiver of consent was requested from the UPMREB panel for this study for the following reasons, in accordance with the National Ethical Guidelines for Health and Health-Related Researches, provisions 17.1-17.4, page 16:

- The research presents no more than minimal risk.
- The waiver or alteration will not adversely affect the rights and welfare of the participants.
- This research cannot be practicably carried out without the waiver of informed consent.

Autonomy

Collection of the data through chart review as well as its interpretation were not foreseen to directly affect the patient's welfare. More importantly, ensuring confidentiality in handling patient's data was consistently implemented throughout the study. Reference numbers were assigned to cases reviewed to maintain patient's anonymity.

Beneficence

Despite the absence of direct benefit to included subjects in the study, determining the clinical profile, presence of gastrointestinal manifestations and possibly establishing clinical associations to morbidity and mortality among laboratory confirmed COVID-19 positive patients shall significantly guide clinicians in the prioritization and formulation of a comprehensive diagnostic and management plan for future patients involved. No financial compensation were offered for participation.

Disclosure of Conflict of Interest

The investigators declared that there were no competing interests existing.

RESULTS

Characteristics of Study Participants and Frequencies of Gastrointestinal Manifestations

The baseline characteristics of the participants included in this study are seen in table 1. A total of 597 observations of gastrointestinal symptoms were reported with diarrhea (16.4%) being the most frequent symptom. All gastrointestinal symptoms were reported by 370 patients comprised mostly of those patients classified as moderate COVID infection (38.38%).

Table 1. Clinical characteristics of patients with COVID-19 included

Characteristics	*N=1212*
Sex	
Male	637 (52.56%)
Female	575 (47.42%)
Comorbidities	
Hypertension	582 (48.02%)
Diabetes Mellitus	310 (25.58%)
Heart Disease	165 (13.62%)
Chronic Kidney disease	107 (8.83%)
Chronic Liver Disease	11 (0.91%)
COPD	29 (2.40%)
Asthma	87 (7.18%)
Active TB	34 (2.81%)
HIV	7 (0.58%)
Malignancies	69 (5.69%)
Neurologic	83 (6.90%)
Vices	
Smoker Significant Alcohol Use Illicit Drug Use	258 (21.29%) 287 (23.68%) 22 (1.82%
Severity of Illness:	
Mild Moderate Severe Critical	203 (16.75%) 487 (40.18%) 182 (15.02%) 340 (28.05%)
Outcomes:	
Need for ICU Admission	459 (37.87%)
Need for O2 Support	661 (54.54%)
Need for Invasive Ventilation/Intubation	241 (19.98%)
Need for Renal Replacement Therapy	113 (9.32%)
Discharged/Recovered Expired	993 (81.93%) 219 (18.06%)

Table 2. Frequencies of GI Manifestations

	N = 597
Anorexia	161 (13.3%)
Ageusia/Dysgeusia/Hypogeusia	94 (7.7%)
Nausea	21 (1.7%)
Vomiting	55 (4.5%)
Diarrhea	199 (16.4%)
Abdominal Discomfort	58 (4.7%)
GI Bleeding	9 (0.7%)
Coffee-ground vomiting	0
Hematemesis	1 (0.08%)
Melena	6 (0.5%)
Hematochezia	2 (0.16)

Table 3. Over-all frequency of patients presenting with GI symptoms and over-all COVID disease severity of these patients stratified from mild to critical

	N = 370
Mild	71 (19.2%)
Moderate	142 (38.38%)
Severe	58 (15.68%)
Critical	99 (26.75%)

Association of Health Determinants/Risk Factors with Gastrointestinal Symptoms

Table 4.1 shows the different p-values showing associations between the different surveyed health determinants/risk factors and the different surveyed GI manifestations reported for this study with values <0.05 considered as significant associations.

The following associations were observed:

- DIARRHEA - A history of illicit drug use, HIV infection, cancer and neurologic disease were significantly associated with the presentation of diarrhea.
- NAUSEA - A history of hypertension, chronic kidney disease and neurologic disease were significantly associated with the presentation of nausea.
- VOMITING - Chronic kidney disease was significantly associated with the presentation of vomiting.
- ABDOMINAL PAIN/DISCOMFORT - Diabetes Mellitus, HIV infection as well as malignancy were significantly associated with the presentation of abdominal pain/discomfort.
- MELENA - A history of heart disease and chronic kidney disease were significantly associated with the presentation of melena.

Table 4. Cross-table reference for health determinants/risk factors with the different GI manifestations

		DIARRHEA			NAUSEA			VOMITING			ANOREXIA			ABDOMINAL PAIN / DISCOMFORT		
		(-)	(+)	p-value	(-)	(+)	p-value	(-)	(+)	p-value	(-)	(+)	p-value	(-)	(+)	p-value
SMOKER	(-)	785	169		937	17		915	39		825	129		908	46	
	(+)	228	30	0.018	254	4	1.000	242	16	0.176	226	32	0.680	246	12	1.000
ALCOHOL BEVERAGE DRINKER	(-)	764	161		908	17		889	36		805	120		883	42	
	(+)	249	38	0.101	283	4	0.797	268	19	0.072	246	41	0.552	271	16	0.526
ILLICIT DRUG USE	(-)	991	199		1169	21		1135	55		1030	160		1132	58	
	(+)	22	0	0.037*	22	0	1.000	22	0	0.620	21	1	0.344	22	0	0.621
DM	(-)	749	153		887	15		858	44		788	114		851	51	
	(+)	264	46	0.424	304	6	0.801	299	11	0.429	263	47	0.286	303	7	0.013*
HPN	(-)	527	103		624	6		604	26		560	70		596	34	
	(+)	486	96	1.000	567	15	0.045*	553	29	0.493	491	91	0.022	558	24	0.346
HEART DISEASE	(-)	868	179		1028	19		1000	47		908	139		996	51	
	(+)	145	20	0.115	163	2	0.757	157	8	0.840	143	22	1.000	158	7	0.846
CHRONIC LIVER DISEASE	(-)	1004	197		1180	21		1146	55		1040	161		1145	56	
	(+)	9	2	0.699	11	0	1.000	11	0	1.000	11	0	0.377	9	2	0.094
CHRONIC KIDNEY DISEASE	(-)	919	186		1090	15		1062	43		956	149		1054	51	
	(+)	94	13	0.273	101	6	0.007*	95	12	0.002*	95	12	0.654	100	7	0.344
COPD	(-)	985	198		1162	21		1129	54		1026	157		1127	56	
	(+)	28	1	0.071	29	0	1.000	28	1	1.000	25	4	1.000	27	2	0.646
ASTHMA	(-)	946	179		1107	18		1071	54		977	148		1073	52	
	(+)	67	20	0.098	84	3	0.187	86	1	0.175	74	13	0.623	81	6	0.300
ACTIVE TB	(-)	983	195		1158	20		1126	52		1023	155		1122	56	
	(+)	30	4	0.639	33	1	0.453	31	3	0.197	28	6	0.440	32	2	0.676
HIV	(-)	1011	194		1184	21		1150	55		1045	160		1149	56	
	(+)	2	5	0.002*	7	0	1.000	7	0	1.000	6	1	1.000	5	2	0.040*
CANCER	(-)	947	196		1123	20		1092	51		994	149		1094	49	
	(+)	66	3	0.004*	68	1	1.000	65	4	0.549	57	12	0.277	60	9	0.004*
NEUROLOGIC DISEASE	(-)	934	195		1112	17		1079	50		983	146		1075	54	
	(+)	79	4	0.002*	79	4	0.050*	78	5	0.419	68	15	0.181	79	4	1.000

Table 4. continued

		AGEUSIA / HYPO / DYSGEUSIA			HEMATEMESIS			COFFEE-GROUND VOMITING			MELENA			HEMATOCHEZIA		
		(-)	(+)	p-value	(-)	(+)	p-value	(-)	(+)	p-value	(-)	(+)	p-value	(-)	(+)	p-value
SMOKER	(-)	879	75		953	1		954	0		950	4		952	2	
	(+)	239	19	0.896	258	0	1.000	258	0	no test	256	2	0.613	258	0	1.000
ALCOHOL BEVERAGE DRINKER	(-)	854	71		924	1		925	0		921	4		923	2	
	(+)	264	23	0.899	287	0	1.000	287	0	no test	285	2	0.632	287	0	1.000
ILLICIT DRUG USE	(-)	1099	91		1189	1		1190	0		1184	6		1188	2	
	(+)	19	3	0.240	22	0	1.000	22	0	no test	22	0	1.000	22	0	1.000
DM	(-)	833	69		901	1		902	0		896	6		901	1	
	(+)	285	25	0.806	310	0	1.000	310	0	no test	310	0	0.347	309	1	0.446
HPN	(-)	587	43		629	1		630	0		627	3		628	2	
	(+)	531	51	0.237	582	0	1.000	582	0	no test	579	3	1.000	582	0	0.500
HEART DISEASE	(-)	964	83		1047	0		1047	0		1044	3		1045	2	
	(+)	154	11	0.642	164	1	0.136	165	0	no test	162	3	0.036*	165	0	1.000
CHRONIC LIVER DISEASE	(-)	1107	94		1200	1		1201	0		1195	6		1199	2	
	(+)	11	0	1.000	11	0	1.000	11	0	no test	11	0	1.000	11	0	1.000
CHRONIC KIDNEY DISEASE	(-)	1019	86		1105	0		1105	0		1102	3		1103	2	
	(+)	99	8	1.000	106	1	0.088	107	0	no test	104	3	0.011*	107	0	1.000
COPD	(-)	1089	94		1182	1		1183	0		1177	6		1181	2	
	(+)	29	0	0.161	29	0	1.000	29	0	no test	29	0	1.000	29	0	1.000
ASTHMA	(-)	1038	87		1124	1		1125	0		1119	6		1123	2	
	(+)	80	7	0.836	87	0	1.000	87	0	no test	87	0	1.000	87	0	1.000
ACTIVE TB	(-)	1085	93		1177	1		1178	0		1173	5		1176	2	
	(+)	33	1	0.511	34	0	1.000	34	0	no test	33	1	0.157	34	0	1.000
HIV	(-)	1111	94		1204	1		1205	0		1199	6		1203	2	
	(+)	7	0	1.000	7	0	1.000	7	0	no test	7	0	1.000	7	0	1.000
CANCER	(-)	1052	91		1142	1		1143	0		1137	6		1142	1	
	(+)	66	3	0.358	69	0	1.000	69	0	no test	69	0	1.000	68	1	0.111
NEUROLOGIC DISEASE	(-)	1042	87		1129	0		1129	0		1124	5		1127	2	
	(+)	76	7	0.831	82	1	0.068	83	0	no test	82	1	0.347	83	0	1.000

Association of Gastrointestinal Manifestations with In-Hospital Health Outcomes

The Fisher Exact test was used to determine associations between the presence of gastrointestinal symptoms and the outcomes that were studied, specifically the need of oxygen support, need for invasive ventilation, need for renal replacement therapy, need for ICU admission and mortality. The subsequent tables show the different p-values showing these associations.

Table 5. Cross-table reference of GI manifestations with need for oxygen support

		NEED FOR O2 SUPPORT					
		(-)		(+)		Total	
		Count	Row %	Count	Row %	Count	p-value
Diarrhea	(-)	456	45.0%	557	55.0%	1013	
	(+)	95	47.7%	104	52.3%	199	0.485
Nausea	(-)	542	45.5%	649	54.5%	1191	
	(+)	9	42.9%	12	57.1%	21	0.830
Vomiting	(-)	533	46.1%	624	53.9%	1157	
	(+)	18	32.7%	37	67.3%	55	0.054
Anorexia	(-)	512	48.7%	539	51.3%	1051	
	(+)	39	24.2%	122	75.8%	161	<0.001*
Abdominal Pain / Discomfort	(-)	522	45.2%	632	54.8%	1154	
	(+)	29	50.0%	29	50.0%	58	0.501
Ageusia / Hypo / Dysgeusia	(-)	505	45.2%	613	54.8%	1118	
	(+)	46	48.9%	48	51.1%	94	0.518
Gastrointestinal Bleeding	(-)	551	45.8%	653	54.2%	1204	
	(+)	0	0.0%	8	100.0%	8	0.009*
Hematemesis	(-)	551	45.5%	660	54.5%	1211	
	(+)	0	0.0%	1	100.0%	1	1.000
Coffee-ground Vomiting	(-)	551	45.5%	661	54.5%	1212	
	(+)	0	0.0%	0	0.0%	0	no test
Melena	(-)	551	45.7%	655	54.3%	1206	
	(+)	0	0.0%	6	100.0%	6	0.035*
Hematochezia	(-)	551	45.5%	659	54.5%	1210	
	(+)	0	0.0%	2	100.0%	2	0.504

The manifestations of anorexia (p = <0.001) and gastrointestinal bleeding (p = 0.009) were significantly associated with the need for oxygen support among the population included in this study. Sub-analysis of gastrointestinal bleeding showed that melena (p= 0.035) was significantly associated with this outcome. (Table 5)

Table 6. Cross-table reference of GI manifestations with need for invasive ventilation or intubation

		NEED FOR INVASIVE VENTILATION OR INTUBATION					
		(-)		(+)		Total	
		Count	Row %	Count	Row %	Count	p-value
Diarrhea	(-)	804	79.4%	209	20.6%	1013	
	(+)	167	83.9%	32	16.1%	199	0.146
Nausea	(-)	956	80.3%	235	19.7%	1191	
	(+)	15	71.4%	6	28.6%	21	0.282
Vomiting	(-)	934	80.7%	223	19.3%	1157	
	(+)	37	67.3%	18	32.7%	55	0.023*
Anorexia	(-)	861	81.9%	190	18.1%	1051	
	(+)	110	68.3%	51	31.7%	161	<0.001*
Abdominal Pain / Discomfort	(-)	928	80.4%	226	19.6%	1154	
	(+)	43	74.1%	15	25.9%	58	0.240
Ageusia / Hypo / Dysgeusia	(-)	891	79.7%	227	20.3%	1118	
	(+)	80	85.1%	14	14.9%	94	0.228
Gastrointestinal Bleeding	(-)	969	80.5%	235	19.5%	1204	
	(+)	2	25.0%	6	75.0%	8	0.001*
Hematemesis	(-)	971	80.2%	240	19.8%	1211	
	(+)	0	0.0%	1	100.0%	1	0.199
Coffee-ground Vomiting	(-)	971	80.1%	241	19.9%	1212	
	(+)	0	0.0%	0	0.0%	0	no test
Melena	(-)	970	80.4%	236	19.6%	1206	
	(+)	1	16.7%	5	83.3%	6	0.002*
Hematochezia	(-)	970	80.2%	240	19.8%	1210	
	(+)	1	50.0%	1	50.0%	2	0.358

The manifestations of vomiting (p = 0.023), anorexia (p = <0.001) and gastrointestinal bleeding (p= 0.001) were significantly associated with the need for invasive ventilation among the population included in this study. Sub-analysis of the gastrointestinal bleeding showed that melena (p=0.002) was significantly associated with this outcome. (Table 6)

Table 7. Cross-table reference of GI manifestations with need for renal replacement therapy

		NEED FOR RENAL REPLACEMENT THERAPY					
		(-)		(+)		Total	
		Count	%	Count	%	Count	p-value
Diarrhea	(-)	919	90.7%	94	9.3%	1013	
	(+)	180	90.5%	19	9.5%	199	0.894
Nausea	(-)	1081	90.8%	110	9.2%	1191	
	(+)	18	85.7%	3	14.3%	21	0.434
Vomiting	(-)	1056	91.3%	101	8.7%	1157	
	(+)	43	78.2%	12	21.8%	55	0.003*
Anorexia	(-)	964	91.7%	87	8.3%	1051	
	(+)	135	83.9%	26	16.1%	161	0.003*
Abdominal Pain / Discomfort	(-)	1047	90.7%	107	9.3%	1154	
	(+)	52	89.7%	6	10.3%	58	0.816
Ageusia / Hypo / Dysgeusia	(-)	1011	90.4%	107	9.6%	1118	
	(+)	88	93.6%	6	6.4%	94	0.361
Gastrointestinal Bleeding	(-)	1093	90.8%	111	9.2%	1204	
	(+)	6	75.0%	2	25.0%	8	0.167
Hematemesis	(-)	1099	90.8%	112	9.2%	1211	
	(+)	0	0.0%	1	100.0%	1	0.093
Coffee-ground Vomiting	(-)	1099	90.7%	113	9.3%	1212	
	(+)	0	0.0%	0	0.0%	0	no test
Melena	(-)	1095	90.8%	111	9.2%	1206	
	(+)	4	66.7%	2	33.3%	6	0.101
Hematochezia	(-)	1097	90.7%	113	9.3%	1210	
	(+)	2	100.0%	0	0.0%	2	1.000

The manifestation of vomiting (p = 0.003) and decreased appetite (0.003) were significantly associated with the need for renal replacement therapy among the population included in this study. (Table 7)

Table 8. Cross-table reference of GI manifestations with need for ICU admission

		NEED FOR ICU ADMISSION					
		(-)		(+)		Total	
		Count	%	Count	%	Count	p-value
Diarrhea	(-)	624	61.6%	389	38.4%	1013	
	(+)	129	64.8%	70	35.2%	199	0.424
Nausea	(-)	741	62.2%	450	37.8%	1191	
	(+)	12	57.1%	9	42.9%	21	0.655
Vomiting	(-)	724	62.6%	433	37.4%	1157	
	(+)	29	52.7%	26	47.3%	55	0.156
Anorexia	(-)	690	65.7%	361	34.3%	1051	
	(+)	63	39.1%	98	60.9%	161	<0.001*
Abdominal Pain / Discomfort	(-)	719	62.3%	435	37.7%	1154	
	(+)	34	58.6%	24	41.4%	58	0.581
Ageusia / Hypo / Dysgeusia	(-)	688	61.5%	430	38.5%	1118	
	(+)	65	69.1%	29	30.9%	94	0.152
Gastrointestinal Bleeding	(-)	752	62.5%	452	37.5%	1204	
	(+)	1	12.5%	7	87.5%	8	0.006*
Hematemesis	(-)	753	62.2%	458	37.8%	1211	
	(+)	0	0.0%	1	100.0%	1	0.379
Coffee-ground Vomiting	(-)	753	62.1%	459	37.9%	1212	
	(+)	0	0.0%	0	0.0%	0	no test
Melena	(-)	752	62.4%	454	37.6%	1206	
	(+)	1	16.7%	5	83.3%	6	0.032*
Hematochezia	(-)	753	62.2%	457	37.8%	1210	
	(+)	0	0.0%	2	100.0%	2	0.143

The manifestations of anorexia (p = <0.001) and gastrointestinal bleeding (p = 0.006) were significantly associated with the need for ICU admission among the population included in this study. Sub-analysis of the gastrointestinal bleeding showed that melena (p= 0.032) was strongly associated with this outcome. (Table 8)

Table 9. Cross-table reference of GI manifestations with mortality

		MORTALITY					
		SURVIVOR		NON-SURVIVOR		Total	
		Count	%	Count	%	Count	p-value
Diarrhea	(-)	822	81.1%	191	18.9%	1013	
	(+)	171	85.9%	28	14.1%	199	0.130
Nausea	(-)	977	82.0%	214	18.0%	1191	
	(+)	16	76.2%	5	23.8%	21	0.564
Vomiting	(-)	953	82.4%	204	17.6%	1157	
	(+)	40	72.7%	15	27.3%	55	0.074
Anorexia	(-)	879	83.6%	172	16.4%	1051	
	(+)	114	70.8%	47	29.2%	161	<0.001*
Abdominal Pain / Discomfort	(-)	948	82.1%	206	17.9%	1154	
	(+)	45	77.6%	13	22.4%	58	0.382
Ageusia / Hypo / Dysgeusia	(-)	913	81.7%	205	18.3%	1118	
	(+)	80	85.1%	14	14.9%	94	0.486
Gastrointestinal Bleeding	(-)	990	82.2%	214	17.8%	1204	
	(+)	3	37.5%	5	62.5%	8	0.006*
Hematemesis	(-)	992	81.9%	219	18.1%	1211	
	(+)	1	100.0%	0	0.0%	1	1.000
Coffee-ground Vomiting	(-)	993	81.9%	219	18.1%	1212	
	(+)	0	0.0%	0	0.0%	0	no test
Melena	(-)	991	82.2%	215	17.8%	1206	
	(+)	2	33.3%	4	66.7%	6	0.012*
Hematochezia	(-)	992	82.0%	218	18.0%	1210	
	(+)	1	50.0%	1	50.0%	2	0.329

The manifestations of anorexia (p = <0.001) and gastrointestinal bleeding (p = 0.006) were associated significantly with mortality among the population included in this study. Sub-analysis of the gastrointestinal bleeding showed that melena (p= 0.012) was strongly associated with this outcome. (Table 9)

DISCUSSION

In terms of symptomatology, diarrhea was the most predominant symptom among the surveyed cohort. At present, it is proposed that SARS-CoV-2, which via the ACE2 receptor can infect and exert a direct cytopathic effect on enterocytes causing diarrhea. Adverse drug reactions can be another possible explanation. Some of the antivirals, antibiotics and immunomodulators, commonly prescribed to COVID-19 patients are known to cause diarrhea.[12] It is yet unclear as to what may be the reason behind this presentation among this surveyed cohort.

With the present data, it is still unclear as to how the different risk factors are associated with the presentation of the specific gastrointestinal manifestations. A further probe on the pathogenesis is needed to further elucidate the mechanisms behind these observed associations.

This study was able to perceive associations between the different gastrointestinal symptoms and in-hospital health outcomes. Most of the published literatures reported mostly on outcomes on ARDS development and mortality. This study was able to look into outcomes of the need for renal replacement therapy and ICU admission. It is hoped that this information be able to fill a gap of knowledge in this aspect.

Across the different literature, most of the studies have not reported of the presence of gastrointestinal bleeding as a gastrointestinal manifestation among infected COVID-19 patients.[12]

This study was able to document 8 observations of gastrointestinal bleeding. Yet due to a small number of observations, it would be premature to completely establish association between the presence of COVID-19 infection and the development of gastrointestinal bleeding. A multitude of factors may be able to explain for the development of gastrointestinal bleeding for the documented cases.

There are limitations to this study. It is based on a retrospective observational study of admitted patients in a tertiary COVID referral system hospital which receives a majority of moderate to critical cases. Mild cases may be underrepresented with these given data. However, given the paucity of literature in the local setting and conflicting results from available international studies on the prognostic significance of GI involvement amidst this unprecedented rapidly evolving pandemic, this study addresses an important issue of GI tract involvement by SARS-CoV-2 and its impact on clinical. Our findings will help local clinicians triage patients better in this resource-limited setting, especially with regards to hospital admission and level of care. Larger prospective studies are necessary to elucidate the complete natural history of this disease and to confirm our findings on an even larger scale.

CONCLUSION

To our knowledge, diarrhea is the most common gastrointestinal manifestation presented by COVID-19 patients included in this study. A history of illicit drug use, HIV infection, neurologic disease, hypertension, chronic kidney disease, malignancy and heart disease may foretell the development of specific gastrointestinal manifestations. The presence of anorexia, vomiting and gastrointestinal bleeding, specifically the presentation of melena, may herald poor clinical outcomes.

RECOMMENDATIONS

Since associations have been seen among the different variables considered in this study, the investigators recommends the following:

- That further investigations be done on the etiology and pathogenesis of the development of specific gastrointestinal manifestations associated with the different health determinants/risk factors identified in this study.
- That further investigations be done to further establish a robust correlation between health outcomes and gastrointestinal manifestations given that the observations for some GI manifestations were small for this study.

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A Randomized Clinical Trial Application of Honey versus Ketoconazole 2% Shampoo for the Treatment of Seborrheic Dermatitis

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INTRODUCTION

Seborrheic dermatitis (SD) is a common chronic relapsing inflammatory skin disorder clinically characterized by poorly defined erythematous patches and scaling. SD primarily affects sebum rich areas, including scalp, face, upper chest and back.[1] Less commonly involved sites include interscapular, umbilical, perineum, and the anogenital crease.[2] The dermatitis presents with pink to erythematous, superficial patches and plaques with a yellow, branny and sometimes greasy scale.[3]

The prevalence of adult SD is estimated at 5%.[4] This condition is more common in males than in females. Among adults, the peak incidence is in the third and fourth decades of life. In the Jose R. Reyes Memorial Medical Center Department of Dermatology, it is one of the most commonly seen cases in the outpatient department with a total of 390 cases seen last 2014. Although the exact cause of SD has yet to fully elucidated, Malassezia yeasts, hormones (androgens), sebum levels and immune response are known to play important roles in its etiopathogenesis.[5] Some researchers propose a pivotal role for Malassezia yeasts (formerly called Pityrosporum ovale) in seborrheic dermatitis.[6] Antifungal therapy leads to decreased colonization with Malassezia spp. and concomitant disappearance of skin lesions, which is probably the strongest evidence that Malassezia spp. Have momentous role in the development of SD.[7] Other therapeutic options include corticosteroids, immunomodulators and antibiotics.

Honey is a by-product of flower nectar and the upper aero-digestive tract of the honey bee, which is concentrated through a dehydration process inside the beehive. Honey has a very complex chemical composition that varies depending on the botanical source. It has been used both as food and medicine since ancient times. Human use of honey is traced to some 8000 years ago as depicted by Stone Age paintings. In addition to important role of natural honey in the traditional medicine, during the past few decades, it was subjected to laboratory and clinical investigations by several research groups and it has found a place in modern medicine. Honey has been reported to have an inhibitory effect on around 60 species of bacteria, some species of fungi and viruses. Antioxidant capacity of honey is important in many disease conditions and is due to a wide range of compounds including phenolics, peptides, organic acids, enzymes, and Maillard reaction products. Honey has also been used in some gastrointestinal, cardiovascular, inflammatory and neoplastic states.[8]

The mainstay management of seborrheic dermatitis includes topical corticosteroids, antifungals, coal tar, metronidazole and topical calcineurin inhibitors. Several studies had shown ketoconazole as an effective treatment for seborrheic dermatitis[9,10]. Most medications for seborrheic dermatitis, however, are expensive, inaccessible, and some are associated with adverse side effects. Hence, it is important to find a cost-effective alternative treatment especially for use in a developing country such as the Philippines.

An open label pilot study was done in Jose R Reyes Memorial Medical Center on 2016 by the primary investigator and Dr. Zharlah Gulmatico-Flores, M.D, F.P.D.S which showed significant improvement from the patients treated using diluted honey.

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METHODOLOGY

This study started upon receiving the approval from the Institutional Review Board and Institutional Ethics Committee of Jose R. Reyes Memorial Medical Center. The nature and purpose of the study were described to potential subjects. Comprehensible verbal and written (English and Tagalog) instructions were given in detail. All patients who were voluntarily willing to participate were asked to sign a written informed consent before admission to the study. Eligible patients were initially seen and examined by the primary investigator. The skin was gently cleansed with hypoallergenic soap prior to measurement of erythema index using Mexameter®. The sites measured were indicated in the data sheet and were the same throughout the course of the study. Subjects for both honey group as well as ketoconazole group were instructed to apply the (dilution 1:1) solution once every other day on the lesions with gentle rubbing for 2-3 minutes. For the honey group, honey was rinsed with warm water after three hours. While for the ketoconazole group, the solution was rinsed with water after 10 minutes. No soap or cleanser needed. The patients were monitored for changes in color, itching and scaling by the primary investigator with two other co-residents during the treatment period every two weeks until 4 weeks. Firm instruction was given not to apply any other creams, lotions, or powders to areas under active treatment.

Materials

Pure honey was obtained from a honeybee farm "Ilog Maria" in Tagaytay. Virgin honey is produced by Italian honeybees from floral nectar collected in the cool and clean highlands of Silang, Cavite. Nectar was gathered from profuse blooms of sunflower, avocado, mango, coffee, citrus, fruit trees, wild vines and wildflowers. Honey was authenticated by the Institute of Biological Sciences, College of Arts and Science at the University of Philippines Los Baños. Ketoconazole 2% shampoo was obtained from a pharmaceutical company.

STUDY SUBJECTS

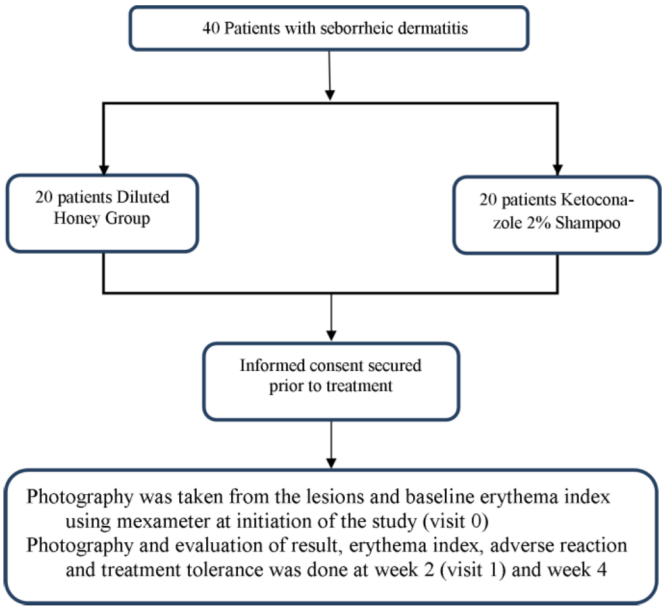
Inclusion criteria:

1. Aged over 18 years old of any gender and race
2. With stable or exacerbating seborrheic dermatitis of the face.
3. Patients without previous treatment or with more than 5 days without any topical or systemic treatment.
4. Patient's written acceptance to participate in the study.

Exclusion criteria:

1. Patients with: decompensated diabetes mellitus, cancer in advanced stage, severe septic stage, hepatopathy, nephropathy, pregnancy.
2. Hypersensitivity to the medications.
3. Patients who receive concomitant topical treatments of the scalp/face or any non-systemic treatments with antifungal agents, corticosteroids, retinoids, erythromycin, tetracycline or derivatives, trimethoprim and/or sulfamethoxazole, or cytostatic or immunomodulating drugs for 4 weeks before the start of treatment.
4. Other medical conditions that prevent compliance with the protocol.
5. Those who are immunocompromised.

Conceptual Flowchart



STATISTICAL ANALYSIS

Statistical analysis was done using SPSS 16.0 to evaluate the comparison between honey and ketoconazole. Descriptive analysis was done by computing the frequency and central tendency measures of demographic variables. Both tests were used to determine the normality of the data. ANOVA of repeated measures was done to determine the difference between means on baseline, day 14 and day 28. A post-hoc comparison test (Tukey) was also done if the p-value from ANOVA was <0.05.

OUTCOME MEASURES

Primary outcome measures are the clinical assessment and erythema index from baseline to end of treatment at the end of visit (week 4). Secondary outcome measure are the presence or absence of adverse reactions and subjective treatment tolerance.
Primary outcome: Clinical assessment on resolution of lesion

1. Color of lesion: change color from erythema to normal skin color was noted. Scoring was given in following manner: 0=absent, 1=mild, 2=moderate, 3=severe
2. Scaling of lesion: scoring was given in following manner: 0=absent, 1=mild, 2=moderate, 3=severe
3. Itching: scoring was given in the following manner: 0=no itching, 1=itching not affecting daily activities, 2=moderate itching affecting daily activities, 3=severe itching disturbing the sleep

Clinical clearing of lesions was assessed by the primary investigator and two co-residents on each visit. The scores were added together and averaged in order to obtain a clinical score. Clinical cure was considered if there is a reduction of ≥2 points from the mean baseline score at the end of the study.

Global physician assessment was assessed by the primary investigator and two co-residents at the end of 4 weeks of the study on each subject using a four-point scale of 4 to 0 (4=clear, 3=almost clear, 2=no change, 1=worse, 0=much worse). A score ≥3 regard as effective, scores ≤2 indicted not effective.

Subjective assessment for overall satisfaction using 5 point scale (5=greatly improved, 4=somewhat improve, 3=no change, 2=somewhat worse, 1=much worse)

Secondary Outcome: clinical and subjective assessment of adverse reaction

Erythema	0 = Absent (no difference with surrounding skin)
	1 = mild (just perceptible erythema without defined borders)
	2 = moderate (uniform erythema with sharply defined borders)
	3 = severe (bright red color and pronounced induration (edema) raised above the surrounding skin)
Itching	0 = Absent (no episode of itching)
	1 = mild (episodic itching, not disturbing daily activity
	2 = moderate (mild continuous itching, slight disturbing daily activity such as sleeping)
	3 = severe (continued itching, very disturbing daily activity, such as sleeping)
Burning	0 = Absent (no episode of burning sensation)
	1 = mild (episodic burning, not disturbing daily activity)
	2 = moderate (mild continuous burning, slight disturbing daily activity such as sleeping)
	3 = severe (continuous burning, very disturbing daily activity, such as sleeping)

A mean score of ≤1 indicated tolerability of the agent.

RESULT

Demographic Profile

Forty patients were included in the study. Majority of the patients enrolled in the study were male 22/40 (55%). The demographic profile of patients is seen in Table 1.

Variable	Honey	2% Ketoconazole	p-value
Age in Year (Mean + SD)	42.3±16.28	45.75±11.63	0.475
Gender M: F	14 (70%): 6(30%)	8 (40%): 12 (60%)	0.058

Table 1. Demographic profile (mean score)

Primary Outcomes

The clinical cure of both groups at baseline (mean of 5.32± 1.286) compared to day 28 (mean of 0.97± 0.830) showed a significantly remarkable

improvement with p-value of < 0.0001. The clinical cure between day 14 and day 28 for both honey and ketoconazole showed significant improvement with p - value of < 0.0001 for honey and 0.009 for ketoconazole. While day 14 and day 28 of treatment for both ketoconazole and honey group showed no significant different with p-value of 0.873 (day 14) and 1 (day 28). A post hoc comparison test was done which showed that as early as day 14 (p < 0.0001), there was a remarkable improvement.

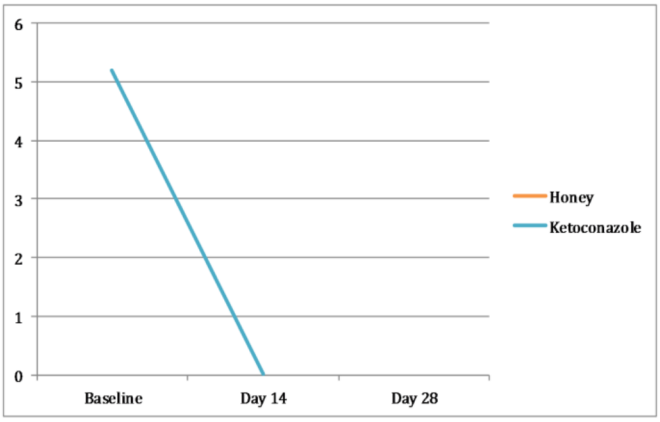


Figure 1. Clinical cure

The mexameter results, which reflects the erythema index in both groups were significantly different (p= 0.342). A post hoc comparison test was done which showed that as early as day 14, there was significant difference in terms of erythema among both groups. However, the improvement observed in between days 14 and 28 were not statistically different (p= 0.342).

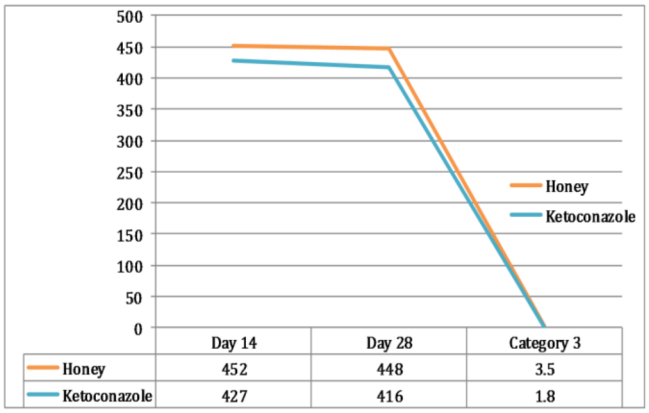


Figure 1. Mexameter results

The parameters such as erythema, scaling and pruritus are shown in Figure 3-5. Erythema, scaling and pruritus in both groups were significantly different (p <0.0001, 0.002, 0.014 respectively). A post hoc comparison test was done which showed that as early as day 14 (p <0.0001), there was a significant improvement in these parameters. However, improvement in erythema observed in between days 14 and 28 were statistically different (p=0.004) in contrast to scaling and pruritus, which showed insignificant improvement from day 14 to day 28 (p= 0.069 and 0.707, respectively).

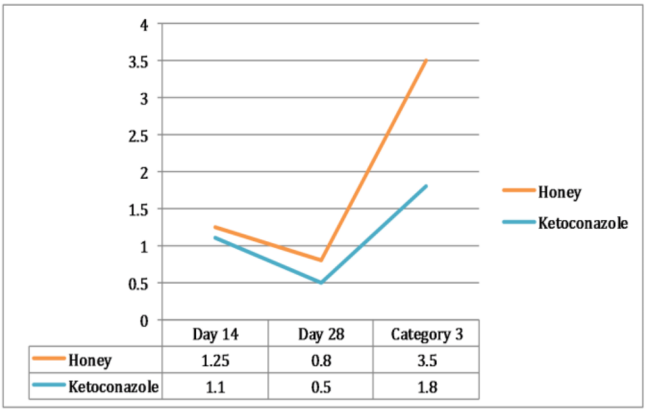


Figure 3. Erythema scores on day 14 and day 28.

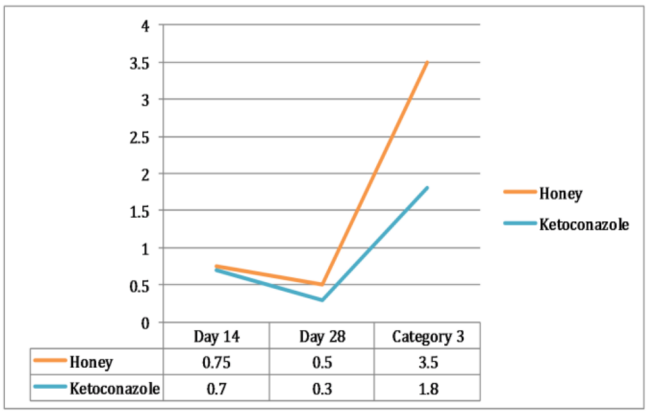


Figure 4. Scaling scores on day 14 and day 28.

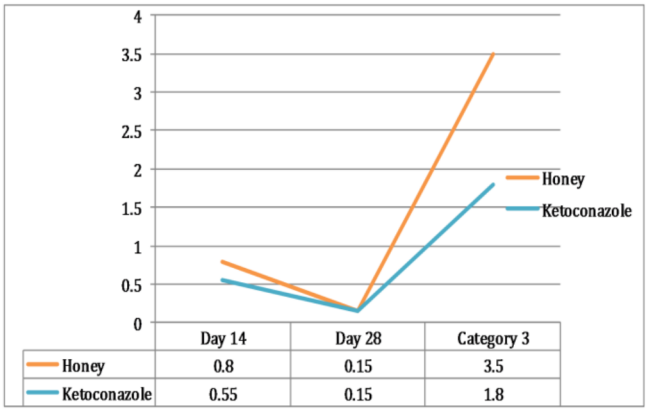


Figure 5. Pruritus scores on day 14 and day 28.

Global Physician Assessment (GPA)

For Global Physician Assessment (GPA), the GPA scores of the honey group are statistically insignificant both on the 2nd and 4th week from the ketoconazole group. GPA scores on the 2nd week showed 19 (95%) subjects who have ≥3 GPA scores in the ketoconazole group and 14 (70%) subjects in the honey group (p=0.059). GPA scores on the 4th week showed 20 (100%) subjects who have ≥3 GPA scores in the ketoconazole group and 20 (100%) subjects in the honey group (p=0.763). *Figures 5* shows difference in GPA score.

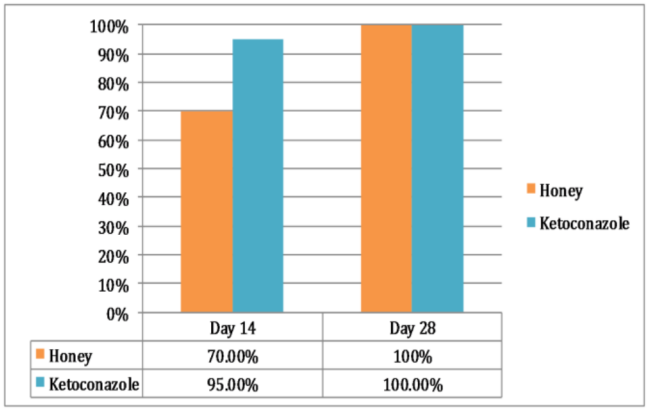


Figure 6. Global physician assessment on day 14 and day 28.

Subjective Assessment

Based on subjective assessment, mean score of honey in 4th week monitoring is 4.6±0.53, while those in ketoconazole group is 4.3±0.47. Using Paired t-test, there is insignificant difference in subjective assessment scores between honey and ketoconazole group, p=0.055.

DISCUSSION

Similar to other studies, the demographic profile of the study participants shows a male predominance with disease occurring mostly during the fourth decade of life.[36] This pattern of prevalence in men may be attributed to the androgen-modulated sebaceous gland activity. Seborrheic dermatitis is usually a chronic disease with different patterns of disease recurrence.[36-37]

The clinical trial of once every other day application of diluted honey compared to ketoconazole showed statistically significant improvement in the clinical cure rate. The decrease in clinical parameters of erythema, scaling and pruritus may be attributable not only to the antifungal effect of honey but also to its anti-inflammatory effect. The antifungal activity of honey is also derived from the osmotic effect of its high sugar content and low moisture content. Honey is characteristically acidic because of gluconic acid, its pH being between 3.2 and 4.5 which is enough to be inhibitory to many animal and fungal pathogens.[38] Another major factor that account for inhibition of honey has been found to be due to hydrogen peroxide produced enzymatically in the honey. Several chemical with antifungal activity has been identified in honey by various researchers. These include pinocembrin, terpenes, benzyl alcohol, 3, 4-dimethoxy-4-hydroxybenzoic acid (syringic acid).[39]

Erythema is an indicator of inflammation. This inflammation is said to be due to *Malassezia* lipases acting on sebaceous triglycerides resulting to the release of inflammatory unsaturated fatty acids. Other factors that affect inflammation are elevation of cytokines IL-1α, IL-1β, IL-2, IL-4, IL-6, IL-10, IL-12, TNF-α anf IFN-γ; neutrophil infiltration; leukocyte infiltration by major histocompatibility complex (MHC) positive lymphocytes and natural killer (NK) cells; and increase in histamine levels. The degree of inflammation was evaluated by means of assessing the erythema index in different facial regions using the mexameter. The results of the study showed significant difference in erythema in both groups as early as the second week among both

groups. However, the improvement observed in between days 14 and 28 were not statistically different.

No significant side effects were recorded in the 40 patients included in the study.

CONCLUSION

Diluted honey exhibited comparable efficacy in the clinical improvement in the signs and symptoms of seborrheic dermatitis and is a safe and cost-effective alternative in clearing the lesions of seborrheic dermatitis. There was noted improvement as early as 14 days of treatment. The degree of erythema as measured by using a mexameter and the erythema scores were significantly improved with diluted honey noted as early as 14 days. However, both groups were comparable in terms of improvement during days 14 to 28. Erythema, scaling and pruritus in both groups were significantly different. As early as day 14, there was a significant improvement in these parameters. However, improvement in erythema observed in between days 14 and 28 were statistically different in contrast to scaling and pruritus, which showed insignificant improvement from day 14 to day 28. Both groups were similar in terms of safety.

RECOMMENDATION

The authors recommend future larger randomized clinical trials using a more frequent dosing, higher concentration or longer treatment duration of diluted honey to determine if a more favorable result may be achieved with this agent. We would also recommend to use other species of honey from other regions of the country which may possibly exhibit higher potency against microorganism. Fungal cultures may also be performed to determine the etiologic agents susceptible to and resistant to honey.

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Metachronous Metastasis to the Stomach from a Primary Colon Cancer in a Filipino Patient – A Case Report*

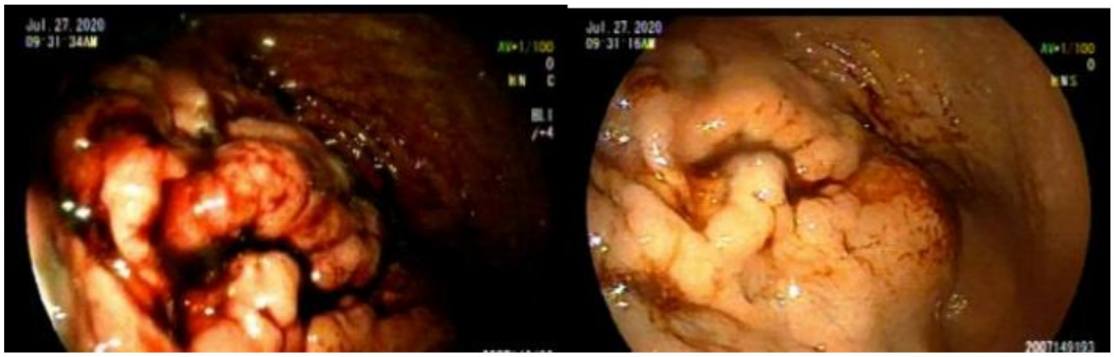
John Alfredo Raphael P. Pangilinan, MD
J Gapasin, MD

Case

We have a 55-year-old male, diagnosed case of Descending Colon Adenocarcinoma who underwent left hemicolectomy in 2018 and received chemotherapy with eight cycles of Capecitabine, Oxaliplatin in the same year who came in due to epigastric pain of 1 month duration. He described this as intermittent and pressure-like, graded 5/10, and non-radiating. This was accompanied with unquantified weight loss. He had no dysphagia but noted nausea and vomiting post-prandially. He had no fever, with no melena, hematochezia or changes in stool caliber. He noted early satiety as well and had bloatedness post-prandially. He was initially given PPI therapy, but persistence of symptoms prompted consult.

An Abdominal CT done a few months prior to his consult showed unremarkable results.

An Upper GI endoscopy and Surveillance Colonoscopy was done which showed a huge, fungating, and friable mass noted at the proximal corpus extending to the distal segment at around 40 cm down to 55 cm level. The antrum was not completely visualized during the study due to the mass, precluding the visualization of the pyloric ring. On retroflexion, the scope was tightly hugged by the cardia. On BLI, the mass showed an irregular surface vessel pattern. Multiple representative biopsies were then taken for histopathology.



The colonoscopy showed unremarkable results with no lesions observed.

Endoscopic ultrasound was also done to determine the depth of tumor involvement.

It showed a heterogenous lesion with central hypoechogenicity measuring 6 x 7 cm. This was noted externally and appeared to be encroaching into the the gastric wall. Multiple perigastric lymph nodes were appreciated as well.

Histopathology of the mass showed adenocarcinoma, and with the history of a previous malignancy in the colon, the question was whether this was a primary gastric malignancy or a recurrence/metastasis from the colon that was previously treated.

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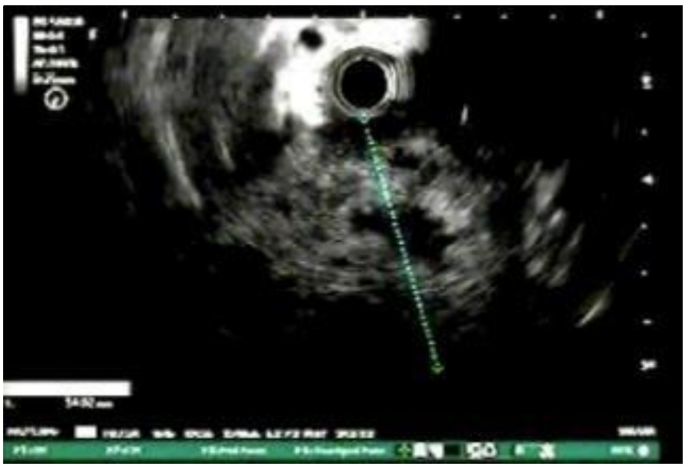
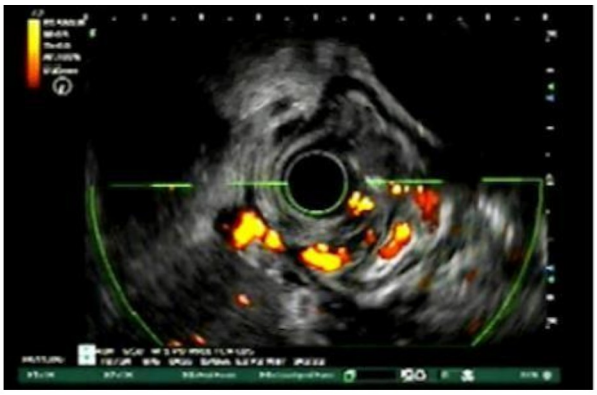
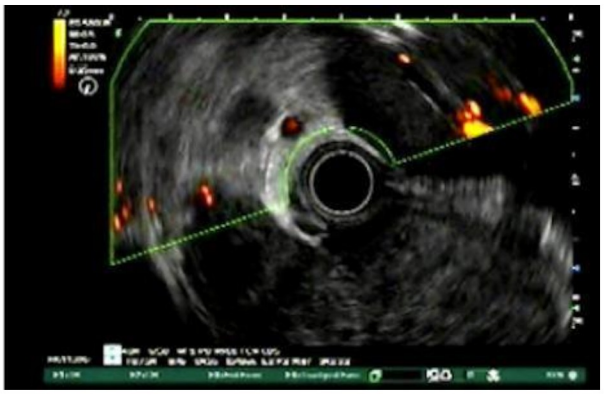
Immunohistochemical studies were done which showed a positive CK20, SATB2, CDX-2 and a negative CK7 and was signed out by the Pathologist as Metastatic Adenocarcinoma with a Colonic Primary

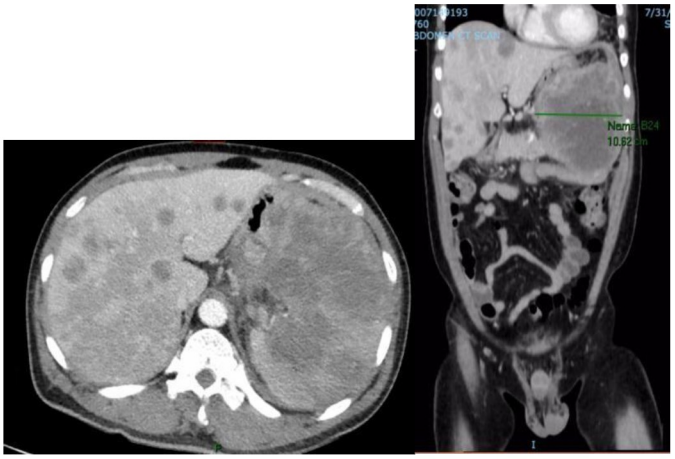






An abdominal CT was also done to further evaluate the lesion as well the surrounding structures which showed that at the level of the gastric fundus, a large mass with predominantly exophytic and necrotic components arising from the greater curvature was evident.

A large, lobulated, heterogeneously enhancing mass with areas of necrosis along the posterolateral gastric wall with an approximate measurement of 16.3 x 10.6 x 13.7 cm. The mass showed no clear plane of cleavage and displaced the spleen, pancreatic tail, left adrenal gland and kidney. The mass was also noted to be closely related to the abdominal wall. The liver was enlarged with a craniocaudal length of 17.1 cm along the midclavicular plane. There were multiple, varisized, ill-defined hypo-enhancing foci with peripheral enhancement scattered in the parenchyma. This was thus signed out as Progressive disease and palliative treatment was recommended.



The patient was admitted, a jejunostomy tube was inserted for nutritional buildup and a plan for chemotherapy was made.

The hospital course was stormy, with the patient developing Pneumonia, tumor bleeding and

eventually deep jaundice. The family decided to take the patient home for palliation. Patient expired a few days after discharge from the hospital.

DISCUSSION

Colorectal Cancer is the 4th most common newly diagnosed internal cancer overall in the USA and third most common cancer worldwide. The risk of development depends on demographic and environmental factors and approximately 20%, or 2 in 10 patients with CRC have metastasis at diagnosis. Spread can be either hematogenous or lymphatic.

Colon cancers can invade transmurally and involve regional lymphatics and then distant lymph nodes. The liver is the most common site of hematogenous spread (via the portal venous system) from colon tumors, and pulmonary metastases from colon cancer usually result from hepatic metastases.

Metastatic neoplasms in the stomach from remote primary tumors are uncommon, and gastric metastases of colorectal origin are rare. These Metastases from Colorectal cancer to the stomach is extremely rare with only a few cases described in medical literature. In one post- mortem study, only 0.8% of colon cancer metastasized to the stomach. Most commonly, these are metastases from Melanoma, Breast and Lung Cancer.

Published data is scarce, with few case reports showing this type of presentation. A 2008 report showed a similar presenting subject, High-risk stage II Colon Cancer who underwent 12 cycles of chemotherapy post-resection. 4 years after, she came in with abdominal symptoms with a CT showing a gastric mass with immunohistochemistry showing Colon adenocarcinoma as well. She underwent resection and subsequent chemotherapy.

Visually, the endoscopic appearance of gastric metastases is variable. Gastric involvement may be characterized by a single lesion or by multiple lesions. The metastases may have the clinical appearance of a primary stromal gastric tumor as in this case. Metastasis to the stomach can be mistaken for a primary gastric cancer and this happens when the primary site is not present at the time of finding a gastric lesion.

Based on a report published in 2019, only 14 cases, excluding this one has been reported worldwide. Analysis done by Terashima et al showed that the mean age was 61.6 and the cases involved 7 males and 7 females. The most common primary site was the transverse colon (n=4) and in all cases, on gross examination, gastric metastases had a submucosal tumor-like appearance which was also seen in our case. Additional sites of metastasis included lung, liver, bone marrow and lymph nodes, with nodal metastasis most prominent (n=5). Ten patients underwent surgical resection with 8 receiving postoperative chemotherapy. Among those who did not receive these interventions, all died within 2 years.

Management of these lesions based on recommendations lean towards operative if feasible. Termed Gastric metastasectomy, selected patients may undergo this surgical procedure with concurrent chemotherapy.

CONCLUSION

Gastric Metastases from Colon Cancer is a rare occurrence with less than 20 cases reported worldwide. Diagnosis includes imaging and possibly endoscopy to evaluate these lesions especially when they present in a solitary manner after successful resection of a primary malignancy. A high index of suspicion and the help of immunohistochemistry can guide the Gastroenterologist in the diagnosis. Management is dependent on a holistic approach, with a median survival of 21 months.

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Effectiveness of Pre-Anesthetic Induction Checklist in Improving General Anesthesia Induction Set-Up in a Simulated Setting during the Covid-19 Pandemic*

Karla Shayne D. Feliciano, MD[1]

Abstract

Background: Anesthesiologists being under high pressure and in a stressful environment may predispose to poor pre-induction preparation. The pre-induction period was identified to be a circumstance where medical errors occur. Thus, routine use of checklists is implemented to prevent these.

Methods: A Pre-Anesthesic Induction Checklist was formulated and validated by the members of Department of Anesthesiology and Perioperative Medicine staff. The study was designed as a pragmatic trial, quality improvement, and quasi-experimental conducted in the hospital's main operating room in a simulated setting. The participants included sixteen (16) anesthesiology residents who were divided into two groups, without a checklist and with a checklist, with an equal number of residents per year level who underwent eight simulated general anesthesia induction set-ups each.

Results: The checklist was used in 64 out of 128 simulations. The group with the checklist had an average completeness score of 95.26% and an average duration of 7.06 minutes compared to the group without the checklist, which had an average score of 70.81% and an average time of 8.75 minutes. Thus, there is an average 24.45% decrease in missed steps and an average 1.69-minute decrease in preparation duration among the residents who used the checklist. In the 128 simulations done, the most common actions and items missed of >20% are the following: Succinylcholine (67.97%), laryngeal mask airways (62.50%), confirmation of identifying factors of patients (55.47%), checking of vaporizer (42.97%), checking of sodasorb (36.72%), checking of breathing circuit (30.47%), video laryngoscope (26.56%), and suction (25.00%).

Conclusion: The mean total duration of preparation and mean completeness score between with checklist and without checklist groups are significantly different, both having a p-value of <0.0001. The Pre-Anesthetic Induction Checklist significantly reduced the number of missed steps and the duration of preparation time of a simulated pre-anesthesia induction period.

Keywords: checklist, general anesthesia induction, simulation

INTRODUCTION

In the year 2020, Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2) that originated from Wuhan, China rapidly spread globally and contagiously thru human respiratory secretions.[1] Infecting millions of people all over the world, COVID-19 was declared a pandemic by the World Health Organization (WHO) on March 11, 2020.

The lack of information about the virus predisposed healthcare workers to infection due to close encounters with aerosol droplets.[1] Anesthesiologists, being the front liners in airway management, were constantly exposed to infected respiratory secretions. Thus, the COVID-19 pandemic brought about challenges and modifications in the operating room to heightened precautions.[2] Healthcare institutions were obligated to implement updated protective measures and modify customary practices to minimize perioperative viral transmission and protect both the patient and healthcare workers.[3] This mandate involved changing anesthetic practices to lessen aerosol-generating procedures during general anesthesia induction.[4]

**3rd Place, 2023 Philippine Society of Anesthesiologists Inc. Research Forum Contest*

[1]from Rizal Medical Center, Pasig City

The practice of anesthesiology has been at the forefront of improving patient safety through the years. However, due to the challenges imposed by the Covid-19 pandemic, the role of anesthesiologists also sheds light on infection prevention.[5] With the changing times and practices, medical errors may be unavoidable. In line with this, the pre-anesthetic induction period was identified as a circumstance where medical errors occur; thus, routine use of checklists are implemented to prevent these. Subsequently, anesthesiologists are under high pressure, and a stressful environment may dispose to poor pre-induction preparation.[6] This study aims to test the effectiveness of the Pre-Induction checklist in improving the set-up of general anesthesia induction in a simulated Covid-19 operating room setting of anesthesiology residents.

METHODOLOGY

Population

The study participants include sixteen (16) residents undergoing training in Anesthesiology. All residents from the first to the third year participated in the study. Pre- residents, pre-fellows, and rotators from other departments and residents who previously consented to the study but later on decided to withdraw, were excluded from the study.

Study Design

The study was designed as a pragmatic trial, quality improvement, quasi-experimental conducted in the hospital's main operating room in a simulated setting.

Statistical Analysis

Descriptive statistics summarized the demographic profile of the participants. Numerical variables were described as mean and standard deviation if the data was normally distributed as assessed by the Shapiro-Wilk test of normality, or median and interquartile range if otherwise. Count and proportion described categorical variables.

Two-way ANOVA was used to compare the mean difference in the total duration of preparation and the mean difference in the completeness score between with checklist and without checklist groups, with the resident as the blocking variable. A subgroup analysis using ANOVA was done to determine if the residency year level affects the duration and completeness score of the participants. The most commonly missed step/item was presented as count and proportion.

Data Collection and Data Analysis

After the approval of the IRB and Ethics Board, several members of the Anesthesiology department conducted an adaptation and content validation of the Pre-Anesthetic Induction Checklist. The panel included residents in training, fellows, junior consultants and medical specialists to ensure the relevance and applicability of the checklist to the local setting.

The checklist was applied in a simulated setting with two test groups, one group using a checklist and one group without a checklist. Residents were asked to prepare stations before general anesthesia induction. The minimum sample size requirement was computed using R version 4.0.3. A sample size of at least eight stations was required to achieve 80% power at a 5% two-tailed significance level in a two-way ANOVA with two groups (without a checklist, and with a checklist) with eight residents participating in each group, to identify a significantly different mean duration and mean completeness score, with medium effect size (Cohen's f=0.25). The study participants were randomly assigned through fishbowl draw into the two test groups with an equal number of residents per year level.

The simulation was conducted in one of the rooms in the hospital's main operating room complex to ensure familiarity with the environment, equipment and items available. A total of eight stations composed of an anesthesia machine, a tray of medications, a box containing anesthesia equipment, a suction machine and an operating table with a dummy patient were prepared. All residents were given eight identical sets of sample cases that were considered the basis for the simulation of the eight general anesthesia induction set-ups they were required to prepare.

Each resident from the no checklist group was asked to prepare eight general anesthesia pre-induction set-ups without using the Pre-Anesthetic Induction Checklist. The principal investigator recorded the time from the entrance of the resident until the time when general anesthesia induction was about to begin when the resident declared "ready for general anesthesia induction." The checklist was used to check the steps done by the resident and take note of the steps missed, each step corresponding to one point. The simulation continued until the resident completed all eight stations. Similar to the no checklist group, the residents from the checklist group were asked to prepare eight general anesthesia induction set-ups based on the same set of sample cases but using the Pre-Anesthetic Induction Checklist. The residents were timed and scored using the checklist. The total simulation scores were recorded, and the investigator also determined the average duration of preparation time and the total number of missed steps.

The two scores and time duration of the no checklist group and the checklist group were statistically analyzed using repeated measures ANOVA. A decrease of at least two minutes in the preparation time and a reduction of 20-30% of missed steps were considered significant.

RESULTS AND DISCUSSION

Anesthesiologists work in a high-risk environment where emergencies and critical conditions require immediate decision-making which makes them susceptible to human medical errors that may lead to patient compromise.[7] It was determined that most of these incidents occur during the pre-induction period.[6] These risks are identified as incidents that are caused by missed steps of even a skilled anesthesiologist.[8] Medical errors may be inevitable, such as missed pre-induction preparation, considering the several roles of the anesthesiologists in the operating room and the heavy workload.[6] Implementation of a checklist may prevent near misses in situations like these. The Pre-Anesthesia Induction Checklist contains a list of equipment that should be prepared and steps that should be done before starting a case. It has been concluded that using a checklist promotes patient safety and decreases morbidity and mortality.[8]

In a study by Boulet et al., the authors discussed that simulation-based assessment in anesthesiology was a developing teaching and grading modality for physicians. It promotes patient safety by identifying deficiencies in skill, medical errors and system problems. Appropriate metrics should be incorporated to ensure the validity of scores, and simulation set-ups should be patterned to real-world settings. Simulation can assess both technical and non-technical skills that may eliminate medical errors in residency training.

The hospital's department of Anesthesiology has a total of sixteen residents who met the inclusion and exclusion criteria set. They were randomly divided into two groups for the simulation testing; with the checklist group and without the checklist group. Each resident completed eight simulations, resulting in 128 simulations. The preparation duration was recorded, and the completeness of the set-up was scored based on the Pre-Anesthesic Induction Checklist.

The total preparation duration and the completeness score were summarized as mean and standard deviation. These were stratified into the intervention groups, i.e., with vs. without a checklist, and into blocks, i.e., by year level. Two-way ANOVA was used to compare the mean total duration of preparation and mean completeness score between with checklist and without checklist groups, and year level as the blocking variable. And the most commonly missed step/item was presented as count and proportion.

Table 1. The comparison of the total preparation duration and the completeness score between the intervention groups and blocks.

	With Checklist n = 8	Without Checklist n = 8	p-value*
Duration, *mins*	7.06 (1.57)	8.75 (2.25)	<0.0001
By year level			0.0001
First years [n=4]	8.09 (1.60)	6.45 (0.61)	
Second years [n=4]	7.22 (1.73)	11.06 (2.03)	
Third years [n=8]	6.47 (1.18)	8.74 (1.63)	
Completeness, *%*	95.26 (2.92)	70.81 (18.63)	<0.0001
By year level			<0.0001
First years [n=4]	94.20 (1.79)	40.18 (3.32)	
Second years [n=4]	94.42 (3.44)	75.67 (4.92)	
Third years [n=8]	96.21 (2.86)	83.70 (4.53)	

***Two-way ANOVA comparing duration or completeness between two intervention groups (with vs without checklist) with year level as blocking variable.**

Results of the comparison of the total duration of preparation and the completeness score between the intervention groups and blocks show that there is sufficient evidence to conclude that the mean total duration of preparation and mean completeness score between those with checklist and without checklist groups are significantly different, both having a p- value of <0.0001.

The results also reveal that there is a longer mean duration of preparation for those without a checklist than those with a checklist and there was a higher completeness score for those with the checklist than those without a checklist with a p-value of <0.0001. The group with the checklist has an average completeness score of 95.26% and an average duration of 7.06 minutes compared to the group without the checklist, which had an average score of 70.81% and an average time of 8.75 minutes. Thus, there is an average 24.45% decrease in missed steps and an average 1.69-minute decrease in preparation duration among the residents who used the checklist, which is considered significant.

In terms of the blocking variable, results show there is sufficient evidence that year level is a significant factor for both duration of preparation and completeness. Post-hoc analysis showed that third years and first years have a significantly shorter preparation duration than second years. There was no evidence of a difference between the third and first years. Third-years who belonged to the checklist group had an average duration of 6.47 minutes, while third-years who belonged to the no checklist group had an average time of 8.74 minutes. Second-years who belonged to the checklist group had an average duration of 7.22 minutes while second-years who belonged to the no checklist group had an average time of 11.06 minutes. First-years who belonged to the checklist group had an average duration of 8.09 minutes while first-years who belonged to the no checklist groups had an average time of 6.45 minutes.

Post-hoc analysis showed that third-years and second-years have significantly higher completeness scores than first-years, and there is no evidence of difference between third and second years. Third-years and second-years from the checklist group have an average completeness score of 96.21% and 94.42%, respectively. On the other hand, third-years and second-years from the no checklist group have an average completeness score of 83.70% and 75.67%, respectively. First-years from the checklist group have an average score of 94.20%, and first-years from the no checklist group have an average score of 40.18%. Results show that there is a 35.49% to 43.52% decrease in the completeness score of first-year residents who did not use a checklist compared to second and third-year residents. First-year residents who did not use a checklist may have performed the pre-anesthetic induction set-up faster than the second years. but their completeness score is significantly decreased.

Table 2. The proportion of instances when the participants miss the preparation step.

Step	Done		Missed	
	n	%	*n*	%
Machine Check Out	111	86.72%	17	13.28%
Vaporizer	73	57.03%	55	42.97%
Leak Test	112	87.50%	16	12.50%
Sodasorb	81	63.28%	47	36.72%
Breathing Circuit	89	69.53%	39	30.47%
ECG	112	87.50%	16	12.50%
NIBP	112	87.50%	16	12.50%
Pulse Oximeter	112	87.50%	16	12.50%
Capnograph	112	87.50%	16	12.50%

Thermometer	112	87.50%	16	12.50%
Laryngoscope with blades	128	100.00%	-	-
Video laryngoscope	94	73.44%	34	26.56%
Suction	96	75.00%	32	25.00%
Face Masks	127	99.22%	1	0.78%
Guedal oral airways or nasal airways	128	100.00%	-	-
ETT tube	125	97.66%	3	2.34%
LMAs	48	37.50%	80	62.50%
Bougie or stylet	117	91.41%	11	8.59%
Emergency medications	128	100.00%	-	-
Anxiolytic drug	128	100.00%	-	-
Opioid drug	128	100.00%	-	-
Sedative drug	128	100.00%	-	-
Non-depolarizing neuromuscular blocker	127	99.22%	1	0.78%
Succinylcholine	41	32.03%	87	67.97%
Identifying factors of patients	57	44.54%	71	55.47%
Monitors attached to the patient	128	100.00%	-	-
Baseline vital signs	118	92.19%	10	7.81%
IVF	104	81.25%	24	18.75%

In the 128 simulations done by the sixteen residents, the most common steps and items missed of >20% are the following: Succinylcholine (67.97%), laryngeal mask airways (62.50%), confirmation of identifying factors of patients (55.47%), checking of vaporizer (42.97%), checking of sodasorb (36.72%), checking of breathing circuit (30.47%), video laryngoscope (26.56%), and suction (25.00%). It was observed that the residents whether they were using the checklist or not, commonly prepared a non-depolarizing neuromuscular blocker and not prepare Succinylcholine on purpose. Laryngeal mask airways are also not routinely prepared by the residents even with the use of the checklist. Checking of the parts of the anesthesia machine was also commonly missed. Video laryngoscope was not usually prepared because the residents preferred to use direct laryngoscopes. Suction was commonly missed by residents who did not use the checklist.

CONCLUSION

Based on the study done by Wetmore et al., it is during the pre-induction period that human medical errors commonly occur. Due to the ongoing pandemic and the increasing work demands, incomplete pre-induction set-up becomes a common mistake. A checklist containing all the essential aspects of anesthesia induction that is presented in a logical order and written using terms commonly used in the operating room setting can significantly reduce medical errors.[10]

In line with the study's result, the Pre-Anesthetic Induction Checklist significantly reduces the number of missed steps and the duration of preparation time of the pre-anesthesia induction period with a p-value of <0.0001. Thus, the Pre-Anesthetic Induction Checklist may be considered as a tool to decrease human medical errors among resident anesthesiologists.

Nonetheless, there are identified limitations of the study. A sample size of at least eight set-ups and a limited number of research participants of only sixteen residents garnered only 80% power of the study. The pre-anesthetic induction checklist was based on the institution's available medications, equipment and materials. Neuromuscular blocker reversal agents were not included in the checklist because it is not available in the institution's drug formulary. Lastly, the checklist only contained medications, equipment and materials commonly used during general anesthesia induction. However, apparatus for possible difficult airways is also limited. The fiberoptic intubating scope is not included due to its current unavailability. Items used during regional anesthesia are also not included.

Due to the mentioned limitations of the study, it is recommended to conduct the study with a similar design to a larger population to achieve a higher statistical power. A more comprehensive checklist that can be applied in both general and regional anesthesia induction set-ups are also recommended. Apparatus for possible difficult airways must also be secured, such as Fiberoptic intubating scope. The study also motivates the inclusion of neuromuscular blocker reversal agents in the drug formulary as it is an essential element in general anesthesia induction.

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