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**Functional Outcome of Hirschsprung's Disease, Post-Surgical Transanal Endorectal
Pull-through at National Children's Hospital**
Meliza Ylaine V. Salvador, M.D.

**Effect of Aspiration and Non-Aspiration of Syringe prior to Intramuscular Administration of
Influenza Vaccine in Pain Perception of Children 9 to 15 Years of Age Consulting at the
Out-patient Department of a Tertiary Government Hospital**
Jovy Anne C. Otero, MD, Michael M. Resurreccion, MD

**A Survey on the Nutrition Risk Level of Patients Subjected to Standard Practice of Enteral
Nutrition Provision Admitted at the Intensive Care Unit of Cebu Doctors' University Hospital:
A One-Year Retrospective Chart Review**
Maricel B. Malazarte, MD, Gerry Tan, MD, FACP

**A Randomized Double-blind Controlled Study on the Efficacy of Spirulina as an Adjunct Therapy
in the Management of Pediatric Community Acquired Pneumonia-C in Patients 6 Months to
5 Years Old Admitted in a Tertiary Government Hospital**
Michael N. Crisostomo, M.D., Michael M. Resurreccion, MD

Patterns of Resolved Medical Malpractice Cases in the Philippines
Natividad Salazar, MD

Annular Pustular Psoriasis in a 6-year-old child: Case Report
Patricia Gaile E. Espinosa, MD, Francisco D. Rivera IV, MD, FPDS

**Classic dermatomyositis in a 36-year-old Filipino female: A case report with emphasis
on the early recognition of cutaneous findings of dermatomyositis**
Maria Cecilia P. Ingente, MD, DPDS, Katrina Carmela M. Belen, MD, DPDS, Maria Jasmin J. Jamora, MD, FPDS

**Trans-Sacral Epiduroscopic Laser Decompression (SELD) for Low back pain secondary to
Herniated Lumbar Disc in the Philippines: A Case Report and Review of Literature**
Wayne V. Paez, MD, Elmer Jose A. Mecedas, MD

**"While finding where the water leaks, you find smoke" - A Case Report: Incidental finding
of Moyamoya for a Filipino worked up for Subarachnoid Hemorrhage**
Christian Emmanuel T. Lim, MD, Maria Felicidad A. Soto MD, Renato Carlos, MD

Bilateral Pallidal stimulation in Parkinsonism predominant XDP
Allister Vincent G. Layog, MD, Roland Dominic G. Jamora, MD

Keratoacanthoma on an Epidermal Nevus in a Filipino Male
Janelle Marie S. Padlan-Ramos, MD, DPDS, Daisy King-Ismael, MD, FPDS

TABLE OF CONTENTS

Journal of the
PHILIPPINE MEDICAL ASSOCIATION
2017 - 2018 VOLUME 96, NUMBER 2

Functional Outcome of Hirschsprung's Disease, Post-Surgical Trans-anal Endorectal Pull-through at National Children's Hospital <i>Meliza Ylaine V. Salvador, MD</i>	1
Effect of Aspiration and Non-Aspiration of Syringe prior to Intramuscular Administration of Influenza Vaccine in Pain Perception of Children 9 to 15 Years of Age Consulting at the Out-patient Department of a Tertiary Government Hospital <i>Jovy Anne C. Otero, MD, Michael M. Resurreccion, MD</i>	13
A Survey on the Nutrition Risk Level of Patients Subjected to Standard Practice of Enteral Nutrition Provision Admitted at the Intensive Care Unit of Cebu Doctors' University Hospital: A One-Year Retrospective Chart Review <i>Maricel B. Malazarte, MD, Gerry Tan, MD, FACP</i>	22
A Randomized Double-blind Controlled Study on the Efficacy of Spirulina as an Adjunct Therapy in the Management of Pediatric Community Acquired Pneumonia-C in Patients 6 Months to 5 Years Old Admitted in a Tertiary Government Hospital <i>Michael N. Crisostomo, M.D., Michael M. Resurreccion, MD</i>	34
Patterns of Resolved Medical Malpractice Cases in the Philippines <i>Natividad Salazar, MD</i>	46

Annular Pustular Psoriasis in a 6-year-old child: Case Report <i>Patricia Gaile E. Espinosa, MD, Francisco D Rivera IV, MD, FPDS</i>	51
Classic dermatomyositis in a 36-year-old Filipino female: A case report with emphasis on the early recognition of cutaneous findings of dermatomyositis <i>Maria Cecilia P. Ingente, MD, DPDS, Katrina Carmela M. Belen, MD, DPDS, Maria Jasmin J. Jamora, MD, FPDS</i>	56
Trans-Sacral Epiduroscopic Laser Decompression (SELD) for Low back pain secondary to Herniated Lumbar Disc in the Philippines: A Case Report and Review of Literature <i>Wayne V. Paez, MD, Elmer Jose A. Meceda, MD</i>	63
“While finding where the water leaks, you find smoke” - A Case Report: Incidental finding of Moyamoya for a Filipino worked up for Subarachnoid Hemorrhage <i>Christian Emmanuel T. Lim, MD, Maria Felicidad A. Soto MD, Renato Carlos, MD</i>	69
Bilateral Pallidal Stimulation in Parkinsonism Predominant XDP <i>Allister Vincent G. Layog, MD, Roland Dominic G. Jamora, MD</i>	74
Keratoacanthoma on an Epidermal Nevus in a Filipino Male <i>Janelle Marie S. Padlan-Ramos, MD, DPDS, Daisy King-Ismael, MD, FPDS</i>	78

Journal of the
Philippine Medical Association
2017 - 2018 VOLUME 96, NUMBER 2

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Philippine Medical Association
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EDITOR'S notes

The commitment to do our share

This present issue proceeds with the intention by the editorial board of being as inclusive as possible in terms of the various fields of medical practice. This promotes for a wider scope of topics and hence might generate a corresponding broader readership and interest. Since our target is both relevance and reach, we are pleased to be able to source the better articles not only from the range of disciplines but also from myriad institutions.

We have in this edition five original research papers and six interesting case reports. While being heterogeneous, we see a common denominator in that the papers are well-crafted, organized, and reflective of the considerable efforts of the authors, not to mention, their supervisors. This is perhaps a pervasive phenomenon in our academic and intellectual environ, that is, putting a premium on the research endeavor. And this is rightfully so, aware of the global direction of attaining credibility and scholarly standing only through the scientific method.

The current trend does not detract from the projection that future issues might in fact have a theme or would be more focused by way of a single specialty. This would be dependent on a number of factors like the volume of submissions and the particular objective of a given time frame. The journal is open to all these and more. The important thing is we continue to provide a venue in fulfilling the need for professional growth and medical advancement.

AJBAJ
May 2018

Journal of the
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Instruction for Authors

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The Journal of the Philippine Medical Association (JPMA) is the official publication of the Philippine Medical Association (PMA).

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The JPMA is a peer-review journal designed to meet the continuing education requirements of PMA members and the medical community. It adheres to the guidelines established by the International Community of Medical Journal Editors (ICMJE); however, for purposes of this issue, the previously circulated JPMA Instructions for Authors, although with some modifications, are still being followed.

Ethical Considerations

In the conduct and reporting of research, the JPMA adheres to the ethical considerations set forth by the ICMJE with respect to authorship and contributorship, editorship, peer review, conflicts of interest, right to privacy and confidentiality of patients, study participants as well as authors and reviewers; and, the protection of human subjects and animals in research.

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Manuscript Preparation

(This section is primarily based on the previous and existing JPMA Instructions to Contributors but with some modifications based on the ICMJE recommendations. A completely revised version based on the guidelines of the ICMJE will be published in the next issue.

Accompanied by a cover letter from the principal author, the manuscripts, figures, tables, photographs, and references should be submitted in duplicate (an original and a copy) and typed double-space (including legends and footnotes) on one side of a white bond paper, 8.5 and 11 inches properly numbered consecutively on the upper right-hand corner of each page beginning with the title page. Illustrations must also be in duplicates. An electronic copy of the articles in a CD must be submitted.

The first page should contain the title, subtitle (if any, all authors' full names and highest earned academic degrees, and hospital or institutional affiliations. It must also include disclaimer, if any.

For the original article, an abstract must be type at the beginning of each paper after the title. It must contain, in structured format, the following: background or context of the study, objectives, methods, results and conclusions of the study, as appropriate. It must not be more than 300 words. No footnotes/references must be in the abstract. For other articles, an unstructured abstract may be preferred. Below the abstract, identify three to ten keywords or short phrases that will assist in indexers in cross-indexing the article.

Abbreviations and nomenclatures: the use of abbreviations should be minimized and preferably confined to tables only; non-standard abbreviations must be accompanied by legends.

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Functional Outcome of Hirschsprung's Disease, Post-Surgical Trans-anal Endorectal Pull-through at National Children's Hospital

Meliza Ylaine V. Salvador, M.D.¹

ABSTRACT

Background: Hirschsprung's Disease, is a congenital illness secondary to lack of ganglion cells in the intestinal tract leading to mechanical obstruction. In the Philippines, Hirschsprung's Disease ranks 9th over the top 10 cases causing morbidity to Filipino children and the mortality rate can reach up to 50%. The treatment is still surgery, such as Soave procedure.

Design: Descriptive cross sectional study

Subjects: The participants of the study were follow up patients at the Surgery Out Patient Department from March 2016 to August 2017, ages 0-7 years old, diagnosed with Hirschsprung's Disease, post Trans-anal endorectal pull-through.

Methodology: Purposive sampling was used to select participants. Sample size was 40 based on the proportion of good functional outcome among patients who underwent trans-anal endorectal pull-through.

Statistical Analysis: Descriptive Analysis using proportion and percentages were used to present the results in all the variables.

Results: Out of the 40, 82 % were diagnosed with the disease as early as the newborn period and 55% of the patients were operated at an age from 1 to 3 years old and about 80% were males. It also showed that post operatively, 60% had normal z scores and 65% of the population still had an abnormal stool. Moreover, the study showed that 95% of the subjects returned to schooling or playing post surgery.

Summary/Conclusion: Comparing it to the 96% result of Dela Merced 2003, this study had 95% of patients who were able to achieve good functional outcome, 4-6 weeks post-surgery.

Hirschsprung's, Endorectal Pull-through, Functional Outcome

¹From the National Children's Hospital, Quezon City, Philippines

INTRODUCTION

Hirschsprung's Disease or aganglionic megacolon, is a congenital illness in which there is a lack of intrinsic nerves (ganglion cells) in the distal segments of the intestinal tract. These abnormal segments produce mechanical obstruction because of failure to relax during peristalsis. (Samuel, 2006).

The incidence of this disease is 1/5000 to 1/10,000 live births, where in males are affected more often (3:1 to 5:1). Based on studies, there is an increased familial incidence in long segment diseases. (Samuel, 2006).

In the Philippines, Hirschsprung's Disease ranks 9th over the top 10 cases causing morbidity to Filipino children and the mortality rate can reach 20 to 50%. (PCMC report, 2013).

Operational intervention is warranted. One of the three surgical procedures (Swenson, Duhamel, Soave (endorectal pull through) is to be performed as standard treatment, the third procedure as the most commonly done.

The use of a primary endorectal pull-through (ERPT) in the management of patients with Hirschsprung's disease represents a significant change from the classic approach to the treatment of this disease. from an article of (Vijaykumar1,2002), because of the simplified nature of this approach and the potential for cost savings, it has been reported that this procedure have shown to be a safe option.

As bowel function is a significant milestone for children to be mastered, studies showed that the functional outcome post pull through is an important determinant, to show the impact of this disease to children physically, socially and psychologically.

As based from Leiri et. Al, (2010), postsurgical treatment of hirschprung's patient creates a great impact and stigma as they continue their development in life. In developed countries, 90% have promising outcomes, regardless of the type of surgery. In developing countries such as in Malaysia and Indonesia, the percent of good outcome is 80%. (Dela merced et. Al, 2003).

The study wishes to determine the functional outcome of National Children's Hospital's patients with Hirschsprung's disease post therapeutic surgery. The researcher deemed it significant to conduct an in-depth investigation regarding the stooling pattern of

of patients with Hirschsprung's disease, after surgical end pull through at the said institution, as one of the specialized training hospital in the Philippine setting. Despite its importance and stigma in the lives children, only a few studies on this have been conducted namely, "Hirschsprung's Disease ten year experience at the Philippine Children's Medical Center" (Dela merced et. Al, 2003), which have documented that approximately 75% of their patients post-surgery are doing well and continued living at their fullest. The results of the study will give the institution a baseline information with regards to the said disease and also the current standing of the hospital, to successful rates post surgically.

Statement of the Problem

What is the functional outcome of patients with Hirschsprung's Disease, Post Surgical Transanal Endorectal Pullthrough at National Children's Hospital?

General Objective

To determine the functional outcome of patients with Hirschsprung's Disease, Post Surgical Transanal Endorectal Pullthrough at National Children's Hospital.

Specific Objectives

1. To determine the demographic profile of patients diagnosed with Hirschsprung's Disease as to:
 - a. Age
 - a1. age of diagnosis
 - a2. age of operation
 - b. Sex
 - c. Nutritional Status
2. To determine the stooling pattern of patients with Hirschsprung's Disease, post surgical transanal endorectal pull through as to:
 - a. Frequency
 - b. Type of stool base on Bristol chart
 - c. Soiling
3. To describe the quality of life of patients with Hirschsprung's Disease, post surgical transanal endorectal pull through 4-6 weeks after surgery.

Significance of the study

The researcher deemed it significant to conduct an in-depth investigation regarding the stooling pattern of patients with Hirschsprung's disease, after transanal endorectal pull through at the National Children's Hospital, as one of the specialized training hospital in the Philippine setting. Despite its importance and stigma in the lives of children, several retrospective studies from other Asian countries have been conducted with regards to this topic and this can be the first prospective study that will be done, locally only a few studies have been conducted namely, at the Philippine Children's Medical Center, which have documented that approximately 96% of their patients post-surgery are doing well and continued living at their fullest. This study may benefit our society by giving our community a glimpse of understanding on how these patients can live a normal life, in spite of their condition. If the community will be able to recognize the capabilities of these patients, discrimination will be lessened and their morale can even be uplifted. By seeing them as an inspiration not as a burden, it can highly create an impact not just to the Filipino community but also to other patients experiencing other kinds of diseases. The outcome of this study may help to further strengthen the prognostication of our future patients and we physicians may further assure them that they can live a better life ahead.

Scope and Delimitation

In this study, the researcher deemed it significant to conduct a baseline data with regards to the functional outcome of patients with Hirschsprung's Disease post surgical transanal endorectal pull through. This was important since our institution still has no study with regards to this topic, and very little data can be found within the Philippine literature. Hirschsprung's disease, in spite of its chronicity that creates great impact with the lives of children, physically as well emotionally and psychologically, has good prognosis and outcome (Dela merced et. Al, 2003). In this study, the researcher limited only her objective to the functional outcome of patients with Hirschsprung's disease post surgical transanal endorectal pull through in terms of the demographic profile and stooling patterns of patients. The population of this study included those patients that were diagnosed with Hirschsprung's Disease, children of 0 -7 yrs old, and those who underwent post surgical transanal endorectal pull through at the National children's Hospital, who followed up at the Surgery Out Patient Department from March 2016 to August 2017.

Definition of Terms

1. **Stooling patterns** – determined by the frequency of stooling, type of stools based from the Bristol chart, and with or without the presence of incontinence.
 - a. Bristol chart: type 1-3 as normal and type 4-7 as abnormal
 - b. Stool Frequency: considered as normal base from clinical practice and related literature
 - i. School aged: 1-2 stool/day
 - ii. Infant: 2-5 stools/day
 - c. Soiling- leading to intermittent loss of bowel contents, including flatus (gas), liquid stool elements and mucus, or solid feces.
2. **Quality of Life**- defined as the ability of the child to return to schooling and or ability to play or socialize with other children, 4-6 weeks after surgery.
3. **Bristol Chart**- is a medical aid designed to classify the form of human feces into seven categories. It was developed by Dr. Ken Heaton at the University of Bristol and was first published in the Scandinavian Journal of Gastroenterology in 1997. The authors of that paper concluded that the form of the stool is a useful surrogate measure of colon transit time. It remains in use as a research tool to evaluate the effectiveness of treatments for various diseases of the bowel, as well as a clinical communication aid.

Type 1: Separate hard lumps, like nuts (hard to pass)

Type 2: Sausage-shaped, but lumpy

Type 3: Like a sausage but with cracks on its surface

Type 4: Like a sausage or snake, smooth and soft

Type 5: Soft blobs with clear cut edges
(passed easily)

Type 6: Fluffy pieces with ragged edges, a mushy stool

Type 7: Watery, no solid pieces, entirely liquid

Types 1 and 2 indicate constipation, with 3 and 4 being the ideal stools (especially the latter), as they are easy to defecate while not containing excess liquid, and 5, 6 and 7 tending towards diarrhea. (Lewis, 1997) However, in patients with Hirschsprung's disease type 4-7 can be considered as normal.

4. **Nutritional status-** using z score for weight for height, defined as no wasting, with wasting, severe stunting, no stunting, with stunting and with severe stunting.
5. **Transanal endorectal pullthrough** - is the removal of diseased rectal mucosa along with resection of the lower bowel, followed by anastomosis of the proximal stump to the anus, to spare the function of the anus. In this study all hirschsprung's disease patients who underwent the said definitive treatment, resulting to the formation of a "neoanus"(new anus), irregardless of with or without colostomy bag usage prior to the pullthrough. Furthermore, these included patients who had completed series of anal dilatation post surgery.

Review of Related Literature

Hirschsprung's disease also called congenital megacolon or congenital aganglionic megacolon, is a developmental disorder of the enteric nervous system, characterized by an absence of ganglion cells in the distal colon resulting in a functional obstruction (Sultan, 2011).

The pathogenesis of Hirschsprung disease results from the absence of enteric neurons within the myenteric and submucosal plexus of the rectum and/or colon. Enteric neurons are derived from the neural crest and migrate caudally with the vagal nerve fibers along the intestine. These ganglion cells arrive in the proximal colon by 8 weeks' gestation and in the rectum by 12 weeks' gestation. Arrest in migration leads to an aganglionic segment. This results in clinical Hirschsprung disease. According to statistics 75% of aganglionic segment are located at the rectosigmoid area, 10% to which all segment of the colon is affected (Marty TL1et.al, 1995).

The definitive diagnosis of Hirschsprung disease rests on histological review of rectal tissue is obtained by suction rectal biopsy or transanal wedge resection. If a suction biopsy is performed, the biopsy is taken 2-2.5 cm above the dentate line on the posterior wall to minimize the risk of perforation. The biopsied specimen is examined for the presence or absence of ganglion cells in the submucous plexus (suction rectal biopsy) or myenteric plexuses (transanal wedge resection).

In the hands of an experienced pathologist, the resulting biopsy and absence of ganglion cells confirm the diagnosis and allow the initiation of treatment.

Skip lesions of aganglionosis have been reported in cases of Hirschsprung disease. Histologic findings include the absence of ganglion cells in the myenteric plexus and hypertrophic extrinsic nerve fibers. Acetylcholinesterase staining of the tissue can be performed to assist with the pathologic assessment. Acetylcholinesterase staining identifies the hypertrophy of extrinsic nerves trunks. In short-segment Hirschsprung disease, the diagnosis can be made with a properly placed rectal suction biopsy alone or in combination with anorectal manometry. Acetylcholinesterase staining and calretinin immunostaining may be helpful in making the diagnosis.

Radiologically, barium enema is requested, wherein a pathognomonic sign will be a transition zone, between the normal dilated proximal colon and a smaller caliber obstructed distal colon caused by non-relaxant of aganglionic bowel. Unprepared single-contrast barium enema is done if perforation and enterocolitis are not suspected, an unprepared single-contrast barium enema may help establish the diagnosis by identifying a transition zone between a narrowed aganglionic segment and a dilated and normally innervated segment. The study may also reveal a nondistensible rectum, which is a classic sign of Hirschsprung disease. A transition zone may not be apparent in neonates, because of insufficient time to develop colonic dilation, or in infants who have undergone rectal washouts, examinations, or enemas.

Nearly all children with Hirschsprung disease are diagnosed during the first 2 years of life. Approximately one half of children affected with this disease are diagnosed before they are aged 1 year (Samuel, 2006). A small number of children with Hirschsprung disease are not recognized until much later in childhood or adulthood. During the newborn period, infants affected with Hirschsprung disease may present with abdominal distention, failure of passage of meconium within the first 48 hours of life, and repeated vomiting. A family history of a similar condition is present in about 30% of cases. Nearly one half of all infants with Hirschsprung disease have a history of delayed first passage of meconium (beyond age 36h), and nearly one half of infants with delayed first passage of meconium have Hirschsprung disease. Unlike children experiencing functional constipation, children with Hirschsprung disease rarely experience soiling and overflow incontinence. Children with Hirschsprung disease may be malnourished. Poor nutrition results from the early satiety, abdominal discomfort, and distention associated with chronic constipation. Older infants and children typically present with chronic

constipation. This constipation often is refractory to usual treatment protocols and may require daily enema therapy.

The worldwide frequency is unknown but the represented occurrence is approximately 1:5000-1:7000 per live births, where in males are affected more often (females 4:1). Based on studies there is an increased familial incidence in long segment diseases.

The overall mortality of Hirschsprung enterocolitis is 25-30%, which accounts for almost all of the mortality from Hirschsprung disease. The disease is generally sporadic, although incidence of familial disease has been increasing. Multiple loci appear to be involved, including chromosomes 13q22, 21q22, and 10q. Mutations in the Ret proto-oncogene have been associated with multiple endocrine neoplasia (MEN) 2A or MEN 2B and familial Hirschsprung disease. Other genes associated with Hirschsprung disease include the glial cell-derived neurotrophic factor gene, the endothelin-B receptor gene, and the endothelin-3 gene (Pini, 2011). Hirschsprung disease is strongly associated with Down syndrome; 5-15% of patients with Hirschsprung disease also have trisomy 21. Other associations include Waardenburg syndrome, congenital deafness, malrotation, gastric diverticulum, and intestinal atresia (Padillar, 2003).

Hirschsprung enterocolitis can be a fatal complication of Hirschsprung disease. Enterocolitis typically presents with abdominal pain, fever, foul-smelling and/or bloody diarrhea, as well as vomiting. If not recognized early, enterocolitis may progress to sepsis and transmural intestinal necrosis (Frykman, 2012).

Operational intervention is warranted. In some patients, colostomy is done first for 6 to 12 months then one of the three surgical procedures (Swenson, Duhamel, Soave) is to be performed as standard treatment. The surgical options vary according to the patient's age, mental status, ability to perform activities of daily living, length of the aganglionic segment, degree of colonic dilation, and presence of enterocolitis.

Surgical options include leveling colostomy, which is a colostomy at the level of normal bowel; a staged procedure with placement of a leveled colostomy followed by a pull-through procedure; or a single-stage pull-through procedure. The single-stage pull-through procedure may be performed with

laparoscopic, open, or transanal techniques. This procedure can be performed at the time of diagnosis or after the newborn has had rectal irrigations at home and has passed the physiologic nadir. Colostomy followed by pull-through procedure is generally reserved for those patients who present with sepsis due to enterocolitis, massive distention of ganglionic bowel prohibiting pull-through procedure, or are otherwise not medically suitable for the pull-through procedure.

The Soave or endorectal pull-through was introduced by Franco Soave at the Institute G. Gaslini in 1955. Use of this procedure has been conventionally approached with the placement of a decompressing colostomy once the diagnosis is made. This is followed by a definitive pull-through procedure once the child's intestine is decompressed and he or she reaches approximately 10 kg body weight (Langer, 2010). The use of a primary endorectal pull-through (ERPT) in the management of patients with Hirschsprung's disease represents a significant change from the classic approach to the treatment of this disease. The first successful modern report of a primary pullthrough for Hirschsprung disease came from (So et. al, 1980). Subsequently, because of the simplified nature of this approach and the potential for cost savings, it has been reported that this procedure have shown to be a safe option (Vijaykumar¹, 2002).

Postoperatively, patients need close follow-up care to assess healing as well as a screen for potential complications (eg, stricture formation). Outpatient dilations may be necessary to alleviate strictures and should be expected in patients who undergo a single-stage pull-through procedure in the newborn period (Zhang, 2005). Postoperative complications may include intermittent fecal soiling and incontinence, anastomotic leak, stricture formation, intestinal obstruction, and enterocolitis.

The outcome in infants and children with Hirschsprung disease is generally quite good. Most children obtain fecal continence and control. However, children with other significant comorbidities, such as major genetic abnormalities, may have lower rates of continence (Vijaykumar et.al, 2002).

Postsurgical treatment of hirschsprung's disease in a patient creates a great impact and stigma as they continue their development in life .

From Yanchar NL1, Soucy P. (1999), 64% of patients interpreted having normal stooling habit, 90% of parents were very satisfied with the child's outcome, post therapeutic surgery. According to this journal entitled Long term outcome after Hirschsprung's disease, perspective articles, most children have significant improvement with respect to soiling and that most parents are satisfied with child's outcome and adapt to their functional abilities along with them.

From Terri L Marty et.al (1995), stated that 15 patients over the age of 4 had excellent anorectal function and appeared well adjusted.

From Dasgupta, Roshni*(2008), during the 6-15 months (average of 8-12 weeks), the follow up period of all of them have had postoperative normal bowel movement.

From Arnold G Corana, b (1997), article titled: Long-term stooling patterns in infants undergoing primary endorectal pull-through for Hirschsprung's disease, concluded that transanal endorectal pullthrough in young infant can yield excellent results including normalization of stool frequency and good to excellent level of continence.

From Hashisha et. Al (2004) Transanal one-stage endorectal pull-through for hirschsprung's disease: a multicenter study, concluded that this technique was associated with excellent clinical functional outcome results.

From Reshma Doodnath, Prem Puri et.al (2010), concluded that majority of patients in whom Hirschsprung's disease is diagnosed during childhood have normal bowel function after surgery.

From Jessica L.A. Mills, David E. Konkin, Ruth Milner, et.al (2008). Long-term bowel function and quality of life in children with Hirschsprung's disease, stated that fecal soiling improved significantly with age, and this is the strongest predictor of quality of life of patients. One effect of this chronic disease is the clinical impairment in the psychosocial development of the child.

In our country, little data or information has been gathered and recorded regarding the functional outcome of patients post-surgery. One study at the Philippine Children's Medical Center, by Dela merced et. Al (2003). Hirschsprung's Disease ten year experience at the Philippine Children's Medical Center, have documented that approximately 96% of

their patients post-surgery had a good survival rate. Furthermore, basing on this study, the age of diagnosis was younger than 30 days in 50% of patients> constipation was the no. 1 complaint followed by abdominal distention. There was also delayed in passage of meconium in 62% if cases. The average time interval for the onset of symptom and diagnosis was 11.5 months, but 71% of case was confirmed within 6 months from onset.

THEORETICAL CONCEPTUAL FRAMEWORK

Figure 1 shows that genetics plays a big risk in the development of Hirschsprung's Disease. The functional outcome post surgical transanal endorectal pull through may be affected by several factors such as the socio demographic profile, by which this may give this study an overview of the prognosis of the disease based on the factor being described.

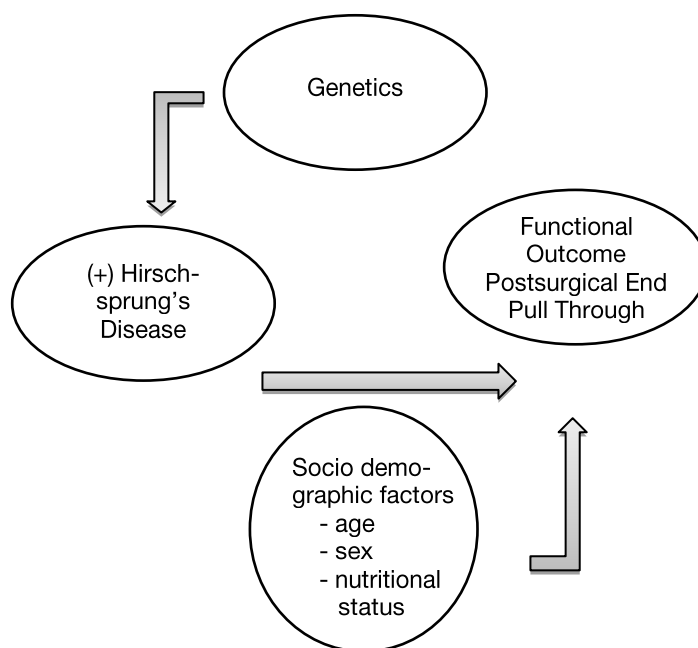


Figure 1: Cause and factors affecting the functional outcome of Hirschsprung's Disease

RESEARCH STUDY DESIGN AND METHODOLOGY

Research Design

A descriptive cross sectional study was conducted by the researchers for this topic.

Sources of Data

The study will be conducted at the Surgery Outpatient Department of the National Children's Hospital, a tertiary pediatric hospital under Department of health.

The participants of the study were patients at the Surgery Out Patient Department from March 2016 to August 2017, who fulfilled the following inclusion criteria:

1. Diagnosed case of Hirschsprung's Disease, s/p Transanal endorectal pullthrough, on follow up.
2. Patients 0-7 y/o who underwent surgical transanal endorectal pull through.

Exclusion Criteria:

- 1) Those with any associated GI anomalies.
- 2) Those with any co-morbidities like Down's syndrome, cardiac anomalies, hydrocephalus and other conditions that can alter the quality of living of patients.
- 3) Severe acute and chronic Malnutrition

Instrument

A patient data collection form was developed based from literature reviews regarding the frequently asked questions post therapeutic surgery, which include: stooling patterns and quality of life of patients.

The variables collected for this study were: age, gender and nutritional status, the frequency of bowel movement, shape and consistency of stools and presence of incontinence.

Furthermore, it also entailed whether the child had returned schooling or at least had the capability to play with other children again.

Procedure

This research protocol was approved by the Institutional Review Board (IRB). The study was conducted at Surgery Outpatient Department of the National Children's Hospital, located at 264 E. Rodriguez Sr. Blvd. Quezon City. The participants who fulfilled the criteria were given a comprehensible consent form, from which they were required to sign.

During the conduct of research, patients' anonymity and confidentiality were ensured. No identified data were out. Each data collection form had a code number, as the basis for data gathering.

Purposive sampling was used to select participants who already underwent end pull through secondary to Hirschsprung's disease. A minimum of 40 participants were considered significant, based on the proportion of good functional outcome among patients with hirschsprung's disease who underwent transanal endorectal pullthrough. Assuming that the proportion of the good functional outcome is 96% (PCMC, Dela Merced et. Al, 2003), with the maximum allowable error of 4% and reliability of 80%.

During follow up, consent form was signed and the physician /researcher used a patient data collection form for data gathering.

Statistical Analysis

Descriptive Analysis using proportion and percentages was used to present the results in all the variables. These included the age, gender and nutritional status, the frequency of bowel movement, shape and consistency of stools and presence of incontinence.

Moreover, it also entailed whether the child has returned schooling or at least had the capability to play with other children again.

Non-probability sample size was used. The sample size computed based on the proportion of postsurgical transanal pull through patients, assuming that the good functional outcome is 96% (from Dela Merced et.al 2003), with maximum allowable error of 4% (plus or minus 4 hence a 92-100% functional outcome for this study) and reliability of 80% ($z=1.29$), the sample size is 40.

Computation:

$N =$ sample size, $z =$ 80% reliability is 1.29 $p = .96$ (96% good functional outcome from Dela Merced Study 2003) $q = 1 - p$ $d =$ maximum allowable error (at 4% or .04)

$$N = (z^2 \times p \times q) / d^2$$

$$N = 40$$

Description of outcome measurements

The primary outcome was, to describe the stooling patterns of these patients post surgically as well their quality of life.

RESULTS OF THE STUDY

The prevalence rate of patients with Hirschsprung's Disease post transanal endorectal pullthrough at the National Children's Hospital was 31% (40/130) from March 2016 to August 2017. There were a total of 40 patients who fulfilled the inclusion criteria of the study. Out of the 40, 82 % were diagnosed with Hirschsprung's Disease as early as the newborn period, while 18% were diagnosed at the infant phase. Based on the data, 55% of the patients were operated at an age ranging from 1 to 3 years old and about 80% of the population in this study were males. It also showed that patients post operatively had no stunting and no wasting, about 60% of the total number.

However, the study shows that 65% of patients post operatively still had an abnormal type of stool, base on the Bristol chart. The latter, belongs to type 5 which was described as more of watery content of stools. The remaining 35% have type 3 stool, which was described as easy to defecate while not containing excess liquid. The stooling pattern of the included patients basing on its frequency revealed to tally in accordance to their respective age group. Only about 2.5 % had soiling even after 4-6 weeks post pull through.

Furthermore, the study showed that 62% of our patients belonged to the school aged bracket and 95% of those were able to get back to schooling or playing 4-6 weeks post operatively. This goes the same with the 38% of the population who were infants and who were all able to return to their respective quality of living, at the same range of time post operatively.

Table 1: Demographic Profile of Patients with Hirschsprung's Disease Post Surgical Transanal Endorectal Pull Through at National Children's Hospital (March 2016 to August 2017)

Profile	N (%)
A. Age of Diagnosis	
Newborn	33(82)
Infant	7 (18)
B. Age of Operation	
<1 y/o	15 (38)
1-3y/o	22 (55)
4-7y/o	3 (7)
C. Sex	
Male	32 (80)
Female	7 (20)
D. Z score (wt for ht)	
No wasting	19 (47.5)
With wasting	14 (35)
Severe wasting	0 (0)
No stunting	5 (12.5)
With stunting	2 (5)
Severely stunting	0 (0)

Table 2: Stooling Patterns of Patients Post Surgical Transanal Endorectal Pullthrough with Hirschsprung's Disease at National Children's Hospital (March 2016 to August 2017) based on Bristol chart, 4-6 weeks post surgery

Criteria	N (%)
Normal	19 (35)
Abnormal	21 (65)

After transanal endorectal pullthrough, 95% of school-aged children all had normal stool frequency (1-2 stools per day), while 100% of infant patients had normal frequency (2-5 tools per day).

In the study, only one patient had soiling after surgery. Further, 95% of the population (n=38) were able to play, socialize and go back to school post-operatively.

DISCUSSION

A cross-sectional descriptive study of patients who underwent transanal endorectal pull through secondary to Hirschsprung's disease was conducted in our institution.

Base on this study, Hirschsprung's Disease was more common in males, affecting around 30 patients (80%), as what most literatures reported such as at Granéli 2017. According to this journal, the said disease had a skewed gender distribution, with a female to male ratio of 1 : 4.

From other literatures, children with Hirschsprung's disease post surgically were malnourished as to the study of Kressmann 2006. According to this journal, 1.5% developed severe malnutrition due to early satiety, abdominal discomfort, and distention associated with or without chronic constipation. Our study, described 24 patients (60%) of the population had a normal z score on weight for height and 35 % were wasted. No patients were described as severely malnourished despite that 69% of the total patients had abnormal type of stool (type 5) based on the Bristol Chart.

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This study signified that comparing it to the result Nakatsuji T. Et. al, 2010, their percent of good outcome was 80% in developing countries such as in Malaysia and Japan, while in developed countries, 90% had promising outcomes. The previous Philippine study from Dela Merced et, al 2003 showed 96% survival rate, our institution's data has almost the same percentage of survival rate (95%) 4-6 weeks post-surgery, and this was 80% reliable. Furthermore, this gave us an idea that, in spite of the disease' chronicity, patients can be able to live their life to its maximum

Despite of the stigma that this disease can brought about, both physically and psychologically, as pediatricians, this study can support and strengthen our prognosis towards the said disease and help re-assure the parents of the condition of their children. This will eventually create a positive view as to how mother and child can cope with the impact of the disease. It has been noted that 2.5 % (1) of the patients had soiling and another 2.5% (1) developed enterocolitis, signifying that the surgery had 5 % chance of developing its complications and would further pave us a way for exploring these factors.

Lastly, this study gave us a baseline data of the functional outcome of patients with Hirschsprung's Disease 4-6 weeks post endorectal pull through, at National Children's Hospital, Philippines.

SUMMARY

The prevalence rate of patients with Hirschsprung's Disease post transanal endorectal pullthrough at the National Children's Hospital was 31% (40/130) from March 2016 to August 2017. Base on this study, from the total of 130 patients who followed up at the Surgery Outpatient Department, there were 40 patients who were diagnosed with Hirschsprung's disease, and underwent trans anal endorectal pull through, were included as study subjects. Among those, 82 % were diagnosed at the newborn period and predominantly were males. The most common age group to which surgery was done, belonged to age 1-3 years old, at around 55%. The study also showed that 60% about 47.5% of the patients had no wasting and 12.5% had no stunting. However, 69% of these patients presented with abnormal stool type based on the Bristol Chart (type 5), with 2.5 % of the total population who still had soiling post operatively. In our study it showed that 95% of our patients were able to go back to playing and schooling, about 4-6 weeks post-surgery. The remaining 2 patients (5%) as follows; one of whom still had soiling and the other developed enterocolitis, readmitted and treated.

CONCLUSION

The prevalence rate of the said disease is 31 % (40/130). Majority of our patients with Hirschsprung's Disease (82%) were diagnosed during the newborn period. The prevalence of this disease is more common to the male gender and the common age group from which trans anal endorectal pull through was done, was at 1-3 years of age. Postoperatively, most of the patients improved with more than half of the study population had normal z scores. In spite the fact that 1 patient had soiling and more than half of the population had an abnormal stool type based on the Bristol Chart (type 5), 95% of our patients were able to go back to playing, socializing and schooling, at about 4-6 weeks post-surgery, signifying a great impact with the prognosis of the disease. Furthermore, this provided the National Children's Hospital a baseline data with regards to Hirschsprung's disease, a chronic disease which created a stigmata in the lives of children as a whole; physically, emotionally and psychologically.

RECOMMENDATION

There are other factors that can affect the functional outcome of Hirschsprung's disease post operatively. These include the length of the segment to be removed. Some studies noted that if a shorter segment is affected, it has better prognosis. Other factors include other comorbidities; such as, Down's syndrome, malnutrition and complications; which include enterocolitis and gastroenteritis. These topics can be further explored and correlated with the functional outcome of the said disease. Furthermore, a comparison of the prognosis between a single-stage versus a multi-stage pull through procedure in the Philippine set-up can be a good area to be investigated as part of this topic.

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ANNEX

Patient Data Collection Form 1

Code: **Age:** **Sex:** **Wt:** **Ht:**

wt/ht z score:

*Operational Definition of Stooling Pattern

1. How many bowel movements does your child have each day?

☐ Once ☐ Twice ☐ Thrice ☐ $\geq$ Four

2. what is the type of the stool?

☐		Separate hard lumps, like nuts (hard to pass)
☐		Sausage-shaped but lumpy
☐		Like a sausage but with cracks on its surface
☐		Like a sausage or snake, smooth and soft
☐		Soft blobs with clear-cut edges (passed easily)
☐		Fluffy pieces with ragged edges, a mushy stool
☐		Watery, no solid pieces ENTIRELY LIQUID

3. Is there any incontinence?

☐ Yes ☐ No

*Operational Definition of Quality of Life

1. (if 4-7 yrs. old) Does the child attends/returned to schooling? Or became active again?

☐ Yes ☐ No

2. (if 0-3 yrs. old) Did the child regain his/her playfulness?

☐ Yes ☐ No

If Child is 0-3 yrs old:

- a. Neonatal period
 - ☐ Visual preference to human face
- b. 1 months
 - ☐ Body movements in cadence with voice of other in social contact
- c. 2 mo
 - ☐ Smiles on social contact
- d. 3 months
 - ☐ Listens to music says "aah, ngah", sustained social contact
- e. 4 months
 - ☐ Laughs out load
- f. 7 months
 - ☐ Babbles
- g. 10 months
 - ☐ Plays peek a boo, waves bye-bye
- h. 15 months
 - ☐ Indicates needs by pointing
- i. 18 months
 - ☐ feeds self, kisses parent pucker
- j. 1 year old
 - ☐ Plays simple ball game
- k. 30 months
 - ☐ pretends in play
- l. 36 months
 - ☐ Plays simple games in parallel with other children

If Child 4-7 yrs. Old

- a. 4-5 yrs. Old
 - ☐ role playing, creation of scenarios that are imaginary, recognition of rules
 - OR
 - ☐ knows basic color, counts 1-10 penies, prints first name (underline if needed to emphasized)
- b. 6-7 yrs. Old
 - ☐ dresses completely, abides with rules
 - OR
 - ☐ formation of group of friends

Effect of Aspiration and Non-Aspiration of Syringe prior to Intramuscular Administration of Influenza Vaccine in Pain Perception of Children 9 to 15 Years of Age Consulting at the Out-patient department of a Tertiary Government Hospital

Jovy Anne C. Otero, M.D., Michael M. Resurreccion, MD¹

ABSTRACT

Objective: To determine the effect of aspiration and non-aspiration of syringe prior to intramuscular administration of influenza vaccine in pain perception of children 9 to 15 years of age consulting at the Out Patient Department of a Tertiary Government Hospital

Design: Randomized controlled clinical Trial

Setting: Out Patient Department of a Tertiary Government Hospital

Participants: One-hundred twenty children 9 to 15 years old consulting at the Out Patient Department

Methodology: Subjects were randomized into two groups and were given influenza vaccine with and without aspiration prior to intramuscular injection.

Outcome Measures: Primary outcome measure is the degree of pain experienced by the subject using the Numeric Rating Scale.

Results: A total of one hundred twenty children were randomized to either Group A or Group B. IBMSPSS version 21 was used as statistical software. Differences in mean heart rate at baseline and after the intervention within group is significantly different (p value < 0.01). Mean heart rate in between group at baseline and after administration of influenza vaccine is not significantly different (p value > 0.05). The difference in mean oxygen saturation at baseline and after immunization within group is significantly different. Mean oxygen saturation between group pre and post immunization is not statistically different (p value 0.309). Analysis showed there is a significant difference in mean pain scores between Group A and Group B (p value 0.046)

Conclusion: This study showed a statistically significant lower pain score for Group A (without aspiration) than Group B (with aspiration). The physiological pain responses, used as outcome measures in this study did not have significant differences between two groups. The result of this study will unleash in health care professionals the burden on whether or not to aspirate before intramuscular administration of vaccine.

Keywords: *aspiration, non-aspiration, influenza vaccine, pain assessment, intramuscular injection*

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INTRODUCTION

Acute pain is one of the most common adverse stimuli experienced by children, as a result of injury, illness, and medical procedures like drug administration and immunizations.¹ In any country, immunization in the pediatric population is essential as it decreases the morbidity and mortality of vaccine-preventable diseases.² However, pain associated with immunization can lead to pre-procedural anxiety, needle fears, healthcare avoidance behaviors, and noncompliance with vaccination schedules.³

Accurate assessment of acute pediatric pain can help dispel myths that children's pain is less severe than that of adults, aid medical staff and clinicians in accurately diagnosing and treating children's pain, and allow researchers to investigate pain and its correlates.⁴

Pediatricians are responsible in alleviating the pain and suffering of children. In order to achieve these goals, pediatricians need to expand their knowledge, use appropriate assessment tools and techniques, anticipate painful experiences and intervene accordingly.¹ A number of strategies are available to diminish pain associated with immunization like procedural interventions (injection techniques), physical interventions (body position and activity), pharmacologic interventions (pain medicine), or even process intervention.³

The guidelines to aspirate prior to an intramuscular injection were originally recommended for reasons of safety, to avoid the inadvertent injection of vaccine material intravenously instead of intramuscularly. The lack of reported publication might suggest that aspiration is effective.⁵ However, the US Advisory Committee on Immunization Practices (ACIP) does not make any recommendations on aspiration during vaccination.⁶

Despite the many recommendations, not all clinicians adopt to such strategies hence more studies were contemplated to support these guidelines. This paper seeks to answer the question: What is the effect of aspiration and non-aspiration of syringe before intramuscular administration of influenza vaccine in pain perception of children nine to fifteen years of age consulting at the Outpatient Department of a Tertiary Government Hospital.

REVIEW OF RELATED LITERATURE

In order for a clinician to manage childhood pain, he/she should be able to assess pain accurately. A child's pain may depend on the child's capability to express their pain. It is also based on a child's age, experience and their changes throughout their developmental changes. Studies have shown that self-report visual analogue and numerical scales are effective pain assessment tools in children and adolescents.⁷

Several studies to reduce pain associated with immunization have been cited. Se Na, Joohyun, et al, showed significantly lower pain scores in children when EMLA was applied prior to venipuncture procedures. The study concluded that the pain scale were significantly lower in the experimental group (EMLA) compared to those in the control group (Placebo) as determined by three rating scale which include the Faces Pain Rating Scale ($p=0.008$), the Procedure Behavior Checklist ($p=0.001$), and the Visual Analogue Scale (VAS) ($p=0.006$). However, the changes in the children's pulse rate and oxygen saturation were not significantly different between the two groups. Nevertheless, the pulse rate and oxygen saturation of the experimental group were more stable during the time of the injections.⁸

A randomized placebo-controlled clinical trial done among pre-school children in Cabiao, Nueva Ecija compared the effectiveness of ice gel compress for five and ten minutes with topical Lidocaine – Prilocaine cream in reducing pain associated with Diphtheria-Pertussis-Tetanus (DPT) vaccination. The study showed that lidocaine-prilocaine was not significantly different between ice gel compress at 5 minutes and ice gel compress at 10 minutes (p values > 0.300). Ice gel at 10 minutes has statistically significant lower pain scores compared with the ice gel at 5 minutes (p value= 0.015).

The placebo group has significantly higher pain score compared to the three other treatment groups (p values < 0.001). Lidocaine-prilocaine and ice gel compress at 10 minutes are not significantly different. Ice gel compress at 5 minutes and placebo are not statistically different. Lidocaine-prilocaine and ice gel compress at 10 minutes are significantly different with the placebo and ice gel compress at 5 minutes (p values < 0.001). There was statistically significant difference in the increase in heart rates (p value = 0.0134) and reduction of O₂ saturation (p value = 0.0109) among treatment groups.⁹

In 2014, Girish, Ravi, et al conducted a randomized controlled trial among 200 infants 6 weeks to one and half years of age receiving routine intramuscular vaccination. They were randomly assigned by computer-generated random numbers into 'Standard group' receiving immunization using standard slow technique with aspiration and 'Pragmatic group' receiving immunization using "pragmatic" technique without aspiration. The entire vaccination procedure was videotaped. Videos were scored for pain using Modified Behavioral Pain Scale (MBPS) by 2 clinical psychologists. Pain was scored within 15 seconds of the immunization. Cry time was measured by a different person from the start of cry till it ends. The author concluded that the "standard" slow technique was significantly more painful and took longer to administer (5-10 second) when compared to pragmatic technique (1-2 second). Cry duration is lesser in the pragmatic group than standard group, but it is statistically not significant.¹⁰

SIGNIFICANCE OF THE STUDY

Childhood immunizations are strategies which widely control the spread of vaccine-preventable diseases. Pain associated with immunizations is a hindrance to the success of this program. Management of pain associated with immunizations can benefit the health care providers, the children and the parents. The key goal is, less pain experienced during immunizations, a more compliant parents and patient to future immunizations.

The result of this study can benefit the health care provider facilitate a faster and convenient way to administer vaccines. This strategy will shorten patient waiting time and improved the quality of health care.

Children with reduced pain during vaccination will have less fear in subsequent clinic visit. An improved compliance to immunizations would mean completion of all the recommended vaccines. Moreover, children will have maximum protection from vaccine-preventable diseases.

A decrease pain during immunization will encourage parents to complete their child's immunization. Parents of a fully immunized child will have less work day of absences from illness and hospitalization and when translated in peso would mean savings. A disease-free child will relieve the parents from stress and worries of the possible complications of the disease.

The results of this study can guide health policy makers formulate guidelines/recommendation on strategies to decrease pain associated with immunization that will enhance parents and patients compliance to childhood vaccination.

GENERAL OBJECTIVE:

To determine the effect of aspiration and non aspiration of syringe prior to intramuscular administration of influenza vaccine in pain perception of children 9 to 15 years of age consulting at the Out Patient Department of a Tertiary Government Hospital.

SPECIFIC OBJECTIVES:

1. To compare the pain level using the Numerical Rating Scale (NRS) among children given influenza vaccine with and without aspiration prior to intramuscular administration.
2. To determine the effect of aspiration and non aspiration of syringe on oxygen saturation and heart rate in children before and after intramuscular injection of influenza vaccine.
3. To determine the adverse effect of aspiration and non aspiration of syringe prior to influenza vaccine.

OPERATIONAL DEFINITION:

1. Primary outcome measure

The primary outcome measure will be the degree of pain experienced by the subject using the Numeric Rating Scale.

Numerical Rating Scale –The primary outcome measure is the degree of pain as reported by the patient using the Numerical Rating Scale (NRS).¹¹ The subjects will give a self-report of pain after the influenza vaccination. The scale will be from zero to ten with zero being 'no pain' and ten being 'severe pain'. A lower average pain score will indicate that intramuscular injection without aspiration is effective in reducing pain associated with vaccination.

2. Secondary outcome measure

2.1 Heart Rate Difference – The difference between pre- and post- injection heart rate as measured by a portable finger-type pulse oximeter. A lower increase in heart rate from the baseline will be interpreted as a lower degree of pain from the injection.⁹

2.2 O₂ Saturation Difference - The difference between pre- and post- injection oxygen saturation as measured by a portable finger-type pulse oximeter. A lower decrease in oxygen saturation from the baseline will be interpreted as a lower degree of pain from injection.⁹

3. Adverse Reactions

Adverse reactions are change in color, itchiness or indurations which may appear during the course of the study on the area of vaccination.

Change in Color – Redness or blanching (change from pinkish to pale) on the area where the vaccine was administered

Itchiness – A tingling or uneasy irritation of the skin that causes a desire to scratch the affected area

Induration – Localized hardening of the soft tissue or the skin.

METHODOLOGY:

1. RESEARCH DESIGN

This is a randomized controlled clinical trial which determined the degree of pain as perceived by children and adolescents after influenza immunization.

2. SETTING AND DURATION

The study took place in the Out Patient Department of a Tertiary Government Hospital.

3. SAMPLE SIZE ESTIMATE

The sample size was computed using the Formula of Cochrane. The minimum sample size requirement is 34 subjects with 17 patients for each group. This is based on mean pain response of 5.6 in the aspiration technique and 3.3 in the non aspiration technique, with a standard deviation of 2, 95% confidence level and 90% power. A 30% allowance for the drop-outs was determined with the minimum sample size increased to 120 subjects. Sixty subjects were allocated for each group.

4. ELIGIBILITY CRITERIA

Included in the study were children 9 to 15 years old consulting at the Out Patient Department; children eligible for influenza immunization; and children with

written informed consent from their parents or guardians and assent signed by the participants in the study.

Excluded in the study were children with acute febrile illness; children with history of convulsions or severe allergic reactions to influenza vaccine; children with history of allergies to egg protein; children with skin lesion over the injection site; and children who could not communicate verbally.

5. STUDY PROCEDURE

A letter was submitted to the Medical Center Chief of the Tertiary Government Hospital requesting permission to conduct a study at the Out-Patient Department. The research was reviewed and approved by the Institutional Review Board.

A research orientation was conducted among the members of the research team. Their duties and responsibilities were discussed with each member of the team. Letters and instructions were distributed to parents/guardians of possible study participants discussing the research objectives and procedures. The principal investigator conducted an interview along with the parents/guardians and performed a thorough physical examination. The subjects were screened based on the inclusion and exclusion criteria. An assistant investigator secured informed consent from the parents/guardians and assent forms from the subjects prior to the study.

A statistician prepared a computer-generated randomization list. The list was unknown to the other members of the research team including the primary investigator. A patient data form was used to collect all relevant clinical information and outcome measures. Data were gathered and analyzed accordingly (Appendix A).

Randomization and Group Allocation

Subjects were assigned into groups by randomization. Results of randomization of treatment allocation were placed in opaque envelopes, arranged chronologically. Each envelope indicated which group the subject would belong. Subjects assigned for the injection without aspiration were included in Group A while those assigned for injection with aspiration were in group B. The paper also denoted a three-digit code which coincided with the designated computer-generated randomization list.

In Group A, the needle was inserted at 90 degrees with steady pressure. No aspiration was performed. The vaccine was rapidly injected and the needle withdrawn. In Group B, the needle was inserted at 90 degrees with steady pressure. Aspiration was performed. The vaccine was rapidly injected and then the needle was withdrawn.

The randomized list of the subjects was kept classified and was revealed only after the completion of the study.

Vaccine Description

The vaccine used in this study was Influvac® 2016 an inactivated influenza vaccine. The vaccine is produced by Abbot Products Operations AG. It is a trivalent subunit influenza vaccine. A 0.5 ml dose contains neuraminidase and 15 mcg of hemagglutinin antigen for each virus strain present in the vaccine. The virus strains used in the vaccine for 2016/2017 are: an A/California/7/2009 (H1N1) pdm09-like virus; an A/Hong Kong/4801/2014 (H3N2)-like virus; and a B/Brisbane/60/2008-like virus. The vaccine is a colorless, clear liquid. It is thimerosal-free, mercury-free, and contains no preservative. Its route of administration is through intramuscular injection or deep subcutaneous injection. In this study, it was administered to children intramuscularly.

Vaccine Administration

Each subject was called to the treatment room of the Out-Patient Department one at a time. A nurse investigator 1 took the heart rate and oxygen saturation with a pulse oximeter prior to the administration of the vaccine. The nurse investigator 1 performed proper hand hygiene by cleansing with a waterless alcohol-based hand rub as recommended by the Centers for Disease Control and Prevention (CDC).¹² The deltoid region was pre-sterilized with a cotton ball damped in 70% isopropyl alcohol.¹³ The nurse investigator number 1 administered the influenza vaccine intramuscularly, with or without aspiration depending on the subject's treatment allocation. The used syringe and needle devices were placed in biohazard containers that were closable, puncture-resistant and leak-proof. Cold chain was maintained until vaccines were administered. Emergency medications like Epinephrine, Diphenhydramine and Hydrocortisone were on hand at the site of the study. The Emergency Department was notified in the event that an adverse reaction would be experienced by any of the subjects.

Outcome Measurement

The assistant investigator number 2 determined and recorded the heart rate and oxygen saturation after the administration of vaccine. The assistant investigator number 2 helped out the subjects in reporting their pain level using the numerical rating scale, wherein 0 is equivalent to no pain, numbers 1, 2, and 3 is mild pain; numbers 4, 5 and 6 is moderate pain and numbers 7 to 10 mean severe pain (Appendix B).

The Primary investigator collated the data, checked them for completeness and accuracy, encoded them in MS Excel. Then they were statistically analyzed.

ETHICAL CONSIDERATION

This study protocol was evaluated by the Institutional Review Board - Ethics Committee of Quirino Memorial Medical Center.

The study was done according to the Principles in the Declaration of Helsinki. Parents and subjects were informed of the purpose, procedures, risk and benefits related to the study. A voluntary informed consent and assent were obtained prior to inclusion to the study. Confidentiality was practiced with utmost care.

Contact numbers of the investigator was provided to the parents/guardians of the subjects.

DATA MANAGEMENT AND ANALYSIS

Continuous data were described using means and standard deviations while categorical data were expressed in frequency and percentages. Differences between two groups with continuous variables were tested using t-test for independent samples while changes of averages from baseline to posttest within group were tested using Paired t-test. Fischer exact test was used in establishing association between gender and groups. Any associated p-values lesser than 0.05alpha were considered significant. IBMSPSS version 21 was used as statistical software.

RESULTS

One hundred twenty children met the inclusion criteria and were randomized to either Group A or Group B. The ages of the children ranges from 9 – 15 years. The mean age for Group A (Without Aspiration) is 11.35 years (2.01 SD). The mean age group for

Group B (With Aspiration) is 12.12 years (2.05 SD). Shown in Figure 1 is the mean age of participants in the two treatment group. The mean age in both groups were statistically significant (p value 0.041). Majority of the participants in both groups were male (61% in Group A and 53 % in Group B). The sex distribution of participants in both study groups showed no statistically significant difference (p value 0.356).

Table 1 Mean Age in Years and Sex Distribution of Participants in Group A and Group B

	Group A		Group B		p – value
	Mean	Std. Deviation	Mean	Std. Deviation	
Age (years)	11.35	±2.01	12.12	±2.05	0.041
Gender:					0.356
Male	37 (61.7)		32 (53.3)		
Female	23 (38.3)		28 (46.7)		

Shown in Table 2 is the mean heart rate of participants at baseline and after intramuscular injection of influenza vaccine. The mean heart rate of participants in Group A (without aspiration) decreased from 93.25 bpm at baseline to 91.25 bpm post injection (p value <0.01). In comparison the mean heart rate in Group B (with aspiration) increased from 92.28 bpm at baseline to 94.43 bpm post injection (p value <0.01). The differences in mean heart rate at baseline and after the intervention within group is significantly different (p value < 0.01). Analysis of the mean heart rate in between group at baseline and after administration of influenza vaccine is not significantly different (p value >0.05).

Table 2 Comparative Mean Heart Rate of Group A and Group B at Baseline and Post Intramuscular Administration of Influenza Vaccine

Phase	Group A		Group B		p value
	Mean	Std. Deviation	Mean	Std. Deviation	
Baseline	93.25	±20.11	92.28	±17.23	0.778
Post	91.25	±19.54	94.43	±21.21	0.629

Table 3 outlines the mean oxygen saturation of Group A and Group B at baseline and after immunization. The mean oxygen saturation in Group A (without aspiration) decreased from 97.68% at baseline to 96.93% post immunization (p value < 0.01). In comparison the mean oxygen saturation in Group B (with aspiration) decreased from 97.57% at baseline to 96.32% at post immunization (p value < 0.01). The difference in mean oxygen saturation at baseline and after immunization within group is significantly different. Analysis of the mean oxygen saturation between group pre and post immunization is not statistically different (p value 0.309).

Table 3 Comparative Mean Oxygen Saturation of Group A and Group B at Baseline and Post Intramuscular Injection of Influenza Vaccine

Phase	Group A		Group B		p value
	Mean	Std. Deviation	Mean	Std. Deviation	
Baseline	97.68	±1.14	97.57	±1.48	0.629
Post	96.93	±3.43	96.32	±3.18	0.309

Table 4 shows the comparative mean pain scores of Group A (without aspiration) and Group B (with aspiration) post-intramuscular injection. The mean pain score of participants in Group A is 1.72. In comparison, the mean pain score of participants in Group B is 2.47. The analysis showed there is a significant difference in mean pain scores between Group A and Group B (p value 0.046).

Table 4 Comparative Mean Pain Scores of Group A and Group B Post Intramuscular Injection of Influenza Vaccine

Phase	Group A		Group B	
	Mean	Std. Deviation	Mean	Std. Deviation
Pain score	1.72	±1.66	2.47	±2.36

DISCUSSION:

Development and administration of immunization is one of the greatest achievements in public health of this generation. Studies have shown that this strategy have markedly decrease vaccine-preventable disease. However, pain associated with procedures like Injection in immunizations hinders its purpose. Pain is

an inherently subjective multifactorial experience and should be dealt accordingly. Clinicians should find efficient and convenient strategies to administer vaccines and achieve health for all in 2020. Aspiration prior to injection is a part of the process of performing vaccinations that has been a wide-spread clinical practice yet has never been substantiated by scientific data.

This study showed that intramuscular administration of influenza vaccine without aspiration in adolescent children 9 to 15 years old is less painful as compared to intramuscular injection with aspiration. Pain scores were significantly lower in the group with no aspiration prior to intramuscular injection (p value 0.046). Physiologic pain responses like heart rate and oxygen saturation were included in the assessment of pain in the study. In children given with influenza vaccine without aspiration, they demonstrated a significant decrease in heart rate from baseline to post-injection (p value <0.01) as compared to a significant increase in heart rate from baseline to post-injection (p value <0.01) in the group given with vaccine with aspiration. This study also showed a quantifiable decrease in oxygen saturation between groups however not statistically significant. No adverse reactions like blanching, itchiness and rashes were observed during the study.

In congruence with this research, the studies made by Ipp, and Girish also determined acute pain response in routine immunizations in infants using different methodology but revealing similar outcomes. In the country, same study was done in school-aged children comparing their response in intramuscular injection of influenza vaccine with and without aspiration. Rayco noted a significant less painful experience in children given influenza vaccine without aspiration. It provided a possible explanation that rapid injection is less painful in children.¹⁵

This study can be relevant in applying interventions in alleviating acute pain in children. This can help improve techniques in vaccination procedures which are performed frequently in clinics. With this, we can expect more compliant parents and patients in immunization that may result to a lesser occurrence of vaccine-preventable diseases.

CONCLUSION

This study showed a statistically significant lower pain score for Group A (without aspiration) than Group B (with aspiration), p value 0.046. The physiological pain responses, used as outcome measures in this study did not have significant differences between two groups (p value >0.05). The result of this study will unleash in health care professionals the burden on whether or not to aspirate before intramuscular administration of vaccine.

LIMITATIONS AND RECOMMENDATIONS

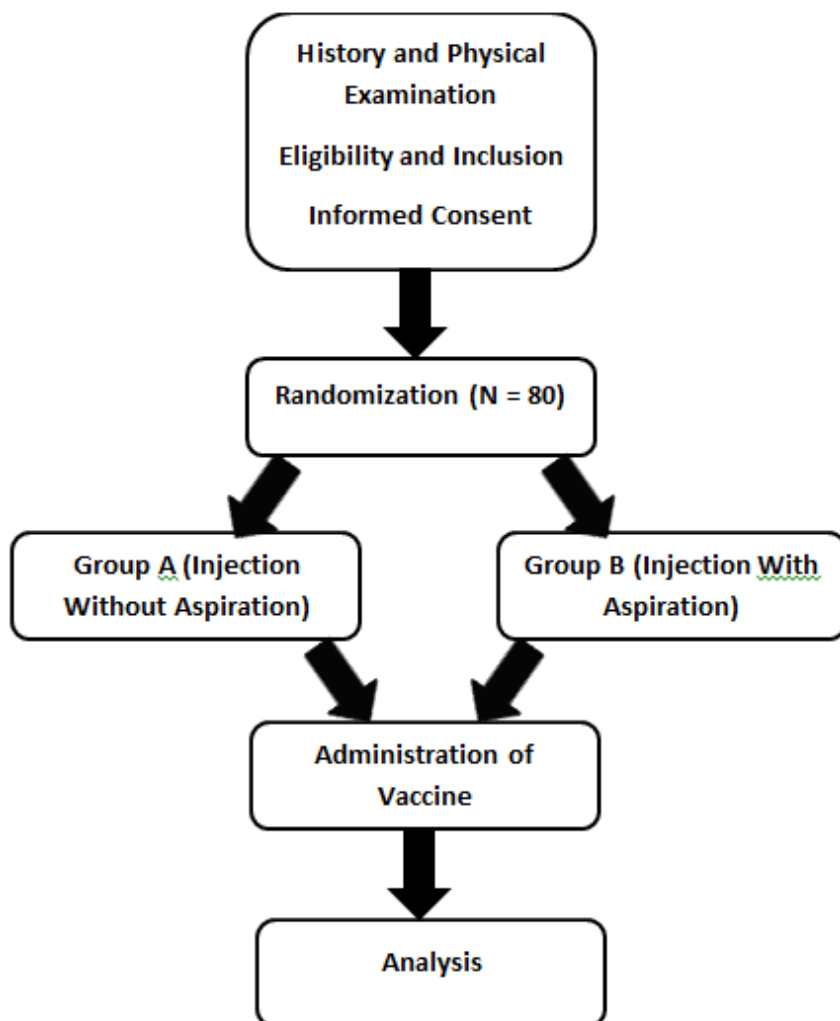
This study is limited to intramuscular immunization only. This is not generalized to all aspiration techniques prior to intramuscular injection procedures like drug administration.

It is recommended that future studies use bigger samples for more accurate determination of statistical significance.

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APPENDIX A**Flow of Procedure****APPENDIX B****Patient Assessment Sheet****Patient number:**

	Before Vaccination	After Vaccination
Heart Rate		
Oxygen Saturation		

Adverse Reactions:

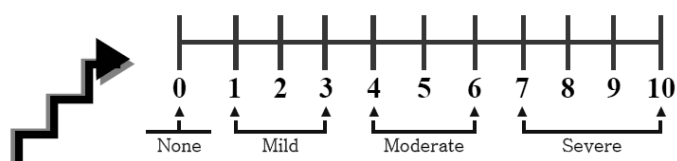
_____ Redness

_____ Blanching

_____ Itchiness

Others: _____

Numeric Rating Scale



Assessor: _____

Date: _____

A Survey on the Nutrition Risk Level of Patients Subjected to Standard Practice of Enteral Nutrition Provision Admitted at the Intensive Care Unit of Cebu Doctors' University Hospital: A One-Year Retrospective Chart Review

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ABSTRACT RETROSPECTIVE - ANALYTICAL

Background: Enteral nutrition is nutrition provided through the gastrointestinal tract, which delivers nutrition distal to the oral cavity. Critically ill patients are at high nutrition risk thus the need for full nutrition assessment. At present, NUTRIC score is one of the reliable assessment tools for quantifying risk of developing adverse outcome in critically ill patients, which may be modifiable by aggressive nutrition therapy.

Objectives: We assessed the nutrition risk levels as measured by NUTRIC score among admitted patients who were given enteral nutrition at the Intensive Care Unit of Cebu Doctors' University Hospital from June 2016 to June 2017.

Methodology: This is a one-year single-center cross-sectional retrospective chart review study on admitted ICU patients from June 2016 to June 2017. Categorical profiles were expressed in frequency and percentage while those continuous variables were described in mean and standard deviations. Moreover, incidence rate of nutrition risk levels of patients was computed. In comparing the required and actual feeding amount of patients was compared using the Paired t-test wherein a p-values lesser than 0.05 alpha were considered significant. IBMSPSS ver 21 was used as software.

Results: This study has shown that 86.4% of the patients admitted in this institution's ICU were started on early enteral feeding within 24 to 48 hours of ICU admission. From the subjects given EN, only 21 (5.8%) were able to achieve the energy requirement. In those subjects who did not achieve the required energy requirement, there is an associated increased length of stay in the ICU (p-value of 0.045). Based on NUTRIC score, out of 52 patients included in this study, 39 patients (75%) were identified to be at low risk while 13 subjects (25%) were at high risk for a 28-day mortality.

Conclusion: Early initiation of enteral nutrition was being practiced among patients admitted to ICU in our institution. However, majority of patients given enteral feeding were not given the required energy requirement. The ICU patients who were given early nutrition feeding were associated with decreased length of ICU stay.

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INTRODUCTION

Most of the patients admitted in the intensive care unit (ICU) have acute critical illness placing them at high nutrition risk. Critical illness is usually associated with catabolic state due to systemic inflammatory response along with complications of infection, multi-organ failure leading to prolonged hospitalization and increased risk for morbidity and mortality.

Previously, nutritional support for the critically ill was regarded as an adjunct to medical therapy in order to help preserve lean body mass and provide support during stress. At present, nutrition has been made into a therapy in itself where feeding is thought to aid in correcting the metabolic response to stress, prevent oxidative cellular injury and help modulate immune responses.¹

Recent studies have shown that early initiation of enteral nutrition (EN) defined as within 24 to 48 hours from admission favorably improved patient outcomes.¹ Providing early enteral nutrition is seen as a proactive therapeutic strategy, which may lessen disease severity, reduce complications as well as decrease length of stay in the ICU.

In this light, this study aims to survey the timing of initiation of enteral feeding in admitted patients in the ICU. The study also aims to determine whether adequate caloric- energy requirements have been provided through the enteral route for this subset of population with nutrition risk.

REVIEW OF LITERATURE

Generally, patients admitted in the intensive care unit are critically ill requiring vital organ support have anorexia and may be unable to feed volitionally by mouth.¹ This subset of patients is at risk of accumulating rapid energy deficits, which leads to lean-tissue wasting and are associated with adverse outcomes.² In acute critical illness, the catabolic response is more pronounced than in healthy fasting persons due to superimposition of energy deficit on severe inflammatory and endocrine stress response as well as immobilization. Those with severe musculoskeletal wasting and weakness during critical illness are associated with a prolonged need for mechanical ventilation and rehabilitation.³

Previous studies have revealed that the degree of energy deficit accumulation in the critically ill patients is strongly associated with length of stay in the ICU

thus increasing incidence of infectious complications and risk of death. Nutrition has become a primary therapeutic intervention to prevent deterioration, loss of body mass and improve outcome of critically ill patients. Considerations in nutrition therapy include the timing of initiation, targeted amount of macronutrients and its route of delivery. A widespread consensus among recent international guidelines has recommended that enteral nutrition is preferred in the critically ill patients without a contraindication. The use of enteral nutrition compared to parenteral nutrition significantly reduced the rate of infectious complications as well as length of ICU stay.⁴

In critically ill patients unable to maintain volitional intake, the guidelines also recommended to initiate nutrition support therapy in the form of early enteral nutrition within 48 hours.¹ It has been stated in the guidelines that all hospitalized patients must undergo an initial nutrition screen within 48 hours of admission.

Patients at higher nutrition risk in an intensive care unit however require a full nutrition assessment. Many screening and assessment tools are used to evaluate nutrition status, such as the Mini Nutritional Assessment, the Malnutrition Universal Screening Tool, the Short Nutritional Assessment Questionnaire, the Malnutrition Screening Tool, and the Subjective Global Assessment. Only the NRS 2002 and the NUTRIC score determine both nutrition status and disease severity.⁵

The energy requirements should be determined to achieve goals of nutrition therapy. The ASPEN guidelines suggested the use of indirect calorimetry when available but in its absence, a simplistic weight-based equation (25-30kcal/kg/day) is to be used to determine energy requirements.¹

In recent studies, critically ill patients with accumulating degree of energy deficit have been strongly associated with the duration of stay in the ICU. This is linked with an increased occurrence of infectious complications and risk of death. Hypermetabolism and malnourishment are common in patients admitted to the intensive care unit. This subset of patients receives specialized nutrition therapy to attenuate the effects of malnourishment. However, the optimal amount of energy to deliver is unknown. It has been suggested that full calorie feeding improves clinical outcomes but other studies have concluded that caloric intake may not be important in determining outcome.⁶

SIGNIFICANCE OF THE STUDY

In recent years, nutrition has become a vital component of therapy especially in the critically ill patients where there is rapid energy deficit accumulation. This subset of patients is at high nutrition risk, which is strongly associated with poor recovery and adverse outcomes. Our local institutions have started to practice incorporating nutrition as a primary therapeutic intervention. Unfortunately, there are concerns as to the timing of initiation, route of delivery and the targeted amount of macronutrients. In the current guidelines and studies, enteral nutrition is preferred over parenteral nutrition in critically ill patients without contraindications. The timing of enteral nutrition initiation is within 24-48 hours of ICU admission with a targeted 25-30 kcal/kg/day. This study would like to determine the institution's current standard practice on enteral feeding, its timing of initiation, the amount of macronutrients provided for and the selected population's nutrition risk. It is the researcher's intent to provide information that may serve as a guide in this institution's future enteral nutrition protocol/s in the critically ill patients.

OBJECTIVES

General Objective

The objective of this study is to determine the nutrition risk levels as measured by NUTRIC score among admitted patients who requires feeding via enteral route at the Intensive Care Unit of Cebu Doctors' University Hospital from June 2016 to June 2017.

Specific Objectives:

1. To determine the timing of initiation of enteral feeding in patients admitted in the ICU:
 - a. Within 24 hours
 - b. Within 48 hours
 - c. Within 3 to 5 days
 - d. More than 5 days
2. To compute the desired caloric-energy requirement of admitted patients requiring feeding via enteral route in the ICU
3. To determine the actual caloric intake provided to admitted patients requiring feeding via enteral route in the ICU

4. To compare the computed caloric requirements versus actual caloric intake given during the patients' ICU admission
5. To determine the rate of high risk nutrition among admitted patients requiring feeding via enteral route in the ICU using the NUTRIC score

MATERIALS AND METHODS

Research Design

This was a one-year single-center cross-sectional retrospective chart review study taken from the medical records of patients admitted in the Intensive Care Unit of Cebu Doctors' University Hospital from June 2016 to June 2017.

Research Locale

The study was conducted at the Intensive Care Unit of Cebu Doctors' University Hospital.

Research Subjects

This study included admitted patients in the ICU on enteral feeding from June 2016 to June 2017 who were included in the selection process which employed purposive sampling technique using the following inclusion and exclusion criteria.

Inclusion criteria:

1. All patients admitted at the ICU with a length of stay (LOS) of more than 3 days
2. Patients 18 years old and above
3. Patients who received enteral feeding during their ICU admission

Exclusion criteria:

1. Patients who did not receive enteral nutrition during the ICU stay due to contraindications to enteral nutrition, instability, or death

Sample Size Determination

A total of 393 patients were admitted in the Intensive Care Unit from June 2016 to June 2017. Out of these patients, only 52 patients were able to fulfill the inclusion criteria. For this study, the following laboratory work-up were included: complete blood count,

serum sodium, serum creatinine, serum total bilirubin level and an arterial blood gas (ABG). From the 393 patients, 245 had incomplete laboratory results required for the computation of the APACHE, SOFA and NUTRIC score systems. A total of 243 patients did not have serum total bilirubin levels while 2 patients lacked arterial blood gas. As to the duration of stay in the ICU, a total of 69 patients had a length of stay of less than 3 days. For those that had complete laboratory results, 3 of these patients were not given enteral feeding. Two of the patients had contraindications to enteral feeding while the third patient was provided with parenteral nutrition. A total of 24 charts lacked the needed data required for this study.

Data Processing and Analysis:

Data was gathered by doing chart review at the institution's medical records for patients admitted to the ICU from June 2016 to June 2017 and properly selected according to the inclusion criteria. Computation for APACHE II, SOFA and NUTRIC scores were done using designated calculator application, *MDcalc* to minimize technical errors as well as avoid bias. Patients included in the study were then assessed for nutrition risk using the NUTRIC Score. Acquired data were tabulated and each patient included in the study was classified as Low Nutrition Risk or High Nutrition Risk.

The researcher computed the desired caloric-energy requirement of each selected patient using the ideal caloric requirement according to the recent ASPEN guidelines of 25 kcal/kg/day based on the patient's estimated body weight. This was compared to the actual caloric intake that each patient under this study has received during his or her ICU stay.

DEFINITION OF TERMS:

Malnutrition: An acute, subacute or chronic state of nutrition, in which varying degrees of overnutrition or undernutrition with or without inflammatory activity have led to a change in body composition and diminished function.

Enteral Nutrition (EN): Nutrition provided through the gastrointestinal tract via a tube, catheter or stoma that delivers nutrients distal to the oral cavity.

Nutrition Screening: A process to identify an individual who is malnourished or who is at risk for malnutrition to determine if a detailed nutrition assessment is indicated.

SOFA Score: The Sequential Organ Failure Assessment (SOFA) score is a mortality prediction score that is based on the degree of dysfunction of six organ systems and assigns a score based on the data obtained in each category as shown in the table below:

Criteria	0	+1	+2	+3	+4
PaO ₂ /FiO ₂ (mmHg)		<400	<300	<200 and mechanically ventilated	< 100 and mechanically ventilated
Platelets (x 10 ⁹ /L)	-	< 150	< 100	<50	<20
Glasgow Coma Scale (GCS)	15	13-14	10-12	6-7	<6
Bilirubin (mg/dL)	-	1.2-1.9	2.0-5.9	6.0-11.9	> 12.0
Mean Arterial Pressure (MAP) or administration of vasopressors required (ug/kg/min)	No hypotension	MAP >70 mmHg	Dopamine < 5 or Dobutamine of any dose	Dopamine < 5 or Epinephrine <0.1 or Norepinephrine <0.1	Dopamine > 15 or Epinephrine > 0.1 or Norepinephrine >0.1
Creatinine (mg/dL) or Urine Output (ml/day)	<1.2	1.2-1.9	2.0-3.4	3.5-4.9	>5

This scoring system predicts ICU mortality based on laboratory results and clinical data gathered. The data was gathered using chart review and the score used for this research has been calculated using values taken within 24 hours of patient's ICU admission or using the worst value during the patient's ICU stay.

APACHE II Score: A severity of disease classification system, which uses a point score, based upon initial values of 12 routine physiologic measurements, age, and previous health status to provide a general measure of severity of disease. In this study, the required variables are taken using data taken within 24 hours of the patient's ICU admission.

Criteria	0	+1	+2	+3	+4	+5	+6	+7	+8
History of Severe Organ Failure or Immunocompromise: Heart Failure Class IV, Cirrhosis, Chronic Lung Disease; Dialysis-dependent; Immunosuppression	No	-	Yes, and elective post-operative patient	-	-	Yes, and non operative or emergency post-operative patient	-	-	--
Age (Years)	< 44	45-54	55-64	65-74	> 74	-	-	-	-
Temperature (°C)	36-38.4	34-35.9 38.5-38.9	32-33.9	30-31.9 39-40.9	< 30 > 40.9	-	-	-	-
Bilirubin (mg/dL)						-	-	-	-
Mean Arterial Pressure (mmHg)	70-109	-	50-69 110-129	130-159	< 50 > 159	-	-	-	-
Heart Rate (beats per minute)	70-109	-	55-69 110-139	40-54 140-179	< 40 > 179	-	-	-	-
Respiratory Rate (breaths per minute)	12-24	10-11 25-34	6-9	35-49	< 6 > 49	-	-	-	-
Arterial pH	7.33-7.49	7.50-7.59	7.25-7.32	7.15-7.24 7.60-7.69	< 7.15 > 7.69	-	-	-	-
Oxygenation (use PaO₂ if FiO₂ < 50% otherwise use A-a gradient)		A-a gradient < 200 (if FiO ₂ over 49%) or pO ₂ > 70 (if FiO ₂ < 50%)	A-a gradient 200-349	A-a gradient 350-499	A-a gradient > 499				
Serum sodium (mMol/L)	130-149	150-154	120-129 155-159	111-119 160-179	< 111 > 179	-	-	-	-
Serum potassium (mMol/L)	3.5-5.4	3-3.4 5.5-5.9	2.5-2.9	6-6.9	< 2.5 > 6.9	-	-	-	-
Creatinine (mg/dL)	0.6-1.4	-	< 0.6 1.5-1.9 and Chronic Renal Failure	2.0-3.4 and Chronic Renal Failure	> 3.4 and Chronic Renal Failure 1.5-1.9 and Acute Renal Failure		2.0-3.4 and Acute Renal Failure		> 3.4 and Acute Renal Failure
Hematocrit (%)	30-45.9	46-49.9	20-29.9 50-59.9	-	< 20 > 59.9	-	-	-	-
White Blood Cell (total/cubic mm in 1000's)	3.0-14.9	15-19.9	1.0-2.9 20-39.9	-	< 1.0 > 39.9	-	-	-	-
Glasgow Coma Scale (GCS) 1-15	15 - (GCS Score)								

NUTRIC Score: This is a scoring system designed to quantify the risk of critically ill patients developing adverse events that may be modified by aggressive nutrition therapy. Based on the scoring system, a score within 0-5 indicates low malnutrition risk while a score within 6-10 has an associated worse clinical outcome. Parameters involved in NUTRIC score determination will be gathered by chart review, the APACHE and SOFA scores will be determined first followed by the input of their respective scores included in the final computation for the NUTRIC score using *MDcalc* application. The final values will be tabulated according to its respective scoring system as shown in table below:

Criteria	0	+1	+2	+3
Age (Years)	<50	50-74	≥75	-
APACHE II Score	< 15	15-19	20-27	> 28
SOFA Score	< 6	6-9	≥ 10	-
Number of co-morbidities	0-1	≥ 2	-	-
Days in hospital to ICU	0	≥1	-	-

RESULTS

Standard Enteral Nutrition

General Characteristics of All Admitted Patients in the ICU

For this study, a total of 393 patients were admitted in the ICU from June 2016 to June 2017 with an average age of 63 years old, male sex, comprising majority of the population with 240 (61.1%) subjects. For associated co-morbidities, 138 (35.1%) subjects had at least one with hypertension as the leading co-morbidity affecting 70% of the study population. The average length of stay in the ICU is 6.93 days with a mean 3.48 days from hospital admission leading to ICU admission.

The study population had an overall positive outcome with 227 (58%) patients discharged improved while 134 (34%) patients expired, 18 (5%) went home against medical advice, 7 (2%) patients were transferred to another institution due to financial constraints, 4 (1%) discharged unimproved and 3 (1%) were directly discharged improved from the ICU

Table 1. General Characteristics of Admitted ICU Patients

General Characteristics	Descriptive (n=393)
Age, years – Average (sd)	63.07(17.86)
Sex	
Female	153(38.9%)
Male	240(61.1%)
Number of Co-Morbidities	
0	99(25.2%)
1	138(35.1%)
2	108(27.5%)
3	9(2.3%)
Co-morbidity Type	
Hypertension	206(70%)
Type 2 Diabetes Mellitus	144(49%)
Bronchial Asthma	18(6%)
Chronic Kidney Disease (CKD)	3(1%)
Chronic Obstructive Pulmonary Disease (COPD)	3(1%)
Length of ICU Stay (Days)	6.93(6.72)
Days from Hospital Admission to ICU Admission	3.48(9.26)
Outcome	
Died	134(34%)
Improved	227(58%)
Directly Discharged	3(1%)
HAMA	18(5%)
Transferred	7(2%)
Unimproved	4(1%)

Frequency and Time of Initiation for ICU Patients Given Enteral Nutrition

Out of 393 admitted ICU patients, 361 (91.9%) patients were provided with enteral nutrition (EN). Those started who were provided EN within 24 hours comprised 212 (59%) patients while 100 (28%) admitted patients received EN between 24 to 48 hours, the remaining subjects were given EN after 3 days of ICU admission.

Table 2: Time of Enteral Nutrition Initiation

Time of EN Initiation	Frequency	Percent
Within 24 hours	212	59%
Within 48 hours	100	28%
Within 3-5 days	39	10%
More than 5 days	10	3%
Total Patients on EN	361	100%

Actual versus Required Energy in kilocalories (kcal) for Patients Given Enteral Nutrition

The mean value for the required kcal in this study was 1555.03 (SD 295.71) kcal while the mean actual kcal provided during the ICU admission in this study is 1495.87 (SD 399.32) kcal with a mean difference of 59.16 (SD 443.03) kcal. Only 21 (5.85%) patients in this study achieved the required 25kcal/kg/day energy requirement based on current guidelines for critically ill patients.

Table 3. Actual versus Required Energy Provision (kcal)

Energy Requirement	kcal	Standard Deviation
Required Kcal (25kcal/kg/day)	1555.03	295.71
Actual Kcal (kcal/kg/day)	1495.87	399.32
Difference (Required - Actual)	59.16	443.03
Feeding status	n=361	Percentage
Achieved energy requirement	21	5.8%
Did not meet energy requirement	340	94.2%

As reflected on Table 1, there were 361 patients who were given enteral nutrition, yet, only 21/361 (5.8%) had achieved the feeding requirement while the rest of the study group was underfed. As shown in Table 4, among those 21 cases provided with adequate energy requirement in kcal, 33% had at least two co-morbidities present, 67% had been fed within 24 hours, with an average ICU length of stay of 6.68 days and mortality rate was 49%.

Moreover, those 340 cases who did not meet the required kcal, 36% had at least 1 co-morbidity present, 58% were started EN within 24 hours of ICU admission, had an average ICU length of stay of 7.13 days, 61% who were discharged improved, and their mortality rate was 31%.

Cross-sectional analysis showed that high proportion of patients in underfed group started within 24 hours (58% vs 34%, $p = 0.003$), longer ICU length of stay (7.13 days vs 6.68 days, $p = 0.045$), and yet, most of them had higher rate of those who had improved condition (61% vs 49%). The differences in rates between underfed and those who had achieved feeding requirement were statistically significant. The results suggested that feeding requirement did not show sufficient requirement in influencing patient's improvement.

Table 4. Variables in Enteral Feeding Energy Requirements

Variables	Adherences to feeding requirement		p-value
	Adhered	Did not adhere	
Total	21	340	
No of morbidities			
1	11(52%)	123(36%)	0.236
2	7(33%)	95 (28%)	0.613
3	1(5%)	8(2%)	0.973
Time of EN Initiation			
Within 24 hours	14(67%)	198(58%)	0.003*
Within 48 hours	6(29%)	93(27%)	0.079
Within 3-5 days	1(5%)	37(11%)	0.231
More than 5 days	1(5%)	8(2%)	0.973
Length of ICU stay			
Average	6.68	7.13	0.045*
Standard deviation	9.80	6.31	
Outcome			
Died	10(48%)	104(31%)	0.019*
Improved	10(48%)	206(61%)	0.146
Direct Discharge	0(0%)	3(1%)	0.546
No improvement	0(0%)	4(1%)	0.485
HAMA	0(0%)	18(5%)	0.131
Transfer	1(5%)	5(1%)	0.638

Nutrition Risk Assessment using the NUTRIC Score

General and Admission Characteristics of Patients with NUTRIC Score Computation

In assessing the nutrition risk, only a total 52 eligible adult patients with completed NUTRIC score computation were included in the study. Among the study subjects, 62% were male with an average age of 62 years old (SD 17.55) and weight of 64kg (SD 19.24), The mean length of ICU stay was 6 days (SD 9.34) with a mean of 5 days (SD 7.1) from hospital to ICU admission. As to the presence of co-morbidities, 23 subjects (44%) had one co-morbidity: hypertension while 12 subjects (23%) had two co-morbidities, namely hypertension and type 2 diabetes mellitus. The frequency of co-morbidities are as follows: hypertension 44%, followed by diabetes mellitus 23%, and lastly bronchial asthma 8%.

Table 5. General Characteristics of Study Subjects with NUTRIC Score

General characteristics	Descriptive (n=52)
Demographics	
Age, mean years (sd)	61.79±17.55
Sex	
Female	20(38%)
Male	32(61.5%)
Weight, average kg(sd)	64.27±19.24
Admission characteristics	
Length of ICU Stay (Days), mean(sd)	6.30±9.34
APACHE Score, mean(sd)	21.22±9.08
SOFA Score, mean(sd)	7.97±3.36
Days from hospital admission to ICU, mean(sd)	4.64±7.1
No. of Co-Morbidities	
0	16(31%)
1	23(44%)
2	13(25%)
Co-morbidity Type	
Hypertension	31(44%)
Type 2 Diabetes Mellitus	12(23%)
Bronchial Asthma	4(8%)

Timing of Initiation of Enteral Nutrition for Patients with Computed NUTRIC Score

As to the timing of enteral nutrition initiation, 23 subjects (44%) were given enteral nutrition within 24 hours, 20 (38%) were started within 24 to 48 hours while 4 (8%) were given feeding within 3 to 5 days and 5 (10%) were started after 5 days of ICU admission.

Table 6: Time of EN Initiation

Clinical profiles	Frequency	Percent
Time of EN Initiation		
Within 24 hours	23	44%
Within 48 hours	20	38%
Within 3-5 days	4	8%
More than 5 days	5	10%

APACHE II Score:

APACHE II score was developed to estimate ICU mortality based on a number of laboratory values and vital signs taking into account both acute and chronic disease. The data were based on values taken from the initial 24 hours of ICU admission. As shown below, a total of 23 subjects (44%) had a history of severe organ failure including those requiring respiratory support (16), chronic obstructive pulmonary disease (2), congestive heart failure NYHA IV (3), chronic liver disease (9), immunocompromised state (5) and chronic kidney disease on maintenance dialysis (3). Fifty-two percent had acute renal failure at the time of ICU admission. In assessing the mortality rate using APACHE score, parameters included the subject's vital signs and laboratory results. Table 3 below shows a mean Glassgow Coma Scale (GCS) score of 11.97 points (SD 4.14) and recorded vital signs with a mean temperature of 36.59°C (SD 1.02), mean arterial pressure (MAP) of 83.47mmHg (SD 12.28), heart rate of 96.30 beats per minute (SD 23.52) and a respiratory rate mean of 24.41 breaths per minute (SD 4.94). The laboratory results taken showed the following blood chemistry values: mean serum sodium of 133.76 mmol/L (SD 28.81), serum potassium of 4.18 mmol/L (SD 0.90) and serum creatinine of 2.2mg/dL (SD 1.65). In the complete blood count test results showed a mean hematocrit of 35.18% (SD 8.08) and white blood count of 16.99 x IOVL (SD 11.36). The arterial blood gas (ABG) results showed a meat) FiO2 of 51.26% (SD 26.80), A-a gradient of 241.22mmHg (SD 129) and PaO2 Of 138.42 mmHg (SD 81.27). In Table 9, APACHE II Score outcome from this study showed a mean of 20.09 (SD 8.69) with 16 subjects (31%) presenting a predicted 40% non-operative ICU mortality.

Table 7. APACHE II Score Variables Set A

Clinical profiles	Frequency	Percent
History of Severe Organ Failure/Immunocompromise	23	44%
Severe Organ Failure/Immunocompromise Type		
Requiring respiratory support	16	31%
Chronic Obstructive Pulmonary Disease	2	4%
Congestive Heart Failure NYHA IV	3	6%
Liver Disease	9	17%
Cirrhosis	3	6%
Upper Gastrointestinal Bleed secondary to Portal Hypertension	2	4%
Hepatic Failure	4	8%
Immunocompromised State	5	10%
Cancer S/P Chemotherapy	4	8%
Leukemia	1	2%
Chronic Kidney Disease on Maintenance Hemodialysis	3	6%
Acute Renal Failure		
No	25	48%
Yes	27	52%

Table 8. APACHE II Score Variables Set B

Laboratory/Vitals	Mean	Standard Deviation
Glassgow Coma Scale	11.97	4.14
Temperature	36.59	1.02
Mean Arterial Pressure	83.47	12.28
pH	7.34	0.10
Heart Rate	96.30	23.52
Respiratory Rate	24.41	4.94
Sodium	133.76	28.81
Potassium	4.18	0.90
Creatinine	2.20	1.65
Hematocrit	35.18	8.08
White Blood Count	16.99	11.36
A-a Gradient If FiO2 > 0.5 (mmHg)	241.22	129.00
PaO2 if FiO2 < 0.5 (mmHg)	138.42	81.27
FiO2	51.26	26.80

Table 9. APACHE II Score Outcome

Outcome profile	Descriptive (n=52)
APACHE II Score, mean(sd)	20.09±8.69
APACHE II Interpretation	
Non-Surgical Mortality	
6%	2(4%)
12%	1(2%)
Non-Operative Mortality	
6%	6(12%)
12%	5(10%)
22%	8(15%)
40%	16(31%)
51%	6(12%)
71%	4(8%)
82%	4(8%)

SOFA Score:

The Sequential Organ Failure Assessment (SOFA) Score is a tool to predict mortality risk and determine the level of organ dysfunction in ICU patients. The score was calculated using subject's clinical data and laboratory results taken within 24 hours of admission to ICU. As shown in Table 10 below, the level of hypotension was also taken into consideration with 22 study subjects not requiring vasopressors followed by those who needed the use of vasopressors of either dopamine $> 15/\mu\text{g/kg/min}$ or norepinephrine $> 0.1/\mu\text{g/kg/min}$. The SOFA score showed a mean outcome of 8.64 (SD 3.41) with 18 subjects (35%) presenting a predicted 33% mortality.

Table 10. SOFA Score Variables

Criteria	Descriptive (n=52)
PaO ₂ (mmHg)	138.42±81.27
FiO ₂ , mean (sd)	51.26±26.80
Platelet, mean (sd)	189.58±109.33
Bilirubin, mean (sd)	5.34±8.21
Creatinine, mean (sd)	2.20±1.65
Glasgow Coma Scale, mean (sd)	11.97±4.14
Level of Hypotension	
0	22(42%)
1	8(15%)
2	2(4%)
3	3(6%)
4	17(33%)

Table 11. SOFA Score Outcome

SOFA Score Outcome	Descriptive (n=52)
SOFA Score, mean(sd)	8.64±3.41
SOFA score Interpretation (Mortality)	
< 33%	11(21%)
33%	18(35%)
40-50%	14(27%)
95%	9(17%)

NUTRIC Score Results

The NUTRIC Score is a tool that can aid in identifying critically ill patients who can benefit from nutrition therapy. Table 12 shows the computation for the nutrition risk of the selected admitted ICU patients with an overall average score was 4.54 (SD 1.64) points which shows ~11% 28-day mortality. Out of the 52 patients included in this study, 39 patients (75%) were identified to be at low risk while remaining 13 subjects (25%) were at high risk for a 28-day mortality.

Table 12: NUTRIC Score

	Descriptive (n=52)
Overall average score (sd)	4.54(1.64)
Nutric Score Category and Interpretation (28-Day Mortality)	
High Risk	13(25%)
Low Risk	39(75%)

Enteral Feeding Required Kcal versus Actual Kcal for Subjects with NUTRIC Score

For the subjects with completed NUTRIC score, the mean required kcal based on 25kcal/kg/day is 1,668.11 kcal/day while the mean actual kcal given was 1,292.93 kcal/day with a percent difference of 22.49% with the actual kcal given lower than the required kcal amount. Using the paired T-test for comparison, the test of paired difference is significant at <0.001 .

Table 13: Enteral Feeding Required Kcal versus Actual Kcal

Feeding requirement	Mean	Std.deviation
Required Kcal (25kcal/kg/day)	1,668.11	627.97
Actual Kcal (kcal/kg/day)	1,292.93	512.51
Difference	375.18	
Percent difference	actual Kcal is lower by 22.49% from required Kcal	
Test of paired difference	<0.001 (significant)	

Clinical Outcome

For the outcome of the study subjects enrolled, 27 subjects (52%) were discharged improved, 20 (38%) patients expired, 3 (6%) went home against medical advice while two (6.1%) were directly discharged from the ICU.

Table 14: Outcome Profile

Outcome profile	Descriptive (n=52)
Improved/Discharged	27(52%)
Direct discharged	2(4%)
HAMA	3(6%)
Died	20(38%)

DISCUSSION

Acute critical illness is associated with a catabolic state, which increases energy expenditure placing this subset of patients at high nutrition risk thereby increasing risk for longer hospital stay and poor outcomes. Inflammation and compensatory mechanisms lead to metabolic changes. These inflammatory-induced stress metabolic changes can lead to increased energy expenditure.²

Actual versus Required Kcal for Subjects on Enteral Nutrition (EN)

The current guidelines recommend giving 25-30 kcal/kg/day based on the patient's ideal body weight. In the study, only 21/361 (5.85%) patients provided with EN achieved the required 25 kcal/kg/day energy requirement based on current guidelines for critically ill patients. In the analysis done, it was noted that there was a high proportion of underfed patients although initiated on EN within 24 hours (58% vs 34%, $p = 0.003$) had longer duration of ICU stay (7.13 days vs 6.68 days, $p = 0.045$).

Achieving Actual Kcal for Subjects on Enteral Nutrition and Subsequent Outcome

A study done by Arabi et. al. concluded that providing enteral nutrition to deliver moderate nonprotein calories to critically ill patients was not associated with lower mortality compared to those given the required amount.⁹ Similarly in our study, it has also shown that most of the patients who were not given the required kcal had a higher rate of improved condition (61% vs 49%). Given that the differences in rates between underfed and those who had achieved feeding requirement were statistically significant, this study revealed that feeding requirement adherence does not guarantee favorable outcome.

Timing of Enteral Nutrition and Subsequent Outcome

In terms of the timing of enteral nutrition, the ASPEN guidelines have recommended that early EN should be initiated within 24 to 48 hours from ICU admission. This study revealed that majority of the ICU patients admitted in this institution had been receiving early EN. A total of 312/361 (86%) patients were initiated with early enteral nutrition within 24 to 48 hours from ICU admission. A total of 219/361 (61%) subjects on enteral nutrition were discharged improved. The results

of our study were similar to a study done by Khalid, MD et al where it was shown that early enteral nutrition might be associated with lesser ICU mortality in patients whose condition is considered hemodynamically unstable.¹⁰

Nutrition Risk Assessment with NUTRIC Score and Patient Outcome

The results in a study done by Rhaman A, et. al., showed that there was an association between nutrition adequacy and a 28-day mortality as demonstrated by the NUTRIC score where the test for interaction had a p-value of 0.029. The study also revealed that patients with high NUTRIC score, there was a strong positive association between nutritional adequacy and 28 day survival. This association diminished with lesser NUTRIC score,¹¹ In our study, the computation for the nutrition risk of the selected admitted ICU patients with an overall average score was 4.54 (SD 1.64) points which showed ~11% 28-day mortality. From the patients with NUTRIC score, majority with 39 patients (75%) were identified to be at low risk while the remaining 13 subjects (25%) were at high risk for a 28-day mortality.

The Joint Commission (United States) has mandated nutrition screening within 24 hours of admission in an acute critical care unit.² Identification of these critically ill patients for nutrition risk using the assessment tool, NUTRIC score can serve as a guide to nutritional intervention. There is noted variability as to patient risk for adverse outcomes related to malnutrition thus markers for both acute and chronic inflammation and starvation are considered. The NUTRIC score is a valid tool that can aid in identifying critically ill patients who will benefit from aggressive nutrition therapy. Scoring systems such as the APACHE II and SOFA score are good mortality prediction tools to aid in identifying critically ill patients who may benefit from aggressive therapeutic intervention including nutritional support. The study was unable to acquire the needed sample size to arrive at a conclusion regarding the institution's practice as to nutrition risk identification. It is however of note that the institution lacks the protocol needed to identify critically ill patients with high risk for mortality.

LIMITATIONS OF THE STUDY

One of the major limitations of this study is that the institution's ICU does not have protocol use of both APACHE and SOFA score systems, which are required in computing for the NUTRIC Score.

Laboratory tests needed for this study, included complete blood count (CBC), serum sodium, serum creatinine, serum total bilirubin and arterial blood gas (ABG). Unfortunately, most of the physicians do not routinely get serum bilirubin levels.

Second limitation is the use of estimated body weight in computing for the energy requirements in enteral nutrition. Ideally, it has been stated in the ASPEN guideline to use 25-30kcal/kg/day based on ideal body weight.

Another limitation is that there were a total of 24 charts that the researcher was not able to access due to unavailability or lack of content.

The small number of subjects included in this study reduces its validity.

CONCLUSION

In the one-year survey done of the institution's standard practice on enteral nutrition (EN) provision for admitted ICU patients based on the NUTRIC score, revealed that most of the admitted patients who were provided with EN were at low risk for a 28-day mortality. However, only 52/393 cases were included in the nutrition risk assessment using the NUTRIC score thus reducing the validity of the results.

It was also shown that majority of the cases were given early enteral nutrition within 24 to 48 hours of ICU admission in accordance to the recent guidelines. It is also noted that there is a possible association between achieving the required energy kcal of 25kcal/kg/day and lesser length of ICU stay.

It is the desire of the researcher that with proper use of APACHE and SOFA scoring systems, critically ill patients with increased risk for mortality can be identified and given immediate therapeutic intervention to avert poor outcomes. Also, these scoring systems can be used for nutrition screen using the NUTRIC score. Proper identification of patients with high nutrition risk can better modify possible adverse outcomes thru aggressive nutritional support if warranted.

RECOMMENDATIONS

1. This study would like to recommend early initiation of enteral feeding within 24 to 48 hours of ICU admission.

2. The study however, cannot verify the benefit of achieving required energy provision basing on 25kcal/kg/day until further indisputable evidence has been shown in larger studies.
3. This study would like to suggest a protocol for ICU admission that includes the use of mortality risk assessment scores namely APACHE and SOFA scoring system.
4. As part of the risk assessment, the researcher would like to suggest inclusion of the following laboratory tests in every ICU admission:
 - a. CBC
 - b. Serum Na
 - c. Serum creatinine
 - d. Serum total bilirubin
 - e. Arterial Blood Gas
5. This study would also like to suggest nutrition risk screening and assessment with the use of an institutional-based Subjective Global Assessment (SGA) and the international NUTRIC Score system.
6. A long-term prospective cohort of enteral nutrition of the same population is suggested for our institution.

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A Randomized Double Blind Controlled Study on the Efficacy of Spirulina as an Adjunct Therapy in the Management of Pediatric Community Acquired Pneumonia-C in Patients 6 Months to 5 Years Old Admitted in a Tertiary Government Hospital*

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ABSTRACT

Objective: To determine the effect of Spirulina among patients with community acquired Pneumonia-C (PCAP-C) based on the resolution of the following symptoms; fever, respiratory rate, chest indrawings, rales, oxygen saturation and compare their length of hospital stay.

Design: A randomized-double blind, placebo controlled clinical trial

Setting: The study was done at a tertiary government hospital

Patients/Participants: Children 6 months to 5 years old with PCAP-C were randomized to either treatment group A or B. The two groups received the standard treatment for pneumonia and adjunct treatment of Spirulina for group A and placebo for group B.

Results: A total of 147 patients participated in the study. Seventy four patients were randomized to group A and 73 patients to group B. Respiratory rate showed greater improvement with Spirulina supplementation starting day 3, 4 and 5. Resolution of chest in-drawing was significant in Spirulina group on day 2 (p- value < 0.05), day 3 (p – value < 0.05) and day 4 (p – value <0.05). There were more patients in Spirulina group with decreased to absent rales on day 2 (p-value 0.02), day 3 (p-value 0.039), day 4 (p-value 0.01) and day 5 (p-value 0.01). Temperature and oxygen saturation on both groups had almost similar trends. The mean hospital stay in Spirulina group (3.09 days) is shorter as compared to the placebo group (p-value 0.02).

Conclusion: Spirulina supplementation showed positive effects in PCAP-C. Its immune-modulating effect played a positive role in the treatment outcome of pneumonia.

Keywords: *pneumonia, Spirulina, PCAP-C*

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INTRODUCTION

Pneumonia is a leading cause of death in children worldwide. In 2013, the World Health Organization (WHO) reported that Pneumonia killed an estimated 1.1 million children less than 5 years of age accounting for 18% of all deaths in children worldwide. Antibiotic remains the core of treatment for Pneumonia. However, despite good antibiotic coverage for pneumonia the mortality and morbidity remain high.¹

In 2004, there were an estimated 12 million deaths in the Asia-Pacific region, of which approximately one quarter (2.8 million) was attributable to respiratory causes. In this region, COPD and lung cancer accounted for 70% of all deaths attributable to respiratory disease. Infection is the other major cause of mortality, with pneumonia comprising 475,000 (16.8%) and TB with 305,000 deaths (10.8%).²

The World Health Organization (WHO) reported that about 156 million new episodes of childhood clinical pneumonia occurred globally in 2000, of which 95% occurred in developing countries. Nine percent of the pneumonia cases occurring in these countries are severe enough to be life-threatening and require hospital admission. In the African and South-East Asian Regions it was estimated that about 2 million deaths from pneumonia occur each year in children less than five years of age. Globally, the Philippines ranks number 10 among fifteen countries with 3 million reported cases.³

In the Philippines, the Department of Health reported that it is the leading cause of mortality and ranks the 2nd most common cause of morbidity in 2010.⁴ Pneumonia also topped the list of 20 illnesses that the Philippine Health Insurance Corporation paid for in claims annually, costing at least 2 billion pesos in 2010. In the first half of 2011 alone, the Philippine Health insurance had spent at least 1.2 billion pesos in pneumonia claims.⁵

Pneumonia can be diagnosed based on clinical signs and symptoms such as tachypnea, chest in drawings, fever and other abnormal chest findings. Chest radiograph and laboratory tests can be used to confirm the presence of pneumonia and identify the causative pathogen. Fever of 38.5 °C and above, a chest x-ray findings of consolidation or atelectasis are features suggestive of bacterial pathogen. Patients with pneumonia of bacterial etiology should be treated

with appropriate antibiotic. Oral Amoxicillin given for an average of 7 days is recommended for an outpatient cases while intravenous Penicillin or Ampicillin for hospitalized patients.⁶

The use of adjunct treatment in pneumonia has been the subject of several researches. Studies have shown that adjunct treatment for pneumonia like Vitamin A and C had minimal effect to none. There are no studies available to warrant recommendation for the use of these immune-modulators. Studies on the efficacy of Zinc, in the treatment of Pneumonia are also equivocal to non-beneficial.⁷ A recent clinical trial done by Cadete et al revealed that supplementation of Spirulina shortened the duration of fever, significantly decreased the heart rate and provided radiologic improvement in children admitted as severe pneumonia.⁸ In the investigators knowledge there are no published studies which use Spirulina as adjunct in the management of pediatric community acquired pneumonia-C (PCAP-C). This study aims to answer the research question; among children six months to five years of age admitted in a tertiary government hospital how effective is Spirulina as an adjunct treatment in PCAP-C.

REVIEW OF LITERATURE

Spirulina is a microscopic and filamentous cyanobacterium that derives its name from the spiral or helical nature of its filaments. It has a long history of use as food and it has been reported that it has been used during the Aztec civilization. Spirulina refers to the dried biomass of *Arthrospiraplatensis*, an oxygenic photosynthetic bacterium found worldwide in fresh and marine waters. It has been used as a source of protein and vitamin supplement in humans without any significant side-effects. It has the ability to modulate immune functions and exhibits anti-inflammatory properties by inhibiting the release of histamine by mast cells. Multiple studies investigating the efficacy and the potential clinical applications of Spirulina in treating several diseases have been performed.⁹

In a journal article it was stated that Spirulina administered 2000mg/day, significantly reduced IL-4 levels by 32% from phytohemagglutinin (PHA) – stimulated cells. These results indicate that Spirulina can modulate the profile patients with allergic rhinitis by suppressing the differentiation of TH2 cells mediated, in part, by inhibiting the production of IL-4.¹⁰

Several local studies showed significant improvement in weight gain, increase in height, correct nutritional anemia in preterm and low birth babies. Presently, however, numerous people are looking into the possible therapeutic effects of Spirulina. One local study done in a tertiary hospital in Manila proved that Spirulina powder is efficacious and safe as an adjunct in management of acute non-bloody diarrhea.¹¹

To date, there is one local investigation that has been published regarding the use of Spirulina for community acquired pneumonia. The study is a randomized double blind controlled trial done at a tertiary government hospital in Iloilo City. The study determined the efficacy of Spirulina as adjunct therapy among patients with Pneumonia severe. Seventy eight patients 2 months to 5 years old admitted from February to August 2012 were enrolled in the study. Clinical and physiologic parameters measured include severity of cough, fever, fast breathing, chest indrawing, tachycardia, rales, chest x-ray, leukocyte count and hospital stay. Demographic profiles of the two groups were comparable ($p>0.050$). The result showed a trend towards improvement within 3 days among patients given Spirulina on clinical parameters and physiologic profile compared to placebo. There was a significant drop in temperature on day 2 (p -value 0.038) and significant decrease in mean heart rate on Day 1 (p -value 0.036) and Day 2 (p -value 0.037) among those who were supplemented with Spirulina.

An improvement on the Chest x-ray finding was noted on Day 3 of treatment among Spirulina group (p -value 0.036). The study showed similar hospital stay in both groups. The study recommended a trial of higher dosing of Spirulina to assess significant effect in both clinical and physiologic parameter.⁸

OBJECTIVE

To determine the efficacy of Spirulina as an adjunct therapy in the treatment of PCAP-C in children 6 months to 5 years old admitted in a tertiary government hospital.

SPECIFIC OBJECTIVES

1. To determine the effect of Spirulina among patients with PCAP-C based on the resolution of the following symptoms: fever, respiratory rate, chest in-drawings, rales and oxygen saturation.

2. To determine the duration of hospital stay among patients with PCAP-C given Spirulina as adjunct therapy and those given with placebo.
3. To determine the adverse effect of Spirulina as adjunct therapy in PCAP-C.

OPERATIONAL DEFINITION

A. PRIMARY OUTCOME MEASURE

The primary outcome measured was the effect of Spirulina on patients based on the following parameters:

1. Resolution of tachypnea refers to the hospital day when the patient's respiratory rate per minute decrease or returns to normal.
2. Resolution of chest in drawing refers to the hospital day when the absence of inward movement/retractions of the chest wall and abdomen was not visible as the child breathes.
3. Resolution of rales refers to the hospital day when absence of crackling sound is not audible on auscultation of the chest area.
4. Resolution of fever refers to the hospital day when normalization of the axillary body temperature ($36.5 - 37.7^{\circ}\text{C}$) was recorded through a standard digital thermometer.
5. Normalization of oxygen saturation refers to the hospital day when normalization of oxygen level of the body (95% and above) was recorded with a standard finger pulse oximeter.

B. SECONDARY OUTCOME MEASURE

The duration of hospital stay from the time of admission until the time of discharge of the patient.

C. ADVERSE REACTIONS

Refers to any new signs or symptoms such as appearance of maculo-papular rashes, erythema, itchiness that the patient may manifest during the clinical trial, which was absent prior to admission.

METHODOLOGY

This is a randomized, double-blind control clinical study conducted at a tertiary government hospital.

The subjects enrolled were infants and children after 6 months to 5 years old; with a primary clinical diagnosis of PCAP-C based on the "Philippine Pediatric Society Guidelines in the Diagnosis and Management of Pediatric Community Acquired Pneumonia, 2004" with a clinical, laboratory and radiographic findings suggestive of bacterial pathogen; requiring monotherapy and with written informed consent signed by the parent or caregiver.

The study excluded infants and children with other co-morbid conditions like pulmonary tuberculosis, measles, meningitis, sepsis, those with hemodynamic instability; those patients with completed Hib vaccination; children with severe malnutrition, severe dehydration, with chronic illness and on maintenance medications and supplement. (i.e. Primary Koch's infection, Leukemia, Nephrotic syndrome, among others)

The sample size was computed based on the study of Cadete et al, where in a 63.16% (60% conservative rate) rate of radiologic improvement was noted in Spirulina group vs. 38.50% (30% conservative rate) rate of radiologic improvement in placebo group after three days of treatment. This study required a sample size of 60 per group with 1:1 allocation. The assumed difference of patients' improvement was tested at 80% power and at 95% (0.05 α) level of significance.

Patients who met the inclusion criteria were randomized to Spirulina (Group A) or placebo (Group B) based on the randomization list prepared by a statistician. The list was prepared using MS Excel 2013 software, where it generated random numbers as basis for assigning treatment grouping.

The Spirulina and placebo was provided by Pharmacia Jimenez the drug company that manufactures "Arthrospiraplatensis (CellLife)". It is distributed in 60mg/sachet and 250mg/tablet available in major pharmaceuticals nationwide. Each sachet and tablet contains 100% Arthrospiraplatensis. The recommended drug intake, if used in conjunction with medications, is 60mg/ kg body weight. There are currently no known side effects, drug interactions or contraindications to this drug. The Spirulina and placebo was of the same color, taste and consistency. The Spirulina and placebo was packed in similar disposable plastic sachet.

The research assistant, subjects, research team was not aware of which group is the Spirulina and which the placebo is. A research assistant, who is a Third Year Resident assigned at the ward determined the primary and secondary outcome measure. A research assistant noted and recorded any adverse effects. Parents were likewise instructed to report any untoward manifestation to the investigator. The principal investigator verifies the accuracy and completeness of the data. Analysis of data was performed to determine the efficacy of Spirulina.

The study was performed in accordance with the Principles in the Declaration of Helsinki. An approval from the Hospital Research Committee and Institutional Review Board was obtained before the implementation of this study. An informed written consent was explained to the parents or caregiver before their inclusion in the study. Complete information on the nature, objectives, benefits and risks related to the study was discussed with the parents or caregiver.

CONDUCT OF THE STUDY

The principal investigator conducted an orientation among the members of the research team. The members of the team were assigned specific duties and responsibilities. The research assistant assigned at the Emergency Department screened and performed a complete history and physical examination to all prospective subjects. The parents or guardians of patients that met the inclusion criteria were oriented on the purpose, benefits and possible risks related to the study. A voluntarily signed informed consent and data information form was secured prior to the study implementation (Appendix A).

The subjects in Group A were given 60mg per kilogram bodyweight of Spirulina three times a day for seven days and subjects in Group B received 60 mg per kilogram bodyweight of placebo three times a day for seven days. The two groups received standard treatment of Ampicillin at 100mg/kg body weight in 4 divided doses until discharged.

The clinical response on both groups were assessed and recorded by the research assistant in the ward every 8 hours based on the following: tachypnea, chest in-drawing, rales, axillary temperature and oxygen saturation until the time the patient is discharged. A standard calibrated digital axillary thermometer and oxygen finger pulse oximeter was used to measure temperature and oxygen saturation,

respectively. Batteries of both thermometer and pulse oximeter were replaced every 10 patients monitored to assure accuracy of temperature and oxygen saturation determination. Adverse reactions were also observed by the research assistant. Patients with marked improvement and positive response to the treatment based on the primary outcome measure was discharged and given oral Amoxicillin 40-50mg/kg in three divided doses as switch therapy based on the recommendation in the "Clinical practice guidelines in the evaluation and management of pediatric community acquired pneumonia, 2004". However, patients who still had presence or worsening signs and symptoms of pneumonia on the third day of treatment was either shifted to another antibiotic or added another antibiotic to the regimen and was considered treatment failure from the study.

The principal investigator collected all the data recorded in the monitoring sheet (Appendix B). Collected data was then analyzed by the statistician. The overall flow of this study is shown in Appendix C.

DATA MANAGEMENT AND STATISTICAL ANALYSIS

Data gathered was encoded in Microsoft EXCEL 2013. Categorical data were expressed in frequency and percentage distribution. Continuous data were presented in mean and standard deviation.

Paired t-test was used to test whether the mean values of continuous variables would significantly change from baseline to post-treatment period. In comparing mean values between the two groups, Z test of mean difference was utilized while Chi square test with 2x2 Fischer exact tests was conducted in comparing categorical data. Any associated p-values lesser than 0.05alpha was considered significant. IBMSPSS ver.21 was used as statistical software in processing the data.

Results

A total of 153 patients met the inclusion criteria. One hundred forty seven of the 153 patients gave an informed consent. Seventy four subjects were randomized to Spirulina Group (Group A) and seventy three subjects were randomized to Placebo Group (Group B). Two (2) of the 74 patients enrolled in Spirulina Group were transferred to the Pediatric Intensive Care Unit (PICU) in less than 24 hours after admission for pneumonia severe. Four (4) patients

were considered unimproved after three days and were shifted to a different antibiotic which was completed for seven days. Ten of the 73 patients enrolled in Placebo Group were dropouts. Two (2) patients were transferred to PICU for progression to severe pneumonia, six (6) patients were considered unimproved after three days and was shifted to another antibiotic which was completed for seven days and two (2) patients went home against medical advised.

The data in this study were analyzed as per protocol. As shown in Table 1, there were more males (57%) in the Spirulina Group as compared to Placebo Group (43%). In comparison, there were more females in the Placebo Group (57%) as compared to the Spirulina Group (43%). The differences in rates of dominant gender in both groups were not statistically significant. (p - value 0.097).

It was noted in Table 1 that the mean age in the Spirulina Group is 1.63, in comparison the mean age in the Placebo Group is 2.70. Those in group B were significantly older than in group (p – value 0.01)

Table 1. Comparative Frequency and Percentage Distribution as to Gender and Age in Spirulina Group and Placebo Group as to Gender

Demographics	Spirulina	Placebo	p-value
	n=68	n=63	
Sex			
Females	29 (43%)	36 (57%)	0.097
Males	39 (57%)	27 (43%)	
Age in years			
mean±SD	1.63±1.33	2.70±1.66	<0.010

The respiratory rate was monitored in both study groups every 8 hours. Table 2 showed that in the Spirulina Group the average respiratory rate in the morning of day 1 is 46.59±8.78 cycles per minute. The respiratory rate decrease in the evening to an average of 42.09±8.37 cycles per minute. The average reduction of respiratory rate in the morning of day 2 was 40.57±8.86 cycles per minute; it continued to decrease in the evening with an average of 37.72±8.27 cycles per minute. A steady decline in respiratory rate was noted at day 3 from 35.59±6.40 to 32.80±4.31cycles per minute.

The respiratory rate continues to decrease until day 5 of observation. Analysis indicated that the reduction of average respiratory rate in Spirulina group was statistically significant ($p < 0.01$).

In comparison, participants in the Placebo Group have a decrease in average respiratory rate at 50.62 ± 7.74 cycles per minute at day 1 of observation. The respiratory rate decrease further at 42.02 ± 8.50 cycles per minute at day 2 of the study. The respiratory rate of patients variably changes from 37.71 ± 12.28 cycles per minute to 40.75 ± 6.74 cycles per minute from day 3 to day 4 of the study. The changes in respiratory rate of patients in the placebo Group were statistically significant ($p < 0.001$).

Comparative analysis showed that the average respiratory rate of patients in the Spirulina Group was significantly lower than the patients in the Placebo Group at day 1, day 3, and day 4.

Table 2. Comparison of Mean and Standard Deviation of Respiratory Rate between Spirulina Group and Placebo Group at Different Days and Time Intervals

Respiratory rate	No. of Cases Monitored	SPIRULINA mean $\pm$ SD	No. of Cases Monitored	PLACEBO mean $\pm$ SD	p-value
Day 1					
AM	68	46.59 $\pm$ 8.78	63	50.62 $\pm$ 7.74	0.006
PM	68	43.22 $\pm$ 9.54	63	50.05 $\pm$ 9.32	<0.010
Evening	68	42.09 $\pm$ 8.37	63	46.59 $\pm$ 9.08	0.004
Day 2					
AM	68	40.57 $\pm$ 8.86	63	42.02 $\pm$ 8.5	0.344
PM	68	38.34 $\pm$ 8.16	63	41.21 $\pm$ 9.41	0.064
Evening	65	37.72 $\pm$ 8.27	63	37.52 $\pm$ 8.26	0.892
Day 3					
AM	59	35.59 $\pm$ 6.4	3	48 $\pm$ 0.00	0.001
PM	59	34.49 $\pm$ 5.99	21	37.71 $\pm$ 12.28	0.121
Evening	44	32.8 $\pm$ 4.31	21	38.29 $\pm$ 12.67	0.012
Day 4					
AM	12	29 $\pm$ 3.77	12	40.75 $\pm$ 6.74	<0.010
PM	12	31.25 $\pm$ 3.08	9	39 $\pm$ 5.27	<0.010
Evening	9	29.33 $\pm$ 4.36	9	37.89 $\pm$ 2.42	<0.010
Day 5					
AM	3	22 $\pm$ 0.00	6	35.83 $\pm$ 4.58	0.001
PM	3	19 $\pm$ 0.00	3	38 $\pm$ 0.00	1.000

Paired t-test mean change; Group A: $p < 0.01$, Group B: $p < 0.01$

The resolution of chest in-drawing was observed in the two groups at different days and time interval. Table 3 showed that in Spirulina group, 96% of patients had chest in-drawing at day 1, 74% had chest in-drawing at day 2, and 9% had chest in-drawing at day 3. The reduction implied that there was resolution of patients' chest in-drawings beginning at day 2 to 3.

In the placebo group, the rate of chest in-drawings was at 100% at day 1, 90% at day 2, 29% at day 3, and 10% day 4. The trends indicated that there was a slow resolution of chest in-drawing among the Placebo Group. Analysis revealed that Spirulina demonstrated better effect in the resolution of chest in-drawings at day 2, 3, and day 4 ($p < 0.01$).

Table 3. Comparative Frequency and Percentage Distribution of Chest in-drawings in Spirulina Group and Placebo Group at Different Days and Time Intervals

Chest in-drawings	SPIRULINA Group A N=68	PLACEBO Group B N=63	p-value
Day 1			
AM	65 (96%)	63 (100%)	0.137
PM	65 (96%)	63 (100%)	0.137
Evening	65 (96%)	56 (89%)	0.289
Day 2			
AM	50 (74%)	57 (90%)	0.010
PM	12 (18%)	39 (62%)	<0.01
Evening	9 (13%)	21 (33%)	0.008
Day 3			
AM	6 (9%)	18 (29%)	0.006
PM	0 (0%)	12 (19%)	<0.01
Evening	6 (9%)	6 (10%)	<0.01
Day 4			
AM	0 (0%)	6 (10%)	0.017
PM	0 (0%)	6 (10%)	0.017
Evening	0 (0%)	0 (0%)	1.000

The auscultation findings at different days among patients in Spirulina Group and Placebo Group are shown in Table 4. There were more patients in Spirulina group with absent rales on day 2 (31% vs. 10%, p -value 0.02), day 3 (35% vs. 33%, p -value 0.039), day 4 (100% vs. 38%, p -value 0.01) and day 5 (100% vs. 62%, p -value 0.01).

Table 4. Comparative Frequency and Percentage Distribution of Auscultation Findings in Spirulina Group and Placebo Group at Different Days of Study

Auscultation Findings Resolution	Spirulina N=68 n (%)	Placebo N=63 n (%)	p-value
Day 1	0 (0%)	0 (0%)	1.000
Day 2	21 (31%)	6 (10%)	0.002
Day 3	24 (35%)	21 (33%)	0.039
Day 4	68 (100%)	24 (38%)	<0.01
Day 5	68 (100%)	39 (62%)	<0.01

A comparative analysis of mean axillary temperature among patients in Spirulina and placebo group is shown in Table 5. There is no significant difference in mean axillary temperatures in both study groups on day 1 (37.87 vs. 38.00, p-value > 0.05 α). Further analysis showed a significant difference in mean axillary temperature on day 2 of morning temperature determination (36.97 vs. 37.24, p-value 0.050), day 3 of afternoon temperature determination (36.60 vs. 36.82, p-value 0.013), day 4 of afternoon temperature determination (36.53 vs. 36.23, p-value 0.011) and day 5 of afternoon temperature determination (36.50 vs. 36.13, p-value 0.001). Temperature trends in the two groups showed slight reduction from day 1 to day 4. Despite low average reduction, the changes of temperature in both groups were statistically significant (p-value <0.01).

Table 5. Comparison of Mean and Standard Deviation of Axillary temperature in Spirulina Group and Placebo Group at Different Days and Time Intervals

Axillary Temperature	No. of Cases Monitored	SPIRULINA mean $\pm$ SD	No. of Cases Monitored	PLACEBO mean $\pm$ SD	p-value
Day 1					
AM	68	37.87 $\pm$ 1.19	63	38 $\pm$ 0.94	0.519
PM	68	37.49 $\pm$ 1.09	63	37.72 $\pm$ 0.77	0.159
Evening	68	37.41 $\pm$ 0.88	63	37.47 $\pm$ 0.53	0.677
Day 2					
AM	68	36.97 $\pm$ 0.72	63	37.24 $\pm$ 0.91	0.055
PM	68	37.22 $\pm$ 0.98	63	37.18 $\pm$ 0.69	0.806
Evening	65	37.07 $\pm$ 1.02	63	37.13 $\pm$ 0.57	0.702
Day 3					
AM	59	36.58 $\pm$ 0.53	60	36.54 $\pm$ 0.56	0.667
PM	59	36.6 $\pm$ 0.49	60	36.82 $\pm$ 0.44	0.013
Evening	41	36.63 $\pm$ 0.72	58	36.57 $\pm$ 0.58	0.611
Day 4					
AM	12	36.73 $\pm$ 0.86	18	36.47 $\pm$ 0.37	0.266
PM	12	36.53 $\pm$ 0.36	18	36.23 $\pm$ 0.23	0.011
Evening	9	36.73 $\pm$ 0.48	12	36.45 $\pm$ 0.48	0.193
Day 5					
AM	3	36.8 $\pm$ 0.00	9	37.27 $\pm$ 0.59	0.214
PM	3	36.5 $\pm$ 0.00	9	36.13 $\pm$ 0.13	0.001
Evening			9	36.17 $\pm$ 0.10	1.000
Day 6					
AM	0	-	3	36.3 $\pm$ 0.00	1.000
PM	0	-	3	36.7 $\pm$ 0.00	1.000

Paired t-test mean change; Group A: p<0.01, Group B: p<0.01

Table 6 outlines the comparative mean oxygen saturation of Spirulina group and placebo group. There is no significant difference in mean oxygen saturation in day 1 at different time intervals (96.17 vs. 96.67, p-value >0.05). Oxygen saturation was noted to be significantly different on day 2 of the afternoon determination (97.82 vs. 97.0, p-value <0.01), day 3 of morning and afternoon determination (98.60 vs. 98.05, p-value <0.05), day 4 of afternoon and evening determination (98.50 vs. 96.86, p-value <0.05) and day 5 of the morning determination (99.00 vs. 98.00, p-value <0.05).

Table 6. Comparison of Mean Oxygen and Standard Deviation of Oxygen Saturation in Spirulina Group and

Oxygen Saturation	No. of Cases Monitored	SPIRULINA mean $\pm$ SD	No. of Cases Monitored	PLACEBO mean $\pm$ SD	p-value
Day 1					
AM	68	96.17 $\pm$ 1.89	63	96.67 $\pm$ 1.37	0.089
PM	68	96.56 $\pm$ 1.71	63	96.95 $\pm$ 1.95	0.227
evening	68	97 $\pm$ 1.57	63	96.9 $\pm$ 1.28	0.707
Day 2					
AM	66	97.2 $\pm$ 1.53	63	97.48 $\pm$ 1.23	0.257
PM	66	97.82 $\pm$ 1.02	63	97 $\pm$ 1.24	<0.01
evening	63	93.71 $\pm$ 19.13	63	97.67 $\pm$ 1.85	0.105
Day 3					
AM	57	98.6 $\pm$ 0.73	63	98.05 $\pm$ 0.79	<0.01
PM	57	98.49 $\pm$ 0.76	63	97.86 $\pm$ 1.22	0.001
evening	40	98.58 $\pm$ 0.5	61	98.31 $\pm$ 0.79	0.063
Day 4					
AM	12	98.75 $\pm$ 0.45	21	98.43 $\pm$ 0.51	0.079
PM	12	98.5 $\pm$ 0.9	21	96.86 $\pm$ 1.01	<0.01
evening	9	98.67 $\pm$ 0.5	12	97.5 $\pm$ 0.52	<0.01
Day 5					
AM	3	99 $\pm$ 0.00	9	98 $\pm$ 0.00	0.001
PM	3	100 $\pm$ 0.00	9	97.33 $\pm$ 1	1.000
evening	0	-	9	98.67 $\pm$ 0.5	
Day 6					
AM	0	-	3	99 $\pm$ 0.00	
PM	0	-	3	98 $\pm$ 0.00	

Paired t-test mean change; Group A : p<0.01, Group B: p<0.01

As shown in Table 7, the mean hospital stay in Spirulina group (3.09 days) is shorter as compared to the placebo group (4 days). Analysis showed a significant difference in the mean length of hospital stay (p-value 0.02).

Table 7. Comparison of Mean and Standard Deviation of the Length of Hospital stay in Spirulina Group and Placebo Group

Hospitalization Stay in days	SPIRULINA Group A		PLACEBO Group B		p-value
mean (SD)	3.09	±0.67	3.52	±0.86	0.002
Range (min-max)	2	5	3	6	

There were no reported adverse events noted in both study groups during the study period.

DISCUSSION

Pneumonia is one of the leading causes of death globally among children younger than 5 years of age. The incidence of pneumonia and the childhood related deaths from pneumonia is more than 10 fold higher in developing countries than in developed countries.¹² However, in the Philippines, it still remain as one of the leading causes of morbidity and mortality for children younger than five years of age.

At present, there are still no proven additional interventions in the treatment of pneumonia to ensure early recovery from the disease. In this study, Spirulina supplementation among patients six months to five years of age with PCAP-C had significant results in terms of improvement in respiratory rate, chest in-drawing, auscultation findings and length of hospital stay. The significant improvement in the clinical parameter of the patients' in Spirulina group is explained by the presence of an active ingredient called C-phycocyanin that selectively inhibits the cyclooxygenase 2, a critical enzyme in the biosynthesis of prostaglandin. C-phycocyanin could also enhance the immunologic mechanisms of the lung, which include macrophages in the alveoli and bronchioles, secretory IgA and other immunoglobulins that limit the pathogenic organisms of pneumonia.¹³

Review of literature revealed that Spirulina acts as an immune-modulator. The aqueous extract of Spirulina was found to have a major impact on the immune system by increasing the phagocytic activity of macrophage, stimulating the natural killer (NK) cells. It also played a role in the activation and mobilization of T and B cells due to its stimulatory effects in the production of cytokines and antibodies which are likely accountable for the beneficial effects noted in this clinical trial.¹³ The present study have demonstrated that Spirulina supplementation in children with PCAP-C resulted in a shorter length of hospital stay.

A shorter hospital stay would decrease the risk of infants and children to acquire health care associated infections. Furthermore, a shorter hospital stay would mean a decreased number of missed school days for the patient and work days for the caregiver.

CONCLUSION

Spirulina supplementation in the treatment of PCAP C at a dose of 60 mg per kilogram per day showed clinical benefits in terms of earlier normalization of respiratory rate, resolution of chest in-drawing, improvement in chest auscultatory findings, a faster reversal of oxygen saturation to normal and ensuing a shorter length of hospital days as compared to placebo.

There were no reported side effects with the use of Spirulina supplementation in this study. This study proves that Spirulina supplementation is beneficial, safe, and effective adjunct in the treatment of PCAP C in infants and children.

RECOMMENDATION

This study provided evidence that Spirulina can be used as an adjunct therapy to infants and children with PCAP C. It is recommended to determine the safety and efficacy of Spirulina as an adjunct therapy in the management infants and children with Pneumonia (PCAP A and B) in an outpatient setting, infants and children with underlying malnutrition and Primary Koch's Infection. A research with bigger sample size is recommended for implementation in the future.

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APPENDIX A

DATA COLLECTION FORM

General data:

Name: _____

Age: _____ Sex: _____ Wt. _____ HC: _____ CC: _____ AC: _____ Ht. _____

Address: _____

Parents/Guardian: _____

Consent: _____ Date of consent: _____

Date and time of Admission: _____ Admitting Diagnosis: _____

Admitting MD: _____ Group assignment: _____

Variables	PCAP-A	PCAP-B	PCAP-C	PCAP-D
Co-morbid illness	None	Y/N	Y/N	Y/N
Compliant caregiver	Y/N	Y/N	Y/N	Y/N
Ability to follow-up	Y/N	Y/N	Y/N	Y/N
Presence of dehydration	Y/N	Y/N	Y/N	Y/N
Ability to feed	Y/N	Y/N	Y/N	Y/N
Age		>11mos	< 11 mos	<11 mos
Respiratory rate				
2-12 mos				
1-5 yrs	>50/min	>50/min	>60/min	>70/min
>5 yrs	>40/min	>40/min	>50/min	>50/min
	>30/min	>30/min	>35/min	>35/min
Signs of respiratory failure:				
Retraction				Supraclavicular/
Head bobbing	Y/N	Y/N	Inter/subcostal	inter costal
Cyanosis	Y/N	Y/N	Y/N	Y/N
Apnea	Y/N	Y/N	Y/N	Y/N
Sensorium	Y/N	Y/N	Y/N	Y/N
	Y/N	Y/N	Y/N	Y/N
Complications (effusions, pneumothorax)	Y/N	Y/N	Y/N	Y/N

APPENDIX B

Name: _____ Age: _____

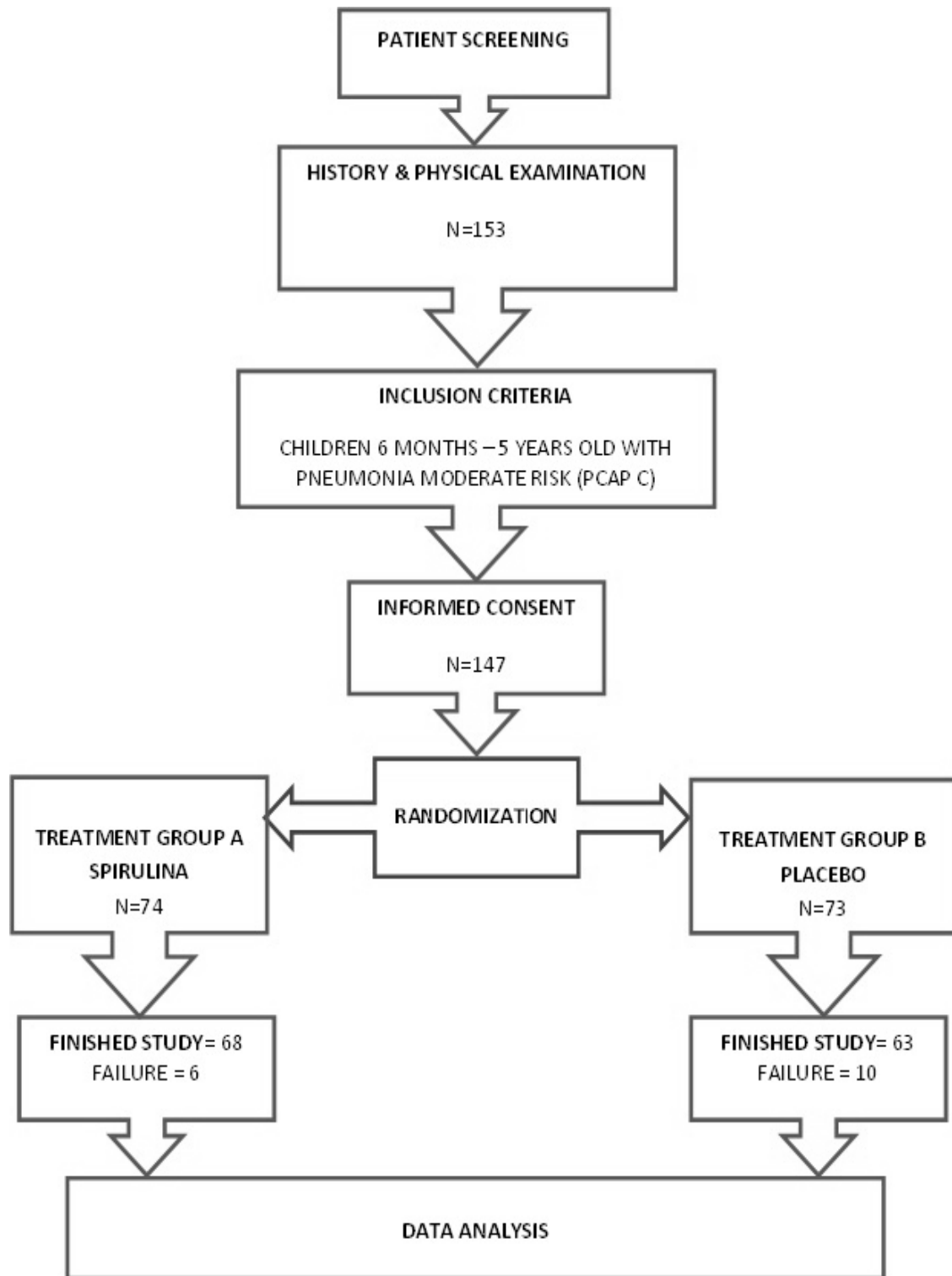
Date admitted: _____ Date discharged: _____

Daily Patient Assessment Form

Clinical Parameters	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Respiratory rate	AM						
	PM						
	Evening						
Chest in-drawings	AM						
	PM						
	Evening						
Auscultation findings	AM						
	PM						
	Evening						
Axillary temperature	AM						
	PM						
	Evening						
O2 saturation	AM						
	PM						
	Evening						
Adverse reaction							

APPENDIX C

STUDY PROCEDURE FLOW CHART



Patterns of Resolved Medical Malpractice Cases in the Philippines

Natividad Salazar, MD¹

ABSTRACT

Background: Medical malpractice is an act or omission by a health care provider that deviates from accepted standards of professional practice leading to injury to the patient. Tort actions of negligence prevail when a plaintiff establishes in court that: (1) the physician had a duty to the patient referred to as patient-physician relationship; (2) a dereliction or breach of that duty occurred (3) the dereliction of duty resulted in damage to the patient, and (4) the patient was, in fact, damaged (Brown, 1976).

Methods: The study was conducted to describe the patterns of the resolved medical malpractice cases in the Philippines. Transcripts of records of resolved medical malpractice cases were retrieved, analyzed and evaluated by 2 lawyers and the researcher.

Results: Negligence was established as the main cause of litigation among the 6 resolved medical malpractice cases. Eight physicians were found liable while 4 were acquitted. The litigation process was protracted, lasting 13-24 years.

Conclusion: The results of the study serve to provide an overview of medical malpractice cases in the Philippines. It is hoped to increase the awareness of health care providers regarding medical malpractice.

Keywords: medical malpractice, negligence, Philippines

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INTRODUCTION

In most countries, medical practitioners are being threatened by litigation, with the first country to report a medical malpractice suit being the United States in 1794 (Monis, 1971). The concept of Mala Praxis (malpractice) extends back to the beginning of the 18th century. Most historical malpractice cases involve negligence based on certain standards of conduct. In the case of doctors, the conduct is judged according to competence and professionalism consistent with specialized training. Deviations from such standards may be judged negligent (Morris, 1971).

Medical malpractice is defined as an act or omission by a health care provider which deviated from accepted standards of practice in the medical community, causing injury to the patient (Medical Malpractice, 2007). This concept is based on the premise that a patient seeks medical consult with the intent of getting the best healthcare possible and a physician is expected to deliver a standard of care. There is an implicit understanding of a patient-physician relationship acceptable to both parties. A breach of this relationship to the point of injury may lead to legal actions.

The most common cause of malpractice is negligence resulting in injury, damage or death. To be found guilty of negligence, the plaintiff must establish in court the criteria for tort or wrongful act. In order for a civil suit to prevail in court, the following conditions should be met: (1) the physician had the duty to the patient or existence of a patient-physician relationship, (2) that there was dereliction or breach of that duty, (3) that the dereliction of duty resulted in damage to the patient, and (4) that the patient was, in fact, damaged (Brown, 1976).

The filing of a litigation claim is guided by regulations, one of which is related to the statute of limitations. This legal term defines the time limit for an individual to initiate a lawsuit, with the length of the statute of limitations depending on the individual's residence. In the Philippines, the prescribed period is two to five years.

There are three social goals of malpractice litigation - to deter unsafe practices, compensate persons injured through negligence, and exact corrective justice (Keeton et al. in Studdert, et al., 2006). The decision to litigate by the relatives is often due to the perceived lack of caring or collaboration in health care delivery (Beckman et al., 1994).

Findings from a US study demonstrated that majority of malpractice suits involved surgical practitioners, with more specialists being sued compared to generalists (Brown, 1976). Another study reported that risk management events were higher among surgeons than non-surgeons (Hickson et al., 2002). In a study identifying defendants from various specialties, majority involved obstetricians, general surgeons, orthopedic surgeons and neurosurgeons (Studdert et al., 2006).

In the Philippines, the first medical malpractice case was filed in 1907 in Davao (SCRA, 1908) followed by a 1957 case in Negros Occidental (SCRA, 1960). In both cases, the accused were unlicensed practitioners. It was only in 1981 that the first case involving licensed medical practitioners was filed in court. Since then, there have been six resolved cases, with the latest in 2007. Hence, while negligence is a common cause of malpractice in the United States, no such pattern has been noted in the Philippines. The researcher is unaware of published studies regarding the prevalence and outcomes of medical malpractice suits in the country. Hence, it would be of interest to explore these patterns of medical malpractice, as the identification of patterns of malpractice suits in the Philippines may provide insights on the litigation risks and consequences that a medical practitioner may face in the course of practice.

METHODS

Study Design and Setting

This was a retrospective descriptive study conducted with the purpose of reviewing resolved malpractice suits filed in the Philippines. Transcripts of resolved cases from Philippine courts from 1907-2007 were reviewed. Resolved malpractice suits were of interest since according to Philippine law, these records were considered to be public records.

Description of Study Procedure

An initial consultation with a justice from the Court of Appeals regarding the process of gathering documents pertaining medical malpractice cases was done. Upon access to the documents, two lawyers were invited to assist in the retrieval and evaluation of the documents. The lawyers were asked to review the transcript of court records and record their comments on the resolved cases, with focus on the cause of the litigation and the resolutions of each case. These annotated documents were then reviewed by the researcher for the purpose of the study.

Ethical approval for the study was secured from the University of the East Ramon Magsaysay Memorial Medical Center, Inc.

Results and Discussion

For the past 100 years (1907-2007), only eight resolved medical malpractice cases were recorded in the Philippines. The reviewed transcript of records of the resolved cases showed that the most frequent reason for filing a suit was negligence.

The first case (GR 86890) was filed in 1981 against a surgeon and an anesthesiologist for negligence due to failure to monitor the patient during the post-operative stage. The next case (GR 11841) in 1984 likewise involved a surgeon and an anesthesiologist who were convicted of negligence due to failure to avert the deleterious effects of an anesthetic. The third case (GR 126467) was reported in 1984, with the surgeon and obstetrician-gynecologist being sued for failing to remove foreign bodies before closure of the abdomen. In 1986, the fourth case (GR 124354) concerning a surgeon and an anesthesiologist was decided for the plaintiff who sued the physicians for the injury resulting to the demise of the patient.

GR 130547 was the fifth case, which was filed in 1987. Unlike the previous cases, physicians practicing non-surgical specialties (internal medicine) were involved due to carelessness in ordering a laboratory procedure and prescribing a medication. The physicians were eventually acquitted.

The last case (GR 122445) reviewed was reported in 1991. The plaintiff sued an anesthesiologist and obstetrician-gynecologist for negligence due to failure to perform necessary preoperative procedures such as medical risk assessment, resulting in the death of the patient. In this case, the court decided to acquit the anesthesiologist but found the obstetrician-gynecologist civilly liable.

Of the six resolved cases involving 12 physicians, eight were convicted for civil liabilities or both civil and criminal liabilities, and four were acquitted. Among those found guilty, four were surgeons, three were anesthesiologists, and one was an obstetrician-gynecologist. The four acquitted doctors were two internists, one obstetrician-gynecologist, and one anesthesiologist.

Negligence was found in the six resolved medical malpractice cases - i.e. failure to perform the standard procedure, with most cases pertaining to negligence prior, during, and after surgical procedures.

In the case of GR 122445, the practitioner failed to request for pre-operative laboratory parameters and baseline procedures required for the assessment of a patient's operative risk. In the case, it was determined that the failure to secure baseline medical parameters was a negligent act resulting to the death of a patient.

Other cases involved negligence during the operative procedure and cases of *res ipsa loquitur*. For example, in a procedure to remove a ureteral stone, the patient developed malignant hyperthermia due to the anesthetic, which the physicians failed to reverse, leading to the death of a patient.

Another instance involved an obstetrician-gynecologist and a surgeon. Two surgical procedures (partial bowel resection followed by a total abdominal hysterectomy) were done, with the obstetrician-gynecologist leaving the operating room prior to closure of the abdomen.

Shortly after this, the surgeon was informed of missing sponges, and despite failure to locate these, he decided to close the abdomen. On a succeeding visit, the patient complained of pelvic pain to both the surgeon and obstetrician-gynecologist who attributed this to wound healing. Several months later, the patient developed a vaginal infection and fistula due to the sponges left behind. While review of the documents was not able to establish who was responsible for leaving the sponges, the case fell under the doctrines of captain of the ship and *res ipsa loquitur*, as the sponges found were enough proof to establish the negligence of the surgeon involved.

Another case of negligence falling under the doctrine of *res ipsa loquitur* was noted in a patient suffering from abdominal discomfort. An initial diagnosis of gallstones required the patient to be admitted for a cholecystectomy; however, the procedure was delayed for three hours as the surgeon was in another hospital. During the operation, the anesthesiologist had difficulties in intubation, and the service of another anesthesiologist was obtained. Despite eventual successful intubation, the patient became comatose and remained so for four months before eventually expiring. The case was decided against the doctors for the injury which needed no further proof.

Negligence after the operative procedure was seen in the case of physicians who were convicted for failing to monitor and correct the adverse effects of anesthesia. In this particular case, it was noted that the physicians failed to monitor post-operative vital signs necessary for the detection of adverse effects of the anesthesia. Furthermore, the patient was transferred out of the recovery room and into a regular room despite not being fully awake, which was contrary to standard protocol. The patient fell into a comatose state and eventually expired.

These cases indicate common practices resulting to negligence, including (1) failure to perform pre-operative laboratory procedures, (2) failure to correct adverse effect of anesthetics, (3) *res ipsa loquitur*, and (4) failure to monitor patients post-operatively.

A pattern observed is the long duration of litigation. The length of time before case resolution is striking, especially when compared to other countries — i.e. litigation lasted for an average of 20 years longer than the mean duration of 10 years in the United States. Aside from the case overload in Philippine trial courts, another contributor to the duration of litigation was the filing of multiple appeals by both the plaintiff and defendants.

For example, the first decision of the case of a patient who underwent bowel resection and hysterectomy was rendered after nine years. A petition for review was filed at the Court of Appeals which affirmed this after three years. Another appeal was elevated to the Supreme Court which rendered a decision after eleven years. It took 24 years before the case was resolved.

In the case of failed intubation, the lower court rendered a conviction of the physicians. An appeal was filed with the Court of Appeals which reversed the decision after 13 years. The family of the patient filed a motion for reconsideration which was denied by the Court of Appeals, and the case was elevated to the Supreme Court which after another three years decided on a conviction. The process spanned 16 years.

In contrast to the previous cases, amicable settlements accounted for the shorter durations of the other malpractice cases. For example, the case of malignant hyperthermia filed in 1997 required 10 years of fact-finding, followed by an amicable settlement.

During the litigation process, all parties involved suffer from psychological distress and financial strain. The large impact of litigation on these aspects of the physicians' lives lead them to prefer the option of amicable settlement whenever possible. For example, two of the physicians found guilty opted for amicable settlement for undisclosed amounts. For other cases, civil liabilities settled varied across the cases reviewed, ranging from Php90,000.00 to Php3,552,000.00.

Damages awarded to the plaintiffs varied depending on the patient's age, earning capacity, health status, and profession. For the cases which were reviewed, the damages to be paid by the defendants were computed by the court.

In contrast to Western countries, the Philippines has a low rate of medical malpractice suits. This may be attributed by patients' perceptions of their physicians as authoritarian healers doing no harm. The collectivist nature of the Filipino society, characterized by *pakikisama*, also dictates that relationships with others, especially those who are perceived to have a higher position in society (such as physicians), are to be valued. Hence, the filing of a lawsuit against a medical practitioner would only cause relational disruption while failing to bring their loved ones back. Finally, as correlated with their perceptions of physicians as authoritarian figures, Filipino patients may have minimal information regarding their rights as patients.

A similarity between the malpractice suits in the Philippines and Western countries is the predominance of surgical specialties involved. In the study, a clear majority of the cases reviewed were concerned with surgical procedures, such as appendectomy, total abdominal hysterectomy, removal of ureteral stone, removal of gallbladder, and bowel resection. The over-representation of surgical specialties is a pattern that has been observed in the United States. In a study done by the Commission on Medical Malpractice under the Secretary of Health Education and Welfare in the United States, more than 90% involved practitioners of various surgical specialties.

In sum, the study identified negligence as the main pattern of malpractice suits in the Philippines, both as omission of and commission against the standards of medical practice. Most cases involved negligence that occurred before, during and after an operative procedure. Medical practitioners should be encouraged to observe proper medical conduct adhering to the norms of the medical profession. Information provision,

particularly in the form of full disclosure, is necessary. Careful patient assessment should be done and informed consent should be secured prior to any procedure/treatment. Finally, medical practitioners should keep clear records of their patient interactions should they be needed in court.

Limitations

This study was a retrospective review of court documents available; hence, information gathered was limited. Furthermore, no interviews with the defendants or plaintiffs were conducted, which could have had an impact on data quality. Finally, the limited number of medical malpractice cases in the Philippines led to a small sample size.

Conclusions and Implications

This study sought to explore the patterns of medical malpractice in the country based on all available resolved cases in Philippine history. Identified patterns included negligence as the primary reason for a malpractice suit, the over-representation of surgical procedures in the cases reviewed, and the lengthy nature of litigation.

It is hoped that this study can serve as a reminder for medical practitioners to practice well within the bounds of their profession and to remain constantly aware that negligence may have adverse effects on their patients, to the point of warranting malpractice suits. Awareness of possible litigation from dissatisfied or injured patients and their families will hopefully heighten the vigilance of health professionals in following accepted standards of medical practice.

Due to the small number of resolved medical malpractice suits in the Philippines, the data which was provided for analysis was likewise limited. Future recommendations include studies assessing the impact of litigation and its long duration to the plaintiff and defendants, continuing studies on the pending malpractice suits filed in the country, and cross-cultural studies on medical malpractice suits, including perspectives from other Asian countries.

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Annular Pustular Psoriasis in a 6-year-old child: Case Report

*Patricia Gaile E. Espinosa, MD, Francisco D. Rivera IV, MD, FPDS **

ABSTRACT

Annular pustular psoriasis (APP) is a rare variant of pustular psoriasis occurring only in about 1-5.4% of children with psoriasis. Pustular psoriasis is triggered by endogenous and exogenous factors. Exogenous factors include stress, upper respiratory tract infection and withdrawal of systemic corticosteroids.

This condition usually requires systemic treatment. However, there are still no randomized controlled trials or standardized guidelines proving the advantage of any specific treatment modality over the other.

We report a case of a 6-year-old male who presented with diarrhea followed by appearance of erythematous annular plaques with pustules and nail changes. Punch biopsy showed pustular psoriasis. Patient was treated with topical betamethasone valerate and calcipotriol, and there was noted to have no recurrence of skin lesions for 4 months.

Keywords: *annular pustular psoriasis, children, pustular psoriasis, psoriasis, topical steroids*

**From the Department of Dermatology, Rizal Medical Center*

INTRODUCTION

Psoriasis is a chronic inflammatory skin disease, with a strong genetic basis, characterized by complex alterations in epidermal growth and differentiation and multiple biochemical, immunologic and vascular abnormalities, and a poorly understood relationship to nervous system function. Its root cause remains to be unknown.¹ Annular pustular psoriasis (APP) is a rare variant of pustular psoriasis occurring only in about 1-5.4% of children with psoriasis.¹⁻²

Treating pediatric psoriasis can be challenging and requires careful compliance to a specific treatment regimen. There are currently no international standardized guidelines for medical treatment of pediatric psoriasis. To date, treatment is primarily based on published case reports, guidelines for adult psoriasis, expert opinions, and experience with these drugs in other pediatric disorders. The range of psoriasis treatments has expanded during the past several years, and multiple topical agents, phototherapy, and systemic and biological agents are available to date.²

This case report involves a 6-year-old child with annular pustular psoriasis and its management.

Case Presentation

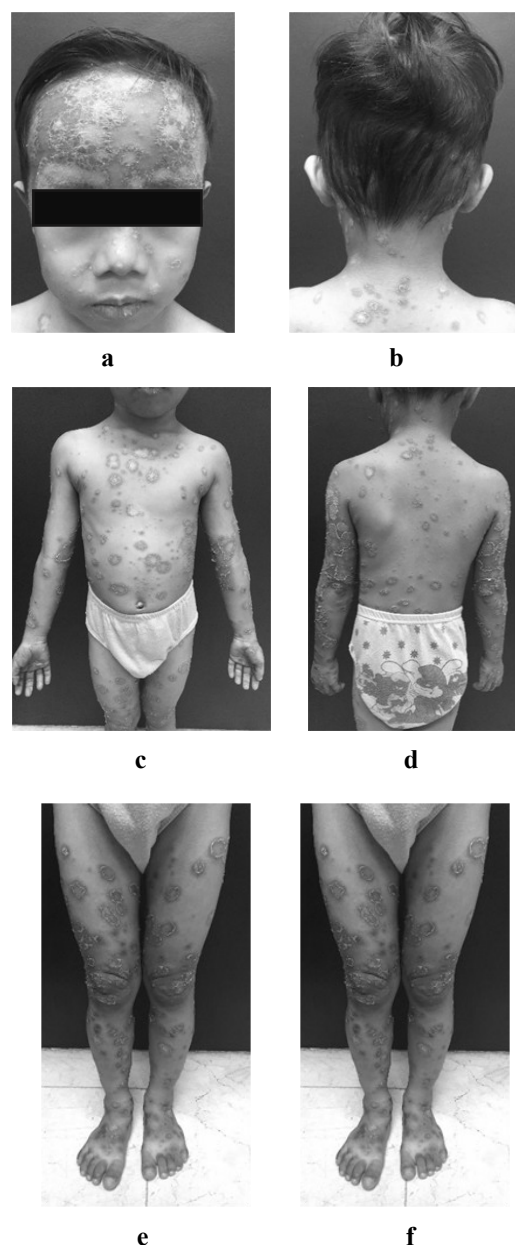
We are presented with a 6-year-old male who initially presented with multiple tender, pinpoint pustules on erythematous base over the right sole. This was preceded by 1 day history of loose, watery stools, accompanied by abdominal pain, decreased activity and poor appetite. There was noted progression of disease over the next 3 weeks, with pustules appearing over the trunk, upper extremities, face and scalp, followed by erythematous annular plaques on the same areas (Figure 1). There was no history of previous skin lesions.

During the course of the disease, patient did not have any cough, colds, fever, weight loss, lymphadenopathy, alopecia, abdominal pain, dysphagia, dental caries, or difficulty breathing. There were no similar lesions were noted from any member of the family.

Based on the history and clinical presentation, patient was assessed to have annular pustular psoriasis. Psoriasis Area and Severity Index (PASI), which is used to assess the severity of psoriasis at a

given point in time, is measured using the following parameters: erythema, scaling and induration of the lesions, and body surface area involvement.³ During initial consult, the patient had PASI score of 21. Skin punch biopsy was performed and complete blood count with platelet (CBCP), urinalysis, erythrocyte sedimentation rate (ESR), blood urea nitrogen (BUN), creatinine, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), and chest radiography were requested which were all unremarkable. Biopsy findings were consistent with psoriasis. (Fig. 2)

Figure 1



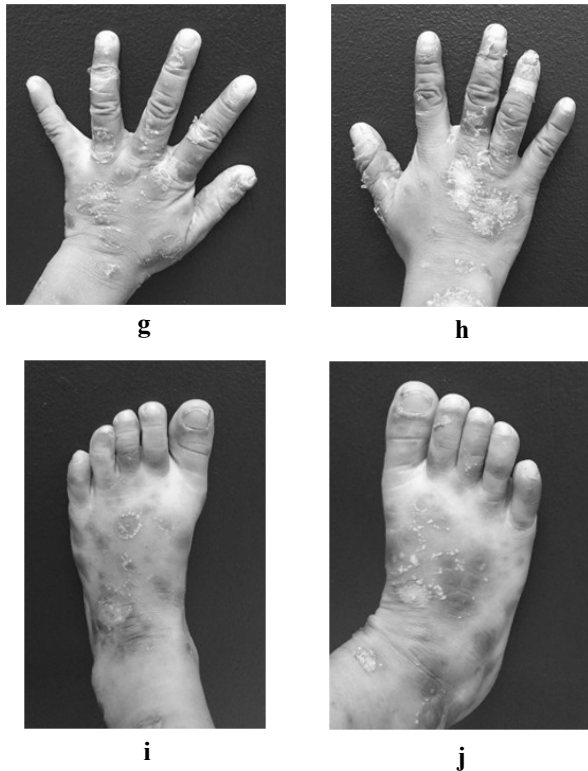


Figure 1 shows patient with PASI 21, with multiple annular erythematous scaly plaques over the head (a,b), trunk and all extremities (c,d, e, f). Some digits have onycholysis, nail pitting and oil spots (g, h, i, j).

Figure 2

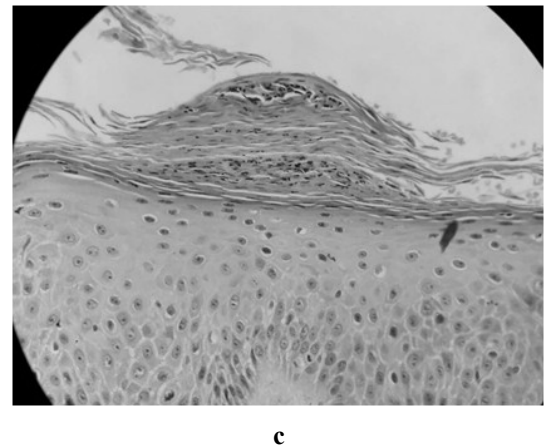
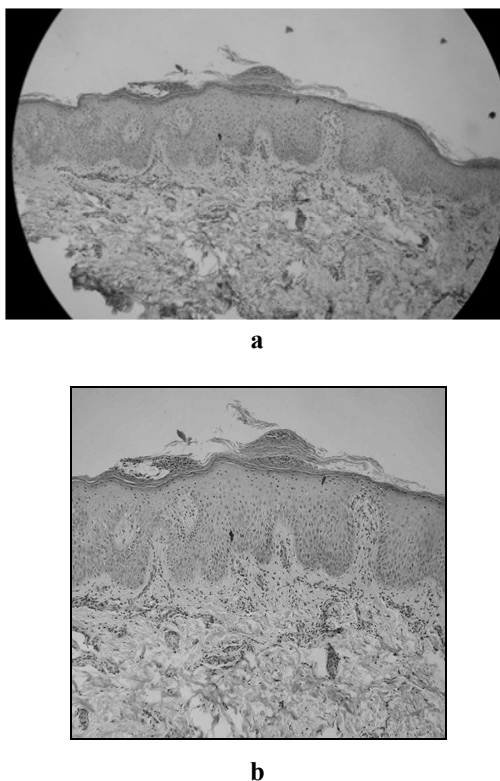
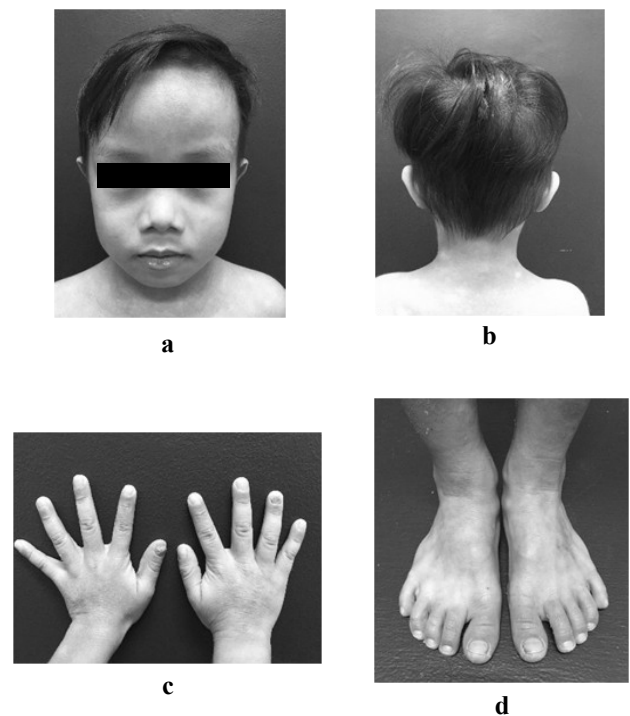


Figure. 2 (a-c) shows histopathologic findings of parakeratosis, hypogranulosis, elongation of rete ridges, neutrophilic aggregates within the stratum corneum, spongiosis in lower third of epidermis, active mitosis near basal layer, dilated blood vessels in the dermis, and perivascular and interstitial lymphocytic infiltrates.

Upon follow-up, he was started on betamethasone valerate lotion applied 2 times a day over the body, calcipotriol gel once a day in the morning over the face and Cetirizine for pruritus. After 9 days of treatment, the patient no longer have pruritus and showed a PASI score of 7.8. There is a 77% improvement of the lesions. There was now marked decrease in erythema and scaling over the whole body. (Fig. 3)

Figure 3



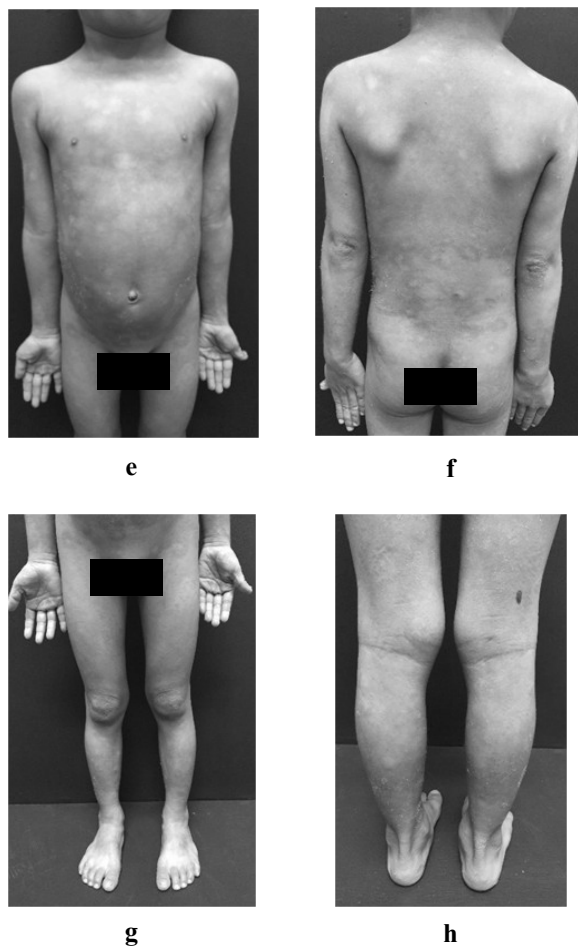


Figure 3 (a-h) shows patient with a PASI score of 7.8.

Discussion

A. Clinical Presentation and Diagnosis

In this case, the child presented with pruritic, annular erythematous scaly plaques and pustules, which is classic of APP.

Psoriasis has a worldwide occurrence, affecting 0.1 – 3% in various populations. It may appear at any age, however, it is uncommon under the age of 10 years.¹ Gelfand et al. found that the prevalence of psoriasis in childhood in the UK was about 0.55% in children aged 0-9 years and 1.37% in children aged 10-19 years.⁴ Pediatric psoriasis was almost absent in an epidemiological study on childhood dermatoses performed in Asia, while pustular psoriasis is seen in only 1.0-5.4% of children with psoriasis.² In a Chinese survey of 277 children, only 1.1% presented with pustular psoriasis.⁵

Commonly, triggers of pustular psoriasis are emotional stress, upper respiratory tract infection or withdrawal of oral corticosteroids. However, in this patient, the child exhibited loose bowel stools and abdominal pain.^{1-3,6}

In this case, pustular psoriasis can be diagnosed clinically, although biopsy can aid in the diagnosis, showing parakeratosis, loss of granular layer, elongation of rete ridges, neutrophilic aggregates within the epidermis (known as microabscess of Munro), dilated blood vessels in the dermis, and perivascular lymphocytic infiltrates.¹⁻²

B. Management

Topical treatment was initially started while patient is awaiting results of laboratory exams.

There is no standard therapy for pustular psoriasis. Disease severity and extent of skin involvement help guide treatment. In children, acitretin, cyclosporine, methotrexate and etanercept are options for first-line therapy. However, no randomized controlled trials exist to prove the efficacy or superiority of a single treatment.⁸

The published first line and second line treatment for childhood generalized pustular psoriasis (GPP) are based on Class III evidences which include non-experimental descriptive studies, such as comparative studies, correlation studies, or case-control studies. First line systemic treatments include acitretin, cyclosporine, methotrexate and etanercept. Second line treatments include adalimumab, infliximab and UVB phototherapy. Topical treatment are started for localized cases and may be used in combination with systemic therapy.^{8,9}

In a journal by Buetner et al., they showed an algorithm for the treatment of childhood psoriasis with greater than 5% body surface area, without psoriatic arthritis. In our case, there was 60% BSA involvement. First line are topical agents, next would be ultraviolet B (UVB) phototherapy treatment. If UVB is not available, systemic treatment is warranted. For oral medications, the following may be considered: Adalimumab, Cyclosporine, Etanercept, Infliximab, Methotrexate, and PUVA.⁹

The use of topical therapy in childhood is the first line of treatment for skin-limited disease, sometimes in combination with oral antibiotics if associated with

infection. With chronicity of illness and in more severe cases, systemic therapy and phototherapy are added to help induce remission.⁵

In this case, we planned on using a topical agent in combination with a systemic treatment. We started the patient on betamethasone valerate lotion, which is a class 3-4 midpotent topical steroid.¹⁰ Topical calcipotriol, a vitamin D analog, was also added to treatment. We planned on giving methotrexate afterwards. The patient responded after twice daily application for 1 week. From a 24 PASI score to a 7.8 PASI score. Improvement was 77% after treatment with both betamethasone valerate and calcipotriol. Since there was marked improvement with topical betamethasone valerate and calcipotriol, the use of oral treatment was no longer needed. There were no noted side effects from the topical used.

Similar to our case, Feicht, et al. also reported in 1982, a case of a 2-year old child who presented with GPP for 3 weeks and was treated with hydrocortisone 1% ointment. 100% clearance was seen. This shows that topical medication can be used and have a favorable outcome in pustular psoriasis.¹¹

In our patient, there were no recurrences for 4 months after treatment. Mother religiously applied emollients over the body. Topical treatment with betamethasone valerate and calcipotriol may be another first line, safer treatment option for pustular psoriasis in children, although randomized controlled trials are still needed.

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Classic dermatomyositis in a 36-year-old Filipino female: A case report with emphasis on the early recognition of cutaneous findings of dermatomyositis*

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ABSTRACT

Introduction: Dermatomyositis is a rare idiopathic inflammatory myopathy with characteristic skin manifestations and proximal muscular weakness. In 30 percent of classic dermatomyositis, skin findings precede muscle weakness. Since the initial skin lesions are not always highly characteristic of dermatomyositis, there may be a delay in diagnosis and treatment.

Case report: This is a case of a 36-year-old Filipino female who initially presented with erythematous patches and plaques on the face, arms, and thighs. One week later, she developed multiple, well-defined, erythematous to violaceous, edematous, tender patches and plaques on the face, V of the neck, upper back, proximal extremities and buttocks. Seven weeks later, she developed proximal muscle weakness described as difficulty in raising her arms and difficulty in standing up from a sitting position. Histopathology was consistent with dermatomyositis. SGPT, C3, ANA, and anti-ds-DNA were normal. SGOT and creatine kinase were 5 and 15 times the normal value, respectively. She was treated with prednisone from the first week of illness and hydroxychloroquine from the fifth week of illness. Her condition greatly improved with no progression of the disease for the succeeding 3 years.

Conclusion: Even in the absence of muscle weakness, there should be a high index of suspicion for dermatomyositis in patients with confluent, erythematous patches and plaques on the face, trunk and proximal extremities. Adequate work-up and clinical monitoring will pave the way for early diagnosis and consequently early treatment and a better patient outcome.

Keywords: *dermatomyositis, inflammatory myopathy, corticosteroids*

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INTRODUCTION

Dermatomyositis is a rare autoimmune disorder that targets the skin, skeletal musculature, and other organs. Little is known about the basic mechanisms underlying the pathogenesis. Skin findings are characteristic and play a significant role in its diagnosis. These include violaceous patches and edematous plaques in the periorbital area (heliotrope sign), V of the neck (V-sign), shoulders (shawl sign), proximal extremities and buttocks (holster sign). In classic dermatomyositis, proximal muscle weakness also develops. In majority of the cases, cutaneous manifestations and proximal muscle weakness present simultaneously, making it easy to diagnose dermatomyositis. However, in 30% of the cases, patients initially present with cutaneous manifestations only. Proximal muscle weakness presents several weeks to months after the onset of the condition.¹ To the untrained eye, these skin lesions can be mistaken for skin conditions such as eczema, contact dermatitis and psoriasis. Hence, early and proper recognition of the skin findings of dermatomyositis is crucial.

Advances in the management of dermatomyositis have improved the prognosis of the patients. Early recognition and aggressive treatment are important in decreasing the mortality and morbidity of this disease. This case illustrates an example of dermatomyositis initially presenting with skin manifestations only, followed by muscle weakness after 7 weeks. Early recognition and treatment resulted in a good patient outcome.

CASE REPORT

A 36-year-old Filipino female presented with a one-week history of erythematous patches and plaques on the glabella, periorbital and nasolabial area, arms, and thighs. One week later, the lesions became edematous and painful bruise-like lesions. The lesions were also seen on the V of the neck, upper back, proximal extremities and buttocks. There was no associated fever or weakness; no medication taken nor consultation sought. The review of systems and past medical history and family history were unremarkable.

Physical examination revealed multiple well-defined erythematous to violaceous, tender patches and edematous plaques on the eyelids, glabella, periorbital area, nasolabial area, upper chest, V of the neck, upper extremities (Figure 1), lower extremities (Figure 2) and buttocks. Working diagnosis was dermatomyositis. Differential diagnoses considered

were lupus erythematosus, contact dermatitis and photocontact dermatitis. She was given prednisone at a dose of 0.5mg/kg/day (30mg/day), loratadine 10mg/day, betamethasone dipropionate 2% lotion twice a day and sunscreen SPF 30.



Figure 1. Multiple, erythematous to violaceous patches and plaques on the eyelids, glabella, periorbital area, nasolabial area, upper chest, V of the neck and upper extremities on the first week of illness



Figure 2. Multiple, violaceous patches and plaques on the lower extremities during the 1st week of illness

Skin punch biopsy was done on the first day of consult and the result came out after two weeks. The biopsy finding was consistent with the diagnosis of dermatomyositis; compact hyperkeratosis, flattened epidermis, and vacuolar interface change with lymphocytes appearing within the dermis. There was superficial and deep perivascular and peri-adnexal infiltrate of lymphocytes, histiocytes, neutrophils, and melanophages with leukocytoclastic vasculitis. (Fig 3).

On the third week of illness, the lesions worsened despite the consistent use of advised medications. She had periorbital edema of both eyelids, edema and blisters on the extremities, fever, generalized weakness, easy fatigability, and muscle pains. Complete blood count, BUN, creatinine, and lipid profile were normal, while urine WBC and LDH were slightly increased. She was maintained on prednisone, loratadine, betamethasone dipropionate lotion and sunscreen.

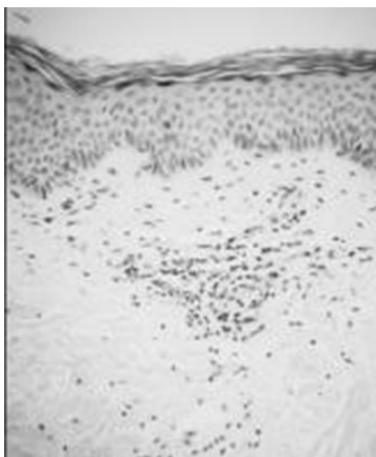


Figure 3. Photomicrograph of the skin punch biopsy specimen showed interface vacuolar dermatitis and leukocytoclastic vasculitis, consistent with dermatomyositis (hematoxylin-eosin stain, 10x)

On the fifth week of illness, 12-lead echocardiogram, kidney, urethra and bladder ultrasound, urine culture and sensitivity, SGPT, C3, ANA and anti-ds-DNA showed normal results. However, SGOT was elevated five times the the normal value. She was started on hydroxychloroquine 200mg twice a day and prednisone was increased to 50mg/day.

On the seventh week of illness, there were no new lesion, however she complained of difficulty in raising her arms and standing up from a sitting position. Her proximal muscles had fair contraction with the ability to overcome gravity, while her distal muscles had good contraction with ability to offer some resistance, and muscle strength tests were 3/5 and 4/5, respectively (Figure 4). During this time, she had multiple well-defined erythematous to violaceous, edematous plaques on the of the forehead, eyelids, malar area (Figure 5), V of the neck (Figure 6), trunk (Figure 7), buttocks, and upper and lower extremities (Figure 8), consistent with the characteristic distribution of dermatomyositis. Creatine kinase was elevated fifteen

times the normal value, further supporting the diagnosis of dermatomyositis. Over a span of 4 weeks, her skin symptoms and muscle weakness resolved leaving poikilodermatous skin changes with areas of atrophy. Hydroxychloroquine 200mg twice a day was continued while prednisone was tapered off at 10mg/week on the 11th week of illness. She was referred to other specialties and there were no signs of cardiac, respiratory, gastrointestinal, gynecological and ophthalmologic involvement.

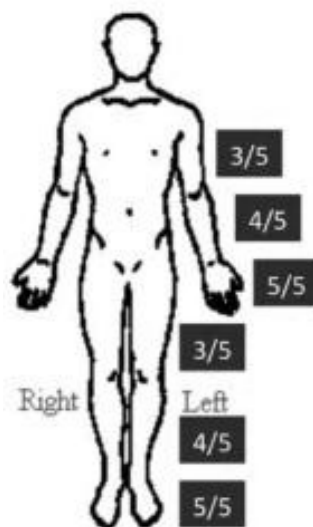


Figure 4. Muscle strength test showed proximal muscle weakness as compared to the distal muscle

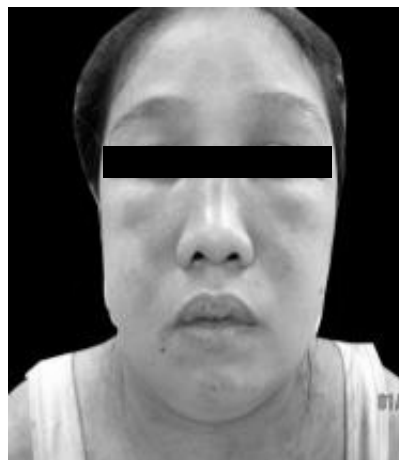


Figure 5. Heliotrope rash manifests as erythematous to violaceous edematous plaques on the eyelids. She also had multiple erythematous to violaceous plaques on the forehead, malar area and during the 7th week of illness



Figure 6. V-sign is seen as multiple, violaceous patches and plaques on the V of the neck and upper chest



Figure 7. Multiple, violaceous patches and plaques the upper back and shoulders define shawl sign, a characteristic finding in dermatomyositis.

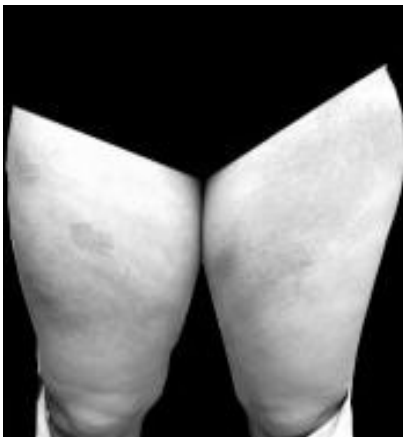


Figure 8. Holster sign manifests as violaceous patches and plaques on the lateral aspect of the hips and thighs.

Dermatomyositis is an idiopathic inflammatory myopathy that targets the skeletal musculature and the skin.²⁻⁴ The etiology remains uncertain. There is a biphasic age of distribution with an initial peak at age 5-14 years and second peak at 45 to 54 years old, and is twice more common in females.⁵ The prevalence rate ranges from 9.54 to 32.74 cases per 100,000 individuals.⁶ Based on the Philippine Dermatological Society Health Information System database, there were 90 new cases of DM among 398,455 new patients seen from 2011 to February 2017.⁷

The pathogenesis of dermatomyositis begins with exposure of genetically predisposed patients to ultra-violet light or a virus. This leads to the loss of tolerance to self-antigens that cause the specific clinical manifestations.¹ Myositis-specific autoantibodies are found in 50-70 percent of patients with dermatomyositis which likely cause the tissue destruction.³

Skin findings are the distinguishing clinical feature of dermatomyositis. The classic skin lesions are symmetric, confluent, macular, violaceous to erythematous patches and plaques. These are seen on the central aspect of the face, periorbital areas, forehead and scalp, V of the neck and upper chest, posterior shoulder, extensors of the fingers, hands, forearms, arms, deltoid areas, and lateral hips and thighs. Gottron's sign, a pathognomonic feature of dermatomyositis, presents as violaceous papules on the interphalangeal or metacarpophalangeal joints.¹ Since the skin lesions of dermatomyositis gradually appear and may not be highly suggestive of the disease from the beginning, a high index of suspicion is important in diagnosing and treating dermatomyositis. Our patient developed these skin lesions over 7 weeks before muscle weakness became evident.

Other common skin lesions include: excoriation with secondary infection and ulceration; sub-epidermal vesicles and bullae in areas of intense inflammation; post inflammatory hyperpigmentation; deep, irregular ulcers; and non-scarring alopecia.^{1,5}

Muscle weakness affecting the shoulders and hip girdle muscle present as difficulty raising the arms and standing up from a sitting position, respectively. In 60 percent of patients, cutaneous lesions and muscle weakness are present concomitantly, while in 10 percent, muscle weakness precedes the cutaneous findings.¹ In these groups of presentation, dermatomyositis can easily be diagnosed clinically. However, in 30 percent, cutaneous findings present without

muscle weakness initially. Muscle weakness only develops after weeks to months. In these cases, clinical diagnosis alone is more difficult and proper treatment may be delayed. Our patient initially had skin lesions alone.

In case of doubt, a skin biopsy is advisable. Characteristic histopathology of dermatomyositis shows hyperkeratosis, basement membrane degeneration, vacuolar alteration of basal keratinocytes, melanin incontinence dermal edema, and interstitial mucin deposition with sparse perivascular lymphocytic infiltrate, acanthosis and epidermal atrophy.⁵

Table 1. Classification Criteria for Polymyositis and Dermatomyositis⁸

Patients presenting with at least one finding from item 1 and four findings from items 2 through 9 are said to have dermatomyositis (sensitivity, 94.1% and specificity, 90.3%)
1. Skin lesions: heliotrope sign, Gottron's sign, or erythema on the extensor surface of extremity joints, slight raised red-purple erythema over elbows or knees
2. Proximal muscle weakness (upper or lower extremity and trunk)
3. Elevated serum creatine kinase or aldolase level
4. Muscle pain on grasping or spontaneous pain
5. Myogenic changes on electromyography
6. Positive anti-Jo-1 antibody test
7. Nondestructive arthritis or arthralgias
8. Systemic inflammatory signs (temperature > 37° C, elevated serum C-reactive protein level or accelerated erythrocyte sedimentation rate >20 mm/hr)
9. Pathologic findings compatible with inflammatory myositis

Our patient fulfilled the classification criteria for dermatomyositis by Tanimoto et al.⁸ She had 1 of the 3 skin lesions: heliotrope sign. She also had 4 findings from items 2 to 9: proximal muscle weakness from the 7th week of illness, elevated serum creatine kinase which was 15 times the normal value, spontaneous muscle pain and pathologic findings compatible with inflammatory myositis.

Organ systems can also be involved and present as weakness of the upper third of the esophagus, diffuse interstitial fibrosis (15-30 percent), non-erosive arthritis of the knees, wrists, elbows, and fingers (20-65 percent); and arrhythmia or conduction defect.¹

Non-invasive procedures such as magnetic resonance imaging and ultrasound are currently being utilized to localize affected muscles. More invasive procedures, such as muscle biopsy and electromyography, are performed in cases that are difficult to diagnose. However, practitioners defer invasive procedures in patients with no muscle symptoms due to sampling errors and low specificity in such patients.⁹

Since dermatomyositis involves internal organs, imaging studies including chest x-ray, CT scan, esophageal motility study, and electrocardiogram are also utilized. During treatment, it is important to monitor muscle enzymes, such as creatine kinase, aldolase, lactate dehydrogenase, SGOT and SGPT to monitor response to treatment.¹

Adult-onset dermatomyositis has been associated with increased risk of malignancy specially those who are older than 40 years old.¹⁰ In a study by Mebazaa et al., among 130 dermatomyositis cases, 20 were associated with cancer (15.38%); of which, breast cancer (35%) and nasopharyngeal cancer (25%) predominated.¹¹ In another study by Airio et al., they concluded that the patients with dermatomyositis had a 6.5-fold risk of malignancy like ovarian, stomach, non-melanoma skin, lung and male genital organ cancers.¹² Diagnosis can be made by physical examination, routine laboratory and radiologic examination while imaging techniques like CT scan and magnetic resonance imaging are not routinely done.¹ Since approximately 15% of adult dermatomyositis patient have either a pre-existing malignancy or will develop a malignancy in the future, they should be screened for malignancy and regularly monitored.¹⁰

In treating the patients, rapid aggressive treatment is indicated in early, active dermatomyositis. Delayed initiation of treatment will result in worsening of the patient's condition and a worse outcome. The mainstay for therapy of dermatomyositis is immunosuppression. Prednisone, the most widely used treatment, ranges from a dose of 0.5 to 1.5 mg/kg/day and is gradually tapered.⁵ Non-steroid agents such as hydroxychloroquine 400 mg/day, azathioprine 50mg/day, methotrexate 15mg/week, cyclosporine 3-4 mg/kg/day, cyclophosphamide 300-800 mg/m² IV every four weeks and human immunoglobulin 1 g/kg/day over two days can be used as an adjunct to oral steroids.¹³

In a study by Dalakas et al., 15 patients on prednisone 25 mg/day were randomly assigned to receive one infusion of immune globulin (IV Ig) 2mg/kg/day or placebo for three months. Eight patients on IV Ig had significant improvement in scores of muscle strength and neuromuscular symptoms, while seven patients on placebo did not improve. This suggests that high-dose IV Ig is a safe and effective adjuvant treatment for refractory dermatomyositis.¹⁴

Dinh et al., report three cases of dermatomyositis refractory to prednisone. The patients were given rituximab at 375 mg/m² weekly for four consecutive weeks. Lesions significantly improved eight weeks after the last dose of treatment.¹⁵

Long term effects of dermatomyositis vary from mild rash to life threatening muscle weakness or lung involvement.¹⁶ Morbidity and mortality of dermatomyositis are worsened by poor prognostic factors include the following: progressive disease, presence of malignancy, older age, delayed initiation of therapy, esophageal, cardiac and pulmonary involvement, and extensive cutaneous lesions on the trunk. The one-year survival rate ranges from 83-95 percent, while the 5-year survival ranges from 63-95 percent. Before the advent of corticosteroid treatment, survival rate was at 50%.¹⁷ Initiation of treatment is the only factor that the physicians can control, hence early recognition and treatment of dermatomyositis is imperative. Our patient was treated with prednisone starting on the first week of illness and hydroxychloroquine starting on the fifth week of illness. She has been regularly monitored for the past 3 years and she has not developed any signs of progression of the disease and systemic manifestations. The plan for the patient is regular biannual checkup for 2 more years then yearly to monitor for any progression of the disease and systemic involvement, internal medicine and obstetrics and gynecology checkups for any malignancy and ophthalmologic checkup for retinal toxicity secondary to hydroxychloroquine.

CONCLUSION

This case illustrates that even in the absence of muscle weakness, there should be a high index of suspicion for dermatomyositis specially in cases where confluent, erythematous patches and plaques present on typical areas of involvement such as the face, chest and the proximal extremities. A high index of suspicion with adequate work-up will pave the way for early diagnosis and, consequently, early treatment and a better patient prognosis.

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Trans-Sacral Epiduroscopic Laser Decompression (SELD) for Low back pain secondary to Herniated Lumbar Disc in the Philippines: A Case Report and Review of Literature

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ABSTRACT

LBP has a lifetime prevalence ranging from 54% to 80%, an annual prevalence of 15-45%, and a point prevalence of 30%. Lumbar radicular pain often results from a Lumbar disc herniation. With recent advances in technique and access in instrumentation, minimally invasive spine surgery has ushered in a renaissance of spine care. SELD has promising positive effects in controlling LBP following HLD.

This is a case of a 26 year old with radicular LBP of 2 years duration secondary to HLD, underwent conservative management of LBP but offered no relief and improvement, hence he became the case for the pioneering procedure of SELD in the Philippines. Immediate and significant improvement in the patient was noted. SELD was proven to be an effective therapeutic modality for patients with LBP secondary to HLD.

Keywords: *Herniated Lumbar Disc (HLD), Trans-Sacral Epiduroscopic Laser Decompression (SELD), Minimally Invasive Spine Surgery (MISS), Low back pain (LBP), Epiduroscopy*

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INTRODUCTION

Trans-sacral epiduroscopic laser decompression (SELD) is reported to have strong positive effects in controlling low back pain (LBP) or radicular pain following Herniated Lumbar Disc (HLD). This is one of the advances in practice of Minimally Invasive Spine Surgery (MISS), a less invasive surgical alternative to traditional open surgery.¹

The endoscope was first invented by Adolf Kussmaul in 1868.² In 2003, Ruetten used epiduroscopy to guide intervention in 93 participants with chronic back pain syndrome.³

Epiduroscopy, also known as epidural spinal endoscopy, requires the insertion of a fiberoptic endoscope into the epidural space through the sacral hiatus to treat a symptomatic herniated disc that has failed to respond to conservative treatment. In recent years, considerable progress has been made in the area of epiduroscopic diagnosis and treatment of spinal lesions using a laser as a less invasive surgical alternative to traditional open surgery for lumbar disc herniation. The remarkable mechanical and technical advances of these medical optical devices have allowed more detailed imaging during procedures, which allows surgeons to see things in new ways and leads to better and more successful results. Epiduroscopy accesses through the body's natural opening, namely the sacral hiatus, to permit direct visualization of lumbar epidural lesions and surrounding structures with minimal impact on patient's musculoskeletal structures, using a flexible catheter and epiduroscopy. This steerable flexible epiduroscopic laser system is used to confirm epidural pathologic findings, and provide precise and directed therapy at the same time.⁴

In this case report, we attempt to elucidate the mechanism and use of a minimally invasive procedure for the management of HLD specifically the SELD in the Philippine setting, to provide surgeons with ocular and MRI proof of the value of SELD as one of the effective treatment modalities for HLD, and understand the mechanism of pain relief in SELD (**Table 1**) and the indications and contraindications (**Table 2**).

Table 1. Mechanism of Pain Relief⁸

Decrease size of herniated lumbar disc
Fragmentectomy (neural Decompression)
Mechanical Adhesiolysis of epidural space
Burn away the Sinu-vertebral nerve, ingrowth nerve
Reduce the inflammatory mediators by irrigation

Table 2. Indications and Contraindications of SELD⁸

Indications	Contraindications
Lumbar disc herniation, up migrated and down migrated	Central Stenosis.
Annular tear Syndrome.	Foramina Stenosis
Adhesiolysis for postoperative syndrome	Calcified lesion
Discal Cyst	Extraforaminal HNP
Biopsy, Diagnosis	Instability, listhesis

Patient Information

Patient is a 26 year old Male, Filipino, Nurse from Legazpi, Albay, Philippines, came in the hospital with a complaint of low back pain of 2 years duration described to be 3-8/10 on Pain Score, limiting his movement and functionality at work, it was described to be sharp non radiating, localized at the lumbar area, noted upon prolonged sitting and standing, aggravated by flexing and lifting heavy objects, relieved by lying down. The low back pain was noted to be gradually progressing which prompted consult to a physician, radiographic xray of the lumbosacral area done revealed normal findings. Several months had passed with the persistence of symptoms, patient now notices paresthesias at the L4, L5 distribution on the R lower extremity. Rehab consult done, for which patient was advised regular session with PT for 3 months, 2-3x per week for upperback and core body exercises offered no relief of symptoms. Consult done at a Neurosurgeon, patient was advised to do an MRI which revealed Disc bulge, L3/L4 and L5/S1 with mild thecal sac indentation and mild bilateral neural foramina narrowing, patient was then scheduled to be the 1st patient for SELD procedure in the Philippines at UERMMCI. Upon General Survey, patient was awake, not in distress, ambulatory, with stable vital signs, Wt: 72 kg Ht: 167 cm BMI: 25 kg/m². Unremarkable General Physical Examination, motor strength of 5/5 all extremities with good bulk and tone, (+) sensory level at L4 and L5 right, for light touch and pin prick. Patient had intact joint, vibration and position sense both lower extremities. Upon examination of the spine, no gross anatomic deformity, no scoliosis, and no tenderness noted. However, pain was notable upon flexion, relieved by extension (+) SLR R DRE: good sphincter tone, (+) bulbocavernosus reflex. Lumbosacral radiograph revealed: Intact Disc Spaces, straightening of the lumbar lordosis (Figure 1 A,B), Lumbosacral MRI revealed: Disc bulge, L3/L4 and L5/

S1 with mild thecal sac indentation and mild bilateral neural foramina narrowing. An Oswestry Low Back Pain Disability Questionnaire was used to evaluate low back pain, with an ODI of 21 categorized as Moderate disability.



Figure 1. A. AP view, intact disc spaces (arrow); B. Lateral View, straightening of the lumbar lordosis C. T1W Disc Bulge L3/L4 and L5/S1 (Arrow) with mild thecal sac indentation and mild bilateral neural foramina narrowing, Lumbar lordosis is maintained. No spondylolisthesis observed. There is no loss of vertebral body and intervertebral disc height, no facet joint nor ligamentum flavum hypertrophy. The rest of the visualized soft tissues are unremarkable. D. T2W Disc Bulge L3/L4 and L5/S1 (Arrow)

Inclusion and Exclusion Criteria.¹⁰

Inclusion Criteria

1. Contained disc herniation, or discal or synovial cyst demonstrated on MRI or CT
2. Neurological findings referring to a single nerve root, leg pain of greater intensity than back pain, and a positive straight-leg-raising test
3. No improvement after 2 weeks of conservative treatment

Exclusion Criteria

Hemorrhagic diathesis
Infection
Spondylolisthesis
Spinal stenosis
Previous surgery at the indicated disc level
Significant psychological disorder
Significant narrowing of the disc space Pathologic findings at the sacrum epidural space

Patient Selection

Preoperative multidisciplinary measures were done including radiographic, clinical, as well as basic laboratory results. A precise medical history and the correlation of symptoms with MRI findings were done. The patient was provided with an informed consent explaining the procedure and its probable risks and complications. Preoperative evaluation was done by the anesthesia service.

The patient was selected based on the inclusion criteria mentioned above, low back pain and radicular pain of the lower extremities caused by HLD proven by MRI, with refractory pain even after medical and physical therapy for > 2 weeks, a contained disc herniation demonstrated on MRI.

Staff and Manpower

Procedure was headed by a trained MISS surgeon specifically for SELD procedure, assisted by a trained SELD nurse from Korea, second assist was a Neurosurgery resident, 2 newly trained nurses assisted in preparing the laser and tower, Anesthesiologist for IV sedation and intraoperative anesthesia care, and a Radiology technician manning the C ARM.

Materials and Equipment

The procedure was performed using the Ho:YAG laser (Sphinx Laser Machine), the laser has a 550 nm wavelength, and 0.4 mm depth of penetration. To deliver the laser and a 15-K pixel flexible fiberoptic scope with a 1.2 mm diameter to the epidural space, a video guided catheter (VGC) with a 3.0mm outer diameter (3mm Video Guided Catheter) was used. It has a radiopaque shaft with 1.3mm dual working channels and dual infusion ports for infusing saline for irrigation. The epiduroscopic equipment consisted of an epidural endoscope, a video camera system, and a video monitor.

Procedure

The procedure was performed with the patient under local anesthesia, utilizing lidocaine with epinephrine over the sacral hiatus, and the patient was monitored by an anesthesiologist. The patient was placed in the prone position on a radiolucent operating table (Figure 2.A). All the time the patient was awake, allowing a free conversation with the anesthesiologist and surgeon throughout the procedure.

A 5 mm skin incision was made over the sacral hiatus using a #11 blade. The sacrococcygeal ligament was punctured with a Tuohy needle under fluoroscopic guidance followed by a guide wire and dilator, and the Myelotec spinal introduction system was inserted into the sacrococcygeal ventral epidural space. Subsequently, a 3.0mm steerable VGC was introduced (Figure 2.D). A C-arm fluoroscope was used to provide images in both the anterior/posterior and lateral views to verify the position of the catheter in the ventral epidural space (Figure 2.B,C)

Through the, epiduroscope and the Ho:YAG laser were advanced into the end of the catheter to visualize the epidural space and perform HNP ablation. After introducing the VGC, fluoroscopy and epiduroscopy were used to confirm that the tip of the catheter was located at the most inferior part of the targeted disc, covering the PLL.

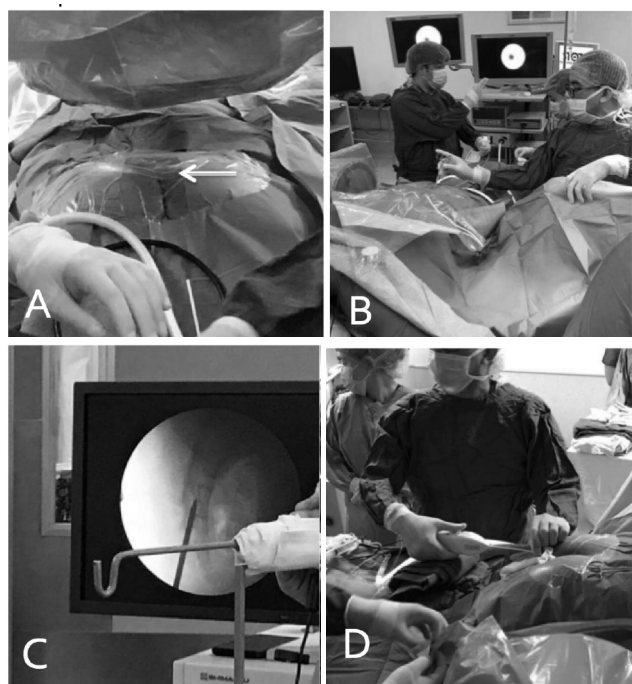


Figure 2: A. Prone Position, with Sacral Hiatus entry point (Arrow) B. Localization with C ARM guidance C. C ARM trocar insertion, D. 3.0mm steerable VGC was introduced

Under direct vision with epiduroscopy, adhesiolysis and morcellation technique was used to by the Ho:YAG laser (Figure 3. A,B,C). After the surgeon was able to sufficiently decompress the ruptured disc using the laser. The floating and sequestered HNP was removed using 1mm forceps. The ruptured discs were decompressed until the epiduroscopic images confirmed nerve root decompression, the epidural space between the dura and bulging PLL with an underlying HNP became wider. The wound was closed by one-point skin suture. The suture was removed 1 week after SELD.

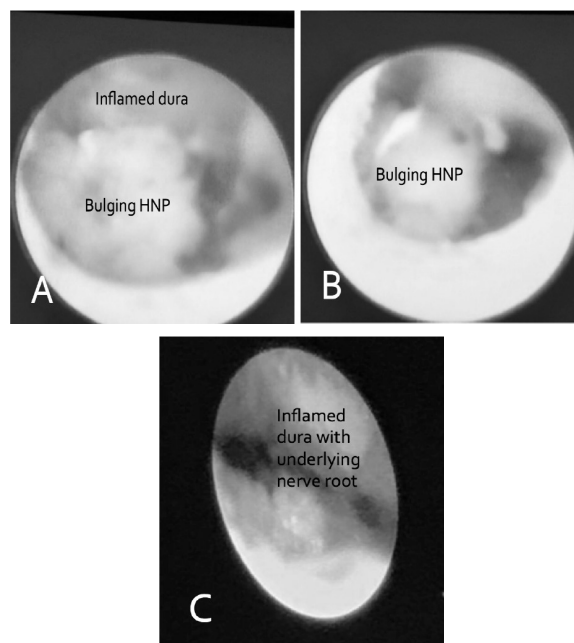


Figure 3 A. Initial epiduroscopic view (white) bulging HNP, (red) inflamed dura with nerve root B. Midpoint during Laser Application C. Exposure of Inflamed root

Follow up and Outcome

Immediately post op, from preoperative SLR at 250 noting significant improvement in SLR >600 post operatively (Figure 4. A,B). On the first post-operative day without any pain medications taken, the patient noted relief of back pain, patient was able to ambulate without assistance, able to flex his hips without any pain. With an ODI score of 10, and an Excellent score for MacNab, denoting no pain and restriction to activity. Post-operative site was dry, with no signs of hematoma or CSF leak. Repeat MRI done on the first postoperative day revealed decompression of the spinal canal at the level of L3/L4, L5/S1. Subsequent follow up done at 2 months and 6 months noted no recurrence of back pain or any radicular pain.

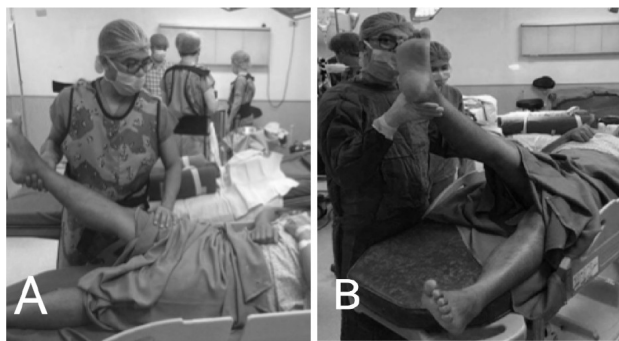


Figure 4: A. Preop SLR at 25 degrees B. Postop SLR no pain >60 degrees raised

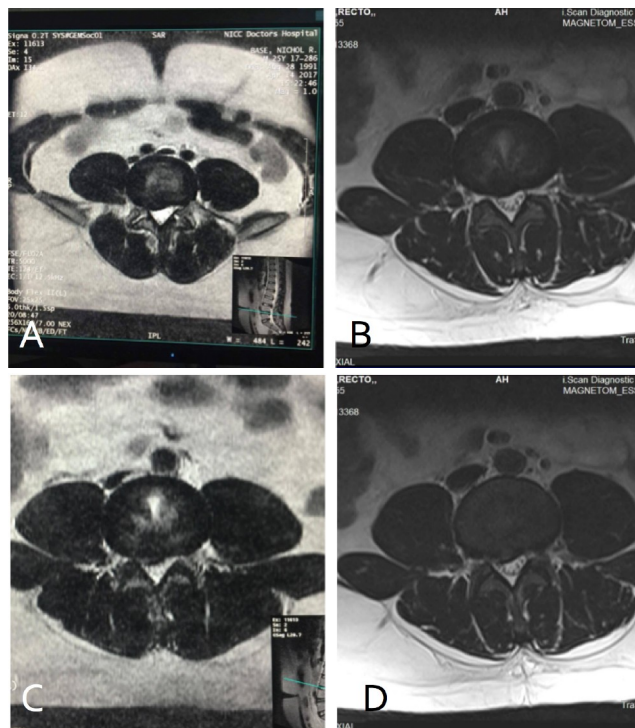


Figure 5: A. Preop MRI L3/L4 disc level B. Postop MRI MRI L3/L4 disc level C. Preop MRI L5/S1 disc level D. Post op MRI L5/S1 disc level

Discussion

With recent advances in technique and access instrumentation, minimally invasive spine surgery has ushered in a renaissance in spine care. As more patients receive minimally invasive spine surgery treatments, stronger long-term outcome data are supporting this change in practice pattern.⁵

Patient outcomes are improved compared with traditional open surgery and cost are reduced, partly due to reduced hospital stays and recovery times. Approach-related morbidity is significantly reduced because normal anatomical structures are preserved

to a greater extent, reducing the incidence of delayed progressive deformity and degenerative changes. Minimally invasive surgical procedures of the spine can be just as efficacious as traditional open procedures with respect to the operative pathology. Unnecessary approach dissection and ligamentous and muscular disruption are minimized, potentially leading to a reduced incidence of repeated operations and scar formation.⁶

The epiduroscopic laser method also showed that lumbar disc decompression resulted in well-controlled pain and improved quality of life during the follow-up period after the procedure in a previous study that included eight centers.⁷

The advantages of SELD are as follows: A good view of Anatomical structures before removal of disc fragment, these includes the nerve root, disc, dura, adhesions and inflammation; for small amount of disc to be removed, there is a lower rate of subsidence; there are no additional, unnecessary annulus injury or nucleus pulposus injury leading to a lower rate of recurrence; the procedure can also be used as a multi level diagnostic and therapeutic modality; and lastly it can be used to identify adhesion and at the same time ablate of sinuvertebral nerves.⁸

In the study of Jung-Woo Hur et al, Reports the preliminary clinical and radiologic results of SELD for the treatment of LDH in a single center experience. There were twenty-one patients who underwent SELD for the treatment of single-level LDH were retrospectively evaluated for minimal 12-month follow-up. Outcome measures used were visual analog scale (VAS) scores for back and leg pain and functional status was measured with Oswestry disability index (ODI). Radiologic outcome were evaluated by comparing the changes of disc size on MRI scans, preoperatively, postoperatively and at final follow-up. They have found out that there significant improvements of VAS score and ODI after SELD for LDH with back and leg pain at minimal 12 months of follow-up. Postoperative MRI scans revealed significant decrement of the disc size and reduction of neural compression.⁹

In the Prospective case series of Sung Ho Lee et al, which intends to determine the outcomes of SELD with regard to reducing pain and improving the functional status in patients with LBP and radiculopathy caused by definitive neural compression confirmed by MRI. A total of 250 patients with LBP and simultaneous radiculopathy underwent SELD by applying a

Ho:YAG laser. Clinical outcomes were evaluated using the VAS score for LBP, and radiculopathy and functional status were measured using the ODI. Patients showed good clinical outcomes in the early period and at 3 months after the procedures, and there were no significant complications affecting the clinical outcomes, such as nerve damage caused by thermal injury, infection, or post-operative hematoma. They have concluded that the VAS score and ODI significantly improved after SELD in HNP patients with LBP and radiculopathy. Postoperative MRI showed a notable decrease in the HNP size and a reduction in neural compression. SELD is suggested to be an effective therapeutic modality for patients with symptomatic HNP.¹⁰

Epiduroscopy permits direct visualization of the epidural space with minimal impact on patients' musculoskeletal structures. The higher the resolution of the epiduroscope, the better the visualization of anatomical structures in the narrow epidural space and closer the monitoring of the laser, which enables securing the safety of the nerve root.¹⁰

The goal of the approach is to go to the ventral epidural space simply because you will find most of the pathology in the degenerative spine. The presence of the meningo vertebral ligaments will be an obstacle in navigating the spinal epidural space.⁸

Morcellation is a surgical method used for division and removal of large masses of tissues during epiduroscopic surgery. In Epiduroscopic fragmentectomy the fragment is minced up, or morcellated, into smaller pieces inside the fragment space in order to extract from the epidural space.⁸

The concept of SELD is based on the sacral hiatus introduction of epiduroscopy and the insertion of a fiberoptic laser system into the ventral lesion of the epidural disc space. This procedure enables the vaporization of discs in the herniated part, cauterization of the sinuvertebral nerve, lysis of adhesion nearby the nerve root, and irrigation of inflammation. Laser decompression of HNP was limited between the PLL and posterior annulus to avoid doing more damage to posterior annulus. A damaged posterior annulus is prone to cause herniation of the nucleus to recur. Laser application is performed with an optic fiber that is placed directly into the herniated disc, which generates heat, reduces the water content of the disc, and changes the protein structure of the disc, permanently decreasing its ability to absorb water. Slow and continuous irrigation with cool saline allowed visualization of the anatomical structures by preventing distension of the epidural space, and thermal damage

to the nerves was significantly reduced by using the Ho:YAG laser and irrigating bleeding during the procedure. The most important aim of the endoscopic procedure is to avoid bleeding. We confirmed the anatomical structures by endoscope and avoided the blood vessels, especially arteries. However, during the laser decompression, venous bleeding occurred sometimes. If there was bleeding during the procedure, we secured the endoscopic view by continuous cool saline irrigation. After the procedure, expansion of thecal sac and other structures compressed bleeding points.¹⁰

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“While finding where the water leaks, you find smoke” - A Case Report: Incidental finding of Moyamoya for a Filipino worked up for Subarachnoid Hemorrhage

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ABSTRACT

Moyamoya Disease was initially reported in 1957 as vessels resembling a puff of smoke, alongside hypoplasia of bilateral internal carotids. The true incidence remains elusive. Genetic studies point to familial occurrence of the disease, however some studies refute this, claiming that environmental factors are to blame. The treatment strategies remain an enigma, more so in our country where data is scarce. We present a case of an asymptomatic Moyamoya disease incidentally diagnosed in the work - up of Subarachnoid Hemorrhage. The basis of the management is being provided.

Keywords: Moyamoya disease, intracranial aneurysm, headache

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INTRODUCTION

Moyamoya is a Japanese word meaning puffy, obscure, or hazy like a puff of smoke in the air. Thus, the term was used to describe the smoky angiographic appearance of the vascular collateral network.¹

It has been used to refer to an extensive basal cerebral rete mirabile (a network of small anastomotic vessels at the base of the brain, around and distal to the circle of Willis, associated with segmental stenosis of both internal carotid arteries. This form of cerebrovascular disease is predominant but not limited to the Japanese². Originally considered to affect predominantly persons of Asian heritage, but now observed around the world in people of many ethnic background^{3,4}.

We treated a patient who presented with Subarachnoid hemorrhage with incidental Moyamoya disease, and was discharged in good functional status.

Case Presentation

A 39 year old female, right handed, with a degree in education, currently working as an online tutor.

Seven hours prior to admission, while watching a movie alone, the patient suddenly felt pulsating headache, that initially started on both frontal area, radiating to the back and to the nape. This was rated to be 10/10, and described to be the worst headache of her life. She tried to contain the pain for approximately 30 minutes because she was into the movie, until she could no longer tolerate, she went to the bathroom to void, thinking that voiding would help ease the pain. To her dismay, the pain persisted, she went back to her seat. The person seated 2 seats away noticed her agonizing in pain, and offered to bring her to the clinic.

She was then brought to the mall clinic, where her blood pressure was noted to be 150/100, she was given clonidine 75 mcg sublingually, and was allowed to rest in the clinic. While she was resting, she felt nauseated, and vomited previously ingested food, approximating 200 cc. Due to the persistence of the pain, she was advised ER consult.

She was brought to a nearby emergency room (3 hours PTA). On the assessment of the ER physician, the patient was advised admission, however she opted to transfer to our institution.

The patient has no known co morbidities, the family history reveals both her parents are of pure Filipino origin. Her mother has hypertension, while her father has type 2 diabetes mellitus, and neither has suffered a stroke. The nearest relative who suffered a stroke is a paternal uncle who had a stroke in his 60s. Social history includes an eight pack per year smoking history, consuming 8-10 sticks per day for the past 17 years, and an occasional alcoholic beverage drinker, consuming one to two glasses of wine a week.

The physical exam reveals an awake lady, not in acute cardiorespiratory distress, with regular respirations, and spontaneous movements of all extremities. Vital Signs: blood pressure: 110/80, heart rate: 62 beats per minute, respiratory rate: 18, temperature 37.1 degrees Celsius and saturating 97% at room air. The rest of her physical examination, as well as her neurologic examination were all normal, except a nuchal catch.

At the emergency room, neuroimaging with a CAT scan was done, and revealed a subarachnoid hemorrhage. The patient was then referred to interventional radiology for conventional four vessel angiogram, and possible coiling. Neurosurgery service was also informed for possible clipping of the aneurysm. The angiogram revealed an A1 secular aneurysm measuring 3.54 mm x 2.73 mm and a neck of 1.95 mm with a teat-like extension note at its fundus denoting recent site of rupture. An ACOM saccular aneurysm measuring 3.26 mm x 2.12 mm with a 2.31 mm neck. There was a severe narrowing noted at the take off site of the proximal M1 segment of the left middle cerebral artery. This is fair but slightly restricted ante-grade flow into the more distal branches of the left middle cerebral artery. There are multiple ill defined vessels around the distal supraclinoid segment of the left internal carotid artery and around the stenotic area in the proximal left middle cerebral artery they represent Moyamoya vessels.

The A1 aneurysm was coiled using GDC 10 360 4 mm x 8 cm and GDC 10 360 3mm x 6 cm, which showed complete occlusion of the lumen of the aneurysms on check angiograms. In consultation with the family of the patient, a decision to clip the ACOM aneurysm, was made. The question then was whether a by-pass procedure will be done.

Discussion

First described in 1957 as "hypoplasia of the bilateral internal carotid arteries,"⁵ Moyamoya disease is thought to be an abnormal proliferation of thalamo-perforating vessels occurring in the Japanese population. It was later learned that the associated network of abnormally dilated collateral vessels on angiography was later likened to "something hazy, like a puff of cigarette smoke," which is, in Japanese, Moyamoya.⁶

The disease was originally considered to affect predominantly persons of Asian heritage but is now observed around the world in people of many ethnic backgrounds, with ⁷ an incidence of 0.086 case per 100,000 persons. The incidence ratio in the United States is: 4.6 Asian Americans, 2.2 Blacks, and 0.5 for Hispanics⁸. In the East Asian area, the incidence is 3.16 - 10.5 per 100,000⁹ with a bimodal presentation: children (5 years old), and adults (mid 40s) presentation; and a sexual predilection: twice as many female to male ^{10,11}

The most common presentations are typically localized to the regions of the brain supplied by the internal carotid arteries and middle cerebral arteries: frontal, parietal and temporal lobes. Others may present as seizures, visual deficits, syncope, or personality changes that can be mistaken for psychiatric illness ¹². It is common in adult patients with Moyamoya disease to present with a hemorrhagic stroke with the location of hemorrhages in descending order: intraventricular, intraparenchymal, subarachnoid¹³. Less common presentations would be headache, or choreiform movements.

Stenosis occurs in the distal internal carotid artery and often involves the proximal anterior and middle cerebral arteries. Pathologic analysis has revealed that affected vessels do not show arteriosclerotic or inflammatory changes leading to occlusion. Rather vessel occlusion results from a combination of hyperplasia of smooth muscle cells and luminal thrombosis. The media is often attenuated, with irregular elastic lamina. Caspase dependent apoptosis has been implicated as a contrictrubitory mechanism, the associated degradation of the arterial wall¹⁴

Genetic factors appear to play a major role in Moyamoya. The proportion of patients who have affected first degree relatives is 10% in Japan and 6% in the United States. Associations with loci on chromosomes 3, 6, 8 and 17, as well as specific HLA

haplotypes have been described^{15,16}. Literature search reveals that these haplotypes have been conducted only in East Asian population, and in series, no Filipino patient was included.

Familial cases appear to be polygenic or inherited in an autosomal dominant fashion with incomplete penetrance.¹⁷ Ringfinger 213 (RNF 213) gene in the 17q25-ter region was identified as the strongest susceptibility gene for MMD in East Asian People but not for South Asians¹⁸. p.R4810K variant was identified in 95% of patients with familial MMD, 80% in sporadic MMD, and 1.8% in control subjects¹⁹. The p.R4810L RNF213 variant is related to the ischemic type of MMD, while the non p.R4810L RNF213 variants particularly A4399T, were associated with the hemorrhagic type of Moyamoya disease²⁰. Securing decreasing normal Identical twin with only one affected sibling would point to environmental factors²¹, contesting the genetic theory.

Smooth muscle progenitor cells collected from the peripheral blood of patients with MMD showed that the SPC in MMD group tended to make more irregularly arranged and thickened tubules, as well as express differential genes compared to that of the healthy controls. Endothelial progenitor cells (EPCs) originate from the bone marrow and help maintain the vasculature and blood flow in infarcted areas²². EPC potentially contribute to the neovascularization at the ischemic brain injury site in patients with MMD²³. However, the EPCs were noted to have defective angiogenic functions in MMD. Aberrant angiogenesis was an active angiogenetic process that may cause both stenosis through the proliferation of endothelial and or smooth muscle cells and abnormal collateral formation²⁴.

The natural history of Moyamoya disease is variable. Disease progression can be slow with rare, intermittent events or fulminant, with rapid neurologic decline^{25,26}. However, regardless of the course, Moyamoya progresses in the majority of patients. A 2005 report indicated that the rate of disease progression is high even among asymptomatic patients, and that medical therapy alone does not halt disease progression²⁷. It has been estimated that up to two thirds of patients with Moyamoya have symptomatic progression over a 5 year period.

Asymptomatic adult Moyamoya disease is not a permanent disease. In particular, reduced cerebrovascular reserve capacity is an indication of Moyamoya disease progression²⁸.

The outcome is poor without treatment. In contrast the estimated rate of symptomatic progression is only 2.6% after surgery, according to a meta analysis involving 1156 patients²⁹. In general, neurologic status at the time of treatment more than the patient's age predicts long term outcome. Thus early diagnosis of Moyamoya coupled with expeditious institution of therapy is of paramount importance.

The diagnosis of Moyamoya was first established in Japan, the most recent revision of this first diagnostic criteria is contained in the Research Committee on the Pathology and Treatment of Spontaneous Occlusion of the Circle of Willis; Health Labour Sciences Research Grant for Research on Measures for Intractable Diseases: Guidelines for diagnosis and treatment of Moyamoya disease. This was published in 2012. The diagnosis of Moyamoya disease required the bilaterality of the vessels.

In 2016, the Korean Stroke Society published a new guideline³⁰. The diagnostic criteria for definitive MMD were revised to include patients with unilateral terminal ICA steno - occlusion. Definitive diagnosis of MMD requires catheter angiography in unilateral cases, while bilateral cases can be promptly diagnosed by either catheter or MRA.

Asymptomatic Moyamoya disease is defined as Moyamoya vessels without neurological deficit and ischemic or hemorrhagic episodes³¹

In patients where surgery appears to present a high risk or when patient has mild disease, medical management is employed. Approximately 38% of medically managed patients underwent surgery for worsening symptoms³² In patients that present Anti platelet agents have been used to prevent emboli from micro thrombi at sites of arterial stenosis, anticoagulants are rarely used. Calcium Channel blockers may be useful in ameliorating intractable headaches or migraines³³

Surgical therapies uses the external carotid artery as a source of new blood flow.

Direct: a *branch of the external carotid artery* (superficial temporal artery) is directly anastomosed to a cortical artery.

Indirect: placement of *vascularized tissue* supplied by the external carotid artery in direct contact with the brain

The bypass procedure does not come without complication, with post operative stroke with permanent neurologic deficits occurring in 1.6-16%. Hemodynamic status of patient is the most important factor, the other two being advanced Suzuki stage and lower cerebral blood flow³⁴.

The rate of asymptomatic Moyamoya disease developing ischemic stroke is 0.8%, while 2.5% would develop a hemorrhagic stroke³⁵.

The impracticality to screen the general population for asymptomatic Moyamoya disease as well as for asymptomatic intracranial aneurysms robs us of the information of the actual prevalence of these conditions, much more leaves us at an enigma of the incidence of these two diseases occurring concurrently in a patient.

This case report aims to contribute data into this void of information.

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Bilateral Pallidal Stimulation in Parkinsonism Predominant XDP *

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ABSTRACT

X linked Dystonia Parkinsonism (XDP) is a progressive movement disorder among male inhabitants of the island of Panay in the Philippinesⁱ, it would start as a focal dystonia then become generalised. The disease is believed to be due to a founder mutation of some 50 meiotic generations agoⁱⁱ. Although initially seen in male population, current data shows otherwise. Reports of about 11 female cases are detected and listed in the registry. Male more than female predilection is seen with a ratio of 75:1ⁱⁱⁱ. XDP is a very disabling degenerative disease causing involuntary torsion of the body, torticollis, blepharospasm and eventually parkinsonian features^{iv}. There is no known treatment, and alleviation of symptoms is difficult to achieve, some patients even die due to infection and self harm. This report will present a case of XDP with predominating parkinsonian feature, who has undergone bilateral Globus Pallidus Interna(GPi) Deep brain Stimulation (DBS). After the operation, return to functionality and improvements in activities in daily living is seen. The UPDRS and FMDRS scores show improvement noted on regular follow up. However adverse effects such as slurring of speech and minimal blepharospasm are still observed.

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INTRODUCTION

X-linked Dystonia Parkinsonism (XDP) is a progressive movement disorder, manifesting predominantly with dystonia in combination with parkinsonism^v. It is seen predominantly on male population, however recent data shows that female gender can also be affected. Focal dystonia is the most common initial presentation at 93.4% while Parkinsonism are seen in only 5.7%^{vi}. The latest XDP Philippine registry demographic data shows a total of 838 individuals with XDP, 827 are males and 11 are females (Philippine XPD Registry 2016) with a ratio of 75.2:1. Challenges in treatment currently faces this disease condition, medications such as Levodopa/Carbidopa, Benzodiazepines, anticholinergic agents and antipsychotics fail to show adequate improvement. One drug that shows benefit is Zolpidem however no clinical trials are yet available. Another strategy for the treatment is the use of Botulinum Toxin type A injection, although this is only limited to focal, multifocal and multisegmental dystonia and the effects would last temporarily and would require frequent injections^{vii}. Surgery is the new trend in the management of movement disorders. Deep Brain stimulation (DBS) is being done in Parkinson's Disease and other forms of dystonia, which targets the Subthalamic nuclei and Bilateral Globus Pallidus interna (GPi). The results of these surgeries were impressive. Nonetheless, GPi is the target of choice between the two nuclei due to its proven effectiveness in off dysonias and dyskinesias in Parkinson's disease^{viii}. To my knowledge there are five XDP patients who have undergone bilateral GPi DBS from 2009 - 2015 at the Philippine Movement Disorder Surgery Center. All of them have positive outcome and minimal adverse effects like wound dehiscence in IPG site. A continuous success in controlling Dystonia and Parkinsonism noted on 3 cases at 3 years follow up. This is the 2nd case done in 2016 at Philippine Movement Disorder Surgery Center.

Case Presentation:

The patient is a 34 year old Right handed Teacher from Ibajay Aklan an Island in Panay, Philippines. His maternal roots are from that island and has relatives with the same condition. His initial symptoms started as tremors on the right hand which eventually progressed which involved his left hand. He has a tendency to drop hand held objects and is observed both when resting and when in use.

6 months after the onset of his symptoms, the patient developed abdominal muscle spasm and involuntary contractions of the abdominal muscles, lasting for approximately 10 seconds that would spontaneously resolve and would recur infrequently. His posture was now noted to be stoop with difficulty ambulating. Slowness on movement was also noted at this time. Consult was made and Biperiden 2mg/tab three times a day and Clonazepam 2mg/tab three times a day are started. Despite the medications no relief of symptoms were noted. Progression of abdominal muscle contraction and length as well as bowing of posture was observed. Botulinum Toxin A (BOTOX) therapy was injected to the abdominal muscles provided temporary relief lasting for 3 months, he had 7 sessions of Botox.

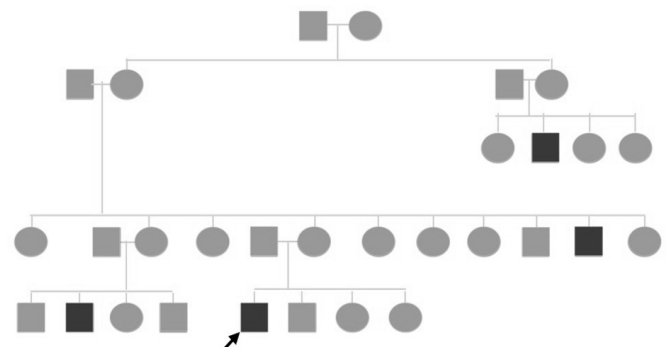
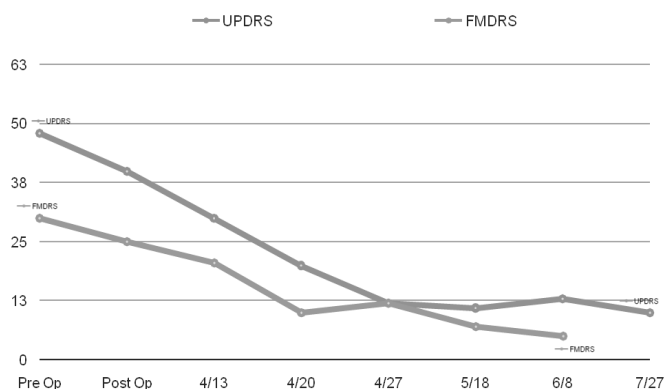


Figure 1: Pedigree of the patient

4 months prior to operation the patient experienced bilateral lower extremity weakness which lead him to require assistance in performing daily activities of living. Slurring of speech was noted thus he resigned as a teacher and became bed bound. He was referred to a neurologist in Cardinal Santos Medical Center for DBS.

The patient would fit to the criteria for a "probable" diagnosis of XDP by the Philippine XDP study group because this patient has a cousin, maternal uncle, and Grandfather with a history of Dystonia. Molecular genetic testing however was not done on this patient.

The pre operative Unified Parkinson's disease rating scale (UPDRS) part III is 48 (out of 108) and the initial Fahn-Mardsen dystonia rating scale (FMDRS) score is 30 (out of 120). The patient underwent Bilateral Pallidal (GPi) DBS last March 2016. Immediately post operatively the UPDRS score and FMDRS score are both recorded and showed great improvement. No immediate post operative complication is observed and he is discharged after 4 days.

Figure 2: UPDRS and FMDRS scores

2 days post operatively, the UPDRS score is 30 and FMDRS score is 20.5, noting marked improvement again. The bowed posture is improved, his gait is now stable and can walk without support, however dysarthria is still noted. Medications are adjusted, Biperiden is decreased to 2mg/tab, 1/2 tab twice a day and Clonazepam 2mg/tab 1/2 tab three times a day. During this time the IPG is activated. Stimulation set up is: amplitude: 2.0 V, pulse width: 60 us, frequency: 160 Hz in both Left and Right GPi. Patient regularly comes back for follow up.

At 1st month follow up, the patient has 70% improvement on his movements, the UPDRS score and FMDRS score further improves, 18 and 10 respectively. The Stimulation setting is adjusted to amplitude: 2.3 V, the pulse width and frequency are both maintained.

On the 6th month, the posture is more straight, no blepharospasm is noted and speech is improved. Biperiden is discontinued. Further adjustment of stimulus setting is done. At the time of writing he is down to Clonazepam 2mg/tab, 1/4 tab three times a day and stimulation setting of amplitude: 3.0 V, pulse width: 60 us, frequency: 130 Hz in both Left and Right GPi.

Discussion

This is a case of X-linked dystonia parkinsonism that started with Parkinsonian features when the patient is on his 28th years of age. Lee et al (2011) have reported that approximately 5.7% cases present initially with parkinsonian traits, whilst majority 93.4% initially presents with focal dystonia. In the XDP registry update of 2016, the mean age of onset is 43.7 years old, with a range of 23-67 years old, this covers

the age of productivity. In our case, the disease has progressively worsen and developed into generalised type. So as with other cases of XDP, medications and BOTOX fails to control symptoms of both dystonia and parkinsonism. The patient can be classified as a stage IV in the proposed simplified staging go XDP. However this staging is still undergoing local validation.

Surgical management for movement disorders like dystonia in the Philippines has its roots in 1960 where the first documented bilateral chemopallidotomy is done on two XDP cases. However the results are not impressive, these patients experienced left hemiparesis and speech impairment post operatively, and do not note improvement on the XDP. Multiple class 1 studies of DBS on XDP shows promising results, one study shows 1 year mean improvement of FMDRS movement score of 51%. Another study by Kusch et al., (2006) shows 39% improvement in the severity of dystonia and 38% improvement in disability.

After DBS, our patient improved drastically and in a very short time frame. The initial improvement of UPDRS and FMDRS scores post operatively can be attributed to perilesional effects. We can expect that worsening of movement problems and scores (UPDRS and FMDRS) can be seen prior to the activation of the stimulator. The Stimulation of GPi in this patient improved truncal, appendicular dystonia and focal oral dystonia. It also improves the parkinsonian symptoms like stoop posturing, tremors on the hands and bradykinesia. The possible explanation on the response in this patient is because he is a predominantly parkinsonian type.

Comparing our patient with the 5 XDP patients treated with bilateral pallidal DBS from 2009-2015, all of these 5 patients initially present with focal dystonia and then progressed to generalized before surgery^{xii}; but in our patient, the initial feature is parkinsonian then progressed to generalized dystonia. Despite the differences in presentation, there is a note of similarity of results. Seen immediately post operatively the FMDRS scores dramatically fell and would plateau at that point for 6 months. Unfortunately we cannot compare more than 6 months after since our data are still limited. The 1 year follow up of FMDRS scores of the 5 patients has a mean improvement of 66.7% (Range 24.4% to 83.3%)^{xiii}. In our case, the improvement of UPDRS score is 79% and the improvement of 83% in FMDRS score is already seen in 6 months time.

DBS is a safe procedure and a very effective treatment option for XDP. As evidenced by this case, the patient is able to tolerate the procedure well and no peri-operative surgical complications are noted. The intellectual capacity, mood of the patient is maintained and the motor function has improved.

There are several target locations in the Basal ganglia where DBS can be applied, one is the subthalamic nuclei and the GPi. In this case the target nuclei is the GPi, based on a class 1 clinical trial and large blinded studies. It has been found that DBS of GPi is effective for primary generalised as well as segmental dystonia^{xvi}. In a study by Kupsch et al, a 39% improvement in dystonia severity, 38% improvement in disability, and 30% improvement in quality of life at 3 months are seen^{xv}. Thus this case strengthens the evidence in supporting the use of bilateral GPi DBS in patients with XDP. Again comparing our patient with the 5 XDP patients treated with bilateral pallidal DBS from 2009-2015^{xvi}, the stimulation parameters are amplitude of 1.7-4.7 V, pulse width of 60-90 us and frequency of 130 - 160 Hz. While the stimulation setting in our case ranged between amplitude: 2.0 - 3.0 V, pulse width: 60 us, frequency: 130 - 160s Hz in both Left and Right GPi.

The oral medications are tapered off eventually from 2 drug regimen now down to a low dose Clonazepam. The tapering off of this medications strengthens the claim that GPi stimulation in XDP is an effective procedure and a very good alternative to treatment of XDP.

Aside from the scores, the patients nutritional status improved, he is gaining weight and is able to swallow food without dysphagia. However the patient is noted to have slurring of speech or dysarthria. Dysarthria is the most common adverse event of Bilateral Pallidal DBS^{xvii}.

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Keratoacanthoma on an Epidermal Nevus in a Filipino Male

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ABSTRACT

Keratoacanthoma is a cutaneous tumor that most often presents as a solitary lesion in middle-aged to elderly, light-skinned individuals on sun-exposed areas. It is characterized by rapid growth and may be followed by spontaneous involution. This is a case of a seventy-year-old Filipino male who had a one month history of a solitary nodule that suddenly appeared on an epidermal nevus. Histopathologic diagnosis revealed a keratoacanthoma.

INTRODUCTION

Epidermal nevus is a benign epithelial tumor that presents sporadically at birth, or may have an onset in infancy or childhood and may grow or extend in size until puberty. The incidence has been reported to range from 1 to 3 per 1000 live births with equal sex predilection.^{1,2} It may present as localized or widespread tumors which are characteristically skin-colored, brown or dark brown verrucous papules forming warty plaques usually in linear or whorled distribution. Sites of predilection are the trunk and extremities.

Rare cases have been reported on neoplasms such as basal cell carcinomas and squamous cell carcinomas arising on an epidermal nevus, most commonly arising in the middle aged and the elderly.^{1,2,3,4} There are only few cases of reported keratoacanthoma and keratoacanthoma-like lesions arising in an epidermal nevus.

Case Report:

A 70-year-old Filipino male consulted because of sudden appearance of a solitary bud-shaped nodule over a linear verrucous plaque, which extended from the right posterior auricular area to the right lateral side of the neck. The plaque is asymptomatic and has been present since birth.

The condition started four weeks prior to consult, when he noted a pink papule with an adherent central scaly center associated with intermittent mild pain. This gradually enlarged to form a nodule. Patient is a known hypertensive and diabetic. He is a smoker with fifty pack years and an alcoholic beverage drinker. The patient has a history of constant sun exposure for almost forty years, as his hobby includes playing outdoor tennis. His family history was negative for malignant skin tumors.

Physical examination showed a bud-shaped slightly erythematous movable smooth firm nodule measuring 0.8 cm x 0.5 cm topped with white scale on a hyperpigmented verrucous plaque arranged in a linear configuration over the right retroauricular area extending over the lateral side of the neck (Fig. 1). Regional lymphadenopathy was absent. Excision biopsy of the nodule and part of the verrucous plaque was done. Histologic findings of the nodule revealed a keratoacanthoma while that of the verrucous plaque showed an epidermal nevus. He followed up six weeks later, and there was no recurrence nor new growth noted.

Discussion

Keratoacanthoma is a common epithelial tumor of the skin most commonly in elderly males.⁹ Predisposing factors include UV light exposure and smokers, seem to be more affected than non-smokers.^{2,5} Most lesions develop on hair bearing skin, and may arise on a site of previous trauma ex. surgery. It has three clinical stages namely 1) Proliferative or growth phase, which is characterized by a rapidly growing erythematous papule with a smooth surface reaching a size of 1-2 cm. This phase lasts about 2-10 weeks. 2) Mature or stationary phase of similar duration with a central keratotic core on the nodule. 3) Involution or resolving phase that takes around 8-50 weeks characterized by flattening of the nodule leaving a scar.⁶

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The clinical and histopathologic features of the warty papules and plaques in a linear distribution on the right retroauricular area extending to the lateral neck, which has been present since birth is consistent with an epidermal nevus. The sudden appearance of a solitary pinkish papule, which rapidly increased in size over a period of four weeks, forming a firm erythematous nodule with a white scaly center, were likewise consistent with the clinical features of keratoacanthoma. The diagnosis of keratoacanthoma was confirmed by histopathologic findings of keratin-filled invagination of the epidermis with surrounding areas of glassy eosinophilic appearance, keratinocytes with nuclear atypia and mitotic figures, dyskeratosis, irregular acanthosis and dense superficial perivascular lymphohistiocytic cell infiltrates admixed with numerous eosinophils.

Epidermal nevus is a benign proliferation of keratinocytes that usually present at birth or childhood. Lesions may be localized, following linear patterns known as "the lines of Blaschko." When extensive in distribution it is referred to as systematized epidermal nevus and may be associated with extra-cutaneous manifestations such as CNS and skeletal abnormalities.

Previous reports have indicated that the linear epidermal nevus may serve as a site of development for skin tumors.¹ Verrucous and adnexal carcinomas, bowen's disease and basal cell carcinoma although rare have all been reported to arise in linear epidermal nevus. Squamous cell carcinoma arising in an epidermal nevus is extremely rare. According to Massod et.al only less than ten cases of such have been reported in literature.⁴ Such malignant transformations are most common in middle aged and elderly.^{1,2,4} Keratoacanthoma arising in an epidermal nevus is an infrequent phenomenon. Review of literature, showed only two reported cases of such, both in 1982 on a 26 - year-old white woman and a 32-year-old white man. Presentations were on an epidermal nevus on the right arm for the former and the left arm for the latter.³ Other reported cases of keratoacanthoma development were on a nevus sebaceous. This also has a low incidence.⁷

Some authors believe that keratoacanthoma is a subtype of squamous cell carcinoma, where as others say that it is a precursor lesion to SCC.⁸ Some however, believe that it is an abortive malignancy that rarely progresses to invasive squamous cell carcinoma.⁹ Both keratoacanthomas and SCC may

grow rapidly, but regression has been suggested as the gold standard for the diagnosis of keratoacanthoma.⁸ Due to the uncertainty of differentiating one from the other, the recommendation is that it be treated rather than observed. The use of topical, intralesional and systemic treatments like 5-fluorouracil, methotrexate, triamcinolone and interferon- α have proven successful. But in most solitary keratoacanthomas, complete surgical excision is the treatment of choice.^{2,10}

Conclusion

We report a seventy-year-old male, who presented with a neoplasm clinically and histopathologically consistent with keratoacanthoma on an epidermal nevus. We must exercise vigilance with any new growth that develops rapidly within an epidermal nevus and always regard it as suspicious for malignancy. There are no clinical or histologic criteria to classify a potential keratoacanthoma as a benign tumor that might spontaneously regress, or as a neoplasm with metastatic potential.¹¹ Some authors believe that in terms of treatment, it is best to regard a keratoacanthoma as a variant of squamous cell carcinoma hence, treatment should be instituted once diagnosed. Wide excision is the treatment of choice for solitary keratoacanthoma. The rate of recurrence is 4 -8% within a few weeks after surgery and maybe the result of incomplete excision¹¹. Patients should be advised to perform regular skin examination. Sun protective measures should be practiced at all times. This includes the use of sunscreen, protective clothing, wide-brimmed hats and sun avoidance during the peak hours. Predisposing factors like potential carcinogens such as smoking should be avoided.

It is highly recommended that follow-up be done with complete skin examination during each visit at regular intervals between 3-12 months. Sites of previous lesions and treatment should be assessed for recurrences and appearance of any new lesion.

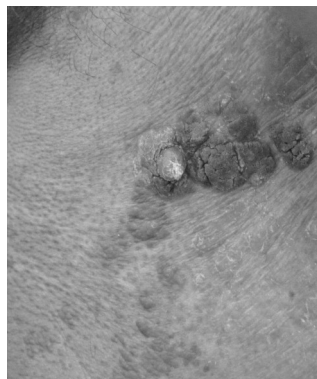
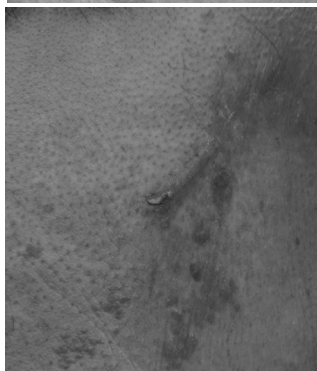


Figure 1. solitary bud shaped pinkish nodule topped with keratotic dry scales on the center of an epidermal nevus



Post-excision of the keratoacanthoma on follow-up six weeks later.

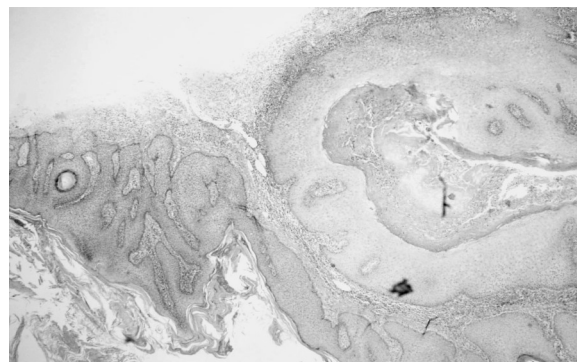


Figure 2. Right side: keratin-filled invagination of the epidermis Left side: hyperkeratosis, focal parakeratosis, papillomatosis, irregular acanthosis with horn cysts (Hematoxylin-eosin stain, magnification x 25)

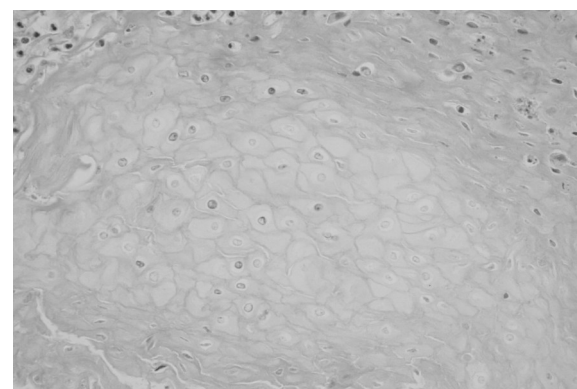


Figure 3. Presence of dyskeratotic cells (above) Surrounding areas with eosinophilic glassy appearance (below) (Hematoxylin and eosin; magnification 40x)

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