JOURNAL OF THE
PHILIPPINE MEDICAL ASSOCIATION

2014-2015 VOLUME 93, NUMBER 1

JOURNAL OF THE
PHILIPPINE MEDICAL ASSOCIATION

2014 - 2015 VOLUME 93, NUMBER 1

TABLE OF CONTENTS

Journal of the
PHILIPPINE MEDICAL ASSOCIATION
2014 - 2015 VOLUME 93, NUMBER 1

RISK FACTORS IN DEVELOPING RETINOPATHY OF PREMATURELY IN A NEWBORN 1
Arejenald U. Meollo, M.D., Marissa Salas, M.D., FPPS, FSPCCMP, FPSCCM

A HOSPITAL BASED CASE – CONTROL STUDY ON RISK FACTORS FOR TEENAGE PREGNANCY AMONG FILIPINO ADOLESCENT GIRLS SEEN IN A TERTIARY GOVERNMENT HOSPITAL 17
Marvin P. Landicho, M.D., Michael M. Resurreccion, M.D.

FOLIC ACID SUPPLEMENTATION IN THE TREATMENT OF ACUTE WATERY DIARRHEA IN CHILDREN 6 MONTHS TO 36 MONTHS OF AGE: A RANDOMIZED DOUBLE-BLIND PLACEDO-CONTROLLED CLINICAL TRIAL 56
Thelma C. Martinez-Lee, M.D., Michael M. Resurreccion, M.D.

PREDICTORS OF RESTENOSIS AFTER PERCUTANEOUS BALLOON MITRAL VALVULOPLASTY 76
Raymund Darius Liberato, M.D., Alexander Ang, M.D.

EYE PROFILE OF CHILDREN AGES 3-5 YEARS OLD IN A DAY-CARE CENTER IN BRYG. BATIS, SAN JUAN 86
Kristine Inopia, M.D., Carlos Chua, M.D., FPAO

OSTEOARTHRITIS OF THE KNEE: CORRELATION OF 1.5 T MRI FINDINGS WITH RADIOGRAPHIC SEVERITY BASED ON KELLEN-LAWRENCE GRADING OF ESTEOARTHRITIS. A RESTROSPECTIVE STUDY FROM JANUARY 2012 TO APRIL 2013 95
Mariaem Andres, M.D., DPBR, Carlos Joshua Espino, M.D., FPCR

COLOSTRUM POWDER SUPPLEMENTATION IN THE TREATMENT OF ACUTE WATERY, NON BLOODY DIARRHEA IN CHILDREN 6 MONTHS TO 36 MONTHS OF AGE WITH SOME SIGNS OF DEHYDRATION: A RANDOMIZED DOUBLE BLIND PLACEBO CONTROLLED CLINICAL TRIAL 113
Ermie Ann V. Badenas, M.D., Michael M. Resurreccion, M.D.

OXYGEN SATURATION (sPO2) LEVELS OF HEALTHY NEWBORNS WITHIN 10 MINUTES OF LIFE 134
Rubelyn F. Aquino, M.D., Marissa G. Salas, M.D.

THE VALIDITY OF USING HAND TOUCH METHOD COMPARED TO DIGITAL THERMOMETRY IN DETECTION OF HYPOTHERMIA AMONG FULL TERM NEONATES DELIVERED AT THE OBSTETRIC ADMITTING SECTION OF A TERTIARY HOSPITAL 152
Josephine Ann G. Santos-Alban, M.D.

Journal of the
Philippine Medical Association
2014 - 2015 VOLUME 93, NUMBER 1

Editorial Office:
2nd Floor PMA Building, North Avenue, Quezon City 1105 Philippines
Contact Numbers: +(632) 929-7361; +(632)929-6366; Fax: +(632) 929-6951
Website: www.philippinemedicalassociation.org;
E-mail: info@philippinemedicalassociation

Journal of the
Philippine Medical Association
2014 - 2015 VOLUME 93, NUMBER 1

MESSAGES

Now more than ever, international indexing and online publication ensures that locally produced research studies are globally cited. This year, the Journal of the Philippine Medical Association will start publishing bi-annual issues of quality original articles in compliance with the minimum requirements for indexing with the Western Pacific Region Index Medicus. The Western Pacific Region Index Medicus (WPRIM) is a project of the WHO Western Pacific Regional Office in collaboration with several institutions in its Member States. This is the Region's contribution to the Global Health Library (GHL) initiative which aims to extend to all the benefits of the knowledge that is essential to the fullest attainment of health. WPRIM will be deployed and hosted, along with the index medici of other WHO Regions, at the Global Index Medicus portal under the GHL platform, where searches can be conducted individually or simultaneously through a federated search engine.

MARIA MINERVA P. CALIMAG, M.D.
President

This first issue of the Philippine Medical Association's Journal would not have been possible with out the unconditional support given by the editorial board under the Chairmanship of Dr. Arnel Asino. Keeping in mind that a medical journal is a forum for the exchange of ideas and valuable information, it is with pride that this journal is presented to all members of the PMA.

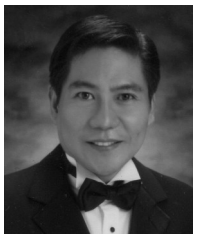
We wish to acknowledge all physicians who have participated by submitting their research papers and case presentations to the PMA. It is to them that we attribute the success of this journal. We fully appreciate their having contributed their work.

A second issue of the PMA Journal will be forthcoming by May, 2015. We encourage all other physicians to have their research papers and case presentations published. The PMA Journal follows the Research Ethics of the Declaration of Helsinski, and we enjoin all participating doctors to do so.

We dedicate this journal to all members of the Philippine Medical Association!
Our sincerest gratitude to all!

MARIANNE L. ORDOÑEZ-DOBLES, M.D.
Secretary General
Chair, Committee on Publications

Journal of the
Philippine Medical Association
2014 - 2015 VOLUME 93, NUMBER 1



Greetings!

The world is a pocket of mystery where things evolve in a very complicated dimension finding solutions to understand unresolved ideas and events. I agree with John F. Kennedy when he said that, "Things do not happen. Things are made to happen." Probably the reason why systematic scientific research are encouraged not to only to harness our curiosity to discover new concepts and modalities, but also to offer new insights, intelligent opinion and strategies. An outcome-based contribution to the human knowledge which may be used as a tool to improve the healthcare system.

Embarking in a research will uncover hidden evidence and encourage investigators to make use of their critical thinking particularly in building theories and conclusion to validate a certain fact in question. It is true that research leads to progress and reduce the rate of errors while improving treatment. According to Thomas Edison, "Our greatest weakness lies in giving up. The most certain way to succeed is always to try just one more time."

I strongly believe that a well-driven researcher always dwell with his work in a formulated thought which reminds me of what Confucius once said that, "The more man meditates upon good thoughts, the better will be his world and the world at large."

God bless us all!

Arnel M. Asino, MD, FPBA
Chair, Sub-Committee on PMA Journal

Journal of the

Philippine Medical Association

Instruction for Authors

General Information

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

The JPMA is published twice in a year at the PMA Office, 2nd Floor, PMA Building, North Avenue, Quezon City 1105, Philippines. It publishes original scientific papers pertinent to medicine and allied fields. It also considers for republications of previously published articles, either in their original or modified forms, provided they are accompanied by written permission from the publisher and principal author.

Statements and opinions expressed the articles and communications herein are those of the author(s) and not necessarily those of the Editor(s) or the publisher. The editor(s) and publisher disclaim any responsibility or liability for such materials and do not guarantee, warrant or endorse any product or services advertised in this publication.

No part of the articles and communications published in the JPMA may be reproduced without the written permission of the publisher.

Editorial Policies

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 Cosiderations

In the conduct and reporting of research, the JPMA adheres to the ethical considerations set forth by the ICMJE with respect to authorship and 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.

All financial or personal relationships that could be viewed as presenting a potential conflict of interest must be disclosed by the author(s) and all participants in the review and publication process.

In experiments involving human subjects, authors must indicate in their reports whatever procedures are complaint with the standards of the responsible institutional and national committee on human experimentation as well as with the Helsinki Declaration of 1975, as revised in 2000. In case of doubts as to the procedures, authors mush show proof of approval of their institutional review body or its equivalent.

In experiments involving animals, authors must indicate in their reports compliance with the institutional and national guide for laboratory animal experimentation.

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 authorsí 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 abstractr, 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.

Generic names of drugs are preferred. Trade names may be given only once at the end of the paper or in the acknowledgement and should follow the generic name in parenthesis.

References are to be cited consecutively in the text as superscripts numbers. At the end of each article, references should be listed consecutively in the numerical order as they appeared in the text

Advertisement

Interested advertisers shall be sent advertising rates and requirements upon request.

The editors and publishers do not guarantee, warrant or endorse any product or service advertised in this publication. Neither do they guarantee any claims made by the manufacturer of such product or service.

Submission

Manuscripts, correspondence, and all materials for review and publication should be sent to the Editor-in-Chief of the Journal of Philippine Medical Association at the Editorial Office.

Subscription and advertisements, including change of address should be sent to the PMA Secretariat at 2nd floor PMA Building, North Avenue, Quezon City, 1105 Philippines.

RISK FACTORS IN DEVELOPING RETINOPATHY OF PREMATURITY IN A NEWBORN

Arejenald U. Meollo M.D.
Principal Author

Marissa Salas MD, FPPS, FSPCCMP, FPSCCM
Co-Author

Our Lady of Lourdes Hospital Department of Pediatrics
Institutional Affiliation

ABSTRACT

I. OBJECTIVE: To identify the risk factors which predispose to retinopathy of prematurity.

II. DATA SOURCES: The population of this study consists of infants born premature admitted at the Neonatal Unit of a private tertiary institution. The medical records of 124 premature infants born from January 2011 to January 2013 were gathered. Presence of known and possible risk factors in developing Retinopathy of Prematurity (ROP) were evaluated using these medical records.

III. REVIEW METHOD: Data were analyzed using Stata version 10 software. Frequency tables were generated to show the distribution of prematures according to maternal obstetrical factors, neonatal factors, course of hospital stay and occurrence of ROP. To determine differences between those who developed and those who did not develop ROP, chi square test and Fishers exact test when applicable were utilized for qualitative variables and independent t-test for quantitative variables. Crude analysis was done to determine the association of selected factors independently with the development of ROP.

IV. RESULTS: Mothers had a mean age of 31 years. Majority had no pre-partum illnesses like preeclampsia, maternal pyrexia and PROM. Most delivered via caesarian section with preeclampsia as the most common indication. Majority of the preterms were 35-36 weeks AOG and weighed between 1500 to less than 2500 grams. Most had Apgar scores of 8 and 9 at 1 and 5 minutes of life, respectively. Almost equal distribution of males and females. Majority did not develop jaundice. The mean length of stay at the NICU was 19 days. For those needing oxygenation, it was given for 8 days on the average. Majority did not require mechanical ventilation. The maximum level of Fi02 (100%) was used in 26% of cases. Out of 124 preterm neonates, 31 (25%) developed ROP. The mean age at detection was 30 days.

V. CONCLUSION: Maternal age was older, duration of PROM was longer, and the proportion of those delivered by caesarian section was higher among those who had ROP. Gestational age was earlier, birthweight was lower and 1-minute Apgar scores were also lower among those who developed ROP. NICU stay and duration of O_2 therapy was longer, level of FiO_2 was higher and a greater proportion placed on mechanical ventilation was seen among those who developed ROP. The final regression model for factors associated with the development of ROP showed birthweight and FiO_2 to be significantly associated with developing ROP.

KEYWORDS: prematurity – retinopathy of prematurity – risk factors

INTRODUCTION

Retinopathy of prematurity (ROP) is a disorder of the developing retina and an important and potentially preventable cause of blindness in childhood. Although treatment options are available, the prevention of ROP is highly desirable. It is widely acknowledged that ROP is a multi-factorial disorder, with low gestational age, low birth weight, oxygen exposure, neonatal sepsis, and bronchopulmonary dysplasia being important risk factors. Some of the risk factors appear to contribute to ROP by affecting the systemic cytokine and growth factor milieu.[1]

ROP is characterized by abnormal neovascular development in the retina of premature infants. These abnormal blood vessels are fragile and can leak or bleed, scarring the retina and pulling it out of position. This causes a tractional retinal detachment, which is the main cause of visual impairment and blindness in ROP.[2] ROP is always correlated with the level of oxygen use in journals. However, some preterms that were not given oxygen support also developed this condition.

Retinopathy of prematurity (ROP) is the main cause of visual impairment in premature infants. The increased survival of extremely low birth weight (ELBW) infants in recent years, due to advances in neonatal care, has produced a population of infants at very high risk of developing ROP. It has been believed for many years that oxygen therapy increases the risk of ROP in preterm infants. However, ROP can occur even with careful control of oxygen therapy. Several factors increase the risk of ROP, especially those associated with short gestation and low birth weight. Other identified risk factors include sepsis, intraventricular hemorrhage, exposure to light, blood transfusions, and mechanical ventilation.[3]

Prematurity has been established as the major risk factor in development of retinopathy. Early diagnosis of retinopathy will give a better chance of preventing loss of sight in these infants. Establishing other conditions other than prematurity in the causation of retinopathy is therefore important in its prevention and management. This study identifies risk factors for ROP other than those established in previous papers.

REVIEW OF RELATED LITERATURE

Prematurity is a term for the broad category of neonates born at less than 37 weeks gestation.[4] The length of a normal pregnancy or gestation is considered to be 40 weeks (280 days) from the date of conception. Infants born before 37 weeks gestation are considered premature and may be at risk for complications.[5]

Retinopathy of prematurity is a serious complication of prematurity treatment and will lead to blindness if not recognized and treated early. It is an important cause of preventable blindness in children. A cohort study by Chen et. al. in 2011 suggests that neonatal sepsis, oxygen exposure and low gestational age are

not only independently associated with a significantly increased risk for ROP, but also interact in a fashion that suggests synergistic effects that go beyond additive and even multiplicative patterns between low gestational age and any sepsis.[6] The currently used international classification of ROP describes the location, extent, and severity of the disease. To delineate location, the retina is divided into three concentric zones, centered on the optic disc. Zone I, the posterior or inner zone, extends twice the disc-macular distance, or 30 degrees in all directions from the optic disc. Zone II, the middle zone, extends from the outer edge of zone I to the ora serrata nasally and to the anatomic equator temporally. Zone III, the outer zone, is the residual crescent that extends from the outer border of zone II to the ora serrata temporally, this area of the retina being vascularized. The extent of involvement is described by the number of circumferential clock hours involved. The phases and severity of the disease process are classified into five stages. Stage 1 is characterized by a demarcation line that separates vascularized from avascular retina. This line lies within the plane of the retina and appears relatively flat and white. Often noted is abnormal branching or arcading of the retinal vessels that lead into the line. Stage 2 is characterized by a ridge; the demarcation line has grown, acquiring height, width, and volume and extending up and out of the plane of the retina. It may change from white to pink. Vessels may leave the plane of the retina to enter the ridge. Stage 3 is characterized by the presence of a ridge and by the development of extraretinal fibrovascular tissue. Stage 4 is characterized by subtotal retinal detachment caused by traction from the proliferating tissue in the vitreous or on the retina. Stage 4 is subdivided into two phases: (1) subtotal retinal detachment not involving the macula and (2) subtotal retinal detachment involving the macula. Stage 5 is total retinal detachment. When signs of posterior retinal vascular changes accompany the active stages of ROP, the term plus disease is used. Patients reaching the point of dilatation and tortuosity of the retinal vessels also frequently demonstrate the associated findings of engorgement of the iris, pupillary rigidity, and vitreous haze.[7]

Advances in neonatal care in the last decade improved the survival rates for premature infants. Consequently, the incidence of ROP has increased in parallel. It is under constant epidemiological study around the world. Early identification of retinal damage and the institution of appropriate treatment prevents blindness and offers the child better overall development. Studies around the world have been conducted to find the relationship between comorbid conditions and maturity of newborns in developing retinopathy.[8]

In a retrospective cohort study by Narong Thongharn in 2010 at Thailand entitled Risk Factors of Retinopathy of Prematurity, data from medical records of premature babies with a gestational age (GA) of ≤32 weeks or a birth weight (BW) of ≤2,000 grams and who were admitted at Roi-Et Hospital between October 2006 and September 2010, were collected and analyzed to identify risk of

ROP by independent t-test and logistic. It concluded that the important risk factors associated with the development of ROP were Respiratory Distress Syndrome (RDS) and hypothermia. The means of gestational ages and birth weight were also noted to be lower in ROP patients than non ROP patients. Prevention of prematurity and avoidance of these risk factors can thus reduce the incidence of ROP.[9]

OBJECTIVES

GENERAL OBJECTIVES

To identify the risk factors which predispose to retinopathy of prematurity among premature infants.

SPECIFIC OBJECTIVES

1. To determine the relationship between retinopathy of prematurity and each of the following risk factors:
    a. Mode of delivery
    b. Age of gestation
    c. Birth Weight
    d. Gender
    E. APGAR score at 5 minutes of life
    f. Number of days on oxygen support
    g. Jaundice
    h. Number of days in phototherapy
    i. Number of days stay in neonatal unit
    J. FiO2 used
    K. Use of mechanical ventilator
    L. Age at which ROP detected
    m. Maximum stage of ROP reached
    n. Maternal age
    o. Preecclampsia in the mother
    p. Preterm Premature Rupture of membrane (PPROM)
    q. Presence of maternal pyrexia

2. To determine which of the abovementioned risk factors are significantly associated with ROP.

STUDY DESIGN

Cross-Sectional Study

PATIENTS AND METHODS

SETTING:

Private tertiary institution

SUBJECTS:

The population of this study consists of infants born premature admitted at the Neonatal Unit of a private tertiary institution.

INCLUSION CRITERIA:

Male and female preterm (<37 weeks AOG) infants born via Cesarean section or normal spontaneous delivery from January 2011-January 2013 in a private tertiary institution.

EXCLUSION CRITERIA:

Neonates who died before the first ophthalmologic examination and infants with congenital anomalies.

STUDY PROCEDURE:

The medical records of 124 premature infants born from January 2011 to January 2013 were gathered. Presence of known and possible risk factors in developing Retinopathy of Prematurity (ROP) were scrutinized using

these medical records. The risk factors included were: mode of delivery, age of gestation, birth weight, gender, APGAR score at 1 and 5 minutes of life, number of days on oxygen support, jaundice, number of days in phototherapy, number of days stay in neonatal unit, FiO2 used, use of mechanical ventilator, age at which ROP detected, maximum stage of ROP reached, maternal age, preecclampsia in the mother, preterm premature rupture of membrane (PPROM), and presence of maternal pyrexia.

Data were analyzed using Stata version 10 software. Frequency tables were generated to show the distribution of prematures according to maternal obstetrical factors, neonatal factors, course of hospital stay and occurrence of ROP. To determine differences between those who developed and those who did not develop chi square test and Fishers exact test when applicable were utilized for qualitative variables and independent t-test for quantitative variables. Crude analysis was done to determine the association of selected factors independently with the development of ROP.

SAMPLE SIZE

For determining factors associated with the development of ROP, current literature provided estimates only for gestational age and birth weight. In the absence of available information from the literature on Apgar score at 1 minute, need for mechanical ventilation, duration of oxygen therapy and level of Fi02, an initial run of the data provided values for these proportions which was used in power calculation and sample size estimation. The largest of these values was the final sample size requirement.

In a study on the incidence and risk factors for ROP (Alpay and Ugurbas, 2012), ROP developed in 43.2% of those <32 weeks AOG and in 50% of those weighing 1500 grams or less. Utilizing the formula for test of hypothesis between two proportions, incorporating the power of the test at 5% level of significance, the estimated sample size was 35 per group (Appendix A).

Appendix A:

$$n = \frac{\left(Z_{1-\alpha}\sqrt{2\bar{P}\bar{Q}} + Z_{1-\beta}\sqrt{(P_1Q_1 + P_2Q_2)}\right)^2}{(P_1 - P_2)^2}$$

Age of gestation:

Where P_1 is the proportion of preterms who developed ROP among those < 32 weeks AOG = .432 (Alpay and Ugurbas, 2012)

P_2 is the proportion of preterms who developed ROP among those ³ 32 weeks AOG = .093 (Alpay and Ugurbas, 2012)

$Z_{1-\alpha}$ is 1.96 corresponding to a two-tailed α error of .05

$Z_{1-\beta}$ is 0.84 corresponding to a one-tailed error of 0.2 or 80% power

$$\bar{P} = \frac{P_1 + P_2}{2} \qquad \bar{Q} = 1 - \bar{P} \qquad Q_1 = 1 - P_1 \qquad Q_2 = 1 - P_2$$

$$n = \frac{\left(1.96\sqrt{2(.263)(.738)} + .84\sqrt{(.432)(.568) + (.093)(.907)}\right)^2}{(.432 - .093)^2}$$

n = 25 per group of gestational age

Birthweight:

Where P_1 is the proportion of preterms who developed ROP among those < 1500 g = .50 (Alpay and Ugurbas, 2012)

P_2 is the proportion of preterms who developed ROP among those ³ 1500 g = .186 (Alpay and Ugurbas, 2012)

$$n = \frac{\left(1.96\sqrt{2(.343)(.657)} + .84\sqrt{(.50)(.50) + (.186)(.814)}\right)^2}{(.50 - .186)^2}$$

n = 35 per group of birthweight

For other selected factors:

The ability to detect a difference in the proportion of those who developed ROP based on the present sample size of the study for the other selected factors is given in the following table :

	Present sample size	Power for present sample size	Sample size needed to achieve 80% Power
Duration of O_2 therapy		100%	
³ 6 days	38		8
< 6 days	86		8
1 minute Apgar Score		NAN	
< 7	5		27
³ 7	119		27
Need for mechanical ventilation		99.9%	
Yes	37		10
No	87		10
Level of FiO_2		100%	
100%	32		7
<100%	92		7

The final sample size was 35 per group of the selected factors.

STATISTICAL ANALYSIS

Data was analyzed using Stata version 10 software. Frequency tables were generated to show the distribution of prematures according to maternal obstetrical factors (maternal age, presence of preecclampsia and maternal pyrexia, duration of PROM, mode of delivery, indication for CS), neonatal factors (gestational age, birthweight, apgar score and gender), course of hospital stay (occurrence of jaundice, length of phototherapy, duration of stay at the NICU, number of days on oxygen therapy, need for mechanical ventilation, level of Fi02 used) and occurrence of ROP (age at which ORP was detected, maximum stage of ROP reached and therapy given).

To determine differences between those who developed and those who did not develop ROP in terms of the above factors, chi square test and Fishers exact test when applicable was utilized for qualitative variables and independent t-test for quantitative variables. A p-value < 0.05 was used as cut-off for significance.

Crude analysis was done to determine the association of selected factors independently with the development of ROP. Risk ratios with 95% confidence intervals were likewise computed.

However, crude analysis has its limitations and so binary logistic regression using backward elimination procedure was carried out to determine factors significantly associated with the development of ROP.

RESULTS

I. General Data

There were a total of 124 preterms delivered from January 2011 to January 2013. Table 1 shows their distribution as to gender, birthweight, and age of gestation.

Table 1: General data Preterm Neonates

Gestational Age	n	%
< 32 weeks	21	17
³ 32 weeks	103	83
total	124	100
Birthweight		
< 1500 grams	22	18
³ 1500 grams	102	82
total	124	100
Gender		
Male	63	51
Female	61	49
total	124	100

II. Profile of Cases

Mothers of the preterm neonates had a mean age of 31 SD ± 5 years, the youngest being 18 and the oldest being 45 years old. Majority had no pre-partum illnesses like preeclampsia, maternal pyrexia and PROM. Most delivered via caesarian section with preeclampsia as the most common indication *(Table 2).*

Table 2: Distribution of Preterm Neonates according to Maternal Obstetric Factors

Maternal Obstetric Factors	No. (%)
Maternal Age (in years)	
Mean, sd	30.9, 5.0
Median (min, max)	31 (18, 45)
Preeclampsia	
With	32 (25.8)
Without	92 (74.2)
total	100
Maternal Pyrexia	
With	1 (0.8)
Without	123 (99.2)
total	100
Duration of PROM (in hours)	
0	107 (86.3)
10	2 (1.6)
12	8 (6.5)
13	2 (1.6)
14	2 (1.6)
18	3 (2.4)
total	100
Mode of Delivery	
Caesarian Section	81 (65.3)
Normal Spontaneous Delivery	43 (34.7)
total	100
Indications for Caesarian Section	
Preeclampsia	32 (39.5)
Twin pregnancy	12 (14.8)
PPROM	11 (13.6)
Repeat CS	10 (12.3)
Non-reassuring Fetal Heart Rate Pattern	7 (8.6)
Placenta Previa	4 (4.9)
Breech	3 (3.7)
Placental Insufficiency	1 (1.2)
Failure of Descent	1 (1.2)
ACD	1 (1.2)
total	100

Table 3: Distribution of Preterm Neonates according to Neonatal Factors

Neonatal Factors	No.(%)
Gestational Age (in weeks)	
24	1 (0.8)
26	1 (0.8)
27	1 (0.8)
28	2 (1.6)
29	4 (3.2)
30	2 (1.6)
31	10 (8.1)
32	6 (4.8)
33	16 (12.9)
34	15 (12.1)
35	34 (27.4)
36	32 (25.8)
total	100
Birthweight (in grams)	
< 1500	22 (17.7)
1500 to < 2500	95 (76.6)
≥ 2500	7 (5.7)
total	100
Apgar Score at 1 minute	
2	1 (0.8)
3	2 (1.6)
5	2 (1.6)
7	26 (21.0)
8	93 (75.0)
total	100
Apgar Score at 5 minute	
7	1 (0.8)
8	19 (15.7)
9	101 (83.5)
	100
Gender	
Male	63 (50.8)
Female	61 (49.2)
total	100

Majority of preterms were aged 35-36 weeks and weighed between 1500 to less than 2500 grams. Most had Apgar scores of 8 and 9 at 1 and 5 minutes of life, respectively. There was almost equal distribution of males and females *(Table 3).*

Majority did not develop jaundice. For those who did, phototherapy was given for a mean duration of 3 SD ± 2 days. The mean length of stay at the NICU was 19 SD ± 16 days, the shortest being 2 days and the longest being 68 days. For those needing oxygen

therapy, it was given for 8 SD ± 7 days on the average, the shortest being a day and the longest being 28 days. Majority did not require mechanical ventilation. The maximum level of FiO_2 (100%) was used in 26% of cases while majority were subjected to room air and FiO_2 ranging from 30% to 90% *(Table 4).*

Table 4: Distribution of Preterm Neonates as to Conditions During Course of Hospital Stay

Conditions during Course of Hospital Stay	No. (%)
Jaundice	
Yes	46 (37.1)
No	78 (62.9)
total	100
Length of Phototherapy (in days)	
Mean, sd	2.6, 2.2
Median (min, max)	2 (1, 9)
NICU stay (in days)	
Mean, sd	18.7, 16.0
Median (min, max)	12 (2, 68)
Duration of Oxygen Therapy (in days)	
Mean, sd	7.5, 7.2
Median (min, max)	4.5 (1, 28)
Need for Mechanical Ventilation	
Yes	37 (29.8)
No	87 (70.2)
total	100
Level of FiO_2 Used (in %)	
21	39 (31.5)
30	49 (39.5)
45	1 (0.8)
60	1 (0.8)
70	1 (0.8)
90	1 (0.8)
100	32 (25.8)
total	100

Out of 124 preterm neonates, 31 (25%) developed ROP. The mean age at detection was 30 SD ± 16 days. The highest stage or most severe ROP in either eye was noted to be commonly stage 2. Observation was the usual therapy given *(Table 5)*. The lone stage 4 case was detected longest at 53 days while stage 1 was detected earliest at 24 SD ± 6 days *(Table 6)*. All of stages 1 and 3 and majority of stage 2 were managed with observation alone while two of stage 2 and the lone stage 4 underwent laser treatment *(Table 7)*.

Table 5: Incidence and Profile of ROP

ROP	No. (%)
With	31 (25.0)
Without	93 (75.0)
	100
Age detected (in days)	
Mean,sd	30.2, 15.5
Median (min,max)	27 (7, 60)
Maximum Stage reached	
Stage 1	6 (19.4)
2	17 (54.8)
3	7 (22.6)
4	1 (3.2)
	100
Therapy given	
Observation	28 (90.3)
Laser IO	3 (9.7)
	100

Table 6: Mean Age detected by Stage of ROP

Stage of ROP	Age Detected (Mean, sd)	No.
1	23.5, 6.2	6
2	30.7, 17.2	17
3	31.6, 15.7	7
4	53.0	1
total		31

Table 7: Therapy given by Stage of ROP

Stage of ROP	Therapy Given			No.
	Laser	Laser , Avastatin	Observation	
1			6	6
2	2		15	17
3			7	7
4		1		1
total				31

III. Comparison between those with and without ROP

There were significant differences in maternal age, duration of PROM and mode of delivery between those who did and those who did not develop ROP (p-value <0.05). Maternal age was older, duration of PROM was longer, and the proportion of those delivered by caesarian section was higher among those who had ROP (Table 8).

As to neonatal factors, there were significant differences in gestational age, birthweight and 1-minute Apgar score. Gestational age was earlier, birthweight was lower and 1-minute Apgar scores were also lower among those who developed ROP. There was no significant difference in gender distribution (Table 8).

Likewise, there were significant differences in length of NICU stay, duration of oxygen therapy, need for mechanical ventilation and level of FiO_2 between the two groups. NICU stay and duration of O_2 therapy was longer, level of FiO_2 was higher and a greater proportion placed on mechanical ventilation was seen among those who developed ROP. No differences were noted on the occurrence of jaundice and duration of phototherapy (Table 8).

Table 8: Comparison by Maternal Obstetric and Neonatal Factors and Course of Hospital Stay

Maternal Obstetric Factors	ROP	No ROP	p-value
Maternal Age in years (mean, sd)	32.7, 3.9	30.2, 5.3	0.0197[a]
Duration of PROM in hrs (mean, sd)	4.5, 6.3	0.9, 3.5	0.0001[a]
Preeclampsia (%)	29.0	24.7	0.6355[b]
Maternal Pyrexia (%)	3.2	0	0.0820[b]
Mode of Delivery (%)			0.0007[b]
CS	90.3	65.4	
NSD	9.7	34.6	
Neonatal Factors			
Gestational Age in weeks (mean, sd)	30.9, 2.6	34.8, 1.3	0.0000[a]
Birthweight in grams (mean, sd)	1412.5, 343.5	2106.9, 323.9	0.0000[a]
1 minute Apgar score (mean, sd)	7.1, 1.3	7.8, 0.8	0.0009[a]
Gender (%)			0.2540[b]
Male	41.9	53.8	
Female	58.1	36.2	

Course of Hospital Stay			
Jaundice (%)	38.7	36.6	0.8300[b]
Length of phototherapy in days (mean, sd)	1.5, 2.2	0.9, 1.7	0.0858[a]
NICU stay in days (mean, sd)	39.4, 14.0	11.8, 9.2	0.0000[a]
Duration of O_2 therapy in days (mean, sd)	12.7, 7.9	2.6, 4.1	0.0000[a]
Need for mechanical ventilation (%)	77.4	14.0	0.0000[b]
Level of FiO_2 in % O_2 (mean, sd)	83.9, 30.3	33.9, 22.6	0.0000[a]

[a]Independent t-test [b]Chi square test

IV. Crude Analysis on the association between selected factors and ROP

Gestational age, birthweight, duration of O_2 therapy, mechanical ventilation and level of FiO_2 were independently significantly associated with ROP (p-value <0.05). ROP was 6 times more among those with gestational age less than 32 weeks, 7 times more among those with birthweight was less than 1500 grams, 12 times more among those on O_2 therapy for more than 6 days, 6 times more among those on mechanical ventilation and 10 times more among those exposed to 100% FiO_2. ROP was 3 times more among those with 1-minute Apgar scores less than 7 but the association was not significant (p-value =.0992) (Table 9).

Table 9: Association between Selected Factors and Development of ROP

Selected Factors	ROP	No ROP	Risk Ratio (95% CI)	p- value
Gestational Age			5.96 (3.51, 10.11)	0.0000[b]
< 32 weeks	17 (81.0)	4 (19.0)		
³ 32 weeks	14 (13.6)	89 (86.4)		
Birthweight			7.34 (4.21, 12.81)	0.0000[b]
< 1500 grams	19 (86.4)	3 (13.6)		
³ 1500 grams	12 (11.8)	90 (88.2)		
Duration of O_2 therapy			11.76 (4.89, 28.3)	0.0000[b]
³ 6 days	26 (68.4)	12 (31.6)		
< 6 days	5 (5.8)	81 (94.2)		
1 minute Apgar score			2.55 (1.16, 5.59)	0.0992[c]
< 7	3 (60.0)	2 (40.0)		
³ 7	28 (23.5)	91 (76.5)		
Need for mechanical ventilation			8.06 (3.81, 17.05)	0.0000[b]
Yes	24 (64.9)	13 (35.1)		
No	7 (8.1)	80 (91.9)		
Level of FiO_2			9.86 (4.70, 20.65)	0.0000[a]
³100%	24 (75.0)	8 (25.0)		
<100%	7 (7.6)	85 (92.4)		

[a]Independent t-test [b]Chi square test [c]Fishers exact probability test

V. Logistic Regression Analysis

Taking into account all of the above selected factors, the final regression model for factors associated with the development of ROP showed birthweight and FiO_2 to be significantly associated with ROP. Those whose birthweight was less than 1500 grams were 47 times more likely to have ROP than those weighing more than or equal to 1500 grams. Likewise those exposed to more than 100% Fi02 were 36 times more likely to have ROP than those exposed to less than 100% Fi02 (Table 10).

Table 10: Final Logistic Regression Model for Factors Associated with the Development of ROP

Factor	Coefficient (b)	Odds Ratio (95% CI)	p-value
Constant	-3.403		
Birthweight <1500 grams	3.846	46.81 (8.20, 267.12)	0.000
Fi02 100%	3.583	35.98 (8.52, 151.99)	0.000

DISCUSSION

Retinopathy of prematurity (ROP) is a major treatable cause of blindness worldwide. The rate of blindness varies considerably in different care units, depending on their level of development and whether effective screening and treatment programs exist.[10]

In this study there were a total of 124 preterms included. Mothers had a mean age of 31 (see table 2). Majority had no pre-partum illnesses like preeclampsia, maternal pyrexia and PROM (see table 2). Most delivered via caesarian section due to preeclampsia (see table 2). According to Yu et. al.[11] preeclampsia was not associated with ROP in preterm births, however, this was not proven in our study.

Majority of the pre terms were aged 35-36 weeks and weighed between 1500 to less than 2500 grams (see table3). Most had Apgar scores of 8 and 9 at 1 and 5 minutes of life, respectively (see table3). Almost equal distribution of males and females (see table3).

Majority did not develop jaundice, but for those who did, phototherapy was given for a mean duration of 3 days (see table 4). The mean length of stay at the NICU was 19 days (see table 4). For those needing oxygen therapies, it was given for 8 days on the average (see table4). Majority did not require mechanical ventilation (see table 4). The maximum level of Fi02 100% was used in 26% of cases while majority were subjected to FiO_2 ranging from 21% to 90% (see table 4).

Out of 124 preterm neonates 31 developed ROP (see table 5). The mean age at detection was 30 days (see table 5). Although guidelines for ROP screening recommends age of gestation less than or equal to 32 weeks, there were 4 neonates 33 weeks AOG, 2 neonates 34 weeks AOG, and 1 neonate 36 weeks AOG who developed ROP in our study.

Retinopathy of prematurity primarily occurs in extremely low birth weight (ELBW) infants. Most research suggests that a low birth weight, a young gestational age, and the severity of illness are associated factors.

Retinal vasculature begins to develop around 16 weeks age of gestation. It grows circumferentially and becomes fully mature at term. Premature birth results in the cessation of normal retinal vascular maturation. Exposure of newborn premature infants to hyperoxia downregulates retinal vascular endothelial growth factor (VEGF). Blood vessels constrict and can become obliterated, resulting in delays of normal retinal vascular development. This hyperoxia-vasocessation is the underlying cause of retinopathy of prematurity.[12]

There were significant differences in maternal age, duration of PROM and mode of delivery between those who did and those who did not have ROP (see table 8). Maternal age was older, duration of PROM was longer, and the proportion of those delivered by caesarian section was higher among those who had ROP (see table 8).

According to a study by Wu et. al. entitled "Retinopathy of Prematurity and Maternal Age": older maternal age is a newly identified risk factor for the development of ROP in premature babies.[13] This is similar with our study. The average age of marriage continues to increase, this might be one of the reasons why advanced maternal age was not an issue in the past and this risk factor was not identified in previous studies.

There are more patients who developed ROP who were delivered via cesarean section which is in contrast with the study by Manzoni et. al. which concluded that vaginal delivery is a significant and independent predictor of threshold ROP in preterm infants.[14] As to neonatal factors, there were significant differences in gestational age, birthweight and 1-minute Apgar score (see table 8). Gestational age was earlier, birthweight was lower and 1-minute Apgar scores were also lower among those who developed ROP. There was no significant difference in gender distribution (see table 8). Although gender is not a significant factor in developing ROP, there were more males than females noted in our study. According to Walsh in 2009: Both birth weight and gestational age were independently associated with severe retinopathy, but gestational age was a stronger predictor.[15] This is comparable with our study where infants born earlier and those with low birth weights developed ROP. This may be due to advancements during the recent years where improvements in neonatal intensive care lead to greater survival among infants born at extremely low gestational ages.

There were significant differences in length of NICU stay, duration of oxygen therapy, need for mechanical ventilation and level of Fi02 between the two groups. NICU stay and duration of O2 therapy was longer, level of Fi02 was higher and a greater proportion placed on mechanical ventilation was seen among those who developed ROP (see table 8). These finding are the same with that of Hakeem et. al. in "Retinopathy of Prematurity: A Study of Prevalence and Risk Factors" which stated that higher level of oxygen during oxygen therapy and use of mechanical ventilator were significant risk factors for ROP.[8] In 1954, Ashton and Cook were the first to establish

that oxygen is important in disrupting retinal blood vessel development.[16] Several recent studies have shown a relationship between a high-oxygen saturation and ROP. It seems that a SaO2>93% increases the risk for severe ROP and need for therapy.[17]

No differences were noted on the occurrence of jaundice and duration of phototherapy (see table 8). Gestational age, birthweight, duration of O_2 therapy, mechanical ventilation and level of FiO_2 were independently significantly associated with the development of ROP (see table 8), which also concurs with the study of Hakeem et. al.[8] ROP was 6 times more among those with gestational age less than 32 weeks (see table 8), 7 times more among those with birthweight was less than 1500 grams (see table 8), 12 times more among those on O_2 therapy for more than 6 days (see table 8), 6 times more among those on mechanical ventilation (see table 8) and 10 times more among those exposed to 100% FiO_2 (see table 8). ROP was 3 times more among those with 1-minute Apgar scores less than 7 but the association was not significant (see table 8).

CONCLUSION

An older maternal age, a longer duration of PROM, and a larger proportion of those delivered by caesarian section are likely to have ROP. Earlier gestational age, lower birthweight, and lower 1-minute Apgar scores were also noted in those babies that developed ROP. Furthermore, a longer NICU stay, a longer duration of O_2 therapy, a higher level of FiO_2, and a greater proportion placed on mechanical ventilation was also seen among those who have ROP.

The final regression model for factors associated with the development of ROP showed birthweight and FiO_2 to be significantly associated with ROP.

LIMITATION OF THE STUDY

Limitation of this study is the short duration of the period included from January 2011 to January 2013, however, adequate sample size was reached. The study only involved one private tertiary hospital. We believe that this is an advantage since there is little variability in practice. In particular, the ophthalmologic examinations were consistent since all neonates were seen by the same ophthalmologist for the entire duration of the study. This study was made to determine risk factors for ROP, but not to test prior hypotheses.

RECOMMENDATIONS

As this is a single hospital-based study, a comprehensive countrywide survey on ROP in the Philippines is recommended to determine any regional differences in ROP prevalence. Larger sample size and additional risk factors is also recommended to yield higher statistical power.

REFERENCES

1. Minghua et. al. *Infection, Oxygen, and Immaturity: Interacting Risk Factors for Retinopathy of Prematurity*. Neonatology. 2011

2. Hakeem et. al. *Retinopathy of Prematurity: A Study of Prevalence and Risk Factors*. Middle East Afr J Ophthalmology. 2012

3. Karna et al. *Retinopathy of prematurity and risk factors: a prospective cohort study*. BMC Pediatrics. 2005

4. Furdon et. al. *Prematurity*. http:// emedicine. medscape.com. 2013

5. Beers et. al. *Premature Infant. Merck Manual of Diagnosis and Therapy.* Whitehouse Station, NJ: Merck Research Laboratories. 2004

6. Chen et. al. *Infection, Oxygen, and Immaturity: Interacting Risk Factors for Retinopathy of Prematurity*. Neonatology. 2010 February. 125–132

7. Behrman et. al. *Disorders of the Retina and Vitreous*. Nelson's Textbook of Pediatrics. 2012

8. Hakeem et. al. *Retinopathy of Prematurity: A Study of Prevalence and Risk Factors.* Middle East Afr J Ophthalmology. 2012 July. 289-294

9. Narong Thongharn. *Risk Factors of Reti nopathy of Prematurity.* http://thailand.digitaljournals.org. 2010

10. Akkoyun I, Oto S, Yilmaz G, et al. *Risk factors in the development of mild and severe retinopathy of prematurity*. J AAPOS 2006; 10: 449–453

11. Yu et. al. *Preeclampsia and retinopathy of prematurity in preterm births*. Pediat ric. 2012 July: 101-7

12. Subramanian et. al. *Retinopathy of Prematurity*. http://emedicine.medscape. com. May 2011.

13. Wu et. al. *Retinopathy of Prematurity and Maternal Age*. National Institute of Health. February 2012. 30(2): 327–331

14. Manzoni et. al. *Mode of delivery and threshold retinopathy of prematurity in pre-term ELBW neonates*. Acta Paediatr. 2007 Feb: 96 (2):221-6)

15. Walsh, N. *Retinopathy Tied to Gestational Age at Birth*. Ophthalmology. October 2009

16. Ashton N, Cook C. *Direct observation of the effect of oxygen on developing vessels*. Br J Ophthalmol 1954; 38: 433-440

17. Askie et. al. *Oxygen-saturation targets and outcomes in extremely preterm infants*. New England Journal of Medicine. 2003; 349: 959-96

A HOSPITAL BASED CASE – CONTROL STUDY ON RISK FACTORS FOR TEENAGE PREGNANCY AMONG FILIPINO ADOLESCENT GIRLS SEEN IN A TERTIARY GOVERNMENT HOSPITAL

Marvin P. Landicho, M.D.
Michael M. Resurreccion, M.D.

Quirino Memorial Medical Center

INTRODUCTION

Teenage pregnancy is defined as an underage girl of 13 to 19 years who becomes pregnant. The definition differs from one country to another but generally refers to women below legal adulthood[1]. In the developing world, one-third to one-half of women become mothers before the age of 20 and pregnancy related complications have become the leading causes of death among them[2,3]. South Asian countries have high proportions of teenage pregnancies, since early marriage is common and there is a social expectation to have a child soon after marriage[4-6]. A study in Southeast Asia showed that nearly 60% of all girls are married by the age of 18 years and one fourth are married by the age of 15 years[7].

Worldwide, early childbearing is associated with higher risk of adverse reproductive outcomes. A younger maternal age is associated with an increased maternal and infant mortality[8,9]. Adolescent pregnancy contributes to the perpetuation of the poverty cycle by exposing these girls at higher risk for low educational and occupational attainment and low socioeconomic status[9,10]. Children born to teenage mothers experience more risk of abuse, neglect and have more behavioural problems[11]. However, abusive early pregnancy is also perceived as a rite of passage a pathway to adulthood that might bring positive consequences and thus is desired in some contexts[11-13]. It may also be seen as an escape from families[11-14].

Teenage pregnancy is widespread in the Philippines, especially amongst the poor. Filipino teens get a higher exposure to sex from the Internet, magazines, TV shows, movies and other media than decades ago, yet without any corresponding increase in information on how to handle the input. During the 21st century, the statistics about this issue continues to rise even though there are a lot of disadvantages that young mothers and fathers can obviously get in the said issue.

According to the 2002 Young Adult Fertility and Sexuality Study done by the University of the Philippines Population Institute and the Demographic Research and Development Foundation, twenty six of our Filipino youth nationwide 15 to 25 years of age admitted to having a premarital sex experience. Thirty eight percent of our youth are already in a live-in arrangement. The 1998 National Demographic and Health Survey (NDHS) reported that 3.6 million of our teenagers got pregnant. In ninety two percent of these teens, the pregnancy was unplanned, and the majority, 78 percent, did not even use contraceptives the first time they had sex. The medical consequence of teenage pregnancies that have been extensively studied include preterm deliveries, stillbirth and fetal distress among others. Social consequences of teenage pregnancies identified are minimal access to higher education , higher divorce rates, premature death of women, population growth, weak and unhealthy children.

Risk factors identification of teenage pregnancy is necessary so as to halt if not to

to prevent it's increasing incidence specially any developing countries like the Philippines. Socio-economic status, educational attainment, cultural factor and family structure were all identified as risk factors for teenage pregnancies in South Asia[20-28].

In our country many studies dealt in an outcome in infants of teenage mother. The literature that focus on the risk factors of teenage pregnancy are limited. This study was conceptualized to determine risk factors for teenage pregnancy and how to determine the association of teenage pregnancy on the following risk factors such as sociodemographic, family psychodynamics and psychosocial factors.

REVIEW OF RELATED LITERATURE

Shrestha et al, conducted a study with the use a questionnaire. The concluded that the incidence of teenage pregnancies is significantly higher in the lower social classes (52%) than in the higher social classes (26%). This study also found that Hindu teenagers are more likely to become pregnant ($p<0.001$) than Buddhist teenagers. Structural and social inequalities, poverty and gender all made young people extremely vulnerable to teenage pregnancy[22,26].

The likelihood of teenage pregnancy and childbearing seemed to be associated with the level of education[23]. However, very few studies have concentrated on education and teenage pregnancies. Sharma et al., in 2001 showed that 19% among teenage mothers were significantly less likely to have studied beyond primary school education compared to among the mothers who were in their twenties (6%)[21]. This needs to be interpreted with caution as the numbers reported are very low, however such differences were also noted by Shrestha in a retrospective study with a bigger sample size[25]. Early age at marriage is acceptable in South Asian culture, which seems to add the risk of teenage pregnancy[21]. Early age at marriage is also taken as a license or social expectation for a woman to enter into reproductive life and to become pregnant immediately after marriage. In rural Nepal, the mean age of marriage is 15.9 years. Some girls who married before the onset of menarche fell pregnant once they were fertile[25].

Low involvement of teenage girls in decision making also contributed to early pregnancy. Most adolescent marriages (80%) were arranged by parents without the girl"s consent[25]. A higher proportion of adolescent pregnant women (67%) were found to be part of an extended family, of which just over half (51%) claimed that the authority over conception remains with their husband in spite of the teenagers" desire to make their own decisions[21]. The study also noted that teenage pregnant women seem to be more likely to have had love marriage (against the wishes of parents/family). Consequently, this leads to negligence of family members towards care and guidance in teenage pregnancies. In addition, teenage girls are also less likely to visit health service clinics without their husband"s permission[28]. These family structures

and social norms have forced teenagers to give birth before they are emotionally or physically ready[26].

Another factors that may contribute to teenage pregnancy are the risk taking behavior, including drug, alcohol, tobacco use, delinquency, and sexual activity occurring among the same groups of teens. Teens who drink or use drugs often are more sexually active and less likely to use contraception when they have sex than teens who take fewer risks. This adolescent also tend to have more sexual partners, and often start having sex at younger ages. Nearly four in ten high school students report having experimented with marijuana at least once, and over one-third of 12th graders report they have used some type of illicit drug[20,21]. Approximately two-thirds of 9th graders report having tried alcohol at least once and one-quarter of all high school students say they drink heavily on occasion[20]. Teens 15 and older who use drugs are more likely to be sexually experienced than are those teens who do not use drugs - 72 percent of teens who use drugs have had sex, compared to 36 percent who have never used drugs[22]. Teens who have used marijuana are four times more likely to have been pregnant or to have gotten someone pregnant than teens who have never used marijuana[23]. More than one-third of sexually active teens and young adults 15 to 24 years of age report that alcohol or drug use has influenced them to do something sexual[24]. Nearly one-quarter of sexually active teens and young adults 15 to 24 years of age report that they have had sex without a condom because they were under the influence of alcohol or drugs. Forty three percent of teens and young adults say that they are concerned that they might do more sexually than they had planned because they are drinking or using drugs[24]. Girls who smoke or drink are even more susceptible. The prior use of alcohol and/or cigarettes increases the risk of early sexual experience by 80 percent[25]. Many teenage girls who use alcohol when they first have sex are too drunk to use birth control successfully[26]. Almost one-quarter of all high school students used alcohol or drugs prior to their last sexual experience. Non-Hispanic white and Hispanic teens are more likely than non-Hispanic black teens to report having used alcohol or drugs before their last sexual experience[20]. Seventh graders who report being sexually experienced are more likely than their sexually inexperienced peers to report having committed a theft, damaged property, or threatened a teacher[27].

Girls who experience menarche early are more likely to use alcohol, initiate alcohol and cigarette use earlier, use more substances at earlier ages, and be drunk more often[28-33]. Although a certain amount of substance use experimentation is considered normative during middle to late adolescence, early initiation of substance use and heavier use at early ages seem particularly problematic and lead to increased longterm negative outcomes including alcohol dependence[34,35,36,37].

Research suggests that alcohol use leads to an increased likelihood of sexual intercourse among adolescents, and a significant portion of female adolescents report

some alcohol use before intercourse[38,39]. A widely held theory known as the "disinhibition effect" posits that the disinhibiting effect of alcohol causes people to engage in riskier sexual behaviors than they would otherwise[40]. However, the disinhibition effect may lead to decreased condom use only when sex is unplanned or occurring for the first time[41]. In fact, unplanned sexual intercourse under the influence of alcohol or drugs has been found to uniquely relate to risky sexual behaviors, including inconsistent condom use[42]. The fact that younger girls are more likely to engage in unplanned sex, they are presumably at heightened risk for unprotected intercourse and pregnancy. In addition, younger girls are more likely to rely on birth control methods that are affected by alcohol use, in comparison to older females, who tend to use the birth control pill[43].

In nine of ten studies regarding consequences of teenage pregnancy found that preterm delivery, still birth, fetal distress, birth asphyxia, anaemia, low birth weight, pregnancy -induced hypertension (PIH) and spontaneous abortion were most frequently encountered complications during teenage pregnancy[44,46-49,51-53]. Apart from medical consequences, there are many adverse social consequences identified within this review. Lower access to higher education, high divorce rates, premature death of women, population growth, weak and unhealthy children and single motherhood are all negative consequence of teenage pregnancy[47,49,50,52].

Sharma et al.,[51] identified that the risk of pregnancy complications was 2.5 times higher among pregnant teenagers compared to mothers in their twenties. A significant number of teenage mothers had Vitamin A and iodine deficiency, which results in night blindness and formation of goiter[51,53]. A north India study has also shown that the prevalence of anaemia is high (46%) among teenage mothers, which occurs due to low intake of dietary iron[53]. In a Sri Lankan study the likelihood of PIH (13%) and pre-eclampsia (5%) was significantly higher ($p<0.001$ and $p=0.03$) among pregnant teenagers compared to the women in their twenties (3% and 1% respectively)[47]. Studies investigating the link between teenage pregnancy and still birth, showed an association 2 to 3% ($p<0.05$) compared to the mothers at 20 to 29 age years group[46,48,49]. There seem to be inconsistent evidence between birth weight and teenage pregnancy. The mean birth weight was found higher (2.81kg) among teenagers[51]; the high birth weight in a study could be because of the small sample size. However, another study showed that the incidence of low birth weight was statistically significant 34% ($p<0.0001$) among teenage mothers compared to the mothers in their twenties[48].

Two studies reported a higher preterm delivery among teenage mothers compared to older women. Shrestha reported 3% preterm delivery in teenage mothers compared to 1% in mature mothers[49]. Goonewardene et al., reported 19% incidence of preterm delivery among teenagers compared to 11% in older mothers, ($p = 0.06$)[47]. A small hospital-based study found that fetal distress

(6%) and birth asphyxia (2%) was commonly reported among pregnant teenagers[51]. There are conflicting findings regarding the link between spontaneous abortion and teenage pregnancy. Shrestha has reported that spontaneous abortion was similar 15 (3%) among teenage mothers and mothers in their twenties[49]. However, Ganatra et al., in 2002 noted that such likeliness is very low (2%) among teenage mothers and very high among matured mothers 166 (14%)[52].

SIGNIFICANCE of the STUDY

This study would contribute to the prevention of early teenage pregnancies by allowing health care professionals to analyze the root cause of teenage pregnancy wether it being lack of education, psychosocial or family psychodynamics. The result can be used in other health care facilities in educating teenagers on the consequence and avoidance of teenage pregnancies. This study would also help educate the Filipino teenagers about the adverse effect of teenage pregnancy, give them knowledge and insight about responsible parenthood and finally allow them to weigh the risk involved in both maternal and baby"s health.

GENERAL OBJECTIVES

To determine the risk factors for teenage pregnancy among Filipino adolescent girls seen in a Tertiary Government Hospital.

SPECIFIC OBJECTIVES

To determine the association of teenage pregnancy and the following risk factors:

a. Sociodemographic profile

b. Family Psychodynamics

c. Psychosocial Factors

MATERIALS AND METHODS

A. Study Design: Unmatched Hospital Based Case Control Study

A quantitative research approach was chosen for this study because it emphasizes objectivity and uses systematic procedures to measure human behavior by using formal structured instruments when collecting data from respondents. This approach has been used to provide hard objective facts about factors that contribute to teenage pregnancy that could be statistically analysed and interpreted. In this study an attempt was made to obtain information from pregnant and non pregnant teenagers.

The descriptive design was selected as it is concerned with gathering more information about the phenomenon studied. This research design was suitable to obtain relevant information and to describe and identify factors that contribute to teenage pregnancy.

B. Setting: Tertiary Government Hospital

C. Study Population

A **CASE** is defined as a female adolescent 13 to 19 years of age as per WHO criteria, who is pregnant at the time of the interview or had been pregnant for the first time during the previous two years.

A **CONTROL** is defined as a female adolescent who had never been pregnant at the time of interview admitted or consulting at this tertiary hospital for other medical illness.

MANAGEMENT and ANALYSIS

Data was encoded and tallied in SPSS version 10 for windows. Descriptive statistics were generated for all variables. Frequencies and percentages was computed for nominal data, mean ± SD were generated for numerical data.

The T test was used to compare two groups with numerical data (compares means). The Mann Whitney U test which is a non - parametric equivalent of T-test was used to compare median instead of means. The Chi-square test was used to compare/ associate nominal data. Fisher Exact test which is a modification of chi-square used to compare/associate nominal data in a 2x2 contingency table. Logistic Regression, a multivariate test was used to identify predictor of an outcome variable.

SAMPLE SIZE CALCULATION

At alpha = 0.05, Beta = 0.20, and assumed difference in the proportion of exposed and unexposed adolescents and teen age of 15% and an OR of 8.51 for early sexual based from a previous study (Adhikari, et al), at least 112 subjects per group is needed, early sexual debut (OR 8.51, 95% CI 1.12-64.90);10% exposed; 25% unexposed;

$$n = \frac{[z_\alpha \sqrt{2pq} + z_\beta \sqrt{P1Q1 + P2Q2}]^2}{(P1 - P2)^2}$$

Where:

n = is the number of subjects needed

P1 = proportion of pregnancy among adolescents = 60% = 0.6

Q1 = 1 - P1 = 1 - 0.6 = 0.4

P2 = proportion of pregnancy among adolescents = 25% = 0.25

Q2 = 1 - P2 = 1 - 0.25 = 0.75

p = (P1+P2)/2 =(0.6+0.25)/2 = 0.425

q = 1 - p = 1 - 0.425 = 0.575

Zα = 95% confidence level = 1.96

Zβ= 80% power of the study = 1.28

SUBJECT SELECTION and DATA COLLECTION

Pregnant/have been pregnant and non pregnant women were selected randomly from any teenage and adolescent consulting at the OPD and currently from January to April 2013

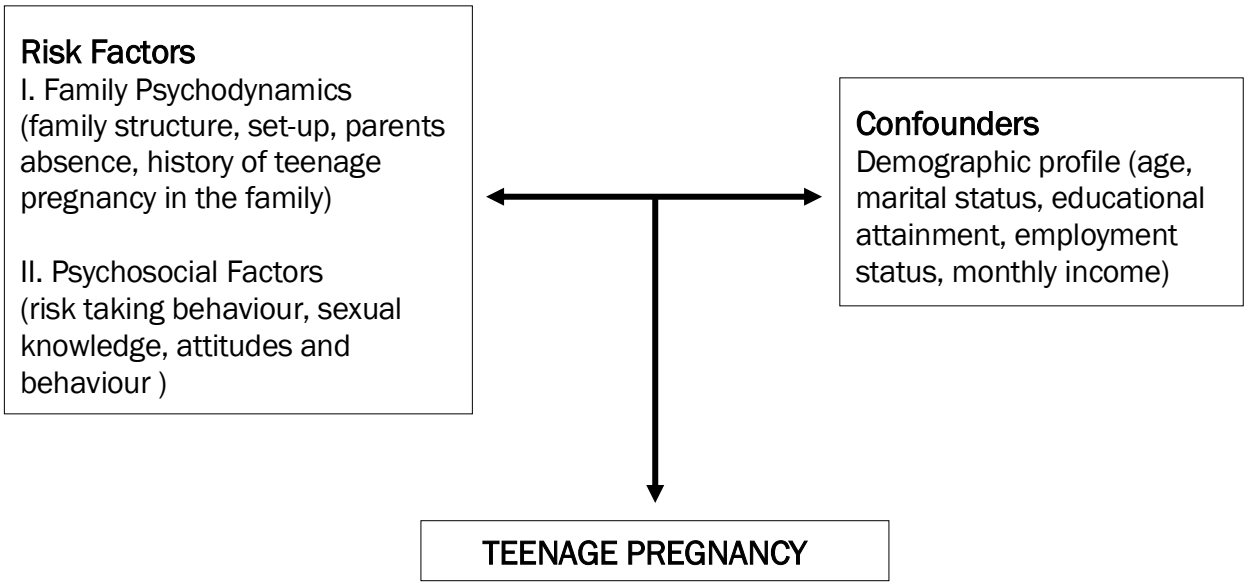
Data were collected through structured self-administered questionnaires (Appendix G). The questionnaires consisted of 30 questions that were divided into three domains namely, sociodemographic data, family psychodynamics and psychosocial factors that

contribute to teenage pregnancy. The statements in the questionnaires were constructed to obtain objective data from the respondents who had met the inclusion criteria.

CONCEPTUAL FRAMEWORK

Figure 1. Outline of the possible risk factors for teenage pregnancy. The risk factors were identified from results of previous studies on risk factors for teenage pregnancy and focus group discussion among teenage mother. The possible confounding factors in this study are demographic profile of the mother and index child.

Figure 1.Conceptual Framework showing the Risk Factors and Teenage Pregnancy



DESCRIPTION OF STUDY PROCEDURES

Preparation prior to conduct of study

The principal investigator wrote a letter to the Medical Director and Chairman of Obstetrics and Gynecology requesting for permission to conduct an interview among nulligravid teenage patients seen at the OPD (Appendix A). A formal letter with necessary documents was given to respective committees and chairman in the hospital for approval and appropriate action. Four research assistants were recruited by the principal investigator. They were oriented to the purpose of the study and were trained on how to conduct the interview.

Ethical Consideration

The protocol was submitted for review and approval of the Hospital Ethics Committee. A letter of request and permission to participate

(informed consent) were given to the subjects. The quality of the research was ensured by adhering to the highest possible standards of research through accountability and the ability to execute the research process.

Permission to sample the pregnant and non pregnant teenagers was obtained from the Out Patient Department. Each pregnant and non pregnant teenager was provided with sufficient and understandable information regarding her participation in the study before signing the consent form. A consent forms was signed by parents or guardians for minor between 13 to 17 years of age (Appendix B). Confidentiality and anonymity were ensured by protecting the participants‟ identity, privacy, selfworth and dignity by not indicating the subjects‟ names on the questionnaires. Refusal to participate in the research was respected.

Research Instrument

Data in this study were collected from direct interview of the patient itself through the use of a structured questionnaire (Appendix G). The questionnaire were composed of three domains which included sociodemographic status, family psychodynamics and psychosocial factors. Sociodemographic status contained patient's age, religion, marital status, educational attainment, employment status and estimated monthly income. The family psychodynamic portion included family structure, set-up, its environment and history of teenage pregnancy.

The psychosocial factors included exposure to risk taking behaviors such as smoking, drinking alcohol, use of illicit drugs, sexual knowledge, attitudes and behaviours, and history of sexual abuse if any.

The questionnaire contained 30 close-ended questions. Likert scale with variable points were devised appropriate for each questions. The questionnaire was pretested and validated to a group of 20 respondents and found to be reliable as shown by the Cronbachs Alpha of 0.65. Item total showed that the cronbachs alpha did not increased that much when individual question was deleted and analyzed for its reliability thus maintaining all the questionnaire in the question and finally used for data collection.

Pretesting and Validating Research Instruments

The questionnaire was pretested to a group of 20 respondents who consulted in the tertiary government hospital. Those 20 respondents were not included in actual conduct of the study. The pretesting of questionnaire helped the investigator to identify problems that encountered during the conduct of the actual interview. Each item were criticized for its clarity, ease of understanding and sensitivity. The questions was revised as necessary.

An approach to assess reliability involved re - interviewing and forming a second review of a sample of respondents then compared it to the response given on the first interview. The repeat interview was done by the same interviewer. This approach holds constant the effect of variability among

interviewer while measuring the consistency of the subjects recall results. Another approach used to check for consistency was by repeating the question in a slightly different manner at different points in the interview. The principal researcher obtained confirmatory information from sources and compare the rates of agreement. No formal test was done to measure test of agreement but validity was based on completeness of the answers in the questionnaire.

Language Translation

The questions were written in English and translated into the Filipino dialect by a Filipino teacher that made all respondents understood the question in a language which they are proficient in. The questionnaire was then translated back from Filipino to English. This process ensured the accuracy of translation.

OPERATIONAL DEFINITION OF VARIABLES

1. Primary outcome - teenage pregnancy

2. Risk Factors
   - 2.1 Family Structure
     - 2.1.1 Nuclear Family - consisting of parents and their still dependent children
     - 2.1.2 Single Parent Family - may result from the loss of spouse by death, divorce, separation or desertion
     - 2.1.3 Blended Family - includes step-parents and step-children
     - 2.1.4 Democratic - parents respect their child's decisions and ideas
     - 2.1.5 Authoritarian - unquestioned obedience conformity to parental guidance

3. Confounders - risk factors of the outcome and are associated with the exposure variable of interest. They are not in the intermediate pathway between the exposure and the outcome variables of interest
   - 3.1 Demographic Profile of the subject
     - 3.1.1 Family Income - combined income of the family in a month
     - 3.1.2 Educational Attainment - highest level of education attained by the subject
     - 3.1.3 Marital Status - marriage status of the subject

RESULTS

A total of 280 respondents were included in the study. One hundred forty pregnant/have been pregnant and 140 non pregnant teenage women.

Table 1 describes the comparison of the demographic character between the cases and controls. The results showed that there was a significant difference in the age of these women as shown by a p value of 0.01. Current age showed that the age of pregnant/have been pregnant teenage women is 17.62 ± 1.33, it was significantly higher compared with 17.20 ± 1.62 years for the group of teenage non-pregnant women. Significantly more proportion of pregnant/have been pregnant women

were Catholics (91.4%). Analysis of marital status showed that significantly more proportion of pregnant/have been pregnant women were either married (29 or 20.7%) or living-in (79 or 56.4%) while significantly more proportion of singles (78 or 55.7%) were found among adolescent non-pregnant women. Sixteen (11.4%) of adolescent pregnant/ have been pregnant women reached at least college level of education. There was no significant difference noted in the employment status as well as the monthly income between the two groups of teenage women as shown by all p values of >0.05.

Table 1. Demographic Characteristics of Pregnant and Non Pregnant Teenage Woman

Characteristics	Pregnant Teenage (n=140)	Non Pregnant Teenage (n=140)	P value
Age in years			
Mean ± SD	17.62 ± 1.33	17.20 ± 1.62	0.01 (S)
Religion			
INC	4 (2.9%)	9 (6.4%)	0.16 (NS)
Adventist	0	1 A(0.7%)	1.00 (NS)
Baptist	1 (0.7%)	3 (2.1%)	0.62 (NS)
Catholic	128 (91.4%)	115 (82.1%)	0.02 (S)
Christian	7 (5.0%)	9 (6.4%)	0.60 (NS)
Mormon	0	1 (0.7%)	1.00 (NS)
Muslim	0	1 (0.7%)	1.00 (NS)
Protestant	1	1 (0.7%)	1.00 (NS)
Marital Status			
Single	21 (15.0%)	78 (55.7%)	<0.000001 (S)
Single Parent	7 (5.0%)	5 (3.6%)	0.56 (NS)
Live in	79 (56.4%)	46 (32.9%)	<0.0001 (S)
Married	29 (20.7%)	8 (5.7%)	0.0002 (S)
Separated	4 (2.9%)	3 (2.1%)	1.00 (NS)
Educational Attainment			
None	3 (2.1%)	0	0.002 (S)*
Elementary Level	4 (2.9%)	5 (3.6%)	
Elementary Graduate	8 (5.7%)	8 (5.7%)	
HS Level	68 (48.6%)	43 (30.7%)	
HS Graduate	32 (22.9%)	37 (26.4%)	
College Level	16 (11.4%)	34 (24.3%)	
College Graduate	9 (6.4%)	7 (5.0%)	
Vocational	0	6 (4.3%)	
Employment Status			
Without	93 (66.4%)	102 (72.9%)	0.24 (NS)
With	47 (33.6%)	38 (27.1%)	
Monthly Income			
<P5,000	76 (54.3%)	64 (45.7%)	0.09 (NS)**
P5,000 - P10,000	44 (31.4%)	43 (30.7%)	
P10,001 - P30,000	11 (7.9%)	3 (2.1%)	
>P30,000	1 (0.7%)	1 (0.7%)	
No Answer	8 (5.7%)	29 (20.7%)	

**** college level and above vs Lower education*** *****between≤P10,00 and >P10,000***

Table 2 shows the comparison of the family psychodynamics between the two groups of teenage women. The results showed that there was no significant difference in the family psychodynamics of these women as shown by p values of >0.05, except for family set-up (p=0.02) and parental presence (p=0.02). Significantly more proportion of teenage pregnant/have been pregnant women have democratic family set-up (67.1%) and are away from both parents (6.4%) than the adolescent non-pregnant women.

Table 2. Comparison of Family Psychodynamics Between the Two Groups of Teenage

Family Structure/ Dynamic	Pregnant (n=140)	Non Pregnant Teenage (n=140)	P value
Family Class			
Nuclear	69 (49.3%)	73 (52.1%)	
Extended	57 (40.7%)	47 (33.6%)	0.50 (NS)
Single	6 (4.3%)	7 (5.0%)	
Blended	8 (5.7%)	13 (9.3%)	
Family Setup			
Democratic	94 (67.1%)	75 (53.6%)	0.02 (S)
Authoritarian	46 (32.9%)	65 (46.4%)	
Parental Presence			
Living with both parents	98 (70.0%)	99 (70.7%)	0.03 (S) (away from both parents only)
Living with only one parent	33 (23.6%)	39 (27.9%)	
Away from both parents	9 (6.4%)	2 (1.4%)	
Family history of teenage Pregnancy			
Yes	62 (44.3%)	58 (41.4%)	0.56 (NS)
No	63 (45.0%)	61 (43.6%)	
Do not know	15 (10.7%)	21 (15.0%)	
Parents gives support to whatever decisions			
Not at all	10 (7.1%)	8 (5.7%)	
Rarely	18 (12.9%)	19 (13.6%)	
Sometimes	51 (36.4%)	44 (31.4%)	0.82 (NS)
Often	32 (22.9%)	33 (23.6%)	
Always	29 (20.7%)	36 (25.7%)	
Experienced Family Feud			
Not at all	17 (12.1%)	10 (7.1%)	
Rarely	40 (28.6%)	36 (25.7%)	
Sometimes	59 (42.1%)	59 (42.1%)	0.20 (NS)
Often	20 (14.3%)	33 (23.6%)	
Always	4 (2.9%)	2 (1.4%)	
Think that negative family relationships affect emotion			
Not at all	17 (12.1%)	18 (12.9%)	
Rarely	22 (15.7%)	29 (20.7%)	
Sometimes	67 (47.9%)	53 (37.9%)	0.47 (NS)
Often	24 (17.1%)	31 (22.1%)	
Always	10 (7.1%)	9 (6.4%)	
Experience hardship in parental caring			
Not at all	42 (30.0%)	37 (26.4%)	
Rarely	29 (20.7%)	37 (26.4%)	0.68 (NS
Sometimes	44 (31.4%)	44 (31.4%)	
Often	19 (13.6%)	19 (13.6%)	
Always	6 (4.3%)	3 (2.1%)	

Tables 3 and 4 shows the comparison of the psychosocial factors between the two groups of teenage women. Thirty eight percent of teenage pregnant/have been pregnant women answered that they would feel rattled/ worried, but significantly more proportion of adolescent non-pregnant women (29.3%) answered that they will feel very rattled/ worried. Sixty percent of teenage pregnant/ have been pregnant women had current relationship in whom they are having sex, 100% of them had sexual intercourse before even at the age of 12. A lower proportion of these teenage pregnant/have been pregnant women had information on birth control (35.0%). It is interesting to note that only 21.0% of teenage pregnant have been pregnant have heard about ways to prevent early pregnancy. The adolescent non pregnant women (40.4%) verbalized that media was very influential for their use of contraceptives.

Table 3. Comparison of Psychosocial Factors Between the Pregnant and Non Pregnant Teenage Woman

Psychosocial Factors	Pregnant Teenage (n=140)	Non Pregnant Teenage (n=140)	P value
Smokers			
Not at all	102 (72.9%)	98 (70.0%)	
Rarely	11 (7.9%)	17 (12.1%)	
Sometimes	19 (13.6%)	16 (11.4%)	0.76 (NS)
Often	6 (4.3%)	6 (4.3%)	
Always	2 (1.4%)	3 (2.1%)	
Alcohol Drinker			
Not at all	67 (47.9%)	54 (38.6%)	
Rarely	35 (25.0%)	33 (23.6%)	
Sometimes	31 (22.1%)	45 (32.1%)	0.26 (NS)
Often	6 (4.3%)	8 (5.7%)	
Always	1 (0.7%)	0	
Use Prohibited Drugs			
Not at all	131 (93.6%)	133 (95.0%)	
Rarely	4 (2.9%)	4 (2.9%)	
Sometimes	4 (2.9%)	0	0.20 (NS)
Often	0	2 (1.4%)	
Always	1 (0.7%)	1 (0.7%)	
Do you think problem can be solve easily?			
Not at all	31 (22.1%)	26 (18.6%)	
Rarely	29 (20.7%)	20 (30.0%)	
Sometimes	59 (42.1%)	68 (48.6%)	0.47 (NS)
Often	16 (11.4%)	18 (12.9%)	
Always	5 (3.6%)	8 (5.7%)	
Think of the life today, how important to you to prevent pregnancy?			
Do not know	13 (9.3%)	10 (7.1%)	
Not that important	4 (2.9%)	8 (5.7%)	
Slightly important	19 (13.6%)	16 (11.4%)	0.59 (NS)
Quite Important?	26 (18.6%)	21 (15.0%)	
Very Important	78 (55.7%)	85 (60.7%)	

Psychosocial Factors	Pregnant Teenage (n=140)	Non Pregnant Teenage (n=140)	P value
Had you known your pregnant, what will you feel?			
Do not know	12 (8.6%)	9 (6.4%)	
Do not care	17 (12.1%)	13 (9.3%)	
Slightly rattled/worried	44 (31.4%)	27 (19.3%)	0.001 (S)
Rattled/worried	53 (37.9%)	50 (35.7%)	
Very rattled/worried	14 (10.0%)	41 (29.3%)	

Table 4. Comparison of Psychosocial Factors Between the Pregnant and Non Pregnant Teenage Women

Psychosocial Factors	Pregnant Teenage (n=140)	Non Pregnant Teenage (n=140)	P value
Are you a victim of sexual abuse?			
Not at all	127 (90.7%)	117 (83.6%)	
Rarely	7 (5.0%)	8 (5.7%)	
Sometimes	3 (2.1%)	8 (5.7%)	0.26 (NS)
Often	3 (2.1%)	5 (3.6%)	
Always	0	2 (1.4%)	
Do you have current relationship whom you are having sex with?			
No	23 (16.4%)	22 (15.7%)	
Do not know	6 (4.3%)	11 (7.9%)	0.005 (S)
Do not have current relationship	27 (19.3%)	49 (35.0%)	
With current relationship	84 (60.0%)	58 (41.4%)	
Did you have sexual intercourse before?			
No	0	55 (30.3%)	<0.0000001 (S)
Yes	140 (100%)	85 (60.7%)	
Have you been influenced by your friends to have sexual intercourse?			
No	109 (77.9%)	105 (75.0%)	0.57 (NS)
Yes	31 (22.1%)	35 (25.0%)	
Did you have any information on birth control or ways to prevent pregnancy?			
No	49 (35.0%)	34 (24.3%)	0.04 (S)
Yes	91 (65.0%)	106 (75.7%)	
Have you heard about ways on how to prevent early pregnancy			
No	29 (21.0%)	17 (12.6%)	0.06 (NS)
Yes	109 (79.0%)	118 (87.4%)	
Who influenced you to use contraceptives?			
Family	28 (21.5%)	16 (15.4%)	0.23 (NS)
Friends	36 (27.7%)	25 (24.0%)	0.52 (NS)
Doctors/Nurse	37 (28.5%)	21 (20.2%)	0.14 (NS)
Media	29 (22.3%)	42 (40.4%)	0.004 (S)

Psychosocial Factors	Pregnant Teenage (n=140)	Non Pregnant Teenage (n=140)	P value
What kind of media do you think can influence youths to have sexual intercourse at an early age?	(n=140)	(n=133)	
Print media	8 (5.7%)	5 (3.8%)	0.44 (NS)
Radio	6 (4.3%)	1 (0.8%)	0.12 (NS)
Internet	57 (40.7%)	51 (38.3%)	0.68 (NS)
TV	69 (49.3%)	76 (57.1%)	0.19 (NS)

Tables 5 describes the univariate analysis of the different variables which shows a p value of ≤0.25. Lower educational attainment or less than college level education was found to be associated with teenage pregnancy. The risk of teenage women who did not reach college level of education to get pregnant was twice the time than teenager who reached at least college level (OR=2.32; 95% CI = 1.33 - 4.05;p=0.003). Although the variables birthplace (rural), employment status, income of P10,000, and experiencing a family feud yielded a p value of >0.05, these are included in the table because the p value is <0.25, which may shows potential association with teenage pregnancy. A married or living-in status have five times higher risk for teen age pregnancy compared to having no partner (single or separated) (OR=5.38; 95% CI = 3.19 - 9.04; p=0.000). A democratic family set-up is also significantly associated with teenage pregnancy. The risk for teenage pregnancy was almost two times higher than an authoritarian family set-up (OR=1.77; 95 % CI = 1.09 - 2.87;p=0.02). Teenager living away to both parents also poses a risk to get pregnant. Results showed that there is an almost five times higher risk for teenage pregnancy among teenager who are away from both parents (OR=4.74; 95% CI = 1.01 - 22.34; p=0.04). There is also a significant association between having a current relationship in have with a sexual intercourse and teenage pregnancy as shown by the p value of 0.002. The risk for teenage pregnancy with a current relationship in whom she have sexual intercourse was two times higher than those who do not have current relationship. Previous sexual intercourse showed a highly significant association with teenage pregnancy (p=0.000). The risk for teenage pregnancy among those with previous sexual intercourse was almost ninety times higher than those without previous sexual intercourse (OR=89.94; 95% CI = 12.21 - 661.95; p=0.000). The result study showed there is a significant association between having no information on birth control or ways to prevent pregnancy and teenage pregnancy as proven by the p value of 0.05. The risk of teenager who do not have information on birth control was almost two times higher than those with information (OR=1.69; 95% CI = 1.00 - 2.82;p=0.05).

Table 5. Univariate Analysis of Risk Factors for Teenage Pregnancy

	OR	95% CI	P value
Lower Education (<College level)	2.32	1.33 - 4.05	0.003 (S)
Birthplace (Rural)	1.50	0.92 - 2.43	0.10 (NS)
Religion (Catholic)	2.17	1.03 - 4.56	0.04 (S)
Marital Status (Live-in or married)	5.38	3.19 - 9.04	0.000 (S)
Employment Status (with)	1.36	0.81 - 2.26	0.24 (NS)
Income (<P10,000)	2.68	0.84 - 8.54	0.09 (NS)
Democratic Family Set-up	1.77	1.09 - 2.87	0.02 (S)
Being away to both parents	4.74	1.01 - 22.34	0.04 (S)
Experienced Family Feud	0.56	0.24 - 1.26	0.16 (NS)
Have current relationship with sex	2.12	1.31 - 3.42	0.002 (S)
Previous Sexual relationships	89.94	12.22 - 661.95	0.000 (S)
Without information on birth control Or ways to prevent pregnancy	1.69	1.00 - 2.82	0.05 (S)

Tables 6 shows the multivariate analysis of the different variables under study. Of the different variables included in the analysis, only lower educational attainment, marital status and previous sexual intercourse showed to be a significant predictors of teenage pregnancy as proven by all p values <0.05. Educational attainment of less than college level education was found to be a significant predictor of teenage pregnancy and the risk of teenage women who did not reach college level of education to get pregnant was almost three times than teenager who reached at least college level (OR=2.86; 95% CI = 1.26 - 6.45;p=0.01). Marital status is also found to be a significant predictor of teenage pregnancy. A married or living-in status, has five times (OR=5.12; 95% CI = 2.30 - 11.43; p=0.000) higher risk for teen age pregnancy compared to having no partner (single or separated). Previous sexual intercourse showed a highly significant prediction with teenage pregnancy (p=0.000). The risk for teenage pregnancy among those with previous sexual intercourse was almost forty times higher than those without previous sexual intercourse (OR=39.71; 95% CI = 4.76 - 331.58; p=0.000).

Table 6. Multivariate Analysis of the Risk Factors for Teenage Pregnancy

	OR	95% CI	P value
Lower Education (<College level)	2.86	1.26 - 6.45	0.01 (S)
Birthplace (Rural)	1.20	0.62 - 2.35	0.57 (NS)
Religion (Catholic)	1.93	0.71 - 5.20	0.20 (NS)
Marital Status (Live-in or married)	5.12	2.30 - 11.43	0.000 (S)
Employment Status (with)	1.82	0.87 - 3.79	0.11 (NS)
Income (<P10,000)	3.30	0.86 - 12.62	0.08 (NS)
Democratic Family Set-up	1.36	0.67 - 2.73	0.39 (NS)

	OR	95% CI	P value
Being away to both parents	2.08	0.29 - 15.10	0.46 (NS)
Experienced Family Feud	0.50	0.22 - 1.08	0.08 (NS)
Have current relationship with sex	0.59	0.27 - 1.26	0.16 (NS)
Previous Sexual relationships	39.71	4.76 - 331.58	0.001 (S)
Without information on birth control Or ways to prevent pregnancy	1.66	0.78 - 3.50	0.18 (NS)

DISCUSSION

Teenage pregnancy is a public health concern both in developed and developing world. Globally 15 million women under the age of 20 give birth, representing up to one-fifth of all births.

Adolescent pregnancy prevention research and programs predominantly focus on factors controlled by the adolescent girl. However, the most important factors linked to early pregnancy in this study are low level of education especially those who reached high school level only, early marriage, democratic family set-up, being away to both parents, have current sexual relationships and those without information on birth control or on how to prevent pregnancy.

The likelihood of teenage pregnancy and childbearing seemed to be associated with the low level of education[47]. In this study majority of the subjects reached high school level (P value 0.002). The study of Sharma et al., showed that teenage mothers were significantly less likely to have studied beyond primary school education compared to mothers who were in their twenties.[51] Low monthly income and non-employment were significantly noted. This can be correlated in the study done by Bissell and Shrestha wherein teenage girls at higher risk for pregnancy were those with low educational, occupational attainment and low socioeconomic status[9,25].

Less than one-third of female adolescents who gave birth before age 18 completed high school. Additionally, for adolescent mothers experiencing a subsequent pregnancy within two years of their first delivery, the prospect of high school graduation is improbable[54]. Hofferth et al. found that adolescent childbearing was greatly associate with reduced chances of completing high school and attending college, thus leading the researchers to conclude that today's adolescent mothers who are unable to obtain some form of higher education are at a disadvantage[55].

There was a significant association between family psychodynamics and teenage pregnancy. In this study, significantly more proportion of pregnant teenage /have been pregnant women who have a democratic family (P value 0.02) and being away from both parents (P value (0.03). This finding was in contrast to the study involving of teenage girls in decision making that contributed to

early pregnancy. Most adolescent marriages (80%) were arranged by parents without the girl's consent[25]. A family, of which just over half (51%) claimed that the authority over conception remains with their husband[21] in spite of the teenagers' desire to make their own decisions[26]. Parental absence or being away to both parents are main indicator for early pregnancy. According to the current study, being away to both parents also poses a teenager to get pregnant. Results showed that there is an almost 5x higher risk for teenage pregnancy among teenage who are away from both parents (OR=4.74; 95% CI = 1.01 - 22.34). In a study of Velez-Pastrana, pregnancy risk increased only for adolescents who experienced absence of both parents (not for adolescents experiencing absence of just one parent). The protective factor for adolescent pregnancy might therefore depend more on maintaining some type of parental watch over adolescent girls at all times than on adhering to the traditional family mode (mother, father, and children)[57]. Family disruption and low levels of communication within the family are also shown to be risk factors along with poor educational indicators and low socioeconomic status[15,17-19].

In this study majority of the subjects both cases and controls has current sexual relationships comprising of 84% and 58% respectively. This is supported by Cooper et al. (2004) who found that amongst teenage girls interviewed in South Africa, 35% were teenagers aged 19 years of which 53% of the pregnancies had either been unplanned at 36% or unwanted at 17%[58]. In addition to that, a study by Morake revealed that the age of the first pregnancies - as a result of the first sexual intercourse - was experienced by teenagers between the age of 13 years and 16 years[59].

Many studies suggest that teenagers have basic knowledge about contraception; mostly related to information about condom use. However, their use was limited and unrelated to lowering teenage pregnancy rates. The studies were not able to explain why young people were inconsistent contraceptive users, even though they have relatively high level of contraceptive knowledge. Most respondents in this study had knowledge about the use of contraceptives and other ways of preventing unwanted pregnancy apart from total abstinence from sexual activity. The results revealed that majority of participants were knowledgeable about the use of contraceptives however they chose not to use it during sexual activity and others keep it as a secret. Other reasons for not utilizing the contraceptives were that teenagers were reluctant to take contraceptive precautions for fear of complications and parental detection, despite their knowledge about the importance of the use of those contraceptives. In a study done by Jejeebhoy et al., clearly notified that much of such knowledge remains superficial and ridden with myths, misperceptions and a sense of invulnerability[60]. In addition, gender power imbalance make risky behaviors acceptable, encourage secrecy and fear of disclosure, and inhibit negotiation among partners.

The findings by Ritcher et al, outlined that teenage pregnancies resulted from lack

of knowledge about contraception and many other misconceptions. It was indicated that injectable contraceptives cause weight gain and watery discharges, whilst contraceptive pills were only taken when they planed sexual intercourse or only after the engagement because it could prevent them from becoming pregnant when used in that way[61].

In a study by Mwaba, teenage girls expressed a preference for receiving the injectable contraceptive and stated that condoms were not their birth control method of choice. In contrast to this, majority of the respondents in this study preferred using oral contraceptive pills and condoms[62].

The study findings pointed out that majority of the respondents didn't use drugs, 3.5% did smoke, and 86% didn't drink alcohol whereas 14% drank alcohol. In support of the study findings of Van Eijk indicated that substance abuse was long recognized as one of the greatest health and social problems in South Africa which resulted in teenage pregnancies because teenagers engaged in sexual intercourse without making calculated decisions due to the influence of alcohol. Additionally it was outlined that drinking became more common as young people moved through their teenage years rising to 45% amongst 15 year olds and this was proven to be a cause of teenage pregnancies[63].

A study done by Julianna et,al., found out that early puberty is associated with earlier age of alcohol use and sexual initiation, which in turn predicted early pregnancy. Age at first sexual intercourse and age at first substance use significantly mediated the relation between age at menarche and age at first pregnancy. They concluded that girls who mature early are more likely to engage in early substance use and sexual intercourse, which in turn puts them at greater risk for adolescent pregnancy[64].

CONCLUSION

Sociodemographic factors, family psychodynamics and psychosocial factors were identified as risk factors for teenage pregnancy among adolescent girls seen in a tertiary government hospital.

Teenage girls who are away from their parents and those with democratic family has five times (OR = 4.74; 95% CI = 1.01-22.34; p = 0.004) and twice the risk (OR = 1.77; 95% CI = 1.09 - 2.87; p= 0.02) for teenage pregnancy respectively.

Teenage girls with past and current sexual relationship (OR = 89.94; 95% CI = 12.21 - 6.61; p = 0.0000). It was determined also that majority of teenage girls in this study did not have any information on birth controls or ways to prevent pregnancy having two times more prone to get pregnant (OR = 1.69; 95% CI = 1.00 - 2.82; p = 0.005).

In multivariate analysis it was shown that low level of educational attainment (OR = 2.86; 95% CI = 1.26 - 6.45; p = 0.01), those with live - in partner or married at a young age

(OR = 5.12; 95% CI = 2.30 - 11.43; p = 0.0000), and those with previous sexual intercourse (OR = 39.7; 95% CI = 4.76 - 333.58; p = 0.001) were found out to be significant predictors of teenage pregnancy.

LIMITATIONS OF THE STUDY

Since this study selected cases and controls based on pregnancy status some girls selected as controls may have, in fact, been cases (i.e., they could have had an abortion but chosen not to disclose the information to the interviewer). Selection may also have been skewed by the fact that girls who lived with their parents could not provide any data without the authorization of their parents, since the interviewer requested permission to conduct the interview from any parents who lived with their adolescent daughters. This aspect of the study design may have indirectly excluded the most vulnerable girls (e.g., those suffering from sexual abuse by family members) by inadvertently providing a means for families to prevent disclosure of sensitive information.

RECOMMENDATIONS

The factors driving teenage pregnancy are complex and varied and therefore require multifaceted intervention strategies. There should be implementation of proper strategies that will prevent teenagers from being pregnant. Health care providers need to design intervention programmes that empower family, school and society in general, so they can play an important role by providing all the necessary information regarding sex education. The family aspect involves parental education and information on sexual health issues, so their children can have a role model. Schools also need to be more focused on offering courses about gender issues, more training for teachers regarding sex education and therefore, society will be more open on sexual health issues.

As a healthcare provider we should also encourage all the females who is pregnant or got pregnant at an early age to continue and finish their school.

It is also suggested that the same study be conducted in other places or private hospitals in order to determine the other factors which contribute to teenage pregnancies amongst the teenagers who attend the clinics for antenatal care.

BIBLIOGRAPHY

1. Langille, D.B.,`Teenage pregnancy: trends, contributing factors and the physician's role` Canadian Medical Association, 2007 vol.176, no.11, pp 1601-1602.

2. UN. The right to reproductive and sexual health. United Nations Department of Public Information (DPI/1877); Available from: http://www.un.org/ecosocdev/geninfo/women/womrepro.htm, Accessed, 1997; 06/04/06.

3. Viegas OA., Wiknsosastro G., Sahagun GH., Chaturachinda K., Ratnam SS. Safe child birth needs more than medical services. World Health Forum. 1992; 13: 59-65.

4. Stone N., Ingham R., Simkhada P. Knowledge of sexual health issues among unmarried young people in Nepal. Asia-Pacific Population Journal. 2003; 18:33-54.

5. Mathur S., Mehta M., Malhotra A. Youth reproductive health in Nepal: is participation the answer? Engender Health, New York. Available from: http://catalog.icrw.org/docs/nepal_0104.pdf, Accessed 2004; 12/02/08.

6. Adhikari R. Early marriage and child bearing: risks and consequences. World Health Organization, Geneva; Available from: http://apps.who.int/reproductive health/publications/towards_adulthood/7.pdf , Accessed 2003; 10/11/08.

7. Mehra S., Agrawal D. Adolescent health determinants for pregnancy and child health outcomes among the urban poor. Indian Pediatrics. 2004;41:137-45.

8. Conde-Agudelo A, Belizan JM, Lammers C. Maternal-perinatal morbidity and mortality associated with adolescent pregnancy in Latin America: cross-sectional study. Am J Obstet Gynecol. 2005;192(2):342-9.

9. Bissell M. Socio-economic outcomes of teen pregnancy and parenthood: a review of the literature. Can J Human Sex 2000; 9 (3):191-204.

10. United Nations Population Fund. Giving girls today and tomorrow: breaking the circle of adolescent pregnancy. New York: UNFPA; 2007.

11. Fessler KB. Social outcomes of early child bearing: important considerations for the provision of clinical care. J Midwifery Women's Health. 2003;48(3):178-85.

12. Spear HJ, Lock S. Qualitative research on adolescent pregnancy: a descriptive review and analysis. J Pediatr Nurs. 2003;18(6):397-408.

13. De la Cuesta C. Taking love seriously: the context of adolescent pregnancy in Colombia. J Transcult Nurs. 2001;12(3): 180-92.

14. Pallitto CC, Murillo V. Childhood abuse as a risk factor for adolescent pregnancy in El Salvador. J Adolesc Health. 2008;42 (6):580-6.

15. Chedraui PA, Hidalgo LA, Chávez MJ, San Miguel G. Determinant factors in Ecuador related to pregnancy among adolescents aged 15 or less. J Perinat Med. 2004;32(4):337-41.

16. Eggleston E. Use of family planning at first sexual intercourse among young adults in Ecuador. J Biosoc Sci. 1998;30 (4):501-10.

17. Peres CA, Rutherford G, Borges G, Galano E, Hudes ES, Hearst N. Family structure and adolescent sexual behavior in a poor area of Sao Paulo, Brazil. J Adolesc Health. 2008; 42(2):177-83. Epub 2007 Dec 3.

18. Guijarro S, Naranjo J, Padilla M, Gutiérez R, Lammers C, Blum RW. Family risk factors associated with adolescent pregnancy: study of a group of adolescent girls and their families in Ecuador. J Adolesc Health. 1999;25(2): 166-72.

19. Peña R, Liljestrand J, Zelaya E, Persson LA. Fertility and infant mortality trends in Nicaragua 1964-1993. The role of women's education. J Epidemiol Community Health. 1999; 53(3):132-7.

20. Centers for Disease Control and Prevention, Youth Risk Behavior Surveillance - United States 2005, in Surveillance Summaries, MMWR. 2006.

21. Johnston, L.D., O'Malley, P.M., Bachman, J.G., & Schulenberg, J.E., Monitoring the Future national results on adolescent drug use: Overview of Key Findings, 2006. 2007, National Institute on Drug Abuse: Bethesda, MD.

22. The National Center on Addiction and Substance Abuse (CASA), Dangerous Liaisons: Substance Abuse and Sex, Analysis of YRBS data. The National Center on Addiction and Substance Abuse at Columbia University New York.1999

23. The National Center on Addiction and Substance Abuse (CASA), Substance Abuse and the American Adolescent: A Report by the Commission on Substance Abuse Among American Adolescents. The National Center on Addiction and Substance Abuse at Columbia University New York, NY.1997

24. Youth Knowledge and Attitudes on Sexual Health: A National Survey of Adolescents and Young Adults. in Dangerous Liaisons: Substance Abuse and Sexual Behavior. 2002.

25. Kandel, D.B., Early onset of adolescent sexual behavior and drug involvement. Journal of Marriage and Family, 1990. 52: p. 783-798.

26. Some Sobering Facts on Alcohol and Teen Pregnancy. The National Campaign to Prevent Teen Pregnancy: Washington, DC. 1998

27. Farrell, A.D., Danish, S.J., & Howard, C.W., Relationship Between Drug Abuse and Other Problem Behaviors in Urban Adolescents. Journal of Consulting and Clinical Psychology, 1992. 60(3): p. 705-712.

28. Dick DM, Rose RJ, Viken RJ, Kaprio J. Pubertal timing and substance use: associations between and within families across late adolescence. Dev Psychol. 2000;36:180–189

29. Aro H, Taipale V. The impact of timing of puberty on psychosomatic symptoms among fourteen-to sixteen-year-old Finnish girls. Child Dev. 1987;58:261–268

30. Wilson DM, Killen JD, Hayward C, et al. Timing and rate of sexual maturation and the onset of cigarette and alcohol use among teenage girls. Arch Pediatr Adolesc Med. 1994;148:789–795

31. Magnusson D, Stattin H, Allen VL. Differential maturation among girls and its relation to social adjustment: a longitudinal perspective. Reports from the Department of Psychology, University of Stockholm. Stockholm, Sweden: University of Stockholm; 1985:62

32. Prokopcakova A. Drug experimenting and pubertal maturation in girls. Stud Psychol (Bratisl). 1998;40:287–290

33. Ruiselova Z. Relationships with parents and teachers in connection with pubertal maturation timing in girls. Stud Psychol (Bratisl). 1998;40: 277–281

34. Baumrind D. The influence of parenting style on adolescent competence and substance use. J Early Adolesc. 1991;11: 56–95

35. Tschann JM, Adler NE, Irwin CE, et al. Initiation of substance use in early adolescence: the roles of pubertal timing and emotional distress. Health Psychol. 1994;13:326–333

36. Chassin L, Flora DB, King KM. Trajectories of alcohol and drug use and dependence from adolescence to adulthood: the effects of familial alcoholism and personality. J Abnorm Psychol. 2004;113:483–498

37. Chassin L, Presson CC, Sherman SJ, Edwards DA. The natural history of cigarette smoking: predicting young-adult smoking outcomes from smoking patterns. Health Psychol. 1990;9:701–716

38. Strunin L, Hingson R. Alcohol, drugs, and adolescent sexual behavior. Int J Addict. 1992;27:129–146

39. Fortenberry JD. Adolescent substance use and sexually transmitted diseases risk: a review. J Adolesc Health. 1995;16:304–308

40. Kellogg ND, Hoffman TJ, Taylor ER. Early sexual experiences among pregnant and parenting adolescents. Adolescence. 1999;34:293–303

41. Halpern-Felsher BL, Millstein SG, Ellen JM. Relationship of alcohol use and risky sexual behavior: a review and analysis of findings. J Adolesc Health. 1996;19:331–336

42. Poulin C, Graham L. The association between substance use, unplanned sexual intercourse and other sexual behaviors among adolescent students. Addiction. 2001;96:607 –621

43. Moore KA, Miller BC, Glei D, Morrison DR. Adolescent Sex, Contraception, and Childbearing: A Review of Recent Research. Washington, DC: Child Trends 1995

44. Brennan L., McDonald J., Shlomowitz R. Teenage births and final adult height of mothers in India. Journal of Biosocial Science. 2005;37: 185-191.

45. Sharma A., Verma K., Khatri S., Kannan A. Determinants of pregnancy in adolescents in Nepal. Indian Journal of Pediatrics. 2002;69: 19-22.

46. Khandait D., Ambadekar N., Zodpey S., Vasudeo N. Maternal age as a risk factor for stillbirth. Indian Journal of Public Health. 2000;44: 28-30.

47. Goonewardena I., Deeyagaha Waduge R. Adverse effects of teenage pregnancy. Ceylon Medical Journal. 2005;50:116-120.

48. Weerasekera D. Adolescent pregnancies - is the outcome different? Ceylon Medical Journal.1997;42:16-17.

49. Shrestha S. Socio-cultural factors influencing adolescent pregnancy in rural Nepal. International Journal of Adolescent Medicine & Health. 2002;14:101-109.

50. Rashid S. Emerging changes in reproductive behaviour among married adolescent girls in an urban slum in Dhaka, Bangladesh. Reproductive Health Matters.2006; 14: 151-159.

51. Sharma A., Verma K., Khatri S. Kannan A. Pregnancy in adolescents: a study of risks and outcome in Eastern Nepal. Indian Pediatrics.2001;38: 1405-1409.

52. Ganatra B., Hirve S. Induced abortions among adolescent women in rural Maharashtra, India. Reproductive Health Matters.2002;10:76-85.

53. Pathak P., Singh P., Kapil U., Raghuvanshi R. Prevalence of iron, vitamin A, and iodine deficiencies amongst adolescent pregnant mothers. Indian Journal of Pediatrics. 2003; 70: 299-301.

54. Kreinin, T. Keep kids from making babies. NEA Today,1998; 17, 25.

55. Hofferth, S. L., Reid, L., & Mott, F. L. The effects of early childbearing on schooling over time. Family Planning Perspectives, 2001; 33, 259-267.

56. Ellis BJ, Bates JE, Dodge KA, Fergusson DM, Horwood LJ, Pettit GS, et al. Does father absence place daughters at special risk for early sexual activity and teenage pregnancy? Child Dev. 2003;74(3):801-21.

57. Vélez-Pastrana MC, González-Rodríguez RA, Borges-Hernández A. Family functionning and early onset of sexual intercourse in Latino adolescents. Adolescence. 2005;40 (160):777-91.

58. Cooper, D., Morroni, C., Orner, P., Moodley, J., Harries, J., Cullingworth, L. & Hoffman, M., 2004, 'Ten years of Democracy in South Africa: Documenting Transformation in Reproductive Health Policy and Status', Reproductive Health Matters Journal 1 (24), 70–85.

59. Morake, A., Factors associated with Teenage Pregnancy in Limpopo Province. Government Printers, Polokwane. 2011

60. Jejeebhoy SJ., Sebastian MP. Actions that protect: Promoting sexual and reproductive health and choice among young people in India. Population Council. Available from:http://www.popcouncil. org/ pdfs/wp/seasia/seawp18.pdf,Accessed, 2003; 04/06/09.

61. Ritcher, M.S. & Mlambo, G.T., 'Perceptions of rural teenagers on teenage pregnancy', Health SA Gesond- heid 10(2), 2005; 61–69.

62. Mwaba, K., 'Perceptions of teenage pregnancy among South African adolescents', Health SA Gesondheid5(3), 2000; 30–35.

63. Van Eijk, R.T., Factors contributing to teenage pregnancies in Rarotonga, United Nations Population Fund (UNFPA), Avarua., 2007

64. Julianna Deardorff, Nancy A. Gonzales, F. Scott Christopher, Mark W. Roosa and Roger E. Millsap, Pediatrics 2005;116; 1451, DOI: 10.1542/peds.2005- 0542.

APPENDIX A

Letter to Hospital Director

Angeles T. De Leon, MD, DPBA, MHSA
Medical Center Chief
Quirino Memorial Medical Center
Project 4, Quezon City

Greetings:

Respectfully requesting authority to distribute questionnaires to pregnant and non pregnant teenagers at the Out Patient Department of Obstetrics and Gynecology and Pediatrics upon prior request from stated subjects.

This is to facilitate my research entitled "A Hospital Based Case Control Study Of Risk factors for Teenage Pregnancy in a Tertiary Government Hospital."

Your favourable response would be greatly appreciated.

Thank you and more power.

Very Truly Yours,

Primary Investigator
Medical Officer III

Noted By:
Research Adviser

APPENDIX B

Letter to Parents

To Our Dear Patients:

Greetings:

I am a resident of Quirino Memorial Medical Center , I would like to ask your permission and help this endeavor by answering the following questionnaire as completely and honestly as possible. Rest assured that your answers would be kept confidential.

This research is being undertaken to help the health administrators and local government officials to come up with the best and practical way of pregnancy prevention strategies of teenagers.

Thank you and God bless.

Primary Investigator
Medical Officer

APPENDIX C

Letter of Agreement

I voluntarily agree to participate in the study being conducted by the primary investigators entitled "A Hospital Based Case Control Study On Risk factors for Teenage Pregnancy in a Tertiary Government Hospital." I freely and honestly answer the questionnaires and other information.

I understand that there are no special risks involved in being a participant. Although I will not benefit individually, it can help the health administrators and local government officials to come up with the best and practical way of pregnancy prevention strategies of teenagers.

---------- ----------

Participants Printed Name Witnessed by

Signature

Date

APPENDIX D

Liham sa Pasyente

Sa Mga Pasyente:

Mabuhay!

Ako po si Dr. Marvin P. Landicho, isang residente sa Departamento Ng Pediatrics ng Quirino Memorial Medical Center ay kasalukuyang gumagawa ng pananaliksik tungkol sa dahilan ng maagang pagbubuntis ng mag tinedyer.

Nais ko po sanang hingin ang inyong tulong at pahintulot sa pananaliksik na ito sa pamamagitan ng maingat na pagsagot sa mga sumusunod na katanungan. Lahat po ng mga kasagutang malilikom mula sa inyo ay kompidensyal.

Ang pananaliksik na ito ay isinasagawa upang makatulong sa mga nangangasiwa ng kalusugan at mga lokal na opisyal n gating gobyerno sa hangaring makapagbigay at prakitakal na paraan kung paano maiiwasan ang maagang pagbubuntis ng mga tinedyer.

Maraming salamat at nawa ang pagpapala ng Diyos ay mapasaating lahat.

Primary Investigator

QMMC

APPENDIX E

Liham ng Pagsang-ayon

Ako ay nagbibigay no boluntaryong pahintulot na sumali sa ginagawang pananaliksik ni Primary Investigator na pinamagatang "A Hospital Based Case Control Study Of Risk factors for Teenage Pregnancy in a Tertiary Government Hospital." Kusang loob buong tapat kung sasagutin ang mga katanungan at ibang impormasyon.

Bilang kalahok, nauunawaan ko na walang kapahamakan na maaring idulot sa akin. Kahit wala na akong pansariling makikinabangan, ito naman ay makaktulong sa mga nangangasiwa ng kalusugan at mga lokal na opisyal n gating gobyerno na makakapagbigay ng mabisa at praktikal na pamamaraan kung paano maiiwasan ang maagang pagbubuntis ng mga tinedyer.

---------- ----------

Pangalan ng Kalahok Saksi

Lagda

Petsa

APPENDIX F

Consent Form for Interview

I have been informed that Dr. Marvin P. Landicho, a resident of Quirino Memorial Medical Center, Department of Pediatrics is conducting a study entitled "A Hospital Based Case Control Study of Risk Factors for Teenage Pregnancy Seen in a Tertiary Government Hospital". The objective of this study is to determine risk factors for teenage pregnancy among Filipino Adolescent Girls seen in a Government Tertiary Hospital.

I voluntarily agree to participate in this study, to be interviewed for approximately 10 minutes concerning data about my present condition as well as other information about my family.

I understand that my participation is voluntary and that I may refuse any questions or withdraw my consent to participate at any time without affecting the health care I receive. I understand that no special risk is involved in being a participant , and even though I will not benefit individually.

I understand that the information elicited from me will be treated in a confidential manner and will not be identified personally in the reporting of the results.

I understand that I may ask any question about this study anytime. If I have further questions, I may contact the Principal Investigator at Telephone number 4212250, Quirino Memorial Medical Center, Project 4, Quezon City.

_____ _____

Participant printed name and signature Interviewer's name and signature

Date:_____

APPENDIX G Questionnaire Risk Factors for Teenage Pregnancy Questionnaire Abstract Form	
Identification Number	
Study Code	
A - Case B - Control	
Date of Interview:	
Interviewer	
Age:	
Birthplace:	
Religion:	
Contact Number:	
Obstetric Score Gravidity: Parity:	
Status	
01 - Single 02 - Single Parent 03 - Live-in 04 - Married 05 - Widower 06 - Separated	
Educational Attainment	
01 - No formal Schooling 02 - Elementary Grade 03 - Elementary Graduate 04 - High School Level 05 - High School Graduate 06 - College Level 07 - Vocational	
Employment Status	
01 - Unemployed 02 - Employed	
Estimated Monthly Income	
01 - less than P5,000 02 - P5,000 to less than P10,000 03 - P10,001 to less than P30,000 04 - P30,000 and above	

I RISK FACTORS	
FAMILY PSYCHODYNAMICS	
A. Family Structure	
1 - Nuclear 2 - Extended 3 - Single-Parent 4 - Blended	
B. Family Set-Up	
1 - Democratic 2 - Authoritarian	
C. Parent's Availability	
1 - Both Parents 2 - Only one parent	
D. Family history of teenage pregnancy	
1 - Yes 2 - No 3 - Don't know	
E. Do your parents give you adequate support regarding decisions and mistakes	
0 - Never 1 - Rarely 2 - Sometimes 3 - Often 4 - Always	
F. Do you experience conflict between family members?	
0 - Never 1 - Rarely 2 - Sometimes 3 - Often 4 - Always	
G. Do you think negative family interaction affects you emotionally	
0 - Never 1 - Rarely 2 - Sometimes 3 - Often 4 - Always	
H. Do you experience poor guidance?	
0 - Never 1 - Rarely 2 - Sometimes 3 - Often 4 - Always	

PSYCHOSOCIAL FACTORS	
A. Do you smoke?	
0 - Never 1 - Rarely 2 - Sometimes 3 - Often 4 - Always	
B. Do you drink alcoholic beverage?	
0 - Never 1 - Rarely 2 - Sometimes 3 - Often 4 - Always	
C. Do you use illegal drugs	
0 - Never 1 - Rarely 2 - Sometimes 3 - Often 4 - Always	
D. Do you think you can solve problems easily?	
0 - Never 1 - Rarely 2 - Sometimes 3 - Often 4 - Always	
E. Thinking about your life right now, how important is it to you to avoid becoming pregnant?	
0 - Don't know 1 - Not at all important 2 - A little important 3 - Somewhat important 4 - Very important	
F. If you found out today that you were pregnant, how would you feel?	
0 - Don't know 1 - Wouldn't care 2 - A little pleased 3 - Upset 4 - Very upset	
G. Are you a victim of sexual abuse	
0 - Never 1 - Rarely 2 - Sometimes 3 - Often 4 - Always	

H. Are you currently in a relationship with whom you are having sex?	
0 - Refused 1 - Don't know 2 - No current partner 3 - Has current partner	
I. Have you had sexual intercourse before?	
1 - No 2 - Yes	If yes, at what age? : _____
J. Does peer pressure influences you to have sex?	
1 - No 2 - Yes	
K. Have you ever gotten information about birth control or pregnancy prevention?	
1 - No 2 - Yes	If yes, from where or when? : _____
L. Have you ever heard of any methods of preventing pregnancy?	
1 - No 2 - Yes	If yes, what type of contraceptive? : _____
M. Who influence you to use contraceptives?	
1 - Family 2 - Friends 3 - Doctors/Nurse 4 - Media	Others: _____
N. What form of media do you think influences teens to have sex at an early age	
1 - Print Media 2 - Radio 3 - Internet 4 - Television	

Risk Factors for Teenage Pregnancy Questionnaire Abstract Form	
Identification Number	
Study Code	
A - Case B - Control	
Date of Interview:	
Interviewer	
Age:	
Birthplace:	
Religion:	
Contact Number:	
Obstetric Score Gravidity: Parity:	
Kasalukuyang katayuan	
01 - Walang asawa 02 - Solong Magulang 03 - May kinakasama 04 - Kasal 05 - Byudo/Byuda 06 - Hiwalay	
Pinakamataas ng antas ng edukasyon	
01 - Hindi nakapag-aral 02 - Elementarya 03 - Nagtapos ng Elementarya 04 - High School 05 - Nakapagtapos ng High School 06 - Kolehiyo 07 - Nakapagtapos ng Kolehiyo 08 - Vocational	
Katayuan sa pagtatrabaho	
01 - Walang trabaho 02 - May trabaho	
Tinatayang buwanang kita	
01 - Mas mababa sa P5,000 02 - P5,000 hanggang P10,000 03 - P10,000 hanggang P30,000 04 - P30,000 at pataas	

I RISK FACTORS	
FAMILY PSYCHODYNAMICS	
A. Klase ng pamilya	
1 - Nuclear (magulang at mga anak) 2 - Extended (magulang, anak at mga kamag-anak) 3 - Single-Parent 4 - Blended (magulang, at mga anak sa dating pamilya)	
B. Family Set-Up	
1 - Democratic 2 - Authoritarian	
C. Presensiya ng Magulang	
1 - Parehong magulang 2 - Isang magulang lang	
D. Kasaysayan sa pamilya ng maagang pagbubuntis	
1 - Oo 2 - Wala 3 - Hindi alam	
E. Ang iyong mga magulang ba ay nagbibigay ng sapat na suporta ukol sa iyong pagkakamali at mga desisyon?	
0 - Hindi kailanman 1 - Bihira 2 - Minsan 3 - Madalas 4 - Palagi	
F. Ikaw ba ay nakararanas ng alitan sa pagitan ng bawat miyembro ng pamilya?	
0 - Hindi kailanman 1 - Bihira 2 - Minsan 3 - Madalas 4 - Palagi	
G. Sa tingin mo, ang negatibong pakikipag-ugnayan ba sa iyong pamilya ay nakakaapekto sa iyong emosyon?	
0 - Hindi kailanman 1 - Bihira 2 - Minsan 3 - Madalas 4 - Palagi	
H. Ikaw ba ay nakararanas ng hirap sa paggabay ng iyong magulang?	
0 - Hindi kailanman 1 - Bihira 2 - Minsan 3 - Madalas 4 - Palagi	

II PSYCHOSOCIAL FACTORS	
A. Ikaw ba ay naninigarilyo?	
0 - Hindi kailanman 1 - Bihira 2 - Minsan 3 - Madalas 4 - Palagi	
B. Ikaw ba ay umiinom ng alak?	
0 - Hindi kailanman 1 - Bihira 2 - Minsan 3 - Madalas 4 - Palagi	
C. Ikaw ba ay gumagamit ng ipinagbabawal na gamot?	
0 - Hindi kailanman 1 - Bihira 2 - Minsan 3 - Madalas 4 - Palagi	
D. Sa tingin mo ba, kaya mong iresolba ang mga problema ng ganung kadali?	
0 - Hindi kailanman 1 - Bihira 2 - Minsan 3 - Madalas 4 - Palagi	
E. Isipin mo ang buhay mo sa ngayon, gaano kahalaga sa iyo ang pagiwas sa pagbubuntis?	
0 - Hindi alam 1 - Hindi mahalaga 2 - Mahalaga ng kaunti 3 - Medyo mahalaga 4 - Napakahalaga	
F. Kung nalaman mong buntis ka ngayon, ano ang iyong mararamdaman?	
0 - Hindi alam 1—Hindi alintana 2 - Kaunting kaguluhan 3 - Maguguluhan 4 - Sobrang maguguluhan	
G. Ikaw ba ay biktima ng pangaabusong sekswal?	
0 - Hindi kailanman 1 - Bihira 2 - Minsan 3 - Madalas 4 - Palagi	

H. Ikaw ba ay kasalukuyang may karelasyon kung saan ikaw ay nakikipagtalik rin??	
0 - Itanggi 1 - Hindi Alam 2 - Walang kasalukuyang karelasyon 3 - Kasalukuyang may karelasyon	
I. Ikaw ba ay nakipagtalik na dati?	
1 - Hindi 2 - Oo	Kung oo, anong edad? : _____
J. Naimpluwensiyahan ka ba ng mga kaibigan mo na makipagtalik?	
1 - Hindi 2 - Oo	
K. Nagkaroon ka ba ng impormasyon tungkol sa birth control o kung paano maiiwasan ang maagang pagbubuntis?	
1 - Hindi 2 - Oo	Kung oo, Saan at kanino? : _____
L. Nakarinig ka na ba ng mga paraan kung paano maiiwasan ang maagang pagbubuntis?	
1 - Hindi 2 - Oo	Kung oo, ano klase ng contraceptive? : _____
M. Sino nakaimpluwensiya sa iyo ng gumamit ng contraceptives?	
1 - Pamilya 2 - Kaibigan 3 - Doctors/Nurse 4 - Media	Iba pa: _____
N. Anong uri ng media sa tingin mo ang maaring makaimpluwensiya sa mga kabataan na makipagtalik sa napakaagang edad?	
1 - Print Media 2 - Radyo 3 - Internet 4 - Television	Iba pa: _____

FOLIC ACID SUPPLEMENTATION IN THE TREATMENT OF ACUTE WATERY DIARRHEA IN CHILDREN 6 MONTHS TO 36 MONTHS OF AGE: A RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED CLINICAL TRIAL

Thelma C. Martinez-Lee, M.D.
Principal Author

Michael M. Resurreccion, M.D.
Co-Author

Quirino Memorial Medical Center
Institutional Affiliation

OBJECTIVE: To determine the efficacy and safety of folic acid supplementation among pediatric patients 6 months to 36 months old with acute, non-bloody diarrhea in Quirino Memorial Medical Center.

STUDY DESIGN: randomized, double- blind placebo-controlled clinical trial

SSETTING: Pediatric Ward of a Tertiary Government Hospital.

PARTICIPANTS: Seventy two subjects aged 6 month to 36 months old with acute non bloody diarrhea of six days duration or less, with some or moderate signs of dehydration based on WHO-CDD protocol.

INTERVENTION: Subjects were randomized into two treatment groups: Group 1 (Folic Acid Group) and Group 2 (Placebo Group)

OUTCOME MEASURES: Efficacy of the folic acid was measured in terms of stool characteristics, frequency, volume and duration

RESULTS: A total of 72 diarrheal cases ages 6 months – 36 months were enrolled to the study. The two groups were essentially similar in terms of age, sex and degree of dehydration. Mean age was 11.3 months for Group 1 and 13 months for Group 2. The character of stool was described as either liquid, semi-formed/semi-liquid, and formed stool. The stools significantly differed in the

two groups by Day 2, 75% of subjects in Group 1 showed semi-formed stool, and 33% in Group 2 (P value – 0.0009). By Day 3, 53% of subjects in Group 1 had formed stools , and only 11% in Group 2. Among the subjects not discharged at days 3 and 4, the proportion of those with formed stools was significantly higher in Group 1 than in Group 2. The volume of stools measured in grams was similar for Day 1 in both groups, but at days 2-3, the volume of stool was significantly lower in Group 1 than in Group 2 (P value 0.0000). It showed that there was a significantly higher proportion and percentage (cumulative) of subjects discharged starting day 3, in Group 1 than in Group 2. By day 5 , 97% of patient in group 1 was discharged while only 75% in group 2. The length of hospital stay was 2.3 days in Group 1 and 3.6 days in Group 2 (P-value 0.0000).

CONCLUSION: Folic acid supplementation to the management of acute diarrhea enabled majority of the subjects in this study to have earlier formed stools, reduce volume of stool earlier and reduce frequency of stooling, resulting in early discharge and shorter hospital stay.

KEYWORDS: acute diarrhea, bloody diarrhea, folic acid, supplemental treatment

INTRODUCTION

Diarrhea remains a leading cause of morbidity and mortality among children less than five years of age around the world.[1] In the year 2000, diarrheal diseases claimed an estimated 1.4 to 2.5 million lives. The incidence and the risk of mortality from diarrheal diseases are greatest among children younger than 1 year of age. The morbidity from diarrhea remained relatively constant during the past two decades, with each child under 5 years of age experiencing an average of three episodes per year. Other direct consequences of diarrhea among children in resource limited countries include malnutrition, diminished growth, and impaired cognitive development.[2]

In the Philippines, diarrhea is one of the ten leading causes of death among children. It's prevalence has not improved in the last five years. In 2003, the National Demographic and Health Survey (NDHS) reported that 11% of the children under five years of age had diarrhea, this figure indicated an increased of 57% from 7% level in the 1998 NDHS data.[3] A slight decreased of 9% was reported in the 2008 NDHS.[4] The 2006 Department of Health Field Service Information System reported that acute watery diarrhea is the second among the ten leading causes of morbidity with the rate of 707.7 per 100,000 population of children under five years of age. Death due to acute diarrhea is usually due to severe dehydration which can be prevented with proper management.[5]

During the past three decades, several factors were noted to have improved the mortality rate of diarrhea, such factors include: widespread distribution and use of oral rehydration solutions (ORS), improved rates of breastfeeding, improved nutrition, better sanitation and hygiene, and increased coverage of measles immunization.[2]

Over the years, supplementation and drugs used for diarrhea were instituted like zinc, multivitamins, minerals, antimotility, and antisecretory agents.[2] Oral rehydration solution (ORS) treatment had reduced significantly the incidence of mortality and morbidity caused by diarrhea but ORS does not shorten the duration, does not change the consistency of stool, and it does not normalize gastrointestinal flora.[6]

The current management of acute diarrhea in infants and children focuses on oral rehydration therapy for the correction of dehydration and appropriate feeding during and after diarrhea.[7]

A randomized controlled trial done in the Philipines by Sanidad R.,MD compared the tolerability between flavored ORS vs unflavored ORS in children. It was found out that unflavored ORS was better tolerated than the flavored ORS preparation among children four months to five years with acute diarrhea having no or some dehydration (P-value 0.05).8

Several studies with zinc as a supplement in the control of diarrheal diseases

were done. A study with zinc along with selected vitamins was done in India which resulted in clinically important reductions in the duration and severity of diarrhea among pre-school age (P-value 0.02).[9] A collaborative study of 5 countries (Brazil, Ethiopia, Egypt, India and the Philippines) was done in 2005. The used of 20 mg zinc tablet dissolved in 5ml water or breastmilk given once daily for 14 days for the treatment of childhood diarrhea resulted in a reduction in the used of other medications without affecting the use of oral rehydration solution (P-value .04).[10]

A study done by Almera-Cirilos, MD at San Juan de Dios Hospital in 2004 with 120 patients 6 months to 36 months old with Acute Diarrhea (P-value .019)[11] and a study by Teodoro-Serillo N.,et al with 150 patients 6 -48 months in 2006 in a Tertiary Government Hospital and Provincial Hospital (P-value 0.000674)[12] showed that administration of zinc had reduced the frequency and consistency of stools in children with acute diarrhea. Zinc was proven to be tolerable and had no side effects[11].

The effect of Vitamin A supplementation on duration of diarrhea was evaluated by Dewan V, et al in India which showed that vitamin A supplementation does not significantly reduced the duration of diarrheal episode. However, this study concluded that children with pre existing vitamin A deficiency particularly those who have associated malnutrition may have beneficial effect (P-value 0.025).[13]

A comparative clinical efficay of Saccharomyces boulardii and yogurt fluid in acute non-bloody Diarrhea in children was done in Turkey. Although, the overall duration of the diarrhea in both groups was not different, normalization of stool composition and frequency was more rapid in the group given Saccharomyces boulardii (P-value <.05).[6]

Probiotic has also been proven to shorten the duration of acute diarrheal illnesses in children less than five years old by approximately one day (P-value <.001)[13] as shown in a meta analysis done by Huang JS in Massachusetts, USA .[14]

Recently, folic acid supplementation in acute nonbloody diarrhea is the subject of several studies. Haffejee in 1988 did a preliminary trial on folic acid supplementation among infants 6 months to 36 months. The study showed favorable results.[15] In 1998, a double blind, randomized controlled trial negated the positive results observed in the Haffejee study.[7] A local study done by Valenzuela and Santos in 2003, concluded that folic acid supplementation is beneficial to patients 6 months to 5 years suffering from acute nonbloody diarrhea (P-value< 0.00001).[16]

The early studies done on folic acid in diarrhea had been controversial. This was followed by a unpublished local study in a private hospital in patients 6 months to 5 years with acute non-bloody diarrhea with no or some signs of dehydration which showed a

good result (P-value < 0.000001).[16] On the other hand, this study was done in a tertiary hospital in 6 months to 36 months old patient with acute watery diarrhea with mild to moderate dehydration.

The objective of this study is to determine the efficacy and safety of folic acid supplementation among pediatric patients 6 months to 36 months old with acute non-bloody diarrhea admitted in a Tertiary Government Hospital. It further aims to compare the effects of folic acid supplementation versus placebo as to: duration of diarrhea; frequency of stool passage; volume and character of stools and to determine the adverse effect of folic acid supplement.

METHODOLOGY

STUDY DESIGN

This is a Randomized, Double-Blind Placebo-Controlled Clinical Trial.

SETTING

This study was conducted at the Pediatric Ward of a Tertiary Government Hospital.

STUDY POPULATION

Included in the study were: Children 6 months to 36 months old with acute non bloody diarrhea of six days duration or less; with some or moderate signs of dehydration based on WHO-CDD protocol.[18]

Excluded in the Study were: Children with diarrhea of more than six days duration with: severe dehydration; bloody diarrhea; previous operation; severe malnutrition; immunocompromised; history of seizure (intake of medications for epilepsy); fecalysis findings of helminthiasis, amoeabiasis, occult blood; and with intake of anti-diarrheal medication.

Sample Size:

Seventy two patients were sampled based on the following assumptions: 95 % Confidence level, 80 % Power, SD of 2 and difference of 2 days duration of diarrhea based on the study of Valenzuela, et al. [16] The sample size for the two groups comparing means was computed with the following formula:

$$n = \frac{(z \times 1-\beta)^2 \times 2 \times SD2}{(d')^2}$$

$$n = \frac{(1.96 \times .84)^2 \times 2 \times SD2}{(2)^2}$$

where:
n = total sample size
z = the standard normal deviation, usually set at 1.96 or more simply

Power = $1 - \beta$ = Probability of rejecting the null hypothesis when it is false
SD = Standard deviation
d' = difference between two samples

Designation of Duties and Responsibilities:

The principal investigator gave a research orientation to the members of the research team prior to the start of the study. Duties and responsibilities were given to each member. A thorough physical examination was done on each patient by a resident physician assigned at the Emergency Room. He/she classified the degree of dehydration according to the WHO/CDD assessment of dehydration. A nurse unknowleadegable of the study objective and treatment assignment administered the Folic acid and the placebo. A Pediatric Resident assigned in the gastroenteritis ward did the daily physical examination and recorded any adverse effect that the children experienced during the treatment.

Treatment Allocation:

The subjects were screened for the exclusion and inclusion criteria through interview of parents and guardians and physical examination of the patients. Name of children with informed consent from parents was included in the list of participants. Subjects were assigned to the 2 treatment groups using a randomization list. Group A was given Drug A (Lot. No. 01) , Group B was given Drug B (Lot. No. 02).

The Folic acid preparation given to each patient was commercially available and provided by a Pharmaceutical Company. Folic acid was repackaged at the University of the Philippines College of Pharmacy, Department of Industrial Pharmacy along with the placebo. The placebo has the same color, taste and odor as that of folic acid and placed in an identical bottle.

Ethical Consideration:

The study was done according to the Principles in the Declaration of Helsinki. Parents of the children were informed about the nature, procedures, benefits and risks related to the study. An informed consent was obtained for their inclusion.

An Assistant Investigator assigned in the gastroitestinal ward noted and recorded any adverse effects. Parents were likewise instructed to report any untoward manifestation to the Assistant Investigator assigned to their ward. The study was approved by Ethics Review Committee.

Randomization:

Random allocation of the subjects to one of two treatment groups was done using pre-drawn block random assignment. The randomization list was prepared using letters A and B. Six 4-letter combinations (which serve as blocks) was made using these 2 letters i.e., ABAB, ABBA, AABB, BABA, BAAB, and BBAA . These 6 combinations became the basis for assigning treatment grouping by substitution with the corresponding number generated from random numbers. The pre-drawn treatment assignments were placed in a sealed envelope.

Definition of Terms

Acute Diarrhea - is the passage of loose or watery stools, at least three times in 24 hours period and may last 2 to5 days.[17]

Dehydration - the amount of fluid loss secondary to diarrhea not replaced adequately. A deficit of water and electrolytes develops.[17]

Tolerability - the ability of the subject to ingest a substance without vomiting.[8]

Actual Conduct of the Study

A physician assigned at the emergency room did the baseline physical examination. He/She classified the degree of dehydration according to the WHO/CDD assessment of dehydration (**Appendix A**). Parents of the subject were informed about the purpose, benefits, and risks related to the study (**Appendix B**). Patient informed consent was obtained prior to their inclusion (**Appendix C**). Once the patient fulfilled the inclusion criteria, he/she was assigned randomnly to either Group A (intravenous fluid and folic acid) or Group B (intravenous fluid and placebo).

A Randomnization list was prepared using letter A for Group A; and letters B for Group B. A total of six (6) combinations of the two (2) letters in random order was formed and was written on separate sheets of paper properly sealed (**Appendix D**). Each random order had an equal chance of being drawn and assigned to each group.

Group A children recieved Folic acid 5ml oral (1mg per 1 ml,equivalent to 5mg) three times a day for 5 days and intravenous fluid. Group B children recieved a placebo 5ml three times a day for 5 days and intravenous fluid. The placebo is of the same color, taste and and appearance. It was kept in a container similar to that of folic acid supplement.

The two assistant investigators who were both blinded evaluated the duration of patient's diarrhea as well as the frequency of stool passage, volume and character of stools (**Appendix E**). Adverse reactions were also observed by the investigators (**Appendix F**). **Figure 1** outline the study procedure.

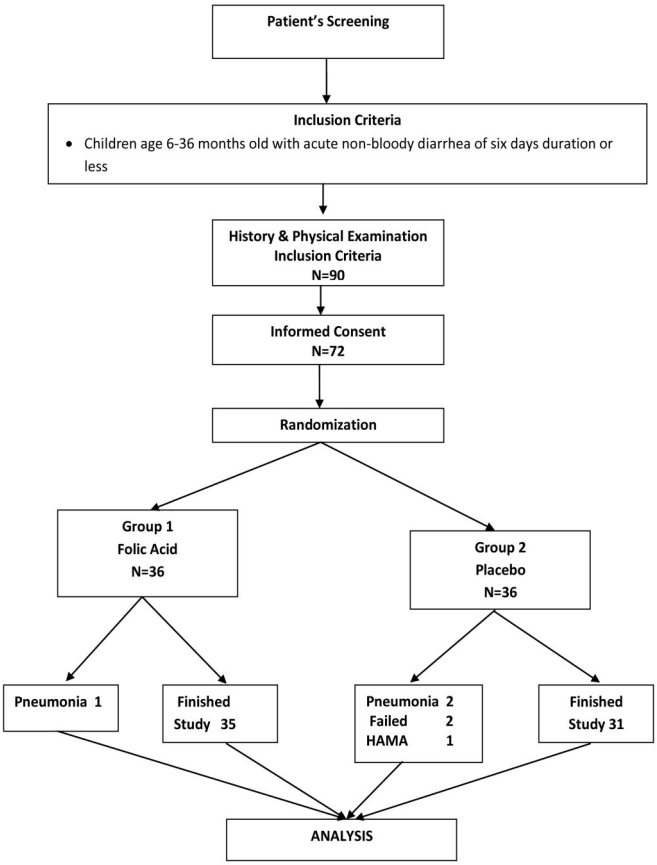


Figure 1: FLOW CHART OF STUDY PROCEDURE

Measures of Outcome

The study outcome measure determined the character, frequency, volume and duration of stool.

The character of stool was determined as follows:

a. Liquid stool – predominantly water.
b. Semi – formed/semi – liquid stool – composed of water and liquid portion.
c. Formed stool – solid stool.

The volume of stool was measured and recorded in grams by weighing the diaper before and after each use. A weighing scale (Silvano Brand - 3 kg) was used and was calibrated every day. The frequency of stool was noted and recorded every 8 hours shift.

Data Analysis

Means and standard deviations, frequency counts and percentage were used to described the data. T-test for independent samples was used to compare continous variables and chi-square and Fischer's exact test for categorical variables. Odds ratio were computed. A 95 % confidence level or P value < 0.05 was considered significant. Minitab ver 16 was used as statistical software.

RESULTS

A total of 90 patients 3 months to 6 months of age qualified to the inclusion criteria. A total of 72 patients gave consent and were randomized to Group A – folic acid (36 patients) and Group B- placebo (36 patients). Out of 36 patients enrolled in Group A, one (1) had Pneumonia and was considered unimproved but completed the medication for 7 days. In Group B ,there were 2 dropouts, one (1) developed Pneumonia and one (1) went home against medical advised (HAMA). Three were considered unimproved who completed the medication for 7 days, one (1) Pneumonia, two (2) had acute gastroenteritis with moderate dehydration.

The two groups were essentially similar in terms of age (P- value 0.239), sex (P-value 0.124) and degree of dehydration (P-value 0.674) on admission. Mean age was 11.3 months for Group 1 and 13 months for Group 2. There was male preponderance for both groups and majority had mild dehydration on admission. The p value was not statistically significant. (See Table 1)

Table 1. Demographic Profile of subjects as to age, sex and degree of dehydration

	Group 1	Group 2	P Value
Age, in months Mean +/SD	11.3+/5.1	13.0+/7.0	0.239
Sex			0.124
Male	22	28	
Female	14	8	
Dehydration			0.674
Mild	34	32	
Moderate	2	4	

The character of stool was described as either liquid, semi-formed/semi-liquid, and formed stool (Table 2). The stools significantly differed in the two groups by hospital day 2 at which time 75% of subjects in Group 1

showed semi-formed stool, and only 33% in Group 2 (P- value 0.0009). In hospital day 3, 53% of subjects in Group 1 had formed stools, and only 11% in Group 2. For remaining subjects not yet discharged at days 3 and 4, the proportion of those with formed stools was significantly higher in Group 1 than in Group 2.

Table 2. Character of Stool in Different Intervals

Character of Stool	Group 1 N (%)	Group 2 N (%)	P value N (%)
Day 1 Liquid Semi-formed Formed	 36 0 0	 36 0 0	--
Day 2 Liquid Semi-formed Formed	 9 (25%) 27 (75%) 0	 24 (67%) 12 (33%) 0	 P- value 0.0009 OR 6.00 95% CI (2.1-16.7)
Day 3 Liquid Semi-formed Formed	 1 16 19 (53%)	 8 24 4 (11%)	0.0000
Day 4 Liquid Semi-formed Formed	 1 3 8 (67%)	 3 17 8 (28%)	0.049
Day 5 Liquid Semi-formed Formed	 1 0 0	 2 5 11	0.158

The volume of stools which was Measured in grams was similar for Day 1 in both groups, at days 2 and 3, the volume of stool was significantly lower in Group 1 than in Group 2. The p-value 0.0000 is statistically significant.

The frequency of stool as shown in table 4 was significantly less in Group 1 as compared in Group 2 for Days 1 to 3 with a P-value 0.036. This is statistically significant.

Table 3. Volume of Stool in Different Intervals

	Group 1 gms.	Group 2 gms.	P value
Day 1 Mean +/SD	608.1+/135.3	620.3 +/142.2	0.714
Day 2 Mean +/SD	383.6+/116.9	494.5+/106.2	0.0000
Day 3 Mean +/SD	355.3+/107.7	402.3+/118.9	0.0000

Table 4. Frequency of Stool in Different Intervals

	Group 1	Group 2	P value
Day 1 Mean +/SD	4.57+/0.81	5.26+/1.05	0.003
Day 2 Mean +/SD	3.0+/0.73	4.06+/1.25	0.0005
Day 3 Mean +/SD	2.7+/0.65	3.5+/1.11	0.036

The duration of diarrhea for both groups was likewise compared. It showed that there was a significantly higher proportion and percentage (cumulative) of subjects discharged starting day 3, in Group 1 than in Group 2 (see Table 5: Fig. 1). By day 5 , 97% of patient in group 1 was already discharged while only 75% in group 2.

Table 5: Cumulative Percentage of Subjects Discharged Per Hospital Day

	Group 1	Group 2	P value
Day 1	0	0	0.0000
Day 2	0	0	
Day 3	24 (67%)	4 (11%)	
Day 4	35 (97%)	19 (53%)	
Day 5	35 (97%)	27 (75%)	

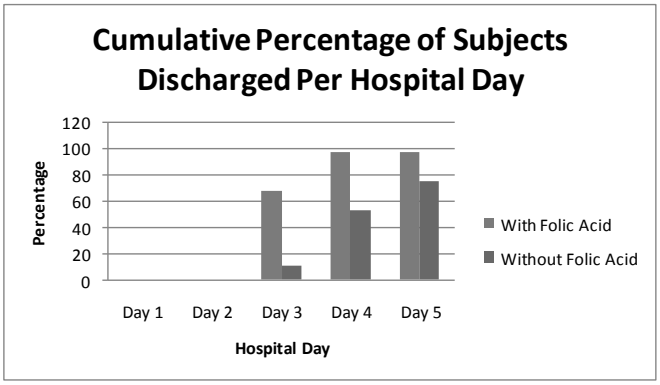


Fig. 1 Cumulative Percentage of Subjects Discharged per hospital day

The Length of hospital stay was 2.3 days in Group 1 and 3.6 days in Group 2. The P value is 0.0000 which is statistically significant.

Table 6 Length of Hospital Stay

	Group 1	Group 2	P value
Mean +/SD	2.3+/0.47	3.6+/1.1	0.0000

Adverse effect

No adverse reaction was noted in the use folic acid.

DISCUSSION

Diarrhea is a common cause of fluid loss in children which can cause dehydration and electrolyte disorders. Most cases can be managed with oral rehydration. Thus, it is important to assess the degree of dehydration, which dictates both the urgency of the situation and the volume of fluid needed for hydration.[18] The outcome of diarrhea range from mild, self-limiting episodes to severe diseases requiring hospitalization.[19] Additional intervention is needed to ensure early recovery and to shorten the course of the disease.

Folic acid supplementation has been shown to have a positive effect in the treatment of acute watery diarrhea in this study. The 2 groups were essentially similar in terms of age (P-value 0.239), sex (P-value 0.124) and degree of dehydration (P-value 0.674). Data on the character of stool showed greater improvement with folic acid supplementation starting day 2 at which time 75% of the subjects in group 1 showed semi formed stool and only 33 % in group 2. The volume of stools was significantly lower in folic acid by day 2 to 3 compared to the placebo group. Frequency of stool was also significantly less in group 1 than in group 2 from day 1 to 3. Comparing the percentage of subject discharged per hospital day there was a significantly higher proportion and percentage

of subjects discharged starting day 3 in group 1 than in group 2. The length of hospital stay was 2.3 days in group 1 and 3.6 days in group 2. The difference was statistically significant. The findings in this study was the same as to age, sex, dehydration to the study done by Valenzuela et al in 2003. However, the mean frequency of LBM/day and the character of stool in the study of Valenzuela started to decreased and improved by day 3 and the volume of stools had no significant difference between the 2 groups.[16]

Folic acid can help repair the damage in lining of the intestine. Folic acid also known as Vitamin 9 or Folacin and folate (the naturally occurring form), are forms of water soluble vitamin B9 which is essential to many body function. It plays a key role in DNA synthesis, which is needed for the regeneration of damaged small-bowel mucosal epithelial cells.[20] Children and adult require folic acid to produce healthy red blood cells and prevent anemia. Folic acid also helps in tissue growth and function. It helps to increase appetite when needed and stimulates the formation of digestive acids and maintains nervous system's integrity and intestinal tract functions. Folic acid is an important nutrient for immune and lymphatic function.[21] It is involved in the production of neurotransmitters such as serotonin, which regulate mood, sleep and appetite.

The data obtained from this study showed beneficial effects of folic acid in acute watery diarrhea. The review of literature revealed that folic acid participates in methylation reactions, it serve as a donor of methyl group to certain substrates involved in metabolic reactions. Two key methylation reactions in which folic acid participates have been identified: The methylation of cobalamin, this substrate then acts as a methyl donor in the interconversion of homocystein and methionine, and the methylation of deoxyuridylate to deoxythymidilate, an important component of cellular DNA and thus would be important in cellular replication and repair. It is this second methylation function of folic acid which is probably responsible for the beneficial effects observed with supplementation in acute diarrheal states.[22]

In the study of Ashraf H, Rahman MM, Fuchs GJ, Mahalanabis D in 1998,[7] the study had shown that folic acid given as adjunct to fluid and electrolyte therapy does not provide any additional clinical benefit to infants and young children with acute watery diarrhea. There were several reasons why these results differ from those of the previous study showing the efficacy of foliate conducted in South Africa.[15] It had a different patient population; they were of different age group (1 to 44 vs 6 to 23 months in the previous and present study), included both male and female patients who were of different socioeconomic and cultural background. Since the previous study was neither randomized nor blind, there was a higher chance of bias in the results. The discrepancy involving the duration of diarrhea between the two studies could be explained as follows: acute diarrheal illness usually resolves spontaneously within 7 to10 days without

treatment. The mean duration of diarrhea prior to admission was 7 days in the previous study, it resolved within 2 to 4 days (in the study and control groups respectively). Similarly, as the mean duration of diarrhea prior to admission was only 2 days in the present study, diarrhea continued beyond 5 days in 40% of the children in both groups.

CONCLUSION

The supplementation of folic acid in the management of acute diarrhea enabled majority of the subjects in this study to have formed stools earlier, reduce volume of stool earlier and reduce frequency of stooling, resulting in early discharge and shorter hospital stay.

The character of stool in this study significantly differed in the two groups by day 2 at which time 75% of subjects in Group 1 (folic acid) showed semi-formed stool, and only 33% in Group 2 (placebo) with a P-value 0.0009. In day 3, 53% of subjects in Group 1 (folic acid) had formed stools, and only 11% in Group 2 (placebo). The frequency of stool was significantly less in Group 1 (folic acid) as compared in Group 2 (placebo) for days 1 to 3 with a P-value of 0.036 which is statistically significant. The lenght of hospital stay was 2.3 days in Group 1 (folic acid) and 3.6 days in Group 2 (placebo). The P.value is 0.0000 which is statistically significant.

There were no reported side effects with folic acid in this study. It is generally tolerated. It maybe taken with or without food.

This study proves that supplementation with folic acid for 5 days with acute watery diarrhea is safe and shortens hospital stay.

RECOMMENDATION

Folic Acid showed importance in cellular DNA synthesis and may help in the repair of the damaged villous cells of the small bowel, making it effective in acute diarrhea. It is recommended to determine its efficacy among infants with chronic diarrhea, infectious diarrhea and intestinal parasitism.

In this study, clinical response to folic acid was assessed during the duration of the subject's hospital stay. It is then recommended that subjects will be evaluated until follow-up as out-patient basis.

APPENDIX A

WHO/CDD

Assessment of Diarrhea patients for Dehydration

	A	B	C
LOOK AT:CONDITION EYES THIRST	Well, alert Normal Drinks normally, not thirsty	Restless, irritable Sunken Thirsty, drinks eagerly	Lethagic Sunken Drinks poorly, or not able to drink
FEEL: Skin Pinch	Goes back slowly	Goes back slowly	Goes back very slowly
DECIDE	The patient has NO SIGNS OF DEHYDRATION	If the patient has two or more signs in B, there is SOME DEHYDRATION	If the patient has two or more signs in C, there is SEVERE DEHYDRATION
TREATMENT	Use treatment Plan A	Weigh the patient if possible, and use Treatment Plan B	Weigh the patient and use Treatment C

APPENDIX B

LETTER TO THE PARENTS

Minamahal na mga magulang,

Ako po si Dr_____, isang residente sa Departamento ng Pediatrics, _____. Nagsasagawa ako ng pag-aaral na "Folic acid in the Treatment on Acute Watery Diarrhea in children 6 months to 36 months: a Double Blind, Randomnized Controlled Trial." Nais kong malaman sa pag-aaral na ito kung ang mga batang bibigyan ng folic acid ay mas mapapadali ang paggaling kumpara sa mga batang walang folic acid.

Ang pagsali sa programang ito ay libre at walang makukuhang pinansyal na bayad.

Bilang mga magulang o taga-pag-alaga, gusto kong ipaalam na magiging bahagi ang inyong anak sa programang ito. Maaaring ang inyong anak ay makakatanggap ng folic acid at maari rin naming hindi. Ang pagpili ng kung sino ang bibigyan ay random na parang pagbunot sa tambiolo.

Magpapapirma ako ng "informed consent" sa inyo bilang patunay na kayo ay sumasang-ayon sa pagsali ng inyong anak sa programa.

Maraming salamat po.

Gumagalang,

_____

Primary Investigator

APPENDIX C

Informed Consent

Katibayan sa Pagpayag

Ako _____, nasa hustong gulang, may asawa, at kasalukuyang naninirahan sa _____
ay nagpapatunay na:

1. Ako ang magulang/ tagapagsubaybay ni _____.

2. Lubos na napaliwanagan tungkol sa kahalagahan at pakay ng pag- aaral na may kinalaman sa epekto ng "folic acid" sa ikabibilis at ikadadali ng paggaling sa sakit na "gastroenteritis" ("pagtatae'). Pati na ang pagsusuri at pamamaraan na kinakailangang gawin. Ako ay sumasang ayon na maisama ang aking anak sa pag aaral na ito.

3. Ang aking anak nay lubos na nasuri at napag alamang may sakit na gastroenteritis ("pagtatae") at walang kaakibat na ibang karamdaman.

4. Ako ay nangangako na magbibigay ng lubos na partisipasyon sa pagtatala ng karakter at dami ng dumi ng aking anak sa loob ng tatlo hanggang limang araw (3-5).

5. Alam ko na ang aking anak ay bibigyan ng "folic acid" 5mg/placebo, tatlong beses (3) sa isang araw, sa loob ng tatlo hanggang limang araw (3-5) na walang kapalit na halaga.

6. Ako ay bibigyan ng kasiguraduhan na lahat ng resulta ng pag-aaral na ito at mananatiling lihim at konpidensyal, na ako ay maaring tumiwalag sa pag aaral na ito sa anumang oras aking naisin.

7. Ako ay may karapatang magtanong ng mga bagay-bagay na may kinalaman sa pag-aaral na ito at ako ay nabigyan ng kasagutan na nagbigay liwanag sa aking kaisipan.

8. Ako ay nabigyan ng kopya ng katibayan na ito.

_____ _____

Magulang/ Tagapagsubaybay Petsa

_____

Pangalan at Lagda ng nagpaliwanag na Doctor

APPENDIX D

Randomization Table

1	A	B	A	B
2	A	B	B	A
3	A	A	B	B
4	B	A	B	A
5	B	A	A	B
6	B	B	A	A

APPENDIX E

Patient Data Form

Name of Patient_____ Age/Sex_____

Date/Time	Character of Stools	Volume of Stools	Frequency of Stools

APPENDIX F

Adverse Reaction Checklist

Name of Patient_____ Age:_____

Date	Vomiting	Abdominal pain	Hypersensitivity reaction	Others

BIBLIOGRAPHY

1. Walker, C et al. Micronutrients and Diarrheal Disease. Oxford Journals Clinical Infectious Disease. Volume 45:Pp. S73-S77: 2007

2. Farthing M., Linberg P., et al. World Gastroenterology Organization Practice Guidelines: Acute Diarrhea: March 2008.

3. National Demographic and Health Survey (NDHS).2003

4. National Demographic and Health Survey (NDHS).2008

5. Republic of the Philippines, Department of Health; Administrative Order: 2007-0045: Zinc Supplementation and Reformulated Oral Rehydration Solution in the Management of Diarrhea Among Children: Dec. 17, 2007.

6. Makbule E, et al. Clinical Efficacy Comparison of *Sacchamyces boulardii* and Yogurt Fluid in Acute Non-bloody Diarrhea in Children. The American Journal of Tropical Medicine and Hygiene; March 2010, Vol. 82, No. 3, 488-491.

7. Ashraf H, Rahman MM, et al. Folic acid in the treatment of acute watery diarrhea in children: a double-blind, randomized, controlled trial. Acta Pediatrica 87:1113-5.1998

8. Sanidad R. A Randomized Clinically Controlled Trial comparing tolerability between Flavored ORS and Unflavored ORS preparation among Children 4 months to 5 years old with Acute Diarrhea seen at ER/ OPD of San Juan Medical Center; PPS Journal; Vol. 54 No. 2; April-June 2005.

9. Sazawal S., et al. Zinc supplementation in Young Children with Acute Diarrhea in India. The New England Journal of Medicine; Vol. 133 No. 13; Sept 1995.

10. Awasthi S., Zinc supplementation in Acute Diarrhea is Acceptable, Does not interfere with Oral Rehydration, and Reduces the use of other medications: A Randomized Trial in Five Countries. Journal Pediatric Gastroenterology and Nutrition. March 2006-Volume 42, Issue3.

11. Almera-Cirilos S. The Effectiveness of Oral Rehydration Solution plus Zinc versus plain Oral Rehydration Solution in the management of Acute Dairrhea: A Randomized placebo controlled trial: PPs Journal, Vol55 No. 1; January-March 2006.

12. Teodosio-Serillo N., et al.Double Blind Controlled Trial on the effect of oral Zinc supplementationin Acute Diarrhea among infants 6-48 months;PPS Journal, Vol. 55 No.3 ;July-September 2006.

13. Dewan V, et al. randomized controlled trial of vitamin A supplementation in acut diarrhea. Indian Pediatrics(1995); Volume 32, Issue1, Pages: 21-25.

14. Huang HS, et al. Efficay of Probiotic use in acute diarrhea in children: a meta-analysis; Dig. Dis.Sci.2002 Nov.; 47(11); 2625-34.

15. Haffejee IE. Effect of Folate on Duration of Acute Infantille Diarrhe. Lancet; ii: 1988;334-35.

16. Valenzuela E., et al. The Role of Folic Acid Supplement in the Treatment of Acute Non-bloody Diarrhea in Children: Unpublished Research Paper: De Los Santos Medical Center; 2003.

17. World Health Organization. A Manual for the Treatment of Diarrhea. Geneva: World Health Organization, p.4 and 8 :2005.

18. Nelson Textbook of Pediatrics. Part 7: p. 902: 19th edition.

19. Mc Farland L. et al. Meta-Analysis of Probiotics for the prevention and treatment of pediatric diarrhea; International Journal of Probiotics and Prebiotics Vol. 1, No.1,pp. 63-76, 2006.

20. Weinstein WM. Epithelial cell renewal of the small intestinal mucosa. Med Clin North Am 1974;58; 1375-86.

21. Beisel WR. Single nutrients and Immunity. The American Journal of Clinical Nutrition.1982;35: 417-68.

22. Bailey LB, et al. Folate Metabolism and Requirements. The Journal of Nutrition. 1999;129:779-782.

PREDICTORS OF RESTENOSIS AFTER PERCUTANEOUS BALLOON MITRAL VALVULOPLASTY

Raymund Darius Liberato, M.D.

Alexander Ang, M.D.

Quirino Memorial Medical Center
Institutional Affiliation

ABSTRACT

INTRODUCTION: Restenosis has been an anticipated occurrence after percutaneous transmitral commissurotomy (PTMC). Factors such as sub-optimal valve area after the procedure and the presence of chronic atrial fibrillation predict a likelihood of restenosis. This study therefore aims to identify the clinical factors that contribute to the development of restenosis, as local studies on adult Filipinos are sparse.

METHODS: This is a 10-year retrospective chart review of patients who underwent PTMC undertaken in a specialized tertiary hospital in the Philippines. A chi-square and t-test were applied to the data to determine the association of each individual factors and multiple logistic regression was applied to determine the independent effect of each factor.

RESULTS: Five Hundred Thirty Five (535) charts were reviewed for 10 years. Of 535 charts, 206 were included in the study. Restenosis rate was computed at 19.42% in 10 years. Among the clinical characteristics, diabetes mellitus was linked with restenosis ($p = 0.021$). Further, the following were linked to restenosis: Wilkins score of >8 ($p = 0.017$), pulmonary hypertension prior to PTMC ($p = 0.017$ for mild, 0.018 for moderate, and 0.029 for severe), heart failure symptoms under NYHA functional class II classification ($p = 0.026$), prior AF ($p = 0.019$), and fusion of the anterolateral commissure ($p = 0.003$). Multiple logistic regression analysis showed relationship with restenosis with age [Odds ratio 1.04, $p = 0.016$ [95% CI (1.00-1.07)] and fusion of the anterolateral commissure [Odds ratio of 3.49 and a $p = 0.012$ [95% CI (1.31-9.24)].

CONCLUSION: There is a high likelihood of restenosis for patients after PTMC if the following are present: increasing age, diabetes mellitus, pulmonary hypertension, high Wilkins score, NYHA functional classification II, atrial fibrillation and fusion of the anterolateral commissures.

KEYWORDS: [Mitral restenosis] [PTMC] [Balloon valvotomy] [Mitral stenosis] [Predictors of Restenosis] [Restenosis rate]

INTRODUCTION

Rheumatic heart disease confers a concurrent disease in the mitral valve[1]. The disease occurs in around 19% of Filipino children with the prevalence increasing with repeated attacks of Rheumatic fever[2]. In 1984, Inuoe introduced the percutaneous mitral balloon valvuloplasty and has recently been considered as the procedure of choice for favorable cases of mitral stenosis.

Restenosis is defined as a loss of > 50% of the initial gain in MVA[3]. The incidence of re-stenosis after a successful mitral valvulopalsty is in the range of 10% and 20% in foreign literatures[4]. In contrast, a local study done by Ang et al showed that the re-stenosis rate after percutaneous mitral balloon valvotomy was at 2.3% after 3 years, 11.3% after 5 years and 26.4% after 8 years[5]. Mainly, re-stenosis is related to the presence of chronic atrial fibrillation at baseline and a suboptimal percutaneous mitral balloon valvotomy[6]. Wilkins score was also an independent risk factor in the development of re-stenosis [7] [8] [9]. Likewise, fluoroscopic Ca $^{++}$[10], presence of Pulmonary Congestion and functional class would likely predict re-stenosis [11].

Unfortunately, there is no available local data that looks on the factors that predispose adult Filipino patients who underwent valvuloplasty to re-stenose hence, the formulation of the study. Therefore, the study aims to determine factors associated with re-stenosis after percutaneous mitral balloon valvuloplasty.

METHODOLOGY

The Institutional Review Board of the Philippine Heart Center approved the conduct of this paper and waiver of informed consent was granted.

Study Design

This study was a 10-year Retrospective Cohort trial from 1998-2008 conducted at the Philippine Heart Center.

Study Population

Inclusion Criteria:

1. Patients 18 years old and above who have Rheumatic Mitral Stenosis who underwent percutaneous mitral balloon valvotomy

Exclusion Criteria:

1. Patients who develop complications immediately after the percutaneous mitral balloon valvotomy that required mitral valve surgery such as the following:
    a. Presence of severe MR
    b. Cardiac perforation

2. Absence of follow-up 2 dimensional echocardiogram within 6 months after the valvuloplasty

Sample Size Determination:

Sample size was computed at n=133 at 95% confidence level, relative error of 10% assumed re-stenosis rate of 26.4% at 8 years follow-up as presented in the paper of Ang et al [5].

Identification of Variables

Patients who had percutaneous mitral balloon valvotomy were included in the study. Baseline demographic characteristics such as the age, sex and the presence of co-morbidities were compiled prior to the start of the study. Further, baseline clinical characteristics such as the presence of atrial fibrillation, mitral valve area post percutaneous mitral balloon valvotomy, pulmonary hypertension, presence of Mitral valve regurgitation, Wilkins score and NYHA Functional classification were also be recorded.

Outcome Measures

The primary outcome measure was re-stenosis after the percutaneous mitral balloon valvotomy.

Study Maneuver

The primary investigator reviewed the medical charts of patients who underwent percutaneous mitral balloon valvotomy at the Philippine Heart Center from 1998-2008. The demographic characteristics of patients and clinical characteristics that underwent percutaneous balloon valvotomy were obtained. These are as follows: age, sex, and presence of co-morbities (eg. hypertension & diabetes). Smoking, Wilkins score, presence of pulmonary hypertension, mitral valve regurgitation post procedure, heart rhythm (atrial fibrillation or sinus rhythm), NYHA classification, and valve area post procedure and commissural opening will also be recorded.

Statistical Analysis

Quantitative data was presented as mean standard deviation (sd) and qualitative in frequency and percent distribution. To determine association of different factor with re-stenosis, Fisher's exact test for categorical variables and t-test for continuous variables were applied. To determine the independent effect of each factor to re-stenosis, multiple logistic regression analysis were applied to the data. A p value 0.050 was considered significant.

RESULTS

Five Hundred Thirty Five charts were reviewed from the year 1998-2008. Of the 535 charts, 206 were included in the study. The rest were excluded due to the following reasons: (1) no follow-up 2D echocardiography within 6 months after PTMC and (2) presence of severe MR. In the reviewed charts, 40 out of 206 were noted to have a loss of ≥ 50% in the initial MVA gain after PTMC. Restenos is rate was computed at 19.42% in 10 years.

Table 1: Demographic Profile of Patients Mitral Stenosis post Percutaneous Balloon Valvuloplasty

	MEAN	Standard Deviation
Age	36.99	11.18
	Frequency	**Percent**
Sex		
Male	36	17.48%
Female	170	82.52%
Hypertension	6	2.91%
Diabetes Mellitus	10	4.85%
Smoking	17	8.25%

The study population had a mean age of 36.99 omprising 17.48% males and 82.52% females. 2.91% were hypertensives, 4.85% were diabetics and 8.25% were smokers.

Table 2. Clinical Characteristics of Patients with Restenosis

	Re-stenosis		P-Value
	(+) n = 40 (%)	(-) n = 166 (%)	
Hypertension	1 (0.006%)	5 (12.5%)	0.863
Diabetes	5 (12.5%)	5 (0.03%)	0.021
Smoking	5 (0.03%)	12 (0.008%)	0.283
Wilkins Score			
>8	10 (25%)	17 (10.24%)	0.017
Pulmonary Hypertension			
Normal	6 (15%)	63 (39%)	
Mild	16 (40%)	49 (30%)	0.017
Moderate	9 (23%)	24 (15%)	0.018
Severe	9 (23%)	27 (17%)	0.029
Mitral Regurgitation post procedure			
None	3 (9%)	35 (21%)	
Trivial	12 (35%)	41 (25%)	0.073
Mild	9 (26%)	56 (34%)	0.370
Moderate	10 (29%)	31 (19%)	0.059
NYHA Functional Class			
I	1 (2.5%)	33 (20%)	
II	38 (95%)	126 (76%)	0.026
III	1 (2.5%)	6 (4%)	0.250
IV	—	—	—
Atrial Fibrillation pre procedure	18 (45%)	43 (26%)	0.019
Valve Area post procedure			
<50% from the initial valve area	14 (40%)	63 (40%)	0.967
≥ 50% of the initial valve area	21 (60%)	96 (60%)	
Commissural Opening post procedure			
Anterolateral Commissure			
Fully open	12 (34%)	78 (49%)	
Partially fused	11 (31%)	63 (39%)	0.779
Fused	12 (34%)	19 (12%)	0.003
Posteromedial Commissure			
Fully open	15 (44%)	90 (56%)	
Partially fused	10 (29%)	49 (31%)	0.649
Fused	9 (26%)	21 (13%)	0.052

For the clinical characteristics, hypertension and smoking were not associated with restenosis having a P value of 0.863 and 0.283 respectively. The presence of diabetes mellitus however, was associated with restenosis compelling a P value of 0.021. Possessing a Wilkins score of >8 were correlated with restenosis with a P value of 0.017. Moreover, pulmonary hypertension prior to PTMC confers the association with restenosis with the following p values: 0.017, 0.018, and 0.029 respectively for mild, moderate and severe pulmonary hypertension. The existence of Mitral regurgitation after the valvuloplasty with any grade (trivial, mild and moderate), were not coupled with restenosis evidenced by a non-statistically significant P value of 0.073, 0.370 and 0.059 respectively. There were no patients who were in NYHA functional class IV. Likewise, the presence of heart failure symptoms classified under the NYHA functional class II classification was somehow linked with restenosis with a P value 0.026.

Existence of prior AF was associated with restenosis having a statistically significant P value of 0.019. The valve area after PTMC was neither associated with the occurrence of the outcome with a non-significant P value of 0.967.

Opening of the commissures matters most for the anterolateral commissure. Non-opening or fusion of this commissure was related with restenosis having a significant P value of 0.003. Partial fusion was not related with the outcome with a P value of 0.779. On the other hand, opening of the posteromedial mitral commissure has no relation with restenosis with the following p values 0.649 and 0.052.

The table with the subcategory of commissural opening post procedure was changed during the course of the study period. This is because the description that was used in the echocardiographic report made the classification in the original protocol difficult to sort-out. Echocardiography detailed the commissural opening as follows: (1) Open; (2) Partially fused and (3) Fused. While, the original protocol described the commissural opening as: Anterolateral commissure open, Posteromedial commissure open and Both commissures open. To coincide with the echocardiographic report, the classification was changed as follows: Open; partially fused and fused.

Multiple logistic regression analysis of all the variables were also done to determine the independent effect of each factor to restenosis. Results showed a significant likelihood of restenosis with age having an odds ratio of 1.04 p = 0.016 [95% CI (1.00-1.07)] and fusion of the anterolateral commissure with a possibility of 3.49 p = 0.012 [95% CI (1.31-9.24)].

DISCUSSION:

The results showed that the patients who underwent PTMC were mostly females and was in accordance with the overall incidence of rheumatic mitral stenosis having a ratio of 2:1 compared to males [20]. Restenosis rate for this study was 19.42% over a 10-year

agreeing with international reports. However, this rate is lower compared to a local study done by Ang et al. In the study, the mean age was 36.99, which was also consistent with the occurrence of mitral stenosis in the Asian population being more frequent in the less than 40-year-old population[20].

The presence of hypertension and smoking seems not to be associated with the occurrence of mitral stenosis. But, the presence of diabetes confers a risk for restenosis. One of the mechanisms involved in the pathophysiology of diabetes involves inflammation leading to impairment of insulin secretion[15]. On the other hand, it was initially thought that a persistent and recurrent rheumatic process was involved in restenosis. However, restenosis occurrence was not found to be so[15]. A plausible explanation between the occurrence of both diabetes and mitral restenosis is likely the involvement of inflammation in both cases. Nevertheless, the specific mechanism has not been completely elucidated. A Wilkin's score of <8 is an indication for PTMC. However, there are patient subsets where a score of >8 had to undergo the procedure with a higher risk for restenosis. As was seen in this study, the likelihood of having restenosis for a score of >8 is high which also coincided with internationally published literatures [7] [8] [9]. Further, the presence of commissural calcification seen by 2D echocardiography is a useful predictor of outcome in patients with otherwise "good" valves (echo score <8). Calcification of one commissure or more predicts a less than 50% probability of achieving a valve area above 1.50 cm^2 [21]. Immediately after a PTMC, PA pressures fell together with reduction in mitral valve gradient. And, the pulmonary arterial pressure taken after the procedure is a factor for the occurrence of restenosis with higher rate if the pressures are [22]. In this study, in contrast to other published reports, the pulmonary artery pressures were measured before PTMC. As the results would show, every grade of pulmonary hypertension from mild, moderate to severe was associated with restenosis achieving a statistically significant connection. A plausible explanation for the occurrence of restenosis in relation to pulmonary hypertension after a PTMC could be related to the vascular changes that occur in the pulmonary tree specially in long standing mitral stenosis. Atrial fibrillation at baseline is associated with a two-fold occurrence of restenosis [25]. In this study, the presence of atrial fibrillation was linked with restenosis that is in parallel with other studies [12] [25].

NYHA class before percutaneous mitral balloon valvotomy was associated with restenosis [23]. This study further illustrates the role of the NYHA classification in restenosis. In particular, having a functional class II confers a likelihood of having restenosis. However, the populations on this study were mostly in the class II category with only sparse distribution on class III and no class IV. Hence, this study is not powered to predict the contribution of each classification to restenosis. Mitral regurgitation was linked also with restenosis [26]. In this paper, the presence of any degree of mitral regurgitation was not linked with restenosis.

Mitral valve area after percutaneous mitral balloon valvotomy predicted the occurrence of restenosis [24]. However on this paper, the valve area was not associated with restenosis. The mechanism for increase in the mitral valve area after a PTMC involves the splitting of the commissures both for the anterior and posterior. A successful splitting can be achieved depending on the subvalvar apparatus and the presence of commissural calcification whereby the less subvalvar and commissural calcification provided the best result for efficacious commissural splitting [27].

It was studied in this paper the independent association of the anterior and the posterior commissural opening in relation to the occurrence of restenosis. Published studies were limited only on describing the occurrence of restenosis in association of splitting of the commissures in general. It was shown interestingly on this study that the fusion of the anterolateral mitral commissure was associated with restenosis having a P value of 0.003.

A multiple regression analysis of all the variables showed that age and fusion of the anterolateral commissures were significantly associated with restenosis. Age confers a 1.04 likelihood of restenosis per year in that an aging patient will eventually have restenosis over time and fusion of the anterolateral commissure confers a 3.49 likelihood of restenosis.

LIMITATIONS OF THE STUDY:

The study was done in a retrospective manner involving review of patients chart admitted with rheumatic mitral stenosis undergoing PTMC. Further, records of patient's data were sometimes incomplete because of losses through time.

RECOMMENDATION

A better study design that involves patient follow-up should be done to determine the magnitude of each characteristic in the development of clinical restenosis.

CONCLUSION

Based on this study, factors such as age, diabetes mellitus, pulmonary hypertension, NYHA functional classification II, high Wilkins score, atrial fibrillation and fusion of the anterolateral commissures were significantly associated with restenosis. However, the presence of an ageing mitral stenosis patient and with fusion of the anterolateral commissure was independently found to have the highest risk for restenosis.

REFERENCES

1. Roberts WC, Perlof JK. Mitral valvular disease. A clinicopathologic survey of the conditions causing the mitral valve to function abnormally. Ann Intern Med. 1972; 77(6): 939-975.

2. Mabilangan LM, Mojica B. A study on rheumatic fever and rheumatic heart disease in 208 Filipino children [online]. Mar 20 [cited 2014 Mar 20]; Available from: URL: http://herdin.ph/index.php?option=com_herdin&controller=research&task=view&cid[0]=26329.

3. Fawzy ME, Stefadouros MA, Hegazy H, Shaer F El, Chaudhary MA, Fadley F, et al. Long term clinical and echocardiographic results of mitral balloon valvotomy in children and adolescents. Heart. 2005; 91 (6):743-748

4. Bonow RO, Carabello B, de Leon AC Jr, Edmunds, HL Jr, Fedderly B, Freed M, et al. ACC/AHA guidelines for the management of patients with valvular heart disease. A report of the American College of Cardiology/American College Association. Task force on practice guidelines (committee on management of patients with valvular heart disease). J Am Coll Cardiol. 1998; 32 (5):1486-1588.

5. Ang AD, Tria RB, Rondilla LWS, Diaz LL. Long-term clinical and echocardiographic follow-up of patients after percutaneous mitral balloon valvotomy at the Philippine Heart Center. Philipp J Cardiol. 2003; 3 (3): 116-120.

6. Langerveld J, Thijs Plokker HW, Ernst SM, Kelder JC, Jaarsma W. Predictors of clinical events or restenosis during follow-up after percutaneous mitral balloon valvotomy. Eur Heart J. 1999; 20(7): 519-26.

7. Palacios IF, Block PC, Wilkins GT, Weyman AE. Follow-up of patients undergoing percutaneous mitral balloon valvotomy. Analysis of factors determining restenosis. Circulation 1989; 79(3): 573-9.

8. Desideri A, Vanderperren O, Serra A, Barraud P, Petitclerc R, Lesperance J, et al. Long-term (9 to 33 months) echocardiographic follow-up after successful percutaneous mitral commissurotomy. Am J Cardiol. 1992; 69 (19):1602-6.

9. Abascal VM, Wilkins GT, Choong CY, Thomas JD, Palacios IF, Block PC, et al. Echocardiographic evaluation of mitral valve structure and function in patients followed for at least 6 months after percutaneous balloon mitral valvuloplasty. J Am Coll Cardiol 1988; 12(3): 606-15.

10. Villanueva K, Panlilio A, Santos R. Valvular restenosis in patients followed for 12 months after percutaneous balloon mitral valvotomy. Philippine Heart Center. 1990. [Unpublished].

11. De Jesus A. Follow-up of patients who underwent percutaneous mitral balloon valvotomy. Analysis determining restenosis. Philippine Heart Center. 1997 [Unpublished].

12. Lung B, Garbarz E, Michaud P, Helou S, Farah B, Berdah P, et al. Late results of percutaneous mitral commissurotomy in a series of 1024 patients. Analysis of late clinical deterioration: frequency, anatomic findings, and predictive factors. Circulation 1999; 99(25):3272-3278.

13. Orrange SE, Kawanishi DT, Lopez BM, Curry S, Rahimtoola SH. Actuarial outcome after catheter balloon commissurotomy in patients with mitral stenosis. Circulation 1997; 95(2):382-9.

14. Akin M, Sagcan A, Nalbantgil S, Ozerkan F, Akilli A, Yavuzgil O, et al. The predictive value of mitral leaflet motion and thickness index scores on early restenosis after mitral balloon valvuloplasty. Tex Heart Inst. J. 2004; 31(3): 251-6.

15. Kohei K. Pathophysiology of type 2 diabetes and its treatment policy. Jpn Med Asso J. 2010; 53(1): 41-46.

16. Thomas MR, Monaghan MJ, Michalis LK, Jewitt DE. Echocardiographic restenosis after successful balloon dilatation of the mitral valve with the Inoue balloon: experience of a United Kingdom centre. Br Heart J 1993; 69(5): 418–23.

17. Reid CL, McKay CR, Chandraratna PA, Kawanishi DT, Rahimtoola SH. Mechanisms of increase in mitral valve area and influence of anatomic features in double-balloon, catheter balloon valvuloplasty in adults with rheumatic mitral stenosis: a Doppler and two-dimensional echocardiographic study. Circulation 1987; 76 (3): 628-36.

18. Reganion J, Azcueta MB, Casas ML, Cantre T. Predictors of outcome after percutaneous mitral balloon valvuloplasty in pediatric patients. Philippine Heart Center. 1997. [Unpublished].

19. Taylor MF. Ethical considerations in European cross-national research. Int Soc Sci J. 1994; 142; 523-32.

20. Fuster V,O'Rourke R, Walsh R, Poole-Wilson P. Hurst's the heart: mitral valve stenosis. 12th ed. Vol. 2. USA: McGraw-Hill Companies; 2007. P1738

21. Sutaria N, Northridge DB, Shaw TR. Significance of commissural calcification on outcome of mitral balloon valvotomy. Heart 2000; 84(4): 398–402.

22. Levine MJ, Weinstein JS, Diver DJ, Berman AD, Wyman RM, Cunningham MJ, et al. Progressive improvement in pulmonary vascular resistance after percutaneous mitral valvuloplasty. Circulation 1989; 79 (5): 1061-7.

23. Dean LS, Mickel M, Bonan R, Holmes DR, O'Neill WW, Palacios IF, et al. Four-year follow-up of patients undergoing percutaneous balloon mitral commissurotomy. A report from the national heart, lung, and blood institute balloon valvuloplasty registry. J Am Coll Cardiol 1996; 28 (6):1452–7.

24. Pavlides GS, Nahhas GT, London J, Gangadharan C, Troszak E, Barth-Jones D, et al. Predictors of longterm event-free survival after percutaneous balloon mitral valvuloplasty. Am J Cardiol 1997; 79(10): 1370-4.

25. Langerveld J, Ernst JMPG, Van Hemel NM, Jaarsma W. Indication and timing of percutaneous mitral balloon valvotomy and the role of atrial fibrillation. Neth Heart J. 2005; 13(1):4-10.

26. Gamra H, Betbout F, Ben Hamda K, Addad F, Maatouk F, Dridi Z, et al. Balloon mitral commissurotomy in juvenile rheumatic stenosis: a ten-year clinical and echocardiographic actuarial results. Eur Heart J. 2003; 24(14):1349-1356.

27. Hasan-Ali H, Shams-Edin H, Abd-Elsayed AA, Maghraby MH. Echocardiographic assessment of mitral valve morphology after Percutaneous Transvenous Mitral Commissurotomy (PTMC). Cardiovasc Ultrasound. 2007; 5:48.

ACKNOWLEDGEMENT

I would like to thank all the staff of the medical records of the Philippine Heart Center for patiently providing me the needed charts for this research. Likewise, a heartfelt gratitude to those who have assisted me in completing this paper namely the research division of the Philippine Heart Center.

EYE PROFILE OF CHILDREN AGES 3-5 YEARS OLD IN A DAY-CARE CENTER IN BRGY. BATIS, SAN JUAN

Kristine Inopia, MD

Carlos Chua, MD, FPAO
Co-Author

Our Lady of Lourdes Hospital
Institutional Affiliation

ABSTRACT

OBJECTIVE: To determine the eye profile of children ages 3-5 years old in a day-care center in Brgy. Batis.

DESIGN: Cross-sectional descriptive study.

METHODS: Visual screening was conducted in 89 preschool children aged 3 to 5 years. The screening involved two basic procedures; the distant visual acuity test and structural eye exam. Those who failed the examination were referred to an ophthalmologist for further examination.

RESULTS: The prevalence of visual impairment was 5.6%. Of the 89 preschool children screened, 4 of them failed the distant visual acuity test. One had strabismus. Refractive errors were the most common cause of visual impairment. Hyperopic astigmatism was the most common type of refractive error seen in these age groups.

CONCLUSIONS: The study is a small but important step in the effort to understand the problem of visual impairment among our preschool children. Although results were low, the mere presence of visual disorders in this study is an important confirmation that there is a need for preventive ophthalmologic examination in these age groups.

KEYWORDS: Preschool children, Eye screening, Prevalence, Visual impairment, Distant visual acuity, Strabismus, Amblyopia

INTRODUCTION

The human eye is the organ which gives us the sense of sight, allowing us to observe and learn more about the surrounding world than we do with any other four senses.[1]

Good vision is essential for proper physical development and educational progress in growing children.[2] Vision is an important requirement for learning and plays a critical role in the development of a child during the first three years of life. Children use their sight to strengthen motor functions, establish parent–child bonding, build picture perception and gain their balance.[3] However, visual system in the young child is not fully mature. Equal input from both eyes is required for proper development of the visual centres in the brain. If a growing child's eye does not provide a clear focused image to the developing brain, then permanent irreversible loss of vision may result. Early detection provides the best opportunity for effective, inexpensive treatment. [2]

The American Academy of Ophthalmology and the American Association for Paediatric Ophthalmology and Strabismus recommend timely screening for the early detection and treatment of eye and vision problems in America's children. This policy includes institution of rigorous vision screening during preschool years wherein common conditions such as reduced vision in one or both eyes from amblyopia, uncorrected refractive errors or misalignment of the eyes (strabismus) can be detected. However, in the Philippines, there is no policy yet established.

REVIEW OF RELATED LITERATURE

In 1899, Connecticut instituted the first state-supported school vision screening test, setting an important precedent despite problems with poorly standardized testing conditions and insufficient funds for following up those who failed the vision screening. Over 100 years later, rates of vision screening among school-aged children remain relatively low, in part because of the controversy over the effectiveness of screening techniques as compared with examinations based on symptoms, and the unclear relationship between undiagnosed visual impairment and academic performance. While some studies have linked undetected or uncorrected visual impairment to poor academic performance, high school dropout rates, and even juvenile delinquency, others have argued that there is little evidence to support such a link. What is irrefutable is that undetected amblyopia, strabismus, and significant refractive errors can have significant long-term effects on visual function and in some patients can cause permanent unilateral or bilateral vision loss.[4]

Amblyopia and amblyogenic factors like strabismus and refractive errors are the most common vision disorders in children.[5]

Amblyopia is a reversible visual deficit that develops during the maturation of the visual system. Amblyopia affects 5% of the preschool children and is potentially treatable. The two common causes of amblyopia are strabismus and refractive errors. Early detection of amblyopia is necessary to avoid permanent

visual deficit by allowing treatment to be undertaken within the sensitive period of neuroplasticity (growth and change) in the visual system, thus, increasing the likelihood of successful treatment. Preschool screening programs may result in better visual outcome than screening at school entry.[6]

Preschool screening programmes for amblyopia were developed in response to experimental data in animals which suggested that early treatment of conditions analogous to human amblyopia is more effective than treatment later in life.[7]

In a systematic review done by Christine Schmucker et al regarding the Effectiveness of screening preschool children for amblyopia, three studies suggested that screening is associated with an absolute reduction in the prevalence of amblyopia between 0.9% and 1.6% (relative reduction: between 45% and 62%).[5]

Furthermore, in the retrospective cohort study of Eibschitz-Tsimhoni et al 2000 (the only study which compared screening versus no screening without implementing a current screening programme), it was observed that the frequency of severe amblyopia (visual acuity ≤5/15) was reduced by a factor 17 in the screening group ($p < 0.001$). [8] Williams et al in 2002 and 2003 also reported that mean visual acuity in the worse eye was better for children who had been treated for amblyopia in the intervention group than for similar children in the control group. [9]

OBJECTIVES

General Objective:

To determine the eye profile of children ages 3-5 years old in a day-care center in Brgy. Batis.

Specific Objectives:

1. To screen children ages 3-5 years old for visual disorders.

2. To assess visual profile of each child in terms of: eye structure, visual acuity, eye alignment and refraction.

3. To analyze the prevalence of various visual disorders such as amblyopia, strabismus, reduced visual acuity, refractive errors and severe visual impairment in these age groups.

Operational Definition

Amblyopia: poor vision in an otherwise normal appearing eye occurs when the brain does not recognize the sight from that eye. Two common causes are strabismus and a difference in the refractive error. If untreated, it can cause irreversible visual loss. The best time for treatment is in the preschool years. Improvement of vision after the child is 8 or 9 years of age is rarely achieved.

Strabismus: misalignment of the eyes in any direction. It may develop when the eyes do not align. If early detection is followed by effective treatment, excellent vision may be restored.

Refractive errors: decreased vision, visual discomfort ("eye strain").The most common form is nearsightedness (poor distance vision) is usually seen in school-age children and is treated effectively, in most cases, with glasses. Farsightedness can cause problems with focusing at near and may be treated with glasses. Astigmatism (imperfect curvature of the front surface of the eye) also requires corrective lenses if it produces blurred vision or discomfort. Uncorrected refractive errors can cause amblyopia particularly if they are severe or are different between the two eyes.

Visual Acuity: The clinical method for using a mathematical fraction that expresses the ratio of two distances, which is also the ratio of one's visual acuity to that of a normal person.[7] *Distance of visual acuity should be tested at 6 meters (20 ft) or 3 meters (10 ft) and at reading distance 30-40 cm from child under good illumination.

** Normal Visual Acuity:

3 years old: 20/50 and below

4years old: 20/40 and below

5 years old: 20/30 and below

METHODS

The Eye Profile screening protocol was approved by the hospital Ethics committee and the Department of Pediatrics. The study was conducted with a written informed consent obtained from parents of all participants.

Design and sample

The eye profile screening was a cross-sectional descriptive study involving 89 preschool children ages 3-5 years old in a daycare center in baranggay batis. Baranggay batis has a population of approximately 1,100 children ages 3-5 years old. The preschool students of the daycare center were chosen as the representative population. A total of 100 preschool students were enrolled at the daycare center. However, only 89 students were able to participate. Sample size was calculated from an expected prevalence rate of 10%.

Site inspection and informed consent

After identification of the preschool children, the respective baranggay health officers and preschool teacher were approached and informed about the study. Upon approval, the day-care centre was inspected for the suitability of the screening process. A place is considered suitable if there is a room with more than 4 meter long which is free from distractions. The light level should be adequate (at least 300 lux in the room and test chart illumination of about 500 lux). Consent forms and information sheets were distributed to the parents one week before the screening procedure. The consent forms and information sheets were written in two major languages (English, Filipino). On the day of screening, the consent forms were collected. Children whose parents gave their written consent to participate in this study were included in the eye screening.

Vision screening

All 89 preschool children underwent two basic screening procedures which included structural eye exam and distant visual acuity test. Measurement of the distant visual acuity was performed using the Allen picture chart. The tests were performed by 3 resident physicians. The children were subjected to structural eye exam first followed by distant visual acuity test. The structural eye exam included inspection for any eye structural abnormalities. This included the cover test to check for alignment disorders. The distant visual acuity test was measured monocularly at a distance of 6 meter. The right eye was tested first before the left eye. The test results of both the eyes were recorded separately. Results were recorded as "pass" if the child can identify the figures in the chart correctly and "fail" if the child was unable to locate the pictures. Children who failed the procedure were referred to a pediatric ophthalmologist for a detailed eye examination.

Referral and further evaluation

Children who failed the eye exam were given a referral letter for a comprehensive eye examination. Examination was performed by a trained ophthalmologist. The examinations included……. Children with underlying refractive errors were prescribed glasses.

Statistical Analysis

Data was analyzed using Stata version 10 software. Descriptive statistics entailed use of means and standard deviation for quantitative variables and counts and proportions for qualitative variables.

Results and Interpretation

A total of 89 children aged 3-5 years old from a day-care center in Barangay Batis underwent screening for visual disorders. Majority were males (56%) and belonged to the 3-year old age group (53%) (Figure 1).

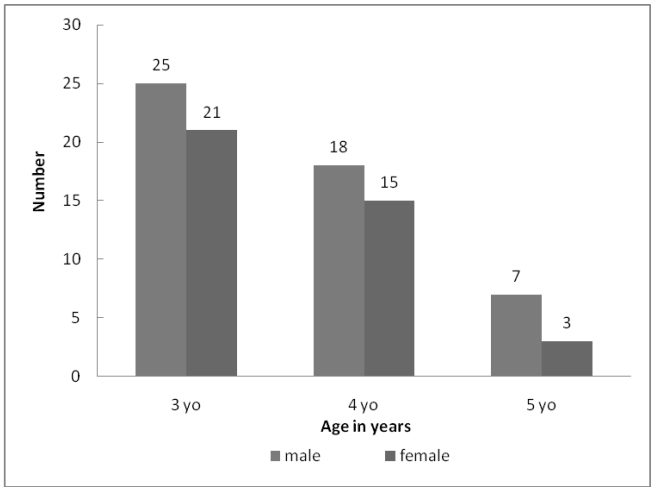


Figure 1: Age-Sex Distribution of Respondents

Visual acuity evaluation of 3-year olds was observed to vary predominantly between 20/20 to 20/30. Readings were consistently similar in both eyes in 80 to 100% of cases. There was one child noted to have a visual acuity of 20/70 and was referred for further evaluation (Table 1).

Table 1: Visual Acuity Profile of 3 year-olds

Visual Acuity, Left Eye	Visual Acuity, Right Eye						Total
	20/20	20/25	20/30	20/35	20/50	20/70	
20/20	8	2	0	0	0	0	10
20/25	0	13	1	0	0	0	14
20/30	0	1	17	0	0	0	18
20/35	0	0	0	1	0	0	1
20/50	1	0	0	0	1	0	2
20/70	0	0	0	0	0	1	1
Total	9	16	18	1	1	1	46

Visual acuity evaluation of 4-year olds was observed to vary predominantly between 20/20 to 20/25. There were two children noted to have a visual acuity above 20/40 and were referred for further evaluation (Table 2).

Table 2: Visual Acuity Profile of 4 year-olds

Visual Acuity, Left Eye	Visual Acuity, Right Eye					Total
	20/20	20/25	20/30	20/40	20/50	
20/20	10	0	0	0	0	10
20/25	3	14	0	0	0	17
20/30	0	0	4	0	0	4
20/50	0	0	0	1	1	2
Total	13	14	4	1	1	33

Visual acuity evaluation of 5-year olds was observed to vary predominantly between 20/25 to 20/30. There was one children noted to have a visual acuity above 20/30 and was referred for further evaluation (Table 3).

Table 3: Visual Acuity Profile of 5 year-olds

Visual Acuity, Left Eye	Visual Acuity, Right Eye				Total
	20/20	20/25	20/30	20/50	
20/25	1	4	2	0	7
20/30	0	0	2	0	2
20/40	0	0	0	1	1
Total	1	4	4	1	10

Out of 89 pre-schoolchildren who underwent evaluation for visual acuity, 96% passed and 4% were referred for further evaluation and management. The prevalence of visual acuity problems in this sample of pre-schoolers was 4%. Of these, 2 were males and 2 were females. Among males a 4-year old and 5 year-old with a visual acuity above 20/40 and 20/30, respectively. And among females, a 3-year old and a 4-year old with a visual acuity above 20/50 and 20/40, respectively (Table 4)

Table 4: Visual interpretation by Age and Gender

Gender-Age	Interpretation		Visual Acuity Defect	
Male	Passed No. (%)	Referred No.(%)	Left Eye	Right Eye
3	25 (100.0)	0		
4	17 (94.4)	1 (5.6)	20/50	20/50
5	6 (85.7)	1 (14.3)	20/40	20/50
Female				
3	20 (95.2)	1 (4.8)	20/70	20/70
4	14 (93.3)	1 (6.7)	20/50	20/40
5	3 (100.0)	0		
Total	85 (96.0)	4 (4.0)		

Of the total sample of pre-schoolchildren who underwent ophthalmologic screening, one had an eye structure problem. This was a 3-year old male evaluated to have strabismus. The prevalence of eye structure problems in this sample of pre-school children was 1% (Table 5).

Table 5: Eye structure profile by age and gender

Gender-Age	Normal	Abnormal
Male		
3	24	1
4	18	0
5	7	0
Female		
3	21	0
4	15	0
5	3	0
Total	88 (98.9)	1 (1.1)

Half of those with visual acuity problems were assessed to have hyperopia and astigmatism. This was a 4-year old female prescribed corrective lenses and a 4-year old male who did not require glasses and was advised close follow-up. The other half failed to follow-up (Table 6).

Table 6: Ophthalmologic Assessment and Intervention of Children referred for Visual Acuity Problems

	Visual Acuity Defect		Ophthalmologic Assessment	Intervention
	Left Eye	Right Eye		
Male				
4	20/50	20/50	Hyperopia/Astigmatism	No need for glasses; Close follow-up advised
5	20/40	20/50	Failed to follow-up	-
Female				
3	20/70	20/70	Failed to follow-up	-
4	20/50	20/40	Hyperopia/Astigmatism	Corrective lenses

DISCUSSION

The prevalence of visual disorders conducted in this study was 5% mostly due to refractive errors (4%). These results were comparable with the study done by Premsenthil et. al regarding visual impairment in preschool children in Malaysia wherein visual screening was conducted in 400 preschool children aged 4 to 6 years. The prevalence of visual impairment was 5%, mostly due to refractive errors.[6] A similar study done by Jamali et al. regarding refractive errors and ambylopia in children in Iran reported that about 6.3% of the children entering school were at risk of amblyopia; mostly due to refractive errors.[10] In a study done in Hongkong by Fans et.al regarding the change in vision disorders among preschoolers, about 4.4% of preschool children had either reduced visual acuity or strabismus.[11] In this study, strabismus was seen in 1% of the population. This was a 3 year old male who was referred for further evaluation but was lost to follow-up. Refractive errors were noted in 4% of the population which prompted referral to an ophthalmologist. However, only 2% followed-up. Hyperopia with astigmatism was the type of refractive error seen in two 4-year old pre-schoolers. Significant refractive errors were not observed.

LIMITATION

This study has the inherent weakness of a cross-sectional study. The data collection was restricted to one baranggay. Data regarding the developmental milestone and nutritional status of the children were not collected. The presence of developmental delay and malnutrition may indicate the presence of associated visual impairment. In addition, the children were only tested for visual acuity and structural eye exam. Comprehensive eye examinations were only offered to those who failed the screening tests.

CONCLUSION AND RECOMMENDATION

The study is a small but important step in the effort to understand the problem of visual impairment among the preschool children. Although results were low, the mere presence of visual disorders in this study is an important confirmation that there is a need for preventive ophthalmologic examination in these age groups. Identification of vision impairment before school entry could help identify children who may benefit from early interventions to correct or improve vision.

BIBLIOGRAPHY

1. Anatomy, Physiology and Pathology of the Human Eye. Ted M. Montgomery O.D. 1998-2003.

2. American Academy of Ophthalmology. Policy statement: Vision Screening for Infants and Children. March 2007

3. Prechtl HF, Cioni G, Einspieler C, Bos AF, Ferrari F: Role of vision on early motor development: lessons from the blind. Dev Med Child Neurol 2001, 43(3):198–201.

4. Elias I. Traboulsi, et al: Vision First, A Program to Detect and Treat Eye Diseases in Young Children: The First Four Years. December 2008.

5. Effectiveness of screening preschool children for amblyopia: a systematic review. Department of Medical Biometry and Statistics (German Cochrane Center), Institute of Medical Biometry and Medical Informatics, University Medical Center, Freiburg, Germany. 2009

6. The screening of visual impairment among preschool children in an urban population in Malaysia; the Kuching pediatric eye study: a cross sectional study Mallika Premsenthil1, Rose Manju2, Asokumaran Thanaraj3, Syed Alwi Syed Abdul Rah man4 and Tan Aik Kah1*)

7. Wiesel TN: Postnatal development of the visual cortex and the influence of environment. Nature 1982, 299:583-591)

8. Eibschitz-Tsimhoni M, Friedman T, Naor J, Eibschitz N, Fiedman Z: Early screening for amblyogenic risk factors lowers the prevalence and severity of amblyopia. Journal of AAPOS 2000, 4:194-199

9. Williams C, Harrad RA, Harvey I, Sparrow JM, ALSPAC Study Team: Screening for amblyopia in preschool children: results of a population-based, randomised controlled trial. ALSPAC Study Team. Avon Longitudinal Study of Pregnancy and Childhood. Ophthalmic Epidemiol 2001

10. Jamali P, Fotouhi A, Hashemi H, Younesian M, Jafari A: Refractive errors and amblyopia in children entering school: Shahrood, Iran. Optom Vis Sci 2009, 86(4):364–369.

11. Fan DS, Lai C, Lau HH, Cheung EY, Lam DS: Change in vision disorders among Hong Kong preschoolers in 10 years. Clin Experiment Ophthalmol 2011, 39(5):398–403.

OSTEOARTHRITIS OF THE KNEE: CORRELATION OF 1.5 T MRI FINDINGS WITH RADIOGRAPHIC SEVERITY BASED ON KELLGREN-LAWRENCE GRADING OF OSTEOARTHRITIS. A RETROSPECTIVE STUDY FROM JANUARY 2012 TO APRIL 2013 IN THE MEDICAL CITY SETTING

Mariaem M. Andres, MD, DPBR
Principal Investigator

Carlos Joshua L. Espino, M.D., FPCR
Consultant Adviser

Radiology Department, The Medical City
Ortigas, Pasig City, Philippines
Institutional Affiliation

RESEARCH OBJECTIVES

General

To correlate magnetic resonance (MR) imaging-defined abnormalities of osteoarthritis (OA) of the knee with radiographic severity based on Kellgren-Lawrence grading of osteoarthritis.

Specific

- To grade the various stages of OA by using Kellgren-Lawrence grading scale
- To evaluate the OA of knee using MRI and describe each findings
- To determine the prevalence of structural lesions evident in MRI that are associated with OA and to correlate them with radiographic Kellgren-Lawrence grading of osteoarthritis
- To aid orthopedic clinicians in the approach to diagnosis of patients with OA

SIGNIFICANCE OF THE STUDY

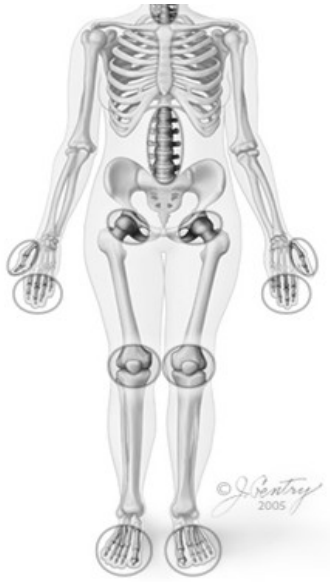
Osteoarthritis (OA) of the knee is a rising prevalent disease of patients with increasing age. Traditional structural changes of OA are assessed with radiographs, mainly the osseous details. However, radiographs lack the sensitivity of soft tissue depiction. MRI, then, will facilitate the evaluation of the soft tissues and cartilage of the knee, thereby, giving a whole-organ approach in assessment. By determining the prevalence of the soft tissue findings in MRI, clinicians could have a picture in mind what to expect in the different grades of OA using only radiography.

INTRODUCTION

Osteoarthritis (OA) is the most frequent form of arthritis, with radiologic and clinical implications that still remains to be under study since no definite effective treatment is available. The committee on OA of the American College of Rheumatology Diagnostic and Therapeutic Criteria Committee defined OA as "A heterogeneous group of conditions that lead to joint symptoms and signs which are associated with defective integrity of articular cartilage, in addition to related changes in the underlying bone at the joint margins" [1].

OA develops when cartilage deteriorates. The degenerative process is usually long and slow. In the early stages of the disease the surface of the cartilage becomes inflamed. The joint loses proteoglycans and water, hence, fissures and pits appears in the cartilage. As the disease progresses and more tissue is lost, the cartilage starts to harden and as a result, it becomes increasingly prone to damage from repetitive use and injury.

This degenerative joint disease frequently affects middle-age to elderly people which is one of the top reasons for functional impairment. It is commonly referred to as "wear and tear" of the joints. Risk factors include genetics, female sex, past trauma, advancing age, and obesity. The clinical diagnosis is based on history of joint pain [2]. ***Figure 1*** shows a schematic depiction of the affected joints in OA.



In the local setting, Filipino patients with OA have the knee as the most common affected site. Majority of the diagnosed patients are females in their 5th decade of life [3].

From an extrapolated data released by US Census Bureau in 2004, the Philippines has an estimated number of more than 6 million individuals diagnosed with osteoarthritis which is approximately 7-8% of the total population. This number is estimated to rise by the hundreds every year.

Figure 1. Schematic illustration of affected joints in osteoarthritis.

BACKGROUND INFORMATION

Radiography

Traditionally, OA structural changes have been assessed with radiographs. The standing anteroposterior (AP) protocol of the knee in extension in the weight-bearing position used to be the most commonly used technique. Standing AP and lateral radiographs suffice for routine clinical assessment of patients diagnosed or suspected with OA.

Radiography is used in clinical practice to establish the diagnosis of OA and to monitor the progression of the disease. Radiographs depict bony features, including marginal osteophytes, subchondral sclerosis, and subchondral cysts, that are associated with OA and provide an indirect estimate of cartilage thickness and meniscal integrity by allowing assessment of joint space width (JSW). Radiographic assessment of OA relies mainly on the evaluation of both osteophytes and joint space narrowing. Osteophytes develop at an earlier stage than joint space narrowing, and they are the most widely applied radiographic criterion for defining the presence of OA, while assessment of the severity of OA relies mainly on joint space narrowing and concomitant subchondral bone abnormalities. The main shortcomings of radiography are its insensitivity to change and its lack of soft-tissue depiction [1], [5], [6].

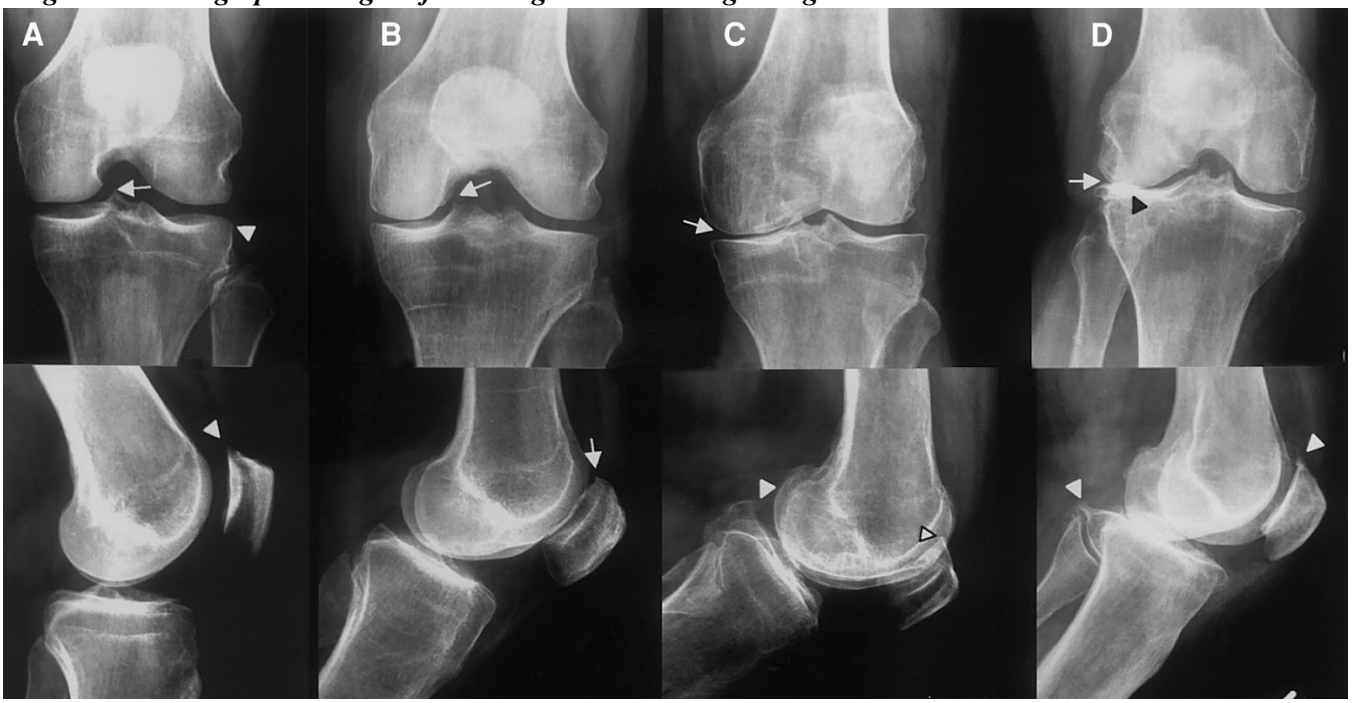
Several grading scales that incorporate combinations of features have also been developed, including the most widely used Kellgren-Lawrence grading scheme, which is the current accepted standard for the diagnosis of OA on radiographs. This scheme was adopted by World Health Organization as the reference standard for cross-sectional and longitudinal epidemiologic studies [7].

Table 1. Kellgren-Lawrence Grading Scheme for OA

Kellgren-Lawrence Grading	Description	Figure
0	No features of OA	
1	Doubtful joint space narrowing and possible osteophyte lipping	A
2	Definite osteophytes and possible joint space narrowing	B
3	Moderate multiple osteophytes; definite joint space narrowing, and some sclerosis and possible deformity of bone ends	C
4	Large osteophytes, marked joint space narrowing, severe sclerosis, and definite deformity of bone ends	D

Source: Kellgren JH , Lawrence JS . *Radiological assessment of osteo-arthrosis* . Ann Rheum Dis 1957 ; 16 (4): 494 – 502 .

Figure 2. Radiographic images of the Kellgren-Lawrence grading scheme



Source: Kellgren JH , Lawrence JS . *Radiological assessment of osteo-arthrosis* . Ann Rheum Dis 1957 ; 16 (4): 494 – 502 .

Magnetic Resonance

Increasingly, MRI has become a useful tool for early detection of OA due to its superior soft tissue contrast that provides maximum diagnostic performance. MRI can visualize various tissues that are clinically relevant not seen on radiography. MRI can show incidental findings in otherwise asymptomatic people. In the knee, MRI visualizes most components of the joint, including articular cartilage, menisci, intra-articular ligaments, tendons, synovium, fat components, bone marrow, and subchondral margins that are not detectable by radiography.

Imaging with a 1.5-T large-bore magnet is still regarded as the clinical standard, and most of the studies in which MR imaging is applied for morphologic and compositional assessment of knee cartilage were performed at this field strength [8], [9].

MRI manipulates image contrast to highlight different tissue types. Common contrast methods include 2D or multi-slice T1-weighted, proton density (PD), and T2-weighted imaging. Spin echo (SE) and Fast-spin echo (FSE) imaging techniques are useful in evaluating focal cartilage defects. Recent improvements in hardware, software, gradients, and radiofrequency (RF) coils have led to the use of fast or turbo-spin echo imaging, fat saturation and water excitation to improve tissue contrast [10],[11].

Recent focus on the acknowledgement that OA as a whole-organ degenerative process, the utility and diagnostic contribution of MRI in the assessment of the disease cannot be overemphasized.

Table 2. Commonly Encountered MRI Findings in OA [11].

MRI Lesion	Description
Cartilage damage	Considered present if there was a small focal loss less than 1 cm in greatest width or areas of diffuse partial or full thickness loss.
Meniscal lesions	Included displaced or non-displaced meniscal tears or evidence of previous surgery (including repair and partial or complete resection) and complete maceration or destruction (that is, loss of normal contour and signal homogeneity within the meniscus) within the Anterior and posterior horns and the body of the medial and lateral menisci.
Osteophytes	Presence of bony projections that form along different margins of the tibiofemoral joint of the knee
Ligamentous abnormalities	Presence of a completely torn anterior or posterior cruciate ligament, or a torn or thickened medial or lateral collateral ligament
Bone marrow lesions	Subchondral bone marrow lesions, also known as "bone marrow edema-like lesions," were considered present if there are non-cystic subchondral areas of ill defined high signal on proton density weighted MR images with fat signal suppression
Subchondral cysts	Areas of markedly increased signal intensity in the subarticular bone with sharply defined rounded margins and no evidence of internal marrow tissue or trabecular bone on the fat saturated proton density weighted images
Synovitis	Synovial cavity was distended and filled with fluid (high signal intensity on fat saturated proton density weighted images), representing synovial thickening and joint effusion
Attrition	Flattening or depression of the articular surfaces of the tibia or femur was termed bone attrition, and any degree of deviation from the normal bony contour was considered abnormal

Source: *BMJ* 2012;345:e5339 doi: 10.1136/bmj.e5339 (Published 29 August 2012

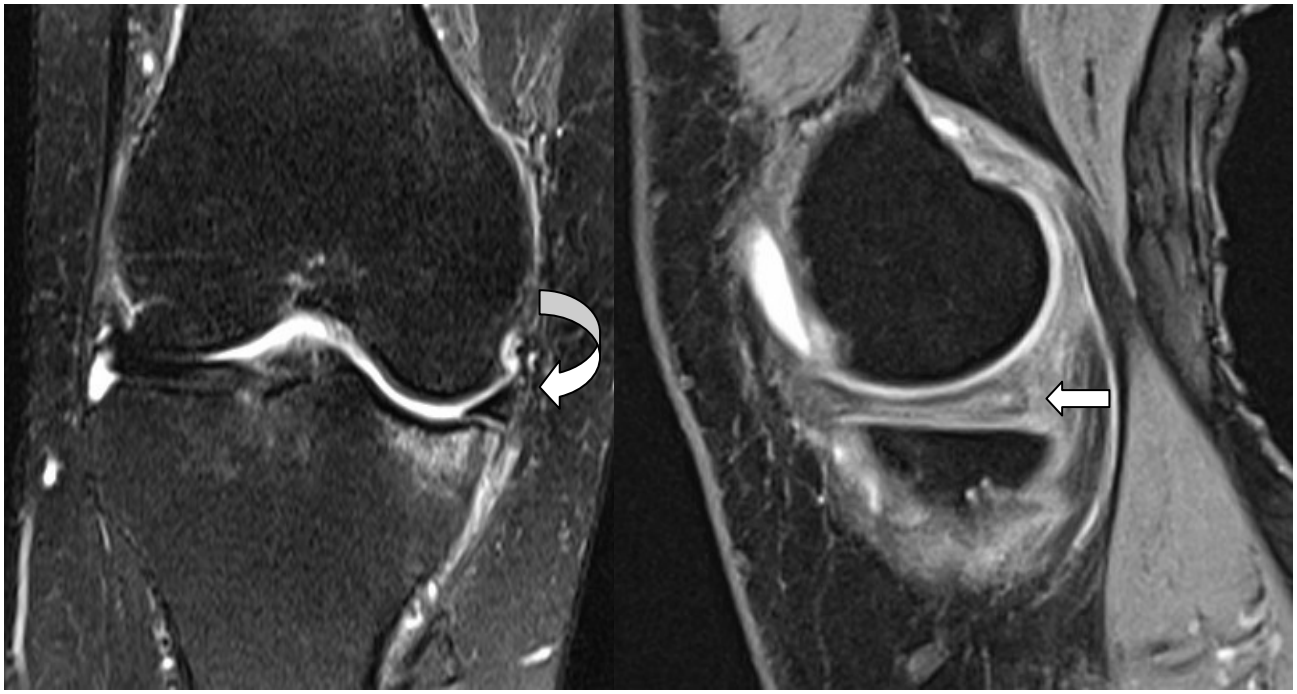


Figure 3. Right knee MRI images of a 58 year old female patient. T2 spin echo coronal fat saturated image of right knee showing full thickness cartilage defect in the medial femoro-tibial compartment (curved arrow) with associated bone marrow edema; the sagittal image showing diffuse hyperintense signals in the posterior root of medial meniscus with extension into inferior articular surface.

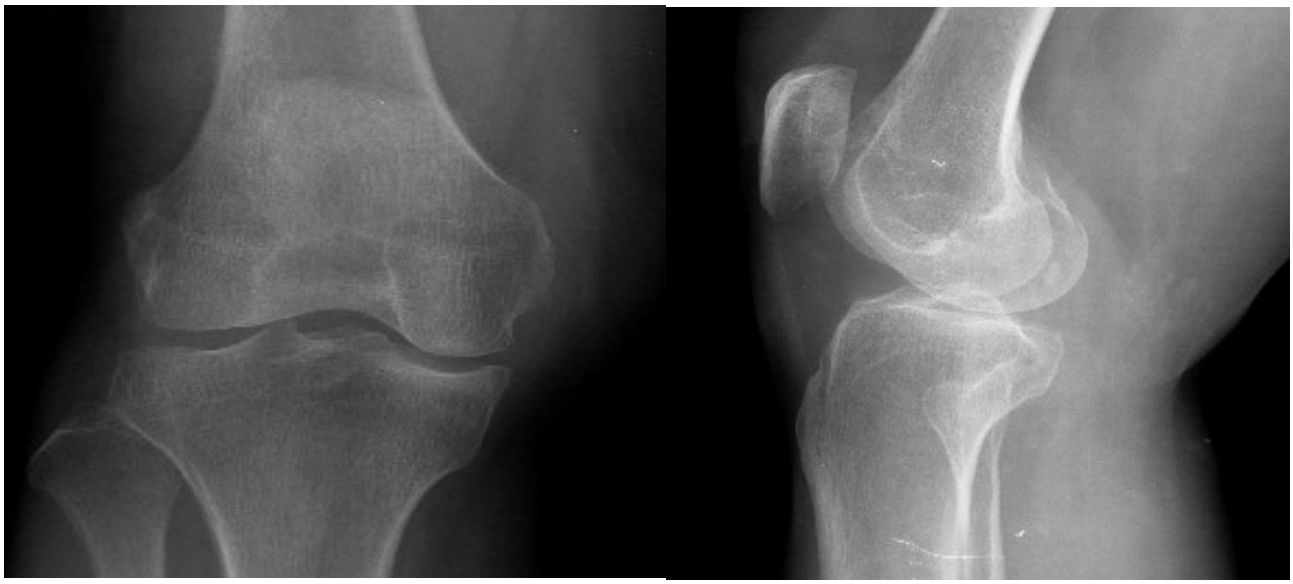


Figure 4. Right knee radiograph images of a 58 year old female patient. Anteroposterior and lateral views demonstrate narrowing of the medial femoro-tibial joint space with concomitant sclerotic changes in the medial tibial plateau associated with sharpening of the intercondylar spines. This was given grade 3 in the Kellgren-Lawrence severity scale of osteoarthritis. (Images were taken from PACS images of the outpatient MRI section of The Medical City)

REVIEW OF LITERATURE

Several studies have proven the fact that osteoarthritis leads to progressive cartilage loss and a number of imaging techniques have been developed and standardized to evaluate this qualitatively and semi-quantitatively. According to an article by Brant and colleagues, OA is not exclusively a disorder of the articular cartilage [12]. Apart from cartilage involvement, there are other associated findings in OA, such as bone marrow edema and synovial and ligamentous or tendinous lesions. Together, these lesions have significant effect on the progression of the disease.

It is a scientific fact that MRI can detect features suggestive of knee OA that cannot be appreciated on conventional radiography. Investigations being conducted enhance OA diagnosis through improvements in sensitivity and specificity in detection of this disease entity, thereby improving immensely clinical decision making.

The correlation of MR-imaging defined abnormalities and radiographically determined OA have been studied in several notable articles. In a study by Hayes et al, MR imaging finding depicting osteoarthritic change is detectable even if no radiographic evidence of OA is present [13]. Amin and colleagues investigated the relationship between radiographic progression of joint space narrowing and cartilage loss seen on MR images in patients with symptomatic knee OA and MR imaging–based cartilage loss. They showed that a substantial proportion of knees exhibit cartilage loss on MR images even when no radiographic progression is observed [14].

In a paper by Link and co-workers, the number of osseous, cartilaginous, synovial, ligamentous, and meniscal lesions depicted on MR images are associated with osteoarthritis and that the extent of these lesions correlates with radiographically determined Kellgren -Lawrence scores.

Type of Research:

Retrospective Cross-sectional Study

Materials and Methods

A. Participants

Patients, ages 30 to 85 years old, who had both radiographic and MRI examination of the knee in The Medical City Radiology Section from January 2012 to April 2013 whose images were stored in the picture and archiving system of the hospital. Excluded in the study are the patients with orthopedic implants on the knee.

B. Radiography

The routine AP and lateral radiographs of the knee through the picture archiving system (PACS) with final impression of OA were reviewed and re-evaluated by 2 consultant radiologists. The grading descriptions of Kellgren -Lawrence scheme were utilized in the assessment of the radiographic changes of the knee. There was no specific laterality required but the radiographs under study should be obtained within the same year the MRI was performed on the same knee being investigated. The consultants were blinded to the MRI findings. The data were pooled and arranged according to grade by the principal investigator.

C. MRI

Data from MRI done with a 1.5 Tesla scanner (Siemens Medical Systems, Erlangen, Germany) with a phased array knee coil was used. The sequences and imaging parameters are summarized in *Table 3*.

MRI images assessment was performed by the investigator wherein the knee cartilages, bony portions, meniscus, ligaments, and synovial cavities were scrutinized for abnormalities. The investigator was blinded to the Kellgren-Lawrence score designated for the knee under study. The morphologic impression of the knee was pooled according to the descriptions enumerated in the previous background information of the research protocol.

Table 3. Imaging Parameters Utilized in 1.5 Tesla Siemens Medical System

Imaging Parameter	Coronal PD FS	Coronal MED2D	Sagittal MED2D	Sagittal PD-T2 FS	Axial T1	Axial PD-T2 FS
TR (msec)	2670	680	20.60	2170	387	3470
TE (msec)	33	23	7.57	75	21	32
Matrix Size	314x448	179x256	288x384	288x384	314x448	192x256
Field of View (cm)	18	18	18	18	16	16
Slice Thickness (mm)	4	4	1.5	3.5	3	3
Bandwidth (kHz)	192	201	191	189	167	190
Signal to noise Ratio	1	1	1.47	1	1	1
Scan Time (min:sec)	2:31	2:41	3:01	3:24	3:29	3:26

Note: FS = fat suppressed, PD = proton density
MED2D = protocol with low sensitivity to artefacts of motion, susceptibility, and chemical shift
PD-T2 DESS Protocol = for orthopedic series that is good for differentiation between synovial liquid and cartilage definition

Statistical Analysis

MR imaging findings evaluation in relation to Kellgren-Lawrence Scores was performed through construction of contingency tables to correlate the frequency of categoric MR imaging findings to Kellgren-Lawrence Scores.

Statistical analyses were performed using SPSS software version 10.1 (Chicago Il, USA). For the testing of relationship between Kellgren-Lawrence score and MRI morphological findings, Chi-Square test was employed. P-values less than or equal to 0.05 were considered statistically significant.

RESULTS

A total of 144 patients were included in the study. The population presented at an age range from 30 to 85 years old, with average age at 51.9 years old (SD of 11.98).

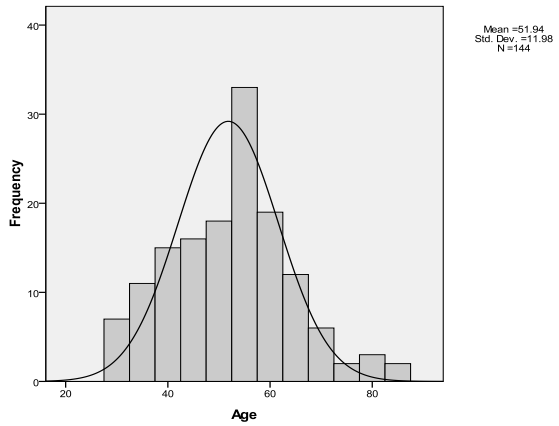


Figure 4. Bar Graph of Age Distribution of Patients

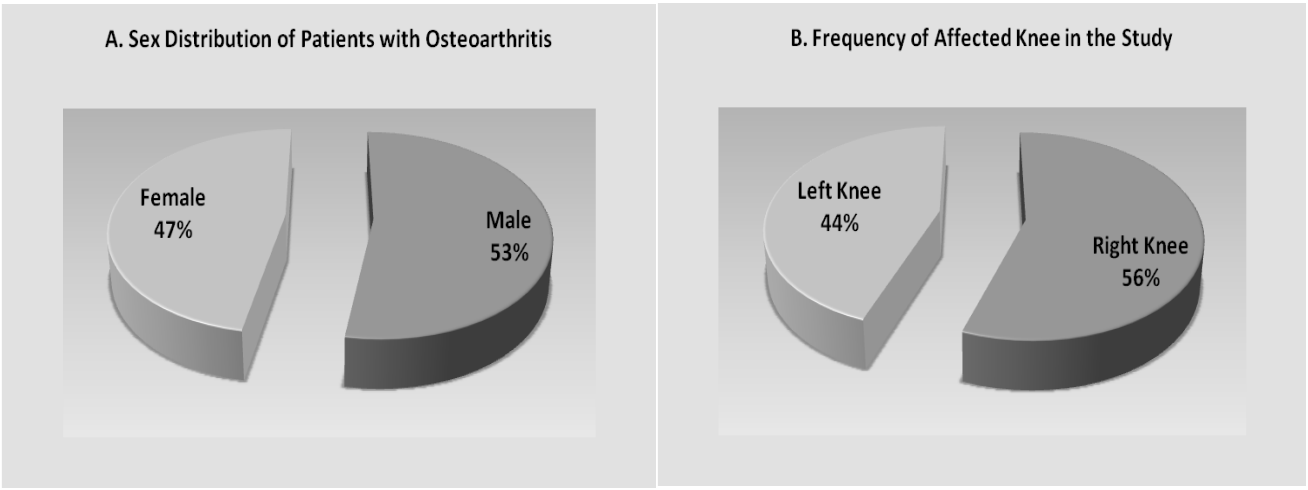


Figure 4. Pie graph representation of A. Sex distribution of patients with osteoarthritis, and B. Frequency of affected knee in the study

Figure 5 shows the study population included 68 females (47%) and 76 males (53%). The affected right knee was demonstrated to be imaged more often in the study.

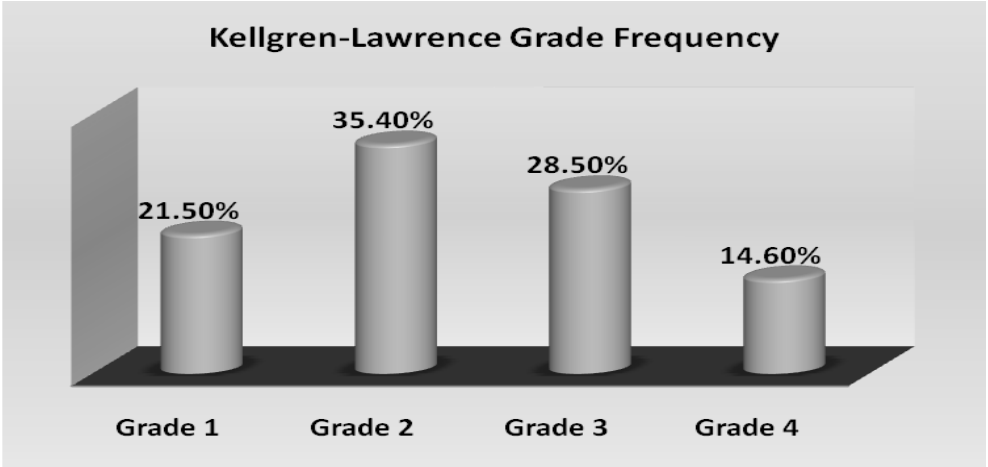


Figure 5. Column graph demonstration of the frequency of Kellgren-Lawrence Grading Scheme

The population was graded by Kellgren-Lawrence scores according to the severity of OA as diagnosed on radiograph features. ***Figure 6*** shows that more than one-third was given a Kellgren-Lawrence Grade of 2 comprising of 35.4%. Next to this value was Grade 3 at 28.5% subsequently followed by Grade 1 at 21.5%. Grade 4 had the fewest number of patients, hence, the lowest frequency value.

The association between various compartment specific MRI findings and KL score has been shown in ***table 4***.

Table 4. MRI findings and their overall prevalence per Kellgren-Lawrence Grade (KL)

MRI Lesions	KL – 1 (Subjects = 31)	KL – 2 (51)	KL – 3 (41)	KL – 4 (21)
Cartilage Damage	50%	62%	100%	100%
Meniscal Damage	56%	70%	85%	100%
Osteophytes	100%	100%	100%	100%
Ligamentous Abnormalities	47%	39%	46%	43%
Synovitis	53%	90%	100%	100%
Joint Space Narrowing	9%	37%	85%	100%

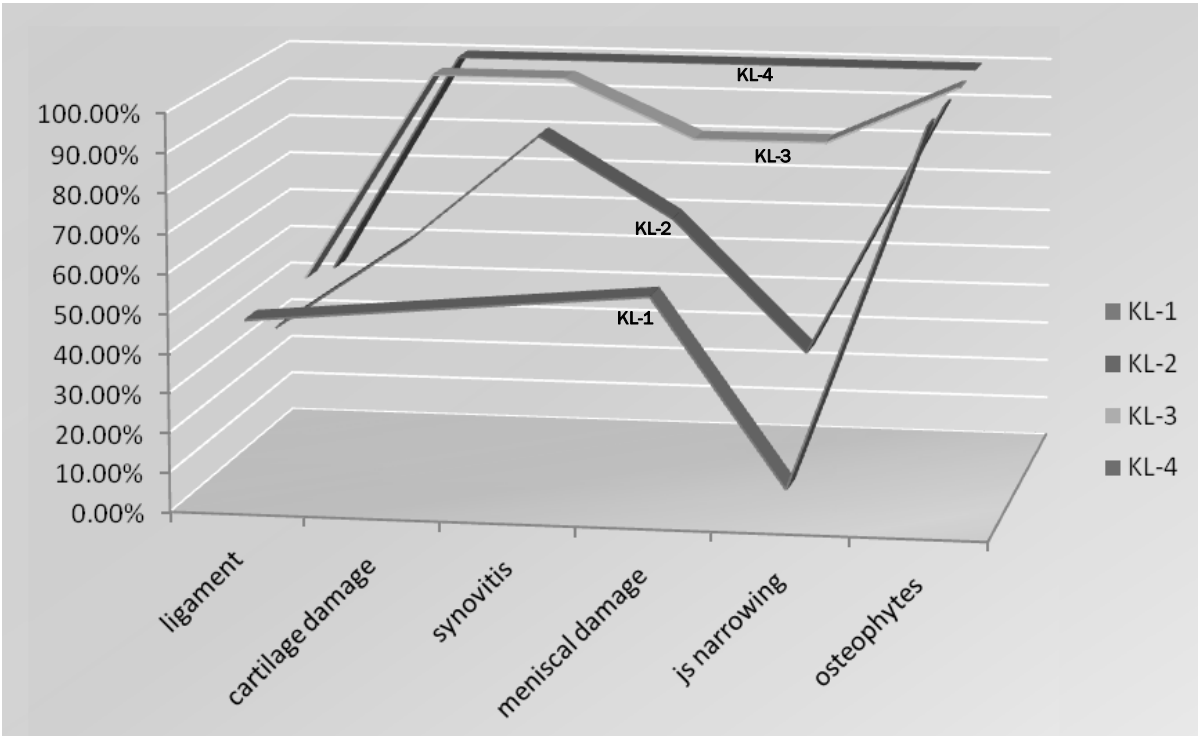


Figure 6. Stacked line graph depicting the frequency of MRI lesions in relation with Kellgren-Lawrence grade

In accordance with the numerous MRI findings, "Sharpening of intercondylar spines" was seen in ALL 144 patients. The next most common finding are "Spurs in patella" with 89.58% incidence, "minimal joint effusion" with 83.33%, "Spurs in femur" with 72.92%, "Spurs in tibia" with 70.83%, "Intrasubstance signal in patello-femoral cartilage" with 56.25%, and "myxoid degeneration, medial meniscus" with 50.69%. "lateral collateral ligament tear" was the least common MRI finding with only 4.17% incidence. Each of the specific frequencies for each of the MRI findings with their corresponding P-values and Chi-square computation are depicted and tabulated in the Appendix.

DISCUSSION

Osteoarthritis (OA) is a chronic and debilitating arthritic lesion that is diagnosed based on radiographic findings and clinical assessment. When radiograph is used, the sensitivity and specificity of diagnosis is at 91% and 85%, respectively [2, 10]. Rising utilization of MRI increases tremendously the effectiveness of early detection of OA lesions.

The noteworthy results of this study had acknowledged the rising fact that OA is a whole-organ disease process, as a brainchild of Dr. Peterfy in 2004 [15].

The male subjects slightly predominated over the female in this study with a 1.1:1 ratio and a mean age 51.9 years old. In a cohort study made by Racaza and colleagues in Philippine General Hospital in 2012, there is a female to male ratio of 3:1, with the female population being diagnosed with OA much more frequently than male. The mean age of OA peak recorded in that study was at 63 years old which is much later chronologically in comparison with the data at hand. According to a paper made by Eckstein et al, males were observed to progress in higher grade of OA over a period of two years than in females.

The data in this study showed there was a high correlation between severity of Kellgren-Lawrence Grade and MRI findings of osteophytes, cartilage, meniscal, and ligamentous damages, synovitis, and joint space narrowing with *P-values of <0.005* at 5% confidence interval. Table 4 and Figure 7 demonstrate the prevalence of MRI findings on each of the Kellgren-Lawrence scores.

Osteophytes. All of the subjects in the population showed osteophytes in the knee from the simple finding of intercondylar spine sharpe-ning prevalent in all the Kellgren-Lawrence grades to more complex osteophytes formations mostly affecting the patello-femoral compartment in grade 2 at 84.3%, grade 3 at 95%, and in grade 4 at 100%. According to Hayes et al in 2005 Radiology journal, there was increased likelihood of MRI detected osteophytes with increasing Kellgren-Lawrence grades.

Cartilage defects. Majority of the patients demonstrate cartilage damage described as focal intrasubstance signals in the femoro-tibial and patella-femoral cartilages

evident in all Kellgren-Lawrence grades with the increasing in area affected proportional to the grade severity. The patella-femoral cartilage was the more involved region at 64.7% in grade 2, 63.4% in grade 3, and 100% in grade 4. In the same study by Hayes et al in 2005, there was a strong association between the Kellgren-Lawrence score and the likelihood that defects of cartilage were present in the knee. 54% of their study population under grade 1 showed cartilage defects, 83% under grade 2, and 88% under grade 3.

Joint narrowing and attrition. The joint space narrowing or attrition changes in this study more severely involved the medial femoro-tibial and patella-femoral compartments, both at 37.5%, in relation with the lateral femoro-tibial region. The greatest prevalence of medial femoro-tibial attrition was detected in Kellgren-Lawrence grade 3 at 56.1% and grade 4 at 100%. Majority of attrition changes and radiographic sclerotic changes were reported by Joshi and colleagues to occur in the femoro-tibial and patella-femoral joints.

Meniscal Damage. Meniscal lesions, comprised of spectrum of changes from simple myxoid degeneration to grank tears of the different parts of the menisci, were shown in all Kellgren-Lawrence grades. The degenerative myxoid changes without frank tears dominated the data affecting mostly the medial meniscus under Kellgren-Lawrence grade 3 and 4 at 58.5% and 100%, respectively. However, the number of meniscal tears was mostly prevalent in grade 3 at 32% affecting the medial meniscus. As stated in the study of Joshi, incidence of medial and lateral meniscal injuries are almost equal at 90.6% and 96.8%, respectively, of which tears were present in 46.9% of medial meniscus and 53.1% of lateral meniscus.

Ligamentous Damage. It is noticeable that anterior cruciate ligament tear was the only ligamentous abnormality that was noted to be statistically significant with the greatest prevalence found at grade 4 at 43%. In the two separate studies by Hayes and Joshi, the ligamentous injuries were uncommon. in the latter research the author stated that 25% of the population under investigation showed ligament injury affecting the anterior cruciate ligament.

Joint effusion or Synovitis. The presence of synovitis or effusion was shown to be apparent in all grades, with grade 3 and 4 demonstrating 100% prevalence. Hayes et al also reported strong correlation of joint effusion and Kellgren-Lawrence score. Joint effusion of varying gradfes was reported in a study by Joshi stating that it was found in 78.1% of the study population.

Other MRI findings. In terms of other MRI findings, Baker's cyst was found in all Kellgren-Lawrence grades most notably in grade 2 and 4 at 24% and 38%, respectively. This was followed by suprapatellar bursitis which was also evident in all Kellgren-Lawrence grades but the most prevalence was seen in grades 2 and 4 at 24% and 29%, respectively.

The contingent data of the study found a statistically significant correlation between majority of MRI changes of OA in patella-femoral and medial femoro-tibial compartments of the knee. These changes include osteophytes, cartilage damage, attrition or joint space narrowing, meniscal damage, and joint effusion. However, there was weak correlation between MRI finding of ligamentous injury and severity of Kellgren-Lawrence grades.

CONCLUSION

In conclusion, MRI has strengthened its indispensable role in diagnosing and defining abnormalities of osteoarthritis of the knee evident in significant correlation between majority of MRI changes of the knee and Kellgren-Lawrence grade.

There was a general pattern that the older age group, the higher the prevalence of the features of OA. All of the participants had at least more than one (1) feature of OA on MRI. There were more frequent and more severe abnormalities detected at MRI as the radiographically determined Kellgren-Lawrence scores increased.

MRI features of OA were highly prevalent in the patella-femoral and medial femorotibial compartments. Osteophytes were the most common finding detected in all of the Kellgren-Lawrence grades. Next was the cartilage defect most prevalent in grades 3 and 4. These were then followed by effusion, attrition, and meniscal damage which were prevalent in grades 3 and 4 as well. Only ligamentous lesions showed no significant MRI and Kellgren -Lawrence grade correlation.

Reinforcement of the concept of assessing OA as a whole-organ disease through significant correlation of MRI and radiographic Kellgren-Lawrence grades were satisfied in this study. Clinicians would have in their references the findings in this study that each of the Kellgren-Lawrence grades could predict the most prevalent soft tissue expected findings that could be encountered in MRI.

LIMITATION

a. Disparity in the number of males and females in the population as well as in the division of the number of subjects per Kellgren-Lawrence grades.

b. Single center data review

RECOMMENDATION

a. Larger and equal distribution of subjects per gender and per Kellgren-Lawrence grade may prove prudent in decision making for better outcome and stronger statistical correlation.

b. Multi-center approach may improve immensely the subject number outcome. in addition, Multicenter research initiative could provide better results that could formulate a uniform diagnostic application of MRI in assessment and definition of OA.

REFERENCES

1. Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K et al. *Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association.* Arthritis & Rheumatism 1986; 29(8):1039-1049

2. Sinusas, Keith. *Osteoarthritis: Diagnosis and Treatment.* Am Fam Physician. January 1, 2012; 85 (1): 49-56.

3. Abao-Lim, Josephine MD, Cortes-Fabia, Stella MD, Hao-Tanopo, Llewelyn MD, Osio-Salido, Evelyn MD, Penserga, Ester MD, Amante, Clemente MD. *The Clinical Profile of Osteoarthritis among Filipino Patients Seen at the UP-PGH Medical Center*. Paper Presentation. PRA Annual Convention. January 1994.

4. US Census Bureau, Population Estimates, 2004.

5. Spector TD , Hart DJ , Byrne J , Harris PA, Dacre JE, Doyle DV. *Definition of osteoarthritis of the knee for epidemiological studies*. Ann Rheum Dis 1993 ; 52 (11): 790 – 794.

6. Kellgren JH, Lawrence JS. *Radiological assessment of osteo-arthrosis* . Ann Rheum Dis 1957 ; 16 (4): 494 – 502 .

7. Link, T, Steinbach, L, Ghosh, s, Ries, M, Lu, Y, Lane, N, and Majumdar, S. *Osteoarthritis: MR Imaging Findings in Different Stages of Disease and Correlation with Clinical Findings.* February 2003 *Radiology,* 226, 373-381.

8. Gerdes CM , Kijowski R , Reeder SB . *Ideal imaging of the musculoskeletal system: robust water fat separation for uniform fat suppression, marrow evaluation, and cartilage imaging.* AJR Am J Roentgenol 2007; 189 (5): W284 – W291 .

9. Yoshioka H, Stevens K, Hargreaves BA, et al. *Magnetic resonance imaging of articular cartilage of the knee: comparison between fat-suppressed three-dimensional SPGR imaging, fat-suppressed FSE imaging, and fat suppressed three-dimensional DEFT imaging, and correlation with arthroscopy.* J Magn Reson Imaging 2004; 20 (5): 857-864.

10. Roemer, F, Crema, M, Trattnig, S, and Guermazi, A. *Advances in Imaging of Osteoarthritis and Cartilage.* Radiology, August 2011: Vol 250 (2): 332-354.

11. Guermazi, A, Niu, j, Hayashi, D, Roemer, F, Englund, M, Neogi, T, Aliabadi, P, McLennan, C, and Felson, D. *Prevalence of Abnormalities in Knees Detected by MRI in Adults without Knee Osteoarthritis: population based study (Framingham Osteoarthritis Study).* BMJ, August 2012; 345: e5339doi.

12. Brandt KD, Radin EL, Dieppe PA, van de Putte L. *Osteoarthritis is not a cartilage disease*. Ann Rheum Dis 2006; (65): 1261–1264.

13. Hayes, C, Jamadar, D, Welch, G, Jannaush, M, Lachance, L, Capul, D, and Sowers, MF. *Osteoarthritis of the Knee: Comparison of MR Imaging Findings with Radiographic Severity Measurements and Pain in Middle Aged Women.* Radiology 2005**;** 237:998–1007

14. Amin S, LaValley MP, Guermazi A, et al. *The relationship between cartilage loss on magnetic resonance imaging and radio-graphic progression in men and women with knee osteoarthritis.* Arthritis Rheum 2005; 52 (10): 3152 – 3159.

15. Peterfy CG, Guermazi A, Zaim S, et al. Whole-Organ Magn Reson Imaging Score (WORMS) of the knee in osteoarthritis. Osteoarthritis Cartilage 2004;12:177–190.

16. Racaza GZ, Salido EO, Penserga EG. Clinical *profile of Filipino patients with osteoarthritis seen at two arthritis clinics.* Int J Rheum Dis. 2012 Aug;15(4):399-406.

17. Eckstein, F, Burstein, D, and Link, T. *Quantitative MRI of Cartilage and Bone: Degenerative Changes in Osteoarthritis.* NMR Biomedicine 2006; 19:822-54.

18. V. Joshi, R. Singh, N. Kohli, U.C. Parashari, A. Kumar, V. Singh: Evaluation Of Os teoarthritis Of The Knee With Magnetic Resonance Imaging And Correlating It With Radiological Findings In The Indian Population. *The Internet Journal of Orthopedic Surgery*. 2009 Volume 14 Number 1. DOI: 10.5580/1860

APPENDIX

More males were included in the study

Table 5. Gender

	Frequency	Percent
Female	68	47.2
Male	76	52.8
Total	**144**	**100.0**

Right knee is more prone to being diagnosed for osteoarthritis

Table 6. Affected Knee

	Frequency	Percent
Left Knee	64	44.4
Right Knee	80	55.6
Total	**144**	**100.0**

Table 7. MRI findings vs. Kellgren-Lawrence Grade

MRI Findings		Kellgren-Lawrence Grade				Total	P-Value
		1	2	3	4		
Affected Knee	Left	16	23	18	7	64	1.709; 0.635ns
	Right	15	28	23	14	80	
Age	Mean (SD)	42.23 (9.49)	49.71 (9.09)	56.37 (9.54)	63.05 (13.18)	51.94 (11.98)	21.991; 0.000**
Gender	Female	10	18	27	13	68	13.224; 0.004**
	Male	21	33	14	8	76	
Thinning of Medial Femoro-Tibial Cartilage	No	29	41	17	3	90	48.287; 0.000**
	Yes	2	10	24	18	54	
Thinning of Lateral Femoro-Tibial Cartilage	No	31	47	33	10	121	29.528; 0.000**
	Yes	0	4	8	11	23	
Thinning of Patello-Femoral Cartilage	No	30	41	17	2	90	55.391; 0.000**
	Yes	1	10	24	19	54	
Intrasubstance Signal in Patello-Femoral Cartilage	No	14	18	25	6	63	8.416; 0.038*
	Yes	17	33	26	15	81	
Intrasubstance signal in Femoro-Tibial Cartilage	No	19	20	28	7	74	11.672; 0.009**
	Yes	12	31	13	14	70	
Spurs in Patella	No	5	8	2	0	15	6.391; 0.094ns
	Yes	26	43	39	21	129	
Spurs in Femur	No	19	19	1	0	39	41.449; 0.000**
	Yes	12	32	40	21	105	

MRI Findings		Kellgren-Lawrence Grade				Total	P-Value
		1	2	3	4		
Spurs in Tibia	No	22	19	1	0	42	50.658; 0.000**
	Yes	9	32	40	21	102	
Sharpening of intercondylar spines	No	0	0	0	0	0	-
	Yes	31	51	41	21	144	
Joint narrowing in Patello-femoral space	No	30	41	17	2	90	55.391; 0.000**
	Yes	1	10	24	19	54	
Joint Narrowing in Medial femoro-tibial space	No	29	40	18	3	90	45.152; 0.000**
	Yes	2	11	23	18	54	
Joint narrowing in Lateral femoro-tibial space	No	31	46	31	9	117	31.008; 0.000**
	Yes	0	5	10	12	27	
Myxoid degeneration, medial meniscus	No	21	33	17	0	71	30.488; 0.000**
	Yes	10	18	24	21	73	
Myxoid degeneration, lateral meniscus	No	23	37	18	0	78	38.508; 0.000**
	Yes	8	14	23	21	66	
Tear, medial meniscus	No	19	40	28	12	99	4.349; 0.226ns
	Yes	12	11	13	9	45	
Tear, lateral meniscus	No	29	44	33	18	124	2.522; 0.471ns
	Yes	2	7	8	3	20	
Tear, MCL	No	23	37	27	9	96	6.954; 0.073ns
	Yes	8	14	14	12	48	
Tear, LCL	No	30	49	38	21	138	2.009; 0.571ns
	Yes	1	2	3	0	6	
Tear, ACL	No	21	44	37	12	114	13.242; 0.004**
	Yes	10	7	4	9	30	
Joint Effusion	(none)	5	5	0	1	11	22.520; 0.001**
	Minimal	26	40	40	14	120	
	Moderate	0	6	1	6	13	
TOTAL		**31**	**51**	**41**	**21**	**144**	

As shown in the ***table 7***, Kellgren-Lawrence Grade is statistically & significantly related at 5% level of significance to Age, Gender, Thinning of Medial Femoro-Tibial Cartilage, Thinning of Lateral Femoro-Tibial Cartilage, Thinning of Patello-Femoral Cartilage, Intrasubstance Signal in Patello-Femoral Cartilage, Intrasubstance signal in Femoro-Tibial Cartilage, Spurs in Femur, Spurs in Tibia, Joint narrowing in Patello-femoral space, Joint Narrowing in Medial femoro-tibial space, Joint narrowing in Lateral femoro-tibial space, Myxoid degeneration-medial meniscus, Myxoid degeneration-lateral meniscus, Tear-ACl, and Joint Effusion.

The table below shows that those graded 4 mostly have "Baker's Cyst", "Suprapatellar Bursitis", and "Synovial cyst, poplieus tendon sheath". On the other hand, those with grade 3 mostly have "Baker's Cyst", "Prepatellar edema", and "Suprapatellar Bursitis".

Table 8. Other MRI Findings vs. Kellgren-Lawrence Grade

OTHER MRI Findings	Kellgren-Lawrence Grade				Total
	1	2	3	4	
Baker's cyst	2	5	3	8	18
Infrapatellar bursitis	0	0	1	0	1
Infrapatellar edema	0	0	0	1	1
Infrapatellar synovitis	0	3	0	0	3
Parameniscal cyst	0	1	0	0	1
Popliteal cyst	1	0	0	0	1
Popliteus tendinitis & suprapatellar tendonitis	0	1	0	0	1
Prepatellar edema	0	3	7	1	11
Sprain, gastrocnemius muscle	2	0	1	0	3
Sprain, quadriceps muscle	1	0	0	0	1
Sprain, sartorius muscle	1	0	0	0	1
Superolateral patellar dislocation	0	0	1	0	1
Suprapatellar bursitis	1	5	4	6	16
Suprapatellar bursitis; hematoma gastrocnemius	0	0	0	1	1
Synovial cyst, popliteus tendon sheath	0	2	2	4	8
Synovial osteochondroma	1	0	0	0	1
Villonodular disease	1	1	0	0	2
Total	**10**	**21**	**19**	**21**	**71**

COLOSTRUM POWDER SUPPLEMENTATION IN THE TREATMENT OF ACUTE WATERY, NON BLOODY DIARRHEA IN CHILDREN 6 MONTHS TO 36 MONTHS OF AGE WITH SOME SIGNS OF DEHYDRATION: A RANDOMIZED DOUBLE BLIND PLACEBO CONTROLLED CLINICAL TRIAL

Ermie Ann V. Badenas, M.D.
Principal Author

Michael M. Resurreccion, M.D.
Co-Author

Quirino Memorial Medical Center
Institutional Affiliation

OBJECTIVE: To determine the efficacy and safety of colostrum powder supplementation among pediatric patients 6 months to 36 months old with acute watery, non-bloody diarrhea in a Pediatric Ward of a Tertiary Government Hospital

STUDY DESIGN: Randomized, double-blinded, placebo controlled clinical trial

SETTING: Pediatric Ward of a Tertiary Government Hospital

PARTICIPANTS: Eighty subjects 6 months to 36 months old with acute non-bloody diarrhea of six days duration or less, with some signs of dehydration based on WHO-CDD protocol

INTERVENTION: Subjects were randomized to either colostrum powder (Group A) or placebo (Group B)

OUTCOME MEASURES: Efficacy of colostrum powder as treatment to acute watery diarrhea was measured in terms of stool characteristics, frequency and volume and duration of hospital stay.

RESULTS: A total of 80 diarrheal cases 6 months to 36 months of age were enrolled to the study. The two groups were essentially similar in terms of age (P value 0.345) and sex (P value 0.135). Mean age was 12.8 months for Group A and 14.5 months for Group B. The character of the stool was described as either watery, semi-formed and formed stool. The stools significantly differ in the two groups by day 3, 62% of subjects in Group A showed formed stools and 16% in Group B (P value – 0.00003). The volume of the stools was significantly higher in Group B than in Group A at all days of observation (P value 0.0001). Group A had lesser frequent stools on days 1-3. The cumulative rate of discharged was higher in Group A than in Group B starting day 3. On day 5, 92% of patient in Group A was discharged while 69% on Group B. The length of hospital stay was 2.21 days in Group A and 3.21 days in Group B (P value 0.0001).

CONCLUSION: Colostrum powder supplementation in the management of acute diarrhea enabled majority of the subjects in this study to have earlier formed stools and reduce volume of stool, reduce frequency of stooling, earlier discharge and shorter hospital stay. There was no adverse effect reported

KEYWORDS: colostrum, acute watery, non-bloody diarrhea, children, randomized controlled study

INTRODUCTION

Diarrheal disease is one of the leading causes of illness and death among young children in developing countries.[1] Children below 5 years of age are mostly affected with deaths occuring in the first two years of life. [2]

In the Philippines, diarrhea is one of the leading cause of morbidity and mortality for all ages. It is the second leading cause of morbidity among children under five years of age. Death due to acute diarrhea is secondary to severe dehydration which can be prevented with proper management.[3]

Over the past years, several measures at improving the health conditions of children were implemented. Oral rehydration therapy, improved nutrition, breastfeeding and immunization contributed to the reduction in the incidence of mortality and morbidity caused by diarrrhea.[2] Deaths from diarrhea in the first five years of life decline from the previous estimates of 13.6 to 5.6 per 1000 per year in a decade.[4] Based on the 2011 Family Health Survey, the estimated under-five mortality rate (U-5MR) or the probability of a child born on a specified year and dying before reaching the age of five years is lower than the estimated deaths per 1,000 live births compared to the 2006 Family Planning Survey (FPS). Under-five mortality levels in the Philippines continue to improve, falling from 64 deaths per 1,000 live births in 1993 to 40 deaths in 2003.[5] This reflects progress at improving the health conditions of children.

The management of diarrhea is primarily supportive and is directed at preventing or treating dehydration. Several measures were implemented to decrease the number of cases. There has been much interest on the use of probiotics, zinc and folic acid supplementation in modifying diseases of the gastrointestinal tract.[6,7] Recently, the use of bovine colostrum as adjunct in the management of diarrheal disorder is receiving attention among child health workers. However, the efficacy of bovine colostrum as supplement in the management of diarrhea is based on testimonials, anecdotal reports and the marketing efforts of its manufacturers and distributors.

The nutritional value of milk is undisputed. Bovine colostrum (BC) is the “early” milk produced by cows during the first several days post-parturition. This “early” milk has a nutrient profile and immunological composition that differs substantially from “mature” milk. In addition to macronutrients found in milk, BC contains oligosaccharides, growth factors, antimicrobial compounds, and immune-regulating constituents either not present in milk or present in substantially lower concentrations.[8] Bovine colostrum is proven to be the most efficacious as it contains much higher levels of Immunoglobulin-G (IgG) than human colostrum (which predominantly contains IgA) and because it is produced in large volumes by cows above and beyond what their calves require.[9]

Preliminary evidence suggests that bovine colostrum might help prevent and

and possibly treat infectious diarrhea. A double-blind, placebo-controlled trial of 80 children with rotavirus diarrhea found that hyperimmune colostrum had significantly less daily total stool output and stool frequency compared to children who received placebo (p value <0.05). The clearance of Rota virus was also earlier in hyperimmune bovine colostrum group (p value <0.001). There were no adverse effects noted in the study.[10]

A double-blind trial done by Mitra, et.al showed similar results. Patients who received bovine colostrum had shorter duration of diarrhea compared to the control (p value <0.001). They have greater reduction in stool output (p value <0.04) with no untoward effects noted in either groups.[11]

In a multi-center study by Rump, et. al., immunodeficient patients with chronic diarrhea were treated with oral Lactobin Immunoglobulin (LIG), an immunoglobulin from bovine colostrum. Among 29 patients, 21 gave good results leading to transient (10 days) or long-lasting (more than 4 weeks) normalisation of the stool frequency. The mean daily stool frequency decreased from 7.4 to 2.2. Intestinal cryptosporidiosis disappeared in 5 patients. [12]

Twenty-five HIV-positive patients suffering from chronic diarrhea were given colostrums bovine colostrum. Participants had negative stool cultures for microbial pathogens with the exception of Cryptosporidium. Seven were positive for Cryptosporidia and 18 were negative for diarrhea-causing organisms. In the 18 subjects with negative stool culture, complete remission of diarrhea occurred in seven cases (39%) and a reduction of 50 percent or more in frequency of diarrhea occurred in an additional four cases (22%). In the persons with positive stool culture for Cryptosporidia, three experienced complete remission and two had partial remission. Stool frequency in the seven cases decreased from an average of 9.4 to 3.7 daily by the end of the 10-day intervention.[13]

The therapeutic effect of bovine milk IgG antibody showed clinical importance demonstrated in a few studies. It is therefore of interest to conduct further study to determine its clinical usefulness among pediatric patients.

The result of this study will give us insights on the use of bovine colostrum as adjunct treatment to acute watery diarrhea to improve the health conditions of Filipino children. This study will provide pediatricians an option to give their patients the bovine colostrum as a safe and accessible adjunct in the treatment of diarrhea. If proven effective and safe, the drug will lessen the number of hospital stay of patients thus days absence from work of parents and relatives resulting to lesser expense, not to forget the ease of psychological burden from illness and hospitalization. The result of the study can guide the health policy makers to come up with an option to improve the treatment of diarrhea in order to achieve the Millennium Development Goal of Reduction in Child Mortality by 2015.

This study was conceptualized with

the following objective: to determine the efficacy and safety of colostrums powder supplementation among pediatric patients 6 months to 36 months old with acute watery, non-bloody diarrhea with some signs of dehydration admitted in a Tertiary Government Hospital. It further aims to compare the effects of colostrum powder supplementation versus the placebo as to: character of stools; volume of stools; frequency of stool passage; duration of hospital stay; and to determine the adverse effect of colostrum powder supplementation.

METHODS AND PROCEDURE

The study is a randomized, double-blind placebo controlled clinical trial conducted at the Pediatric Ward of a Tertiary Government Hospital.

The subjects were screened for the inclusion and exclusion criteria through interview of parents and guardians and physical examination of the patients. The study population included children 12 months to 36 months old with acute watery, non bloody diarrhea of six days duration or less; with some signs of dehydration based on WHO-CDD protocol. Excluded in the study were children with diarrhea of more than six days duration; with severe dehydration; bloody diarrhea; severe malnutrition; history of allergy to milk; history of seizure; postoperative and immunocompromised patient; intake of antidiarrheal medication and stool analysis positive for helminths, amoeaba and occult blood.

Children with informed consent were included in the list of the participants. A minimum of 80 subjects were sampled based on the following assumption: 95 % Confidence level; 80 % Power; SD of 2 and a Difference of 2 days duration of diarrhea based on the study of Martinez, et. al.[8] The formula to determine the sample size for 2 groups comparing means is based on the distribution function of a standardized normal deviate by Julious SA.[15]

$$n = \frac{(z \times 1\text{-}\beta)^2 \times 2 \times SD2}{(d')^2}$$

$$n = \frac{(1.96 \times .84)^2 \times 2 \times SD2}{(2)^2}$$

n = total sample size

z = the standard normal deviate, set at 1.96

Power = 1 - = Probability of rejecting the null hypothesis when it is false

SD = Standard deviation

d' = difference between two samples

Subjects were randomized to two treatment groups. Group A were given colostrum powder, Group B were given placebo powder.

The colostrums powder was commercially available in the market. Its important components are 1.5% Lactoferrin (42mg), 25% Immunoglobulins (720 mg IG) and 3% Proline-Rich Polypeptides (87 mg PRP) per regular daily serving of 3 grams. The colostrums

Powder was repacked into 10 grams per pack which is the recommended daily dose in times of illness or stress. The placebo had the same appearance, color and taste as the colosturm powder. It was kept in a sachet similar to the test drug. The test drug and the placebo was repackaged and prepared, respectively by the Derpartment of Industrial Pharmacy, University of the Philippines, Manila.

Random allocation of the subjects to one of the two treatment groups was done using pre-drawn block random assignment. The randomization list was prepared using letters A and B. Six 4-letter combinations (which serve as blocks) was made using these 2 letters which include ABAB, ABBA, AABB, BABA, BAAB, and BBAA. These 6 combinations were the basis for treatment assignment through substitution with the corresponding number generated from random numbers. The predrawn treatment assignments were placed in a sealed envelope.

The study was done according to the Principles in the Declaration of Helsinki. Parents of the children were informed about the nature, procedures, benefits and risks related to the study. An informed consent was obtained for their inclusion. The study was approved by the Ethics Review Committee prior to its implementation.

CONDUCT OF THE STUDY

A research orientation was conducted by the principal investigator among the members of the research team prior to the start of the study. An assistant investigator did the baseline history and physical examination upon admission. He classified the degree of dehydration according to the WHO/CDD assessment of dehydration **(Appendix A)**. Parents of the subject were informed about the purpose, benefits, and risks related to the study **(Appendix B)**. Patient informed consent were obtained prior to their inclusion **(Appendix C)**. Patient who fulfilled the criteria, was randomly assigned to either group A (intravenous fluid and Colostrum powder) or Group B (intravenous fluid and placebo powder).

A randomnization list was prepared using letter A for Group A; and letters B for Group B. A total of six (6) combinations of the two (2) letters in random order was formed and was written on separate sheets of paper properly sealed (Appendix D). Each random order has an equal chance of being drawn and assigned to each group.

Group A and group B children were given intravenous fluid of D5 0.3 NaCl at 3050cc/kg per 8 hours as deficit therapy. Replacement as maintenance therapy was instituted accordingly. Group A children were given 10g of Colostrum powder dissolved in 20 ml water, given for four days based on the study done by Sarker et al. Group B children were given 10g of placebo powder dissolved in 20 ml water, given for four days. The placebo is of the same appearance, color and taste. It was kept in a container similar to that of Colostrum powder.

An assistant investigator who was blinded of the study evaluated the duration of patient's diarrhea, frequency of stool passage, volume and character of stool (Appendix E). Adverse reactions were also observed by the investigators (Appendix F). A nurse unknowleadegable of the study objective and treatment assignment administered the Colostrum powder and the placebo. Figure 1 outlines the study procedure.

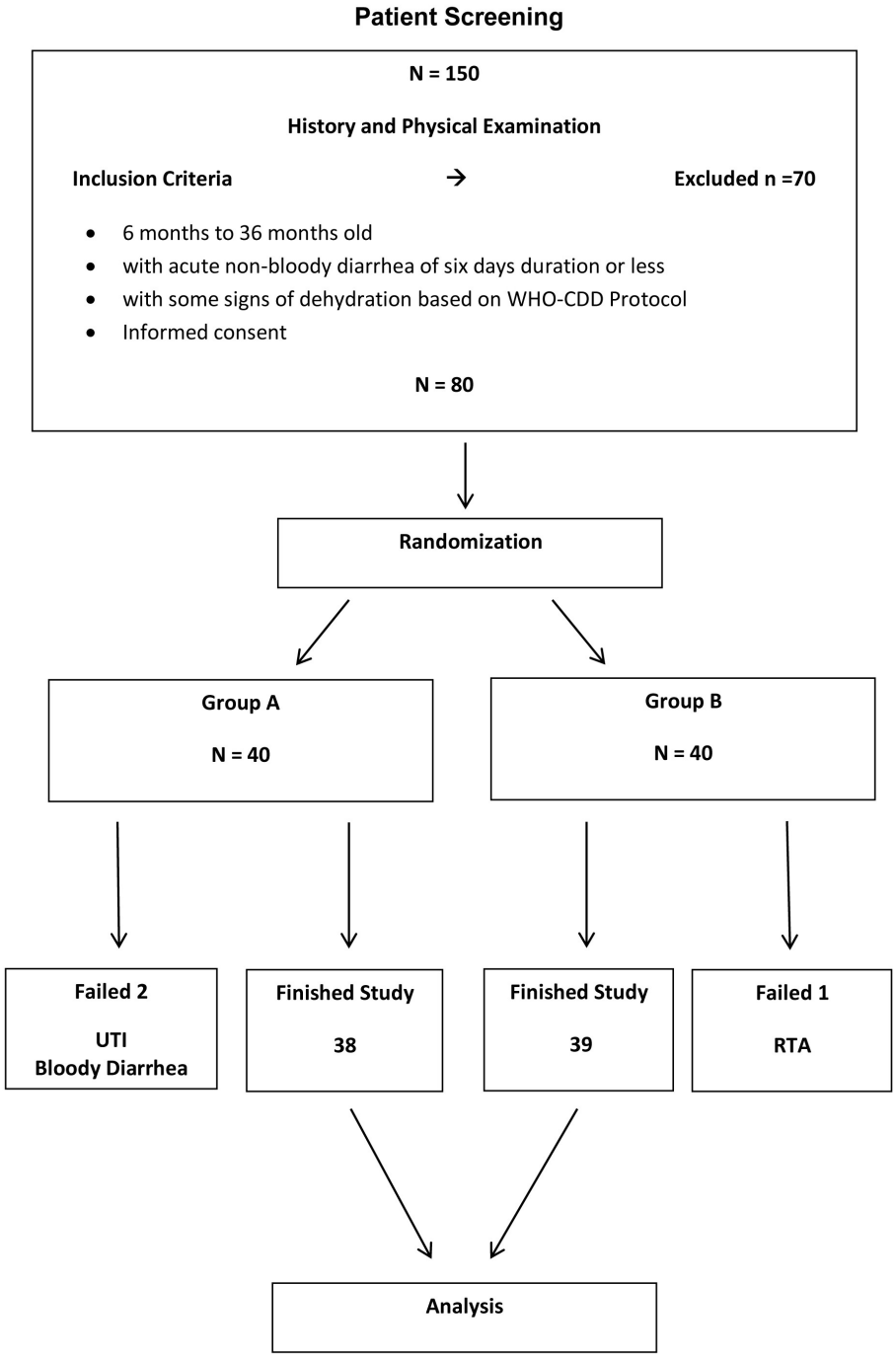


Figure 1: Flow Chart of Study Procedure

DEFINITION OF TERMS

Acute Diarrhea - the passage of loose or watery stools, at least three times in 24 hours period for less than 7 days[16]

Colostrum - the first mammary secretion that a mammal provides for its newborn in the first 24-48 hours of life. It contains numerous immune modulators, growth factors as well as essential nutrients.[9]

Colostrum powder - commercial preparations come which from cows that contain its immune proteins in dry form.

Some Dehydration - degree of dehydration with 5-10% water loss. Patient may present with restlessness or irritability, has sunken eyes, drinks eagerly and skin pinch goes back very slowly[16]

Tolerability - the ability of the subject to ingest a substance without vomiting, nausea and abdominal pain[17]

MEASURES OF OUTCOME

The study outcome measure determined the character, frequency and volume of stool and duration of hospital stay.

The character of stool was determined as follows:

a. Liquid stool - predominantly water.
b. Semi-formed/semi-liquid stool - composed of both liquid and semi liquid stool
c. Formed stool - solid stool

The frequency of the stool was noted and recorded every 8 hours. Mean frequency of stool between treatment group by hospital day was computed.

The volume of stool was weighed and recorded in grams by weighing the diaper before and after each use. A weighing scale (Silvano Brand) was used during the duration of the study. It was calibrated every morning.

Duration of hospital stay is computed as the length of hospital stay of patient in treatment group A and B.

Cumulative rate of discharged is computed to compare the proportion of discharges between two groups.

DATA ANALYSIS

Means and standard deviations, frequency counts and percentage were used to describe the data. T-test for independent samples was used to compare continuous variables and chi-square and Fischer's exact test for categorical variables. Odds ratio were computed. A 95% confidence level or P value of < 0.05 was considered significant. Minitab version 16 was used as statistical software.

RESULTS

A total of 80 patients 6 months to 36 months of age qualified to the inclusion criteria. All patients gave consent and were randomized to either treatment Group A,

Colostrum Powder and treatment Group B, Placebo powder. There were two dropouts in the treatment Group A, one had UTI started on IV antibiotics and one developed bloody diarrhea.

The two groups did not significantly differ in terms of age (P value 0.345) and sex (P value 0.135). The mean age was 12.8 months for Group A and 14.5 months for Group B. (See Table I)

TABLE I. AGE AND SEX DISTRIBUTION OF STUDY PARTICIPANTS OF TREATMENT GROUP A (COLOSTRUM) AND TREATMENT GROUP B (PLACEBO)

	Treatment Group A	Treatment Group B	P Value
Age, Mean + SD	12.8 + 7.5	14.5 + 8.1	0.345
Sex			0.135
Male	8	15	
Female	3024		

The character of the stool was compared between the two treatment groups. It was described as either watery, semiformed, and formed stool (Table 2). On day 1, all subjects in the two groups had liquid stools. On day 2, the proportion of subjects with formed stools was significantly higher in treatment Group A (16%) than in treatment Group B (2.5%). On day 3 of observation, there was no patient in treatment Group A with liquid stool as compared with 12 (31%) patients in treatment Group B. Twenty three (61%)patients in treatment Group A already had formed stools, and 10 (26%) subjects in treatment Group B. There was a significant difference in character of stool between two treatment group on day 3 (p value <0.005).

TABLE II. COMPARATIVE FREQUENCY AND PERCENTAGE DISTRIBUTION OF STOOL CHARACTER BETWEEN TREATMENT GROUP A AND TREATMENT GROUP B BY HOSPITAL DAYS

	Treatment Group A	Treatment Group B	P Value
Day 1	N %	N %	1.00
1 - Liquid	38	39	
2 - Semiformed	0	0	
3 - Formed	0	0	
Day 2			0.0098
1 - Liquid	14 (37%)	30 (77%)	
2 - Semiformed	18 (47%)	8 (21%)	
3 - Formed	6 (16%)	1 (2.5%)	
Day 3			0.00003
1 - Liquid	0	12 (31%)	
2 - Semiformed	9 (24%)	16 (41%)	
3 - Formed	23 (61%)	10 (26%)	
Discharged	6 (16%)	1 (2.5%)	
Day 4			0.728
1 - Liquid	0	4 (10%)	
2 - Semiformed	3 (8%)	8 (21%)	
3 - Formed	6 (16%)	6 (41%)	
Discharged	29 (76)	6 (41%)	
Day 5			1.00
1 - Liquid	0	0	
2 - Semiformed	1 (2.6%)	6 (15%)	
3 - Formed	2 (5.3%)	6 (15%)	
Discharged	35 (92%)	27 (69%)	

We did the comparative analysis of the volume of the stool measured in grams between treatment group A and treatment group B. The volume of stool was significantly higher in treatment Group B than in treatment Group A at all days of observation with P values of <0.0001 (Table 3). Shown in figure 2 is a comparative figure of volume of stool in grams by hospital days.

TABLE III: COMPARISON OF VOLUME OF STOOL IN GRAMS, MEAN + SD BETWEEN TREATMENT GROUP A AND TREATMENT GROUP B BY HOSPITAL DAYS

	Treatment Group A	Treatment Group B	P Value
Day 1	N = 38	N = 39	0.0001
	428.1 + 200.7	578.3 + 159.1	
Day 2	N = 38	N = 39	<0.0001
	198.6 + 102.7	390.4 + 147.4	
Day 3	N = 32	N = 38	
	138.7 + 84.2	293.8 + 133.0	<0.0001
Day 4	N = 9	N = 28	
	137 + 60.3	241.1 + 111.1	

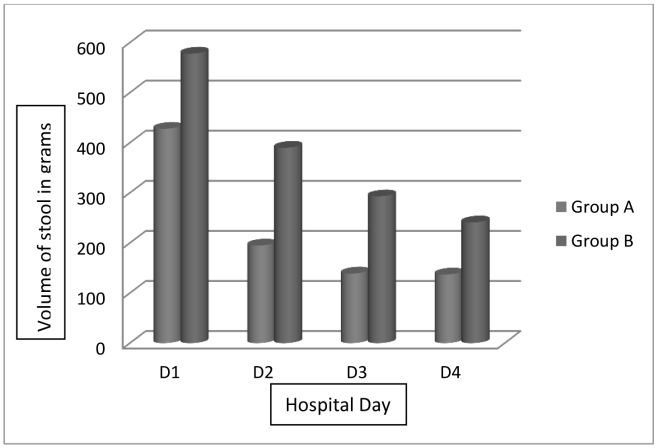


Figure 2. Comparison of Volume of Stools in grams Between Treatment Group A and Group B by hospital days

A comparative analysis of frequency of stool between treatment group A and treatment group B by hospital day is reported as mean and standard deviation in table IV. The result showed that treatment Group B had more frequent stools than treatment Group A from days 1 to 3 of observation. There is a significant difference in mean frequency of stool between two treatment groups with a P value of <0.0002.

TABLE IV: COMPARISON OF STOOL FREQUENCY, MEAN + SD BETWEEN TREATMENT GROUP A AND TREATMENT GROUP B BY HOSPITAL DAYS

Variable	Treatment Group A	Treatment Group B	P Value
Day 1	N = 38	N = 39	0.0008
	2.92 ± 1.3	3.97 ± 1.33	
Day 2	N = 38	N = 39	0.0001
	1.50 + 1.2	2.66 + 1.1	
Day 3	N = 38	N = 39	
	1.22 + 0.444	2.18 + 0.945	<0.0002

The cumulative rate of discharge between the two treatment groups was also compared (see table V and figure 3). It showed that starting at day 3, the cumulative Rate of discharge was significantly higher in Group A than in Group B. At day 5 of the study, 35 (92%) patients in Group A were already discharged compared to 27 (69%) patients in Group B (p value <0.005).

TABLE V. CUMULATIVE RATE OF DISCHARGE BETWEEN TREATMENT GROUP A AND TREATMENT GROUP B

	Treatment Group A	Treatment Group B	P Value
D1	0	0	<0.0001
D2	0	0	
D3	6 (16%)	1 (3%)	
D4	29 (76%)	11 (28%)	
D5	35 (92%)	27 (69%)	
D6	38 (100%)	33 (87%)	
D7		37 (95%)	

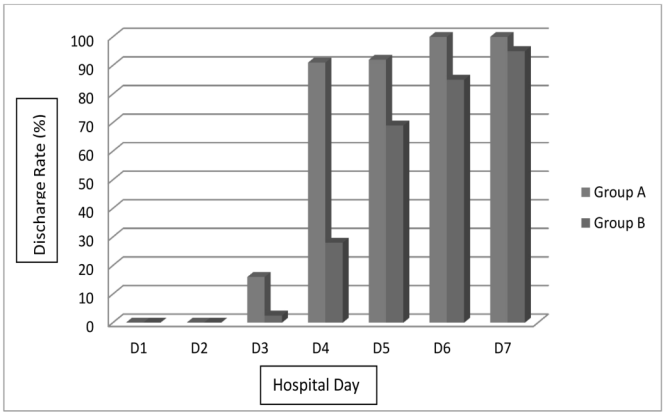


Figure 3. Cumulative Rate of Discharge in Percent Between Treatment Group A and Treatment Group B by Hospital Days

Table VI and figure 4 outline the comparative length of hospital stay between treatment group A and treatment group B. The mean length of hospital stay in treatment Group A was 2.21 days. It is shorter as compared to treatment Group B with a mean hospital stay of 3.21 days. The P value was <0.0001 which is statistically significant.

TABLE VI. COMPARATIVE LENGTH OF HOSPITAL STAY BETWEEN TREATMENT GROUP A AND TREATMENT GROUP B

	Treatment Group A	Treatment Group B	P Value
Length of Hospital stay			
Mean + SD	2.21 + 0.875	3.21 + 1.17	<0.0001
			95% confidence interval of the difference between means -0.994 + 0.468 Or from 0.53 to 1.4 Days

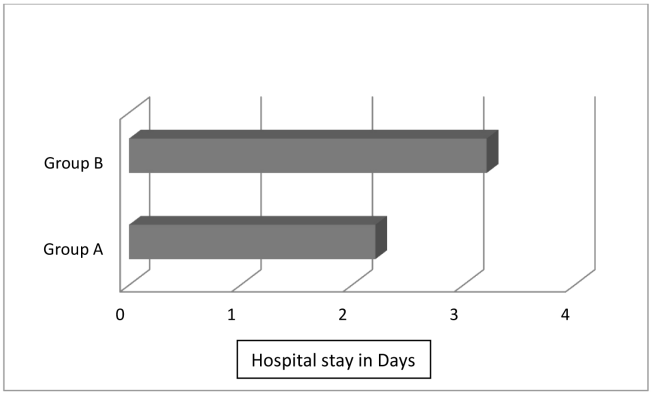


Figure 4. Comparative Length of Hospital Stay in Days Between Treatment Group A and Treatment Group B

There is no adverse reaction noted in both study group.

DISCUSSION

This study conducted among children with acute watery non-bloody diarrhea with some signs of dehydration aim to evaluate the clinical efficacy of orally administered

bovine colostrum. The result of the study has demonstrated a positive effect in the treatment of acute watery, non-bloody diarrhea. The children who received bovine colostrum had lower stool volume similar to the studies done by Sarker et al[11] and Mitra et al[12]. Reduction in stool frequency was also consistent with the study done by Sarker, et al[11]. Although Mitra et al[12] was able to come up with the findings of a shorter duration of diarrhea, it can be deduced from this study that the duration of diarrhea was shorter based on the result of shorter hospital stay.

Although the results of this study are consistent with the findings of Mitra et al and Sarker et al, there were certain important differences to be considered. The study populations in the two studies were confirmed cases of rotavirus diarrhea and used hyperimmune bovine colostrum preparation from immunized cows of human rotavirus. In contrast, the present study was conducted in children with acute watery, non -bloody diarrhea of unspecified cause and was given standard colostrum containing immunoglobulins, lactoferrin, and proline-rich polypetides as the major components. The success of bovine colostrum in this study could be attributed to its major components.

Some studies have focused in the use of colostrum to treat diarrhea, specifically on the advantages of bovine colostrum as an efficient medium in the process of passive immunity in immunocompetent patients.[13,14] Rump et al[13] and Plettenberg et al,[14] studies are also in agreement with the findings in this study in terms of reduction in stool frequency in patients with chronic diarrhea using the standard colostrum preparation.

A noteworthy finding of this study is an earlier formed stool which was not measured in the previous researches.

The clinical benefits of bovine colostrum might be attributed to the presence of intrinsic growth factors and immune factors. Growth factors in bovine colostrum reduce gastrointestinal damage during diarrheal episodes by stimulating cell and tissue growth and are capable of increasing T-cell production. Broad-spectrum antimicrobial factors such as lactoferrin that may have a beneficial effect on the health of the intestinal mucosa by modulating cytokine release which is an important event in immune response.[16,17,18] Immumoglobulins, which are the most abundant immune factors found in colostrum, neutralizes toxins and microbes in the lymph and circulatory system, destroys bacteria and are highly antiviral. Proline-Rich Polypeptide (PRP) regulates the thymus gland, stimulating an underactive immune system or down regulating an overactive immune system. They fuction as signaling peptides produced by activated macrophages and activated T-cells that control the production of all cytokines. Other colostrum components include lysozymes, cytokines, trypsin, lymphokines, orotic acid, oligopolysacharides and conjugates. They also act as agents to boost the immune system. Oligopolysaccharides and glycoconjugates attract and bind to pathogens preventing them from attaching or entering the mucous membranes.[19, 20, 21, 22]

CONCLUSION

Colostrum powder supplementation in the management of children 6 months to 36 months of age with acute watery, non-bloody diarrhea with some dehydration resulted to an: earlier formed stool on day 2 (p value <0.005) and day 3 (p value <0.005); a lower volume of stool at all days of observation (p value <0.005); a higher cumulative rate of discharge (p value <0.001) and shorter mean length of stay (2.21 + 0.875 days), p value 0.001. There was no associated adverse effect noted in all children given colostrum powder.

This study concludes that colostrum powder supplementation given at 10 grams daily for 4 days among children with acute watery, non-bloody diarrhea is effective, safe and can shorten hospital stay.

RECOMMENDATION

In this study, the effectiveness and safety of colostrum powder supplement was assessed during the duration of the participant's hospital stay. It is then recommended that study participants be evaluated and followed up at home and at the out-patient department.

Further studies be conducted on the effectiveness of colostrum powder supplementation in the management of chronic diarrhea and intestinal parasitism.

APPENDIX A

Assessment of Diarrhea patients for Dehydration Based on WHO/CDD Protocol

	No Signs of Dehydration	Some Dehydration	Severe Dehydration
CONDITION	Well, alert	Restless, irritable	Lethargic or unconscious
EYES	Normal	Sunken	Sunken
THIRST	Drinks normally, not thirsty	Thirsty, drinks eagerly	Drinks poorly, or not able to drink
FEEL Skin Pinch	Goes back slowly	Goes back slowly	Goes back very slowly

APPENDIX B

Letter to Parents

Minamahal na mga magulang,

Ako po si _____, isang residente sa Departamento ng Pediatrics, Quirino Memorial Medical Center. Nagsasagawa ako ng pag-aaral na "Colostrum Powder Supplement in the Treatment on Acute Watery Diarrhea in Children 12 months to 36 months: a Double Blind, Randomnized Controlled Trial." Nais kong malaman sa pag-aaral na ito kung ang mga batang bibigyan ng colostrum supplement ay mas mapapadali ang paggaling kumpara sa mga batang walang colostrum supplement.

Ang pagsali sa programang ito ay libre at walang makukuhang pinansyal na bayad. Bilang mga magulang o taga-pag-alaga, gusto kong ipaalam na magiging bahagi ang inyong anak sa programang ito. Maaaring ang inyong anak ay makakatanggap ng colostrum supplement at maari rin naming hindi. Ang pagpili ng kung sino ang bibigyan ay random na parang pagbunot sa tambiolo.

Magpapapirma ako ng "informed consent" sa inyo bilang patunay na kayo ay sumasang-ayon sa pagsali ng inyong anak sa programa.

Maraming salamat po.

Gumagalang,

Tagapagsaliksik

APPENDIX C

Katibayan sa Pagpayag

Ako _____ nasa hustong gulang, may asawa, at kasalukuyang naninirahan sa _____ay nagpapatunay na:

1. Ako ang magulang/ tagapagsubaybay ni _____ .

2. Lubos na napaliwanagan tungkol sa kahalagahan at pakay ng pag- aaral na may kinalaman sa epekto ng "colostrum powder" sa ikabibilis at ikadadali ng paggaling sa sakit na "gastroenteritis" ("pagtatae"). Pati na ang pagsusuri at pamamaraan na kinakailangang gawin. Ako ay sumasang ayon na maisama ang aking anak sa pag aaral na ito.

3. Ang aking anak ay lubos na nasuri at napag alamang may saki na gastroenteritis ("pagtatae") at walang kaakibat na ibang karamdaman.

4. Ako ay nangangako na magbibigay ng lubos na partisipasyon sa pagtatala ng karakter at dami ng dumi ng aking anak sa loob ng tatlo hanggang limang araw (3-5).

5. Alam ko na ang aking anak ay bibigyan ng "colostrum powder" 10g, isang beses (1) sa isang araw, sa loob ng apat na araw (4) na walang kapalit na halaga.

6. Ako ay bibigyan ng kasiguraduhan na lahat ng resulta ng pag-aaral na ito at mananatiling lihim at konpidensyal, na ako ay maaring tumiwalag sa pag aaral na ito sa anumang oras aking naisin.

7. Ako ay may karapatang magtanong ng mga bagay-bagay na may kinalaman sa pag-aaral na ito at ako ay nabigyan ng kasagutan na nagbigay liwanag sa aking kaisipan.

8. Ako ay nabigyan ng kopya ng katibayan na ito.

_____ _____

Magulang/ Tagapagsubaybay Petsa

APPENDIX D

Randomization Table

1	A	B	A	B
2	A	B	B	A
3	A	A	B	B
4	B	A	B	A
5	B	A	A	B
6	B	B	A	A

APPENDIX E

Patient Data Form

Name of Patient_____ Age/Sex_____

Date/Time	Character of Stools	Volume of Stools	Frequency of Stools

APPENDIX F

Adverse Reaction Checklist

Name of Patient_____ Age:_____

Date	Vomiting	Abdominal pain	Hypersensitivity reaction	Others

REFERENCES

1. Walker CL, Black RE. Micronutrients and Diarrheal Disease. Oxford Journals Clinical Infectious Disease. Volume 45:Pp. S73-S77: 2007

2. Farthing M., Linberg G., Dite P., et al. World Gastroenterology Organization Practice Guidelines: Acute Diarrhea: March 2008.

3. Republic of the Philippines, Department of health; Administrative Order: 2007 - 0045: Zinc Supplementation and Reformu-lated Oral Rehydartion Solution in the Management of Diarrhea Among Children: December 17, 2007.

4. Kosek, M., Bern C., Guerrant R,. The Global Burden of Diarrheal Disease, as Estimated from Studies Published Between 1992 and 2000. Bulletin of World Health Organization: 2003

5. Family Health Survey 2011, Republic of the Philippines, National Statistics Office. Sept. 9, 2012

6. Teodosio-Serillo N., et.al., Double Blind Controlled Trial on the Effect of Oral Zinc Supplementation in Acute Diarrhea among Infants 6-48 months. PPS Journal, Vol 55, No. 3, Jul-Sept 2006

7. Huang HS, et.al., Efficacy of Probiotic Use in Acute Diarrhea in Children: A Meta-Analysis; Dig. Dis. Sci. 2002 Nov

8. Martinez T, Resurreccion M,. Folic Acid Supplementation in the Treatment of Acute Watery Diarrhea in Children 6 to 36 months of Age: A Randomized Double Blind Controlled Trial. Quirino Memorial Medical Center. 2011

9. Gopal PK, Gill HS. Oligosaccharides and glycoconjugates in bovine milk and colostrum.Br J Nutr 2000;84:S69-S74

10. Francis GL., Upton FM, Ballard JF, McNeil KA, Wallace JC,. Insulin-like Growth factors 1 and 2 in Bovine Colostrum. Biochem.J.1988.255:p 95 -103

11. Sarker S, Casswall T, Mahanalabis D, et. al. Successful treatment of rotavirus diarrhea in children with immunoglobulins from immunized bovine colostrum. Pedriatric Infectious Disease Journal 1998; 17: 1149-1154

12. Mitra AK, Mahalanabis D, Ashraf H, Unicomb L, Eeckels R, Tzipori S. Hyperimmune cow colostrum reduces diarrhoea due to rotavirus: a double-blind, controlled clinical trial. Acta Paediatr. 1995;84:996-1001.

13. Rump JA, Arndt R, Arnold A, et. al. Treatment of Diarrhea in human immunodeficiency virus-infected patients with immunoglobulins form bovine colostrum. Clinical Investigation; 1992; 70: 588-594

14. Plettenberg A, Stoehr A, Stellbrink HJ, et. at. A preparation from bovine colostrum in the treatment of HIV-positive patients with chronic diarrhea. Clinical Investigation; 1993; 71: 42-45

15. Julious, SA, Sample sizes for clinical trials with normal deviates. Statistics In Med. 2004

16. World Health Organization.A Manual for the Treatment of Diarrhea. Geneva: World Health Organization, p.4 and 8 :2005.

17. Sanidad RA, Randomized Clinically Controlled Trial Comparing Tolerability Between Flavored ORS and Unflavored ORS Preparation Among Children 4 Months to 5 Years Old with Acute Diarrhea seen at ER/OPD of San Juan Medical Center; PPS Journal; Vol 54, No 2; Apr-Jun 2005

18. Playford RJ, MacDonald CE, Calnan DP, et al. Co-administration of the health food supplement, bovine colostrum, reduces the acute non-steroidal antiinflammatory drug-induced increase in intestinal permeability. Clin Sci (Lond) 2001;100: 627–33.

19. Stelwagen K, Carpenter E, Haigh B, Hodgkinson A, Wheeler TT. Immune components of bovine colostrum and milk. J Anim Sci 2009;87:3–9.

20. Van Hooijdonk AC, Kussendrager KD, Steijns JM. In vivo antimicrobial and antiviral activity of components in bovine milk and colostrum involved in nonspecific defence. Br J Nutr 2000;84(Suppl 1):S127–34.

21. Playford, R, Floyd D, Macdonald C, et. al. Bovine colostrum is a health food supplement which prevents NSAID induced gut damage. Gut 1999;44:653-58

22. Rumbo, M, Chirdo F, Anon M, Fossati C. Detection and caharacterization of antibodies specific to food antigens (gliadin ovalbumin and beta-lactoglobulin) in human serum, saliva, colostrum and milk. Clin. Exp.Immunol 1998;112(3):453-58

21. Joseph M, et. al. Research shows colostrum to be one of the nature's most potent broad-spectrum substances Chiropract J1998Mar 12(6):33, 41, 45

OXYGEN SATURATION (sPO2) LEVELS OF HEALTHY NEWBORNS WITHIN 10 MINUTES OF LIFE

Rubelyn F. Aquino, MD

Marissa G. Salas, MD, FPPS, FSPCCM, P, FPSCCm
Co-Author

Department of Pediatrics
Our Lady of Lourdes Hospital
Institutional Affiliation

ABSTRACT

OBJECTIVE: This study aims to determine the oxygen saturation levels of healthy newborns within 10 minutes of life. To correlate sP02 with age of gestation, birthweight, and manner of delivery. To determine the time for infants to reach 90% oxygen saturation.

DESIGN: Prospective observational study design.

SETTINGS: Private tertiary hospital

METHODS: Visual screening was conducted in 89 preschool children aged 3 to 5 years. The screening involved two basic procedures; the distant visual acuity test and structural eye exam. Those who failed the examination were referred to an ophthalmologist for further examination.

PARTICIPANTS: All healthy newborns delivered via NSD and CS with APGAR score 7 and above. Infants who received oxygen or any form of resuscitation were excluded.

METHODOLOGY: The sp02 sensor was applied on the right hand (preductal). Upon clamping of the cord, a stopwatch was then started. The spO2 values were recorded within 10 minutes of life or until sp02 reached 90%. Oxygen saturation values were recorded every 1 minute interval. Analysis of variance (ANOVA) was used to determine the differences in 0_2 saturation at specified time intervals. A p-value <.05 was used as cut-off for significance. Survival analysis using Kaplan-Meier method was used to determine the mean and median time to reach 0_2 saturation of 90%.

RESULTS: A total of 122 newborns were monitored. It took 5 minutes for infants to reach 02 saturation of 80% and 9 minutes to reach $\geq$ 90%. No significant difference was noted in the oxygenation status of babies in different age of gestation and birthweight. However, the oxygen saturation of babies was lower for those delivered by CS than those delivered by NSD, the difference was significant (p-value 0.0000) at every minute interval following birth.

CONCLUSION: Results showed increasing oxygen saturation levels minutes after birth even without intervention, with oxygen saturation reaching > 90% at 9 minutes of life.

KEYWORDS: oxygen saturation, newborn, pulse oximeter

INTRODUCTION

Oxygen is the most common therapy used in the nursery. It has been given to newborns in the past 60 years. Despite this, we still know very little about how much oxygen these babies actually need, or how much oxygen is safe to give, especially in the first few weeks of life. The goal of oxygen therapy is to achieve adequate delivery of oxygen to the tissue without creating oxygen toxicity. [1]

It was not until the epidemic of retrolental fibroplasia, now called retinopathy of prematurity, that physicians began to understand the potential toxicity of high concentrations of oxygen in premature babies. [2]

There is a growing interest relating to oxygen toxicity in newborns. Exposure to high oxygen concentration can produce free radicals and these can damage several organs. Several studies showed that oxygen could be responsible for rising cases of retinopathy of prematurity (ROP), cerebral palsy and bronchopulmonary dysplasia.

It has been a practice to provide oxygen to all newborns. There has been a liberal and unrestricted use of oxygen in delivery rooms. Recent studies say that insufficient and excessive use of oxygen can be both useful and harmful to newborns. Some health care personnel think that providing oxygen will achieve a rapid change in color from cyanotic to pinkish. All newborns are actually 'cyanotic' at birth[3]

The period following delivery is unique in that it is the only time during life when it is normal to have SpO2 values as low as 30%. These values then increase over the next 7 to 10 minutes of life to values of 85% to 95%.[4]

In the delivery room, oxygenation levels of newborns have been assessed clinically. However, there is interobserver and intraobserver variability in assessments of color.[5] Visual inspection of the color is only a crude indicator of oxygenation status. [4] Visual assessment of color is unreliable. The recent guidelines for Newborn Resuscitation recommend the use of pulse oximeter. Pulse oximeter was introduced in the 1980s. It can provide an objective way of measuring oxygenation status. It is also easy and a non invasive way of measuring saturation.

With the use of pulse oximeter, oxygen use can be regulated and adjusted accordingly, thereby reducing oxygen toxicity. However, there are limited information about infants' SpO2 in the minutes after birth. Recent studies showed that it usually takes 5 minutes for newborns to attain 80% and almost 10 minutes to reach 90%.

SIGNIFICANCE OF THE STUDY

Oxygen has been a vital therapeutic tool and an agent of harm in neonatal care. Traditionally, 100% oxygen has been used in all newborns. However, the use of 100% oxygen may increase the load of oxygen free radicals, which can potentially lead to organ

damage. There is considerable growing interest in the effect of oxygen therapy on the morbidity and mortality of newborns.

Newborns developed in a relatively hypoxemic environment. At birth, they are acroyanotic and it will take some time for them to become pinkish. However, visual assessment of color differs from one individual to another. This study monitored the oxygen saturation of newborns at birth using a pulse oximeter. Pulse oximeter is a non-invasive and more objective tool used for continuous monitoring of oxygen. This study also demonstrated that infants have increasing oxygen saturation levels even without intervention.

OBJECTIVES

General Objective

- To determine the oxygen saturation levels of healthy newborns within 10 minutes of life

Specific Objectives

- To correlate sP02 with age of gestation
- To correlate sP02 with birthweight
- To correlate sP02 with manner of delivery
- To determine the time for infants to reach 90% 02 saturation
- To determine the mean sP02 at 5 and 10 minutes of life

METHODOLOGY

Study Design

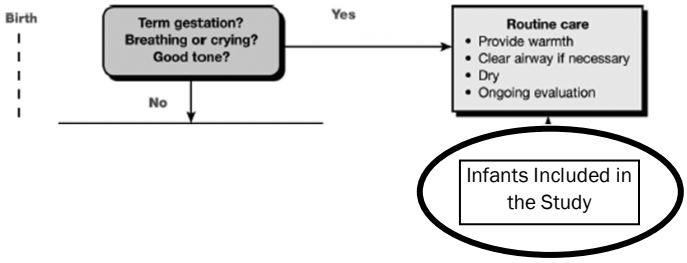
Prospective observational study design

Study Population

All healthy newborns delivered via Cesarean section or normal spontaneous delivery from April 2013-June 2013 in a private tertiary hospital.

INCLUSION CRITERIA

Infants included were term and preterm infants with APGAR $\geq$ 7, breathing with good cry and good muscle tone.



EXCLUSION CRITERIA

Infants were excluded if they received any form of intervention or resuscitation like:

1) oxygen mask
2) positive pressure ventilation
3) suctioning
4) Intubation
5) chest compression

STUDY PROCEDURE

This study was approved by the ethics committee. Consent was asked from the consultants (Pediatrician and Obstetrician) Nurses and Midwives. Before birth, parents gave verbal consent for their infants to participate.

All infants were dried, warmed and covered. Infants were placed on the mother's abdomen. Early skin-to-skin contact between mother and the newborn was done.

The Nellcor pediatric sp02 sensor was applied on right hand (preductal). The sensor was then connected to the oximeter because according to the literature, this leads to fastest acquisition of data. AUTOCORR pulse oximeter was used with continuous monitoring of sp02 at 60-second interval.

Upon clamping of the cord, a stopwatch was then started. The time of birth was taken as the time of cord clamping. Oxygen saturation was recorded at each minute after birth until 10 minutes of life or until the oxygen saturation reached 90%

The sPO2 values at 1, 2, 3 4, 5 6 7 8 9 and 10 minutes were recorded. The manner of delivery, age of gestation and birthweight were also noted.

SAMPLE SIZE ESTIMATION

A. For the objective on determining the 0_2 saturation of newborns within 10 minutes of life.

Based on the study by Rosvik, et al (2009) where the overall mean 0_2 saturation in healthy newborns was 98% SD ± 1.4, and using the formula for estimation of a population mean, with a desired precision of ± 5% and a reliability of 95% the estimated sample size was 3012 newborns (Appendix A)

$$n = \frac{Z^2 S^2}{d^2}$$

To adjust for the limited sample size , e.g. for this institution an average of 95 deliveries in a month, finite population correction was used resulting to a final estimated sample size of 92 newborns (Appendix B) .

$$n^* = \frac{n}{1+\left(\frac{n}{N}\right)}$$

Where n^* is the final sample size

N = 95 is the average number of deliveries in a month for this institution

$$n^* = \frac{n}{1+\left(\frac{n}{N}\right)} = \frac{3012}{1+\left(\frac{3012}{95}\right)} = 92$$

B. For the objective on determining the mean time for infants to reach[3] 90% 0_2 saturation

Based on the study by Omar, et al (2006) where the overall the mean time to reach [3] 90% 0_2 saturation was 5.8 SD

± 3.2 minutes, and using the formula for estimation of a population mean, with a desired precision of ± 5% and a reliability of 95% the estimated sample size was 15,735 newborns (Appendix C).

$$n = \frac{Z^2 S^2}{d^2}$$

$$n = \frac{(1.96)^2 (3.2)^2}{(.05)^2}$$

n = 15,735 newborns

To adjust for the limited sample size , e.g. for this institution an average of 95 deliveries in a month, finite population correction was used resulting to a final estimated sample size of 94 newborns (Appendix D).

$$n^* = \frac{n}{1 + \left(\frac{n}{N}\right)}$$

Where n^* is the final sample size

N = 95 is the average number of deliveries in a month for this institution

$$n^* = \frac{n}{1 + \left(\frac{n}{N}\right)} = \frac{15,735}{1 + \left(\frac{15,735}{95}\right)} = 94$$

STATISTICAL ANALYSIS

Data were recorded using Microsoft excel. Data were analyzed using Stata version 10 software. Frequency tables were generated to show the distribution of newborns according to age of gestation, birthweight, mode of delivery, 0_2 saturation from 1 to 10 minutes of life and time to reach 90% 0_2 saturation. Descriptive statistics entailed use of means and standard deviation for quantitative variables and counts and proportions for qualitative variables.

To determine differences in 0_2 saturation at specified time intervals after birth by age of gestation and birthweight, analysis of variance (ANOVA) was used. Likewise, significant differences in 0_2 saturation at different time points by mode of delivery was determined using independent t-test. A p-value <.05 was used as cut-off for significance.

Survival analysis using Kaplan-Meier method was used to determine the mean and median time to reach 0_2 saturation of 90%. Differences in time to reach 90% 0_2 saturation by age of gestation, birthweight and mode of delivery was determined through the log-rank statistic.

RESULTS

Majority of the 122 newborns included in the study were delivered via normal spontaneous delivery with a mean gestational age of 38.5 SD ± 1.3 weeks and mean birthweight of

3118 SD ± 420 grams. Majority of babies were delivered via normal spontaneous delivery (61.5%) (Table 1).

Table 1: DEMOGRAPHIC CHARACTERISTICS OF THE SUBJECTS

Age of gestation in weeks	
Mean, sd	38.5, 1.3
Median (min, max)	38 (36, 42)
Birthweight in grams	
Mean, sd	3117.6, 420.1
Median (min, max)	3090 (2126, 4309)
Mode of Delivery (no., %)	
NSD	75 (61.5)
CS	47 (38.5)

Table 2: 0_2 SATURATION OF NEWBORNS AND TIME TO REACH 90% 0_2 SATURATION

Time from Birth in minutes	0_2 saturation	
	Mean, sd	Median (min, max)
1	67.2, 4.7	68.5 (59, 75)
2	70.2, 3.8	70 (60, 78)
3	73.7, 4.0	73 (65, 83)
4	76.7, 3.2	77 (68, 85)
5	80.1, 3.3	80 (70, 89)
6	83.0, 3.8	83 (78, 90)
7	85.9, 3.0	86 (78, 92)
8	88.3, 2.8	89 (80, 94)
9	89.5, 1.9	90 (84, 94)
10	90.4, 1.1	90 (86, 94)
Time to reach 90% 0_2 saturation	8.9, 1.2	9 (7, 12)

For all the infants, the mean oxygen saturation at 1,2,3, 4,. 5, 6, 7, 8, 9 and 10 minutes of life were 67.2%, 70.2%, 73.7%, 76.7%, 80.1%, 83% 85.9% 88.3%, 89.3 and 90.4% respectively. It took 8.9 minutes (sd ± 1.2) for infants to reach 90% oxygen saturation.

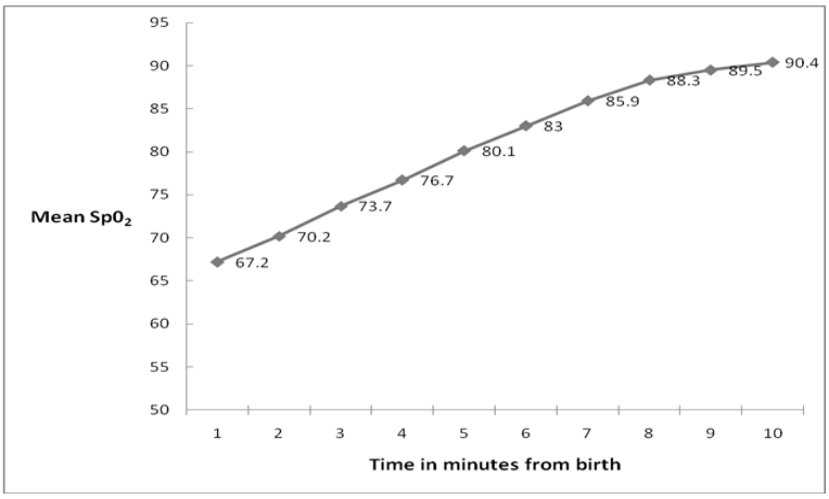


Figure 1: 0_2 saturation of Newborns at 1 to 10 minutes of Life

Oxygen saturation vs age of gestation

There were no significant differences in 0_2 saturation among the three categories of gestational age (p-values ³ 0.05) at each minute interval of life even if the values for those < 37 weeks was slightly higher than those aged 37-39 weeks and ³ 40 weeks (Figure 2)

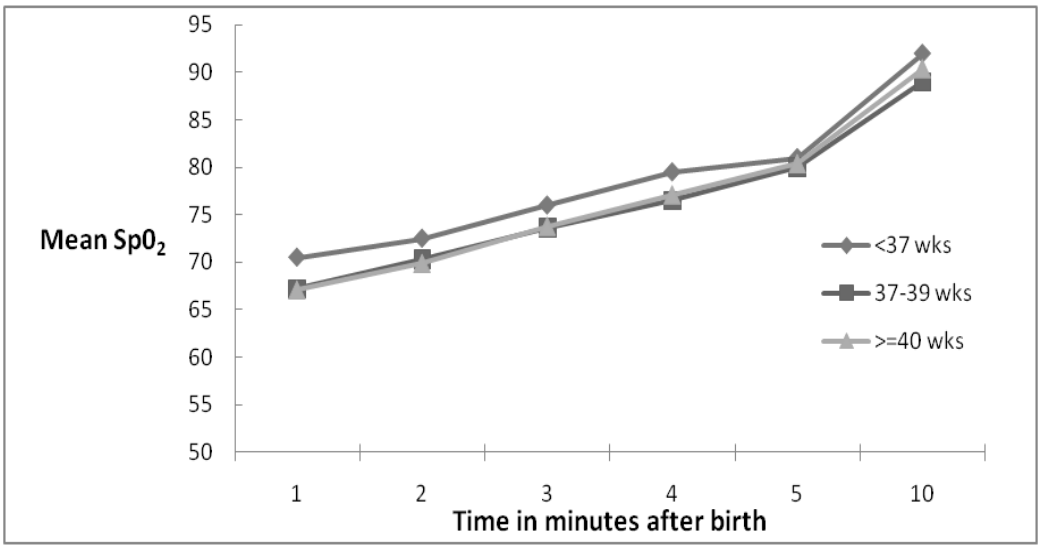


Figure 2: O_2 saturation from 1 to 10 minutes after birth by age of gestation

Oxygen saturation vs Birthweight

Likewise, 0_2 saturation of those weighing <3000g grams did not differ significantly (p-values ³ .05) from those weighing between 3000 to 3900 grams and ³ 4000 grams taken at each minute of life (Figure 3)

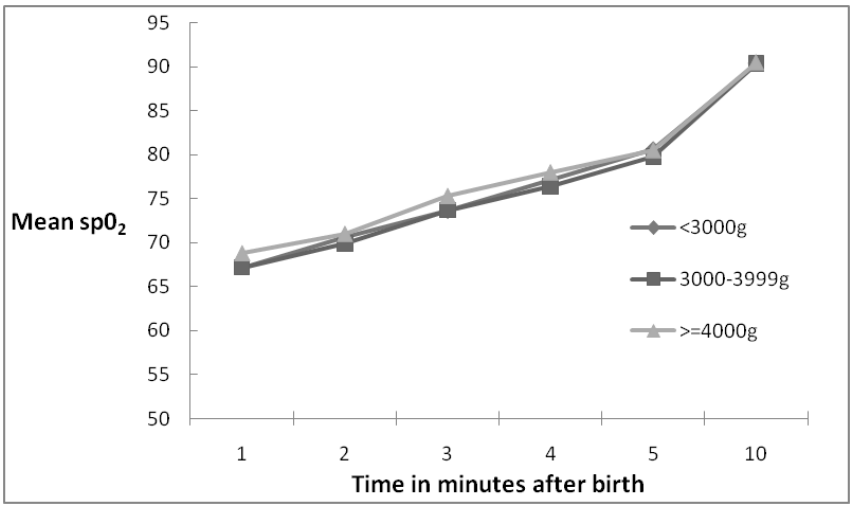


Figure 3: O_2 saturation from 1 to 10 minutes after birth by birthweight

Oxygen saturation vs Manner of Delivery

However, 0_2 saturation was lower for those delivered by CS than those delivered by NSD and the difference was significant (p-value 0.0000) at every minute interval of time from birth (Figure 4)

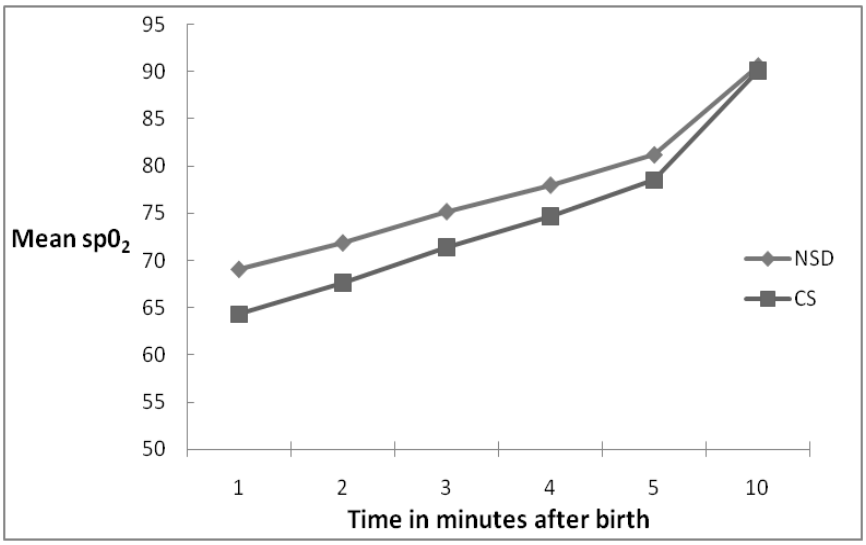


Figure 4: O_2 saturation from 1 to 10 minutes after birth by mode of delivery

The mean time to reach an 0_2 saturation of 90% was slightly earlier for those < 37 weeks than those³ 37 weeks but the difference was not significant (p-value = 0.7349). At 8.5 minutes, 50% of those < 37 weeks have already attained 90% 0_2 saturation compared to 9 minutes among those³ 37 weeks. Likewise those weighing < 3000 grams reached 90% 0_2 saturation earlier than those weighing ³ 3000 grams but the difference was not significant (p-value = 0.7790). However, those delivered by CS took a longer time to reach 90% 0_2 saturation than those delivered by NSD and the difference was significant (p-value=0.0000).

At 8 minutes 50% of those delivered by NSD have already attained 90% saturation compared to 10 minutes for those delivered by CS. (Table 3)

Table 3: COMPARISON OF TIME TO REACH 90% 0_2 SATURATION BY GESTATIONAL AGE, BIRTHWEIGHT AND MODE OF DELIVERY

Time to reach 90% 0_2 saturation in minutes	Age of gestation in weeks			
	< 37 n=2	37- 39 n=89	³ 40 n=31	p-value[a]
Mean,sd	8.5, 0.7	8.8, 1.2	9.0, 1.3	0.7349
Median (min, max)	8.5 (8, 9)	9 (7,12)	9 (7,12)	
	Birth weight in grams			
	< 3000 grams n=45	3000 - 3999 n=73	³ 4000 n=4	p-value[a]
Mean,sd	8.7, 1.2	8.9, 1.2	8.8, 1.7	0.7790
Median (min, max)	8 (7, 12)	9 (7, 12)	8.5 (7, 11)	
	Mode of Delivery			
	NSD n=75		CS n=47	p-value[b]
Mean,sd	8.1, 0.8		10.0, 0.8	0.0000
Median (min, max)	8.0 (7, 10)		10.0 (8, 12)	

[a] ANOVA

[b] Independent t-test

Kaplan Meier estimates showed that the mean time to reach an 0_2 saturation of 90%, was 8.9 minutes (95% CI 8.6, 9.1) and the median time was 9 minutes (95% CI 8, 9) (Figure 5)

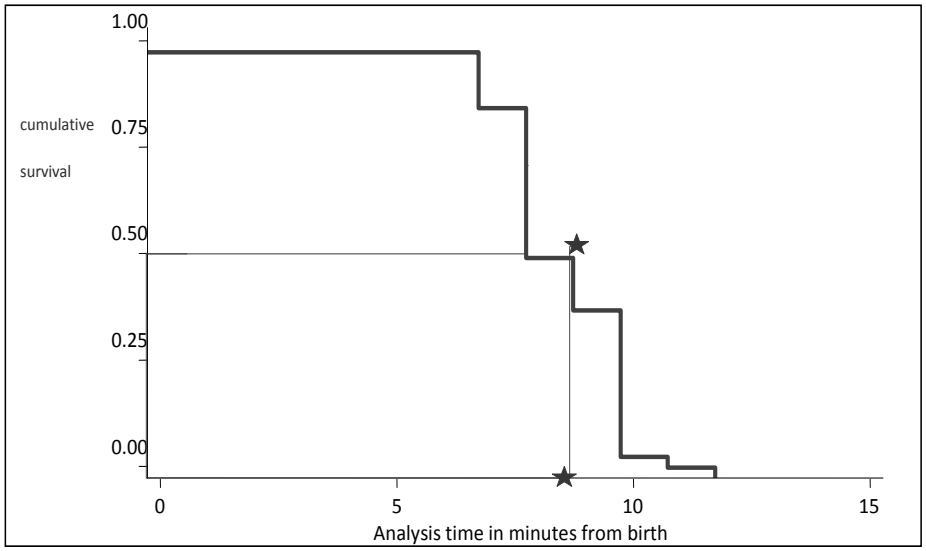


Figure 5: Kaplan Meier curve for time to reach 90% 0_2 saturation of newborns

The curve for those <37 weeks AOG was initially higher but dropped lower and faster than the curves of the 2 other gestational ages. That is, it reached 90% 0_2 saturation faster and earlier. The curve of those ³ 40 weeks AOG was slightly higher than those of 37-39 weeks AOG, that is, it reached 90% 0_2 saturation slower and later than those aged 37-39 weeks. Log rank statistic showed that the 3 survival curves were no different from each other or that there was no significant difference in the time to reach 90% 0_2 saturation among the three gestational ages (p=0.6775) (Figure 6).

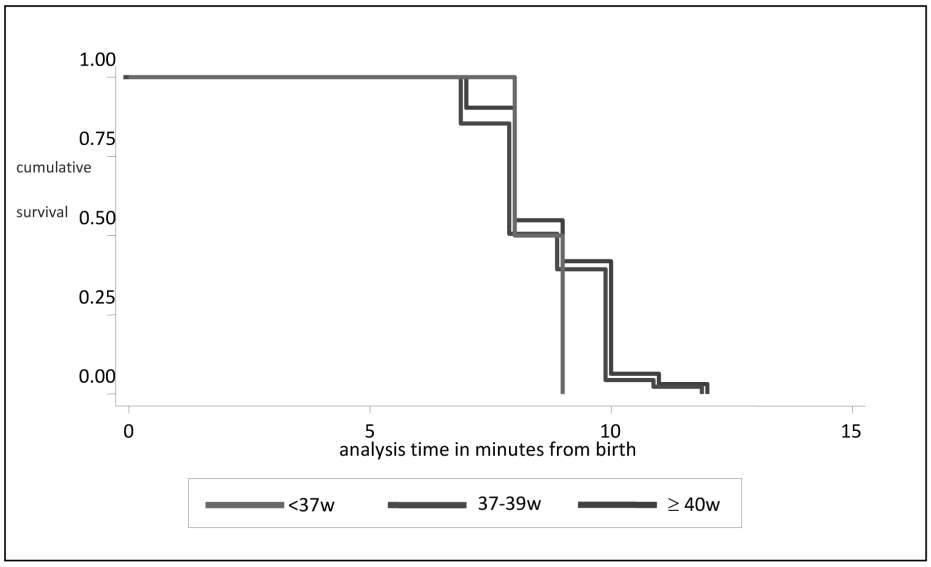


Figure 6: Kaplan Meier curve for time to reach 90% 02 saturation by age of gestation

The curve for those weighing 3000-3999 grams lies above the other birthweights and therefore reached 90% 0_2 saturation slower until 10 minutes from birth and gradually approximated the saturation level of the ³ 4000 grams. The curve was lowest for those weighing < 3000 grams and therefore reached 90% 0_2 saturation faster until 10 minutes from birth and slowed down therafter. The curve of those weighing ³ 4000 grams was midway between the two other birthweights. Log rank statistic showed that there was no significant difference in the time to reach 90% 0_2 saturation among the three categories of birthweight (p=0.7936) (Figure 7).

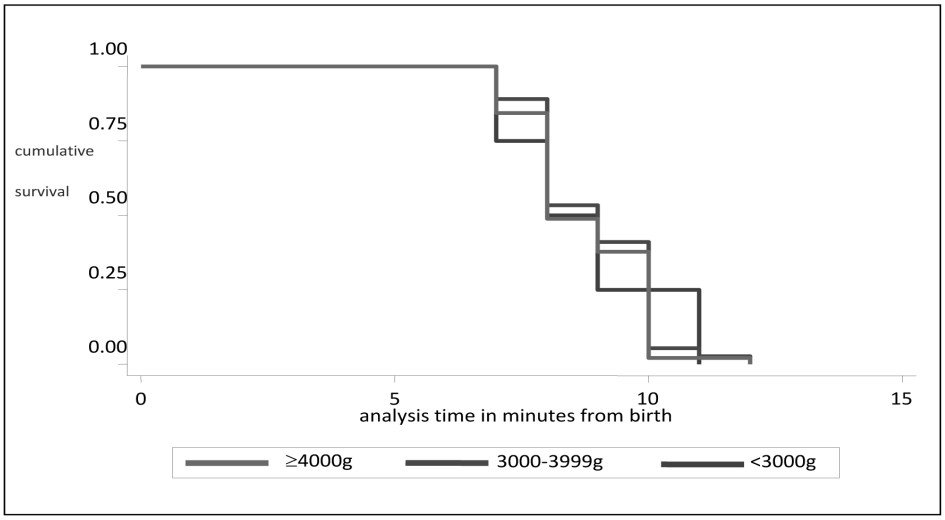


Figure 7: Kaplan Meier curve for time to reach 90% 0_2 saturation by birthweight

Those delivered by CS had a curve above those delivered by NSD indicating that the time to reach 90% 0_2 saturation was longer and slower. Results of log-rank statistic showed that there was a significant difference in the survival curves between the two modes of delivery (p=0.0000) and that those delivered by NSD took faster and earlier to reach an 0_2 saturation of 90% (Figure 8).

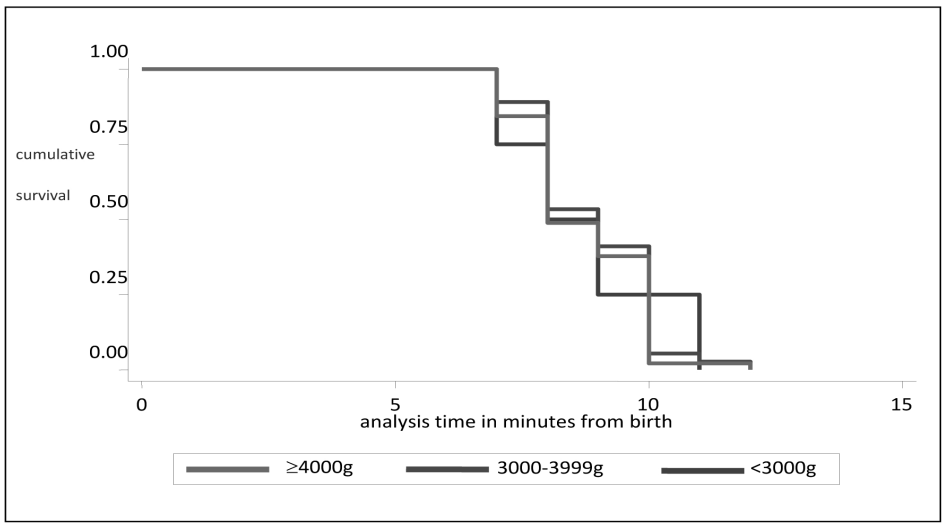


Figure 8: Kaplan Meier curve for time to reach 90% 0_2 saturation by mode of delivery

DISCUSSION

An infant normally grows in an environment with low oxygen. Goldsmith mentioned that fetus develops in a relatively hypoxemic environment (oxygen saturations of 50%–60%), and if hypoxic tissue is abruptly exposed to high concentrations of oxygen during resuscitation, cell and tissue injury are worsened. Oxygen radicals have been shown to play a role in the pathogenesis of many diseases hence unnecessary or excessive oxygen use in newborns may be harmful.

All infants are acyanotic at birth. The transition from an environment with low oxygen content to an environment with high oxygen content usually takes time with ease. According to latest guideline of Newborn Resuscitation, more than 90% of babies make the transition from intrauterine to extrauterine life perfectly smoothly, only few will need aggressive management.

There is a growing interest on the effect of oxygen to newborns. Several studies mentioned that excessive and inadequate use of oxygen can both do harm and good to infants. This study described how sp02 values changed in the first few minutes of life. The sp02 was recorded every minute after cord clamping when the newborn had no oxygen source coming from the placenta. At birth, sp02 of newborns was low with a mean of 67.2 % however over time; the oxygen saturation had steady increased requiring 5 minutes to reach 80% and 9 minutes to reach 90%. The sp02 rose even without any supplemental oxygen.

For all the infants, the mean oxygen saturation at 1, 2, 3, 4,. 5, 6, 7, 8, 9 and 10 minutes of life were 67.2%, 70.2%, 73.7%, 76.7%, 80.1%, 83% 85.9% 88.3%, 89.3 and 90.4% respectively.

The sp02 values obtained in this study were comparable to that of Kattwinkel and colleagues of American Heart Association. They defined the target ranges for 1, 2, 3, 4, 5, and 10 minutes after birth at 60% to 65%, 65% to 70%, 70% to 75%, 75% to 80%, 80% to 85%, and 85% to 90%, respectively.

	Comparison of Oxygen Range		
	Dawson et al.,	American Heart Association Recommendations	This study
1 minute	55-75%	60-65%	59-75%
2 minute	63-82%	65-70%	60-78%
3 minute	69-88%	70-75%	65-83%
4 minute	76-93%	75-80%	68-85%
5 minute	82-95%	80-85%	70-89%
6 minute	85-96%		78-90%
7 minute	88-97%		78-93%
8 minute	90-98%		80-94%
9 minute	90-98%		88-94%
10 minute	92-98%	85-95%	86-94%

	Comparison of Median Oxygen Saturation	
	Dawson et al.,	This study
1 minute	66 %	68%
2 minute	73 %	70%
3 minute	78 %	73%
4 minute	85 %	77%
5 minute	89 %	80%
6 minute	92 %	83 %
7 minute	94 %	86 %
8 minute	95 %	89 %
9 minute	95 %	90 %
10 minute	96 %	90%

Overall, oxygen saturation of newborns in the sample taken at minute intervals from birth showed an increasing trend and on the average reached 90% at 9 SD ± 1.2 minutes of life.

This study also correlates sp02 with different factors like age of gestation, birthweight and manner of delivery.

The findings of this study suggest that age of gestation had no effect on oxygen saturation. There were no significant differences in 0_2 saturation among the three categories of gestational age (p-values ^{3} 0.05) at each minute interval of life. All categories <37 weeks, 37-38 weeks and >40 weeks had increasing trend of oxygen saturation.

This is in contrast with the studies of Dawson et al that Sp02 values for preterm infants increased more slowly than those for term infants (8.1 minute vs 7.9 minutes). The median Sp02 at 5 minutes for preterm infants was 86%, compared with 92% for term infants (*P* > 001).

Kamlin et al also reported that the median Sp02 at 5 minutes for preterm infants was 87%, which was significantly lower than the value for term infants of 90% (*P* >.001).

No difference was observed in the sp02 of infants in different age of gestation group. At 9 minutes, all infants have reached 90% oxygen saturation. This might be attributed to the smaller population of preterm infants included.

Another factor that was investigated was birthweight. Rovrik et al., study measured the sp02 during the first 24 hrs of life, his results showed that sp02 was negatively related to birthweight.The mean Sp02 was higher in infant with a low birth weight (2750–2999 g) 98.3% compared with oyxgen saturation of 97.6% in infants weighing 4500 g and above.

In this study, those weighing < 3000 grams reached 90% 0_2 saturation earlier than those weighing^3 3000 grams but the difference was not significant. At 9 minutes, all infants belonging to different weight group have reached 90%.

The last factor that was studied was the manner of delivery in relation to sp02. The results demonstrated that babies born by cesarean section have lower oxygen saturation compared with babies delivered via NSD. Those delivered by CS took a longer time to reach 90% saturation than those delivered by

NSD and the difference was significant (p-value=0.0000). At 8 minutes 50% of those delivered by NSD have already attained 90% saturation compared to 10 minutes for those delivered by CS.

In a study by Rabi et al., they demonstrated that infants born by cesarean delivery had lower oxygen saturations and required longer to reach stable oxygen saturation ≥ 85% in the immediate newborn period compared with infants born vaginally. Infants delivered by cesarean delivery had a 3% lower Sp02 than infants delivered by vaginal delivery.

Infants born by cesarean delivery also took longer to reach a stable Sp02 > 85. This is consistent with the findings of Kamlin et al that Sp02 values (interquartile range) were 87% (80% to 95%) for infants delivered vaginally and 81% (75% to 83%) for those delivered through cesarean section. However both groups attain 90% oxygen saturation after 8 minutes of life. Dawson also mentioned that oxygen saturation values of infants following cesearean section deliveries are slightly lower than values following vaginal deliveries.

The delayed increase in sp02 of infants delivered by cesarean section maybe secondary to the delayed clearance of lung fluid during operative delivery. Another factor that might play a role was the effect of anesthesia. However, this is beyond the scope of this study.

Rovrik et al mentioned in his study that children born by cesarean section have lower levels of Sp02 during the first minutes of life, probably due to increased amount of lung fluid, However, this difference was equalized within a few minutes. He mentioned also that mode of delivery could affect the sp02 initially but after 2 to 24 hr, sp02 rises comparable to infants delivered vaginally.

Overall, the study showed an increasing trend of saturation without supplemental oxygenation. The study also supports the feasibility of continuously monitoring sp02 using pulse oximeter in the delivery room. This practice can be a helpful guide in titrating oxygen soon after birth, since newborns are most susceptible to oxidant injury. Pulse oximeter is based on the amount of oxygen present in the hemoglobin.

Pulse oximeter can provide continuous non invasive measurement of sp02. Pulse oximeter could potentially play a role in adjusting the oxygen concentration.

CONCLUSION

All infants had increasing trend of oxygenation status immediately after birth. For all the infants, the mean oxygen saturation at 1, 2, 3, 4,. 5, 6, 7, 8, 9 and 10 minutes of life were 67.2%, 70.2%, 73.7%, 76.7%, 80.1%, 83% 85.9% 88.3%, 89.3 and 90.4% respectively. It took 5 minutes for infants to reach 02 saturation of 80% and 9 minutes to reach ≥ 90%. No significant difference was noted in oxygenation status of babies in different age of gestation group and birthweight group.

However the 0_2 saturation of babies was lower for those delivered by CS than those delivered by NSD, the difference was significant (p-value 0.0000) at every minute interval following Birth.

LIMITATION OF THE STUDY

The study only involved one private tertiary hospital with a study period of 3months (April 2013-June 2013). Only few preterm infants were delivered during the study period, majority of the babies were also delivered via normal spontaneous delivery.

RECOMMENDATIONS

Additional factors affecting oxygen saturation of newborns should also be considered such as duration of labor of the mother, effects of anesthesia and whether the mother received oxygen support during labor. For the newborns, temperature should also be considered. These factors might also affect the oxygen saturation of infants following birth.

REFERENCES

1. Tin et al., *Optimum Oxygen Therapy in Preterm Babies*. Child Fetal Neonatology. 2007

2. Goldsmith et al., *The Role of Oxygen in the Delivery Room.* Clinical Perinatology. Elsevier Inc. 2012

3. Rabi et al., *Oxygen Saturation Trends Immediately after Birth.* The Journal of Pediatric 2006

4. Leone et al., *Delivery Room Management of the Term and Preterm Infant*. Elsevier 2009

5. Kamlin et al., *Oxggen Saturation in Healthy Infants Immediately after Birth* The journal of Pediatric 2006

6. Kattwinkel et al., Neonatal Resuscitation: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2010

7. Rovrik et al., *Oxygen saturation in healthy newborns; influence of birth weight and mode of delivery* J. Perinat. Med. 2009

8. Castillo et al., *Pulse Oxygen Saturation Levels and Arterial Oxygen Tension Values in Newborns Receiving Oxygen Therapy in the Neonatal Intensive Care Unit: Is 85%to 93% an Acceptable Range?* Pediatrics May 2008

9. Dawson et al., *Defining the Reference Range for Oxygen Saturation for Infants After Birth Defining the reference range for oxygen saturation for infants after birth*. Pediatrics 2010

10. Rajani et al., *Delivery Room Management of the Newborn* Division of Neonatal and Developmental Medicine, Department of Pediatrics Stanford. Elsevier 2009

11. O'Donnell et al., *Feasibility of and Delay in Obtaining Pulse Oximetry during Neonatal Resuscitation*. Journal of Pediatrics. 2005

12. O'Donnell et al., *Clinical assessment of infant colour at delivery.* Child Fetal Neonatology. 2007

13. Vento et al., *The Use and Misuse of Oxygen During the Neonatal Period.* Clinical Perinatology. 20122012

14. Tin et al., *Oxygen monitoring in preterm babies: too high, too low*

15. Bashambu et al., *Evidence for oxygen use in preterm infants*. Foundation Acta Pædiatrica 2012

16. Dawson et al *Defining the Reference Range for Oxygen Saturation for Infants After Births* Pediatrics 2010

17. Vento et al., *The Use and Misuse of Oxygen During the Neonatal Period* . Clinical Perinatology 2012

18. Guideline on the Basic Newborn Resuscitation World Health Organization 2012

APPENDICES

Appendix A

$$n = \frac{Z^2 S^2}{d^2}$$

Where n is the estimated sample size

Z is 1.96 corresponding to 95% reliability of the estimate

S is the standard deviation of the population = 1.4 (Rosvik, et al , 2009)

d is the maximum error deemed acceptable by the researcher = 0.05

$$n = \frac{(1.96)^2 (3.2)^2}{(.05)^2}$$ n= 3012 newborns

Appendix B

$$n^* = \frac{n}{1+\left(\frac{n}{N}\right)}$$

Where n^* is the final sample size

N = 95 is the average number of deliveries in a month for this institution

$$n^* = \frac{n}{1+\left(\frac{n}{N}\right)} = \frac{3012}{1+\left(\frac{3012}{95}\right)} = 92$$

Appendix C

Where n is the estimated sample size

Z is 1.96 corresponding to 95% reliability of the estimate

S is the standard deviation of the population = 3.2 (Omar, et al 2006)

d is the maximum error deemed acceptable by the researcher = 0.05

Appendix D

$$n^* = \frac{n}{1+\left(\frac{n}{N}\right)}$$

Where n^* is the final sample size

N = 95 is the average number of deliveries in a month for this institution

$$n^* = \frac{n}{1+\left(\frac{n}{N}\right)} = \frac{15,735}{1+\left(\frac{15,735}{95}\right)} = 94$$

THE VALIDITY OF USING HAND TOUCH METHOD COMPARED TO DIGITAL THERMOMETRY IN DETECTION OF HYPOTHERMIA AMONG FULL TERM NEONATES DELIVERED AT THE OBSTETRIC ADMITTING SECTION OF A TERTIARY HOSPITAL

Josephine Ann G. Santos-Alban, MD

CLINICAL ABSTRACT

RATIONALE: Hypothermia is a risk factor for neonatal morbidity and mortality hence it is important to identify a diagnostic test for hypothermia which can be readily available to health care workers.

OBJECTIVE: To determine the validity of using hand touch method in detection of neonatal hypothermia as compared to digital thermometer.

STUDY DESIGN: Cross-sectional study

SETTING: Obstetric Admitting Section of a tertiary hospital

STUDY POPULATION: Full-term neonates who fulfilled the following: delivered within 24 hours, birth weight of at least 2.5 kilograms, without congenital anomalies, not clinically ill, and with consent from the mother/father/guardian were included.

METHODOLOGY: Hand touch method was done on 300 full term neonates by two health care workers who were blinded to each other's assessment followed by rectal temperature determination using digital thermometer. The sensitivity, specificity, positive and negative predictive values, and likelihood ratios of hand touch method against digital thermometer were determined. Age of gestation, birth weight, sex, clinical signs of illness, and maternal risk factors were described.

RESULTS: Of the 300 full term neonates included, 47% were males, with a mean birth weight of 2,969 grams. Prevalence of hypothermia was 37% and presence of maternal risk factor was associated in 38% of cases. The sensitivity and specificity of hand touch method against the digital thermometer were 69% and 97%, while the positive and negative predictive values were 93% and 84%, respectively. The likelihood ratio for hypothermia was 22, and 0.3 for non-hypothermia.

CONCLUSION: Hand touch method can be recommended as an easy, inexpensive, and feasible tool to rule in hypothermia among neonates, especially in areas of the community where thermometer is scarce, after giving adequate training to health care workers.

KEYWORDS: neonatal hypothermia, hand-touch method, sensitivity, specificity, likelihood ratios

I. TITLE

The Validity of Using Hand Touch Method Compared to Digital Thermometry in Detection of Hypothermia Among Full Term Neonates Delivered at the Obstetric Admitting Section of a Tertiary Hospital.

II. INTRODUCTION

Neonatal hypothermia is a widely known risk factor for neonatal morbidity and mortality. In the Philippines, 3.4% of the 2.4 million live births die before 5 years of age annually. In 2006 demographics, there were 32 deaths per 1000 live births among under-five age group, and 37% of these were due to neonatal causes.(1) This makes the Philippines one of the 42 countries accounting for 90% of all global under-five deaths. Around 50% of these deaths occur in the neonatal period and 25% in the first 2 days of life. (2)

The morbidities associated with hypothermia in newborn infants are many and includes hypo/hyperglycemia, respiratory distress, hypoxia, metabolic acidosis and coagulation defects. (3) If adequate thermal protection is not begun immediately after birth, there will be rapid heat loss, with the skin temperature losing up to 4°C in the first minutes of life. (4) Immediate actions are therefore warranted to avoid these consequences, which brings us to the development of essential newborn care. The goal of Essential Newborn Care is to rapidly reduce the number of newborn deaths by following a simple, concise and straightforward guideline which includes: immediate and thorough drying of the newborn, early skin-to-skin contact between mother and newborn, properly-timed cord clamping and cutting, and non-separation of newborn and mother for early breastfeeding. According to the WHO, implementation of this protocol has the potential to avert approximately 70 percent of newborn deaths that are due to preventable causes, without additional cost to both families and hospitals. (5) Among the pillars of essential newborn care, which is prevention of hypothermia, is given emphasis. Therefore, maintaining temperature at the time of birth is one of the primary goals of neonatal resuscitation and is one of the key determinants of neonatal outcome.

Review of Related Literature

All newborn babies are prone to heat loss, particularly in the first few hours after birth because of large surface area per unit of body weight. (4) Newborn loses heat by evaporation, conduction, convection, and radiation. (6) According to studies, heat loss among preterm and underweight babies is more common compared to normal weight or full term babies. This is seen in a study done by Mullany et al in rural Southern Nepal involving 23,240 babies, where almost 30% of infants had low birth weight (< 2500 g) and those between 2000-2499 grams and 1500-1999 grams were at 1.49 and 4.32 times greater risk of hypothermia, respectively. Very low birth weight (VLBW) babies were 11.63 times more likely than normal weight infants to have axillary temperatures of <35.0°C. This is due to larger surface

to mass ratios and rapid transepidermal loss of water through the compromised skin barrier. (4) It therefore shows that the weight of an infant is one of the most important independent factors related to neonatal hypothermia.

World Health Organization (WHO) defines normothermia as a core temperature of 36.5ºC to 37.5ºC. Hypothermia is defined as a core temperature of <36.5ºC and categorized as mild when the temperature is 36.0 to 36.4ºC, moderate when the temperature is 32 to 35.9ºC, and severe when the temperature is <32ºC. (7) Hyperthermia on the other hand, is temperature above 37.5°C. This is usually associated with infection and a search for a possible focus of infection should be done. However, hyperthermia can also be due to increased ambient temperature, hence loosening or removing of clothes can also be done to decrease the neonate's temperature. (6)

Digital thermometer can be used in the newborn for thermal detection. Some studies however, have tried using hand touch method in assessing the newborn's temperature. In a study done by Tuitui et al at Nepal, where the incidence of neonatal hypothermia is as high as 87%, the use of hand touch method among 100 full-term neonates delivered within 24 hours at a local university hospital has a sensitivity and specificity of 95.6% and 70.1% respectively, in detection of neonatal hypothermia against low-reading mercury thermometer. (8) Another study done at Nepal by Ellis et al, shows that the use of touch by health workers to detect hypothermia in 250 newborns examined, has a high sensitivity (80%) but low specificity (36%–74%) compared with axillary thermometry. (9) Agarwal et al also had the same validity testing, involving 152 newborns in Indian slum dwellings, and found that human touch had moderate diagnostic accuracy when compared with axillary digital thermometry (kappa: 0.38, sensitivity: 74.5%, specificity: 68.5%). (10) Despite these, they still recommend peripheral palpation for the detection of hypothermia, at least in the first instance, and if assessed to be cold, further assessment and enhanced thermal care will be done. (9) Also, human touch appeared to be simpler and feasible and just requires adequate training for proper thermal detection. (10)

In developing countries, like the Philippines, where less than half (43%) of all Philippine deliveries occur in hospitals and where most of the deliveries are carried out at home or in local health centers by midwives or traditional birth attendants, hand touch method is a practical way of assessing the baby's temperature, although the most common way of temperature determination is by using a thermometer. (2) As defined by World Health Organization, human touch can detect if the baby is in thermal comfort if with warm and pink feet, is in cold stress if the feet were cold and the trunk warm, and with hypothermia if both feet and trunk were cold to touch. (6)

All hypothermic infants are at increased risk of morbidity and mortality in both home and facility settings. Prevention of cold stress starting immediately at birth is critical and when identified, appropriate steps for warming

must be initiated. Key to this goal is a practical and efficient way of monitoring temperature of neonates so that timely interventions can be made to prevent hypothermia. Presently among our health care workers, there is no standard practice with regards to bringing thermometers in their community. It is then important to identify such a diagnostic which can be available to health care workers especially in areas in the country where resources are scarce. Hence, we would like to determine the diagnostic validity of using hand touch method in detection of neonatal hypothermia as compared to the conventional digital thermometer.

III. RESEARCH OBJECTIVES

a. General Objective

i. To determine the validity of using hand touch method in detection of neonatal hypothermia as compared to digital thermometer.

b. Specific Objectives

i. To describe the characteristics of neonates born at the obstetric admitting section of a tertiary hospital.

ii. To determine the sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratios of using hand touch method compared to digital thermometer in detection of hypothermia among full term neonates.

IV. STUDY DESIGN

This is a cross-sectional study that was done on three hundred full-term neonates delivered at the Obstetric Admitting Section of a tertiary hospital comparing the diagnostic validity of hand touch method versus digital thermometry in detection of hypothermia.

V. METHODOLOGY

Sample size

The sample size for the population of this study is determined using prevalence rates of 74% and 80% in Nepal where the study on hand touch method was already done. The desired level of confidence is at 95% with a standard value of 1.96. The margin of error is at 10% with a standard value of 0.1. The sample size is then multiplied by the design effect (2), hence the sample size is 300 patients. The formula for computing the sample size:

$$n = \frac{t^2 \times p(1-p)}{m^2}$$

n= required sample size
t = confidence level at 95%
p = estimate of prevalence of hypothermia
m = margin of error at 10%

The study was carried out in the catcher's area of the Obstetric Admitting Section of a tertiary hospital. Three hundred full-term neonates were selected who fulfilled the

inclusion criteria: delivery within 24 hours, birth weight of at least 2.5 kilograms and with consent from the mother/father/guardian. Prematurity, those with birth weight less than 2.5 kilograms, congenital anomalies, and clinically ill were excluded from the study. Informed consent was obtained from the neonate's mother/father/guardian before examination.

A. Preparation Prior to the Actual Study

The health care workers (two nurses) who participated in this study underwent one hour lecture on temperature determination. They were taught how to determine hypothermic versus non-hypothermic by comparing glass bottles filled with water with temperatures ranging from < 36.5^{0}C to >/= 36.5^{0}C. They touched the glass bottles using the dorsum of their hand and identified which was hypothermic and not hypothermic. Both of them correctly determined which of the glass bottles were hypothermic or not-hypothermic (10 out of 10 determinations), hence they were included in the study.

Rectal temperature was taken using the digital thermometer (SANITAS Fieberthermometer 01/1, Germany; accuracy ±0.1^{0}C). The health care workers (pediatric resident/nurse/intern/clerk) who did the rectal temperature determination were taught how to use the digital thermometer. The temperature probe was placed in the rectal area until there was temperature recorded on the digital thermometer (this was determined when an acoustic sound was heard few minutes after placing the digital thermometer inside the rectum of the patient). Using digital thermometry, neonates were classified as hypothermic (<36.5^{0}C) or not hypothermic (>/= 36.5^{0}C).

There are factors that may affect the health care worker's determination of the baby's temperature, such as ovulation, hyperthyroidism, ambient temperature, etc. The health care worker who will be doing the hand touch method of temperature determination should therefore, have hands which are not of extreme temperatures. The temperature of their hands was measured by placing the thermometer probe on the palm of the health care worker's hand until the temperature was recorded, once normothermic (36.5-37.5^{0}C), they started the hand touch method.

B. Study Proper

The study was done at the Obstetric Admitting Section of a tertiary hospital. The procedure was explained to the mother/ father/guardian of the baby. The consent was secured prior to the examination, from the mother if obtained before the delivery or from the father or guardian after the delivery of the baby. The health care workers did hand washing first, followed by temperature determination of their hands, to make sure that the hands were normothermic. This was followed by placing the dorsum of the hand on the trunk of the neonate for a few seconds, until it was determined if the baby was hypothermic or not. By this hand touch method, neonates were classified as hypothermic (<36.5^{0}C) or not hypothermic (>/= 36.5^{0}C). The health care workers washed their hands after the

procedure. Another health care worker (pediatric resident/nurse/intern/clerk), then measured the rectal temperature of the baby, by first wiping the probe of the digital thermometer with alcoholised cotton, then inserting it to the rectum of the baby. The probe was wiped again with alcoholised cotton after the temperature was determined. The health care workers were blinded to each other's assessment. If the baby were determined to be hypothermic or hyperthermic, appropriate measures were then done to keep the patient within normal temperature.

DATA ANALYSIS.

Using the digital thermometer reading as the reference test, the sensitivity, specificity, positive and negative predictive values, and likelihood ratios of hand touch method with 95% confidence interval were determined and compared. Age of gestation, birth weight, sex, clinical signs of illness, maternal risk factors were described for each participant. Data compilation and analysis were done using the Microsoft Office Excel program.

VI. ETHICAL CONSIDERATIONS

This research is about comparison of the diagnostic validity of hand touch method to digital thermometry in detection of neonatal hypothermia among full term neonates delivered at the Obstetric Admitting Section of a tertiary hospital. This involved human touch and placement of digital thermometer in the rectal area of the neonate. As a participant in this study, the child was not exposed to any serious risk. Determination of temperature did not disturb the routine care being provided to the neonates at the neonatal resuscitation area.

The use of a digital thermometer for temperature determination has no record of any risk. The benefit to the child was that he/she was provided close monitoring for hypothermia by the health care worker during their stay at the neonatal resuscitation area. The results of this study might not benefit the child directly but will benefit future patients by providing information that may justify the use of hand touch method in assessing for hypothermia among neonates. No payment was given to the child as a result of participation in the study.

The health care workers (two nurses) who participated in this study got the consent from the neonate's mother prior to the delivery. Otherwise, consent was taken from the father or guardian if the mother has already delivered prior to examination. The risks, benefits, and the methodology were explained to the mother or father. All their questions were answered accordingly.

The protocol of this study was submitted to the Ethics Review Board of a tertiary hospital for ethical review and approval. The study was conducted only upon approval from the Ethics Review Board. All patient information collected in this study will be kept strictly confidential, except as may be required by the law. The child or family will not be identified by name when the results of the study are published. They are given the right to know the results of the study at the end of the trial. Any

additional information about the study results are provided to them at its conclusion, upon their request. Expenses of the study were funded by the investigator.

VII. RESULTS

The results of this study showed that out of the 300 full term neonates who were included in this study, 47% were males, with a mean birth weight of 2,969 grams (range: 2,500 – 4,150 grams). The presence of maternal illness or risk factor was associated with hypothermia in 38% of cases as shown in Table 1. In Table 2, the prevalence of hypothermia (<36.5^{0}C) was 37% (mean: 36.5^{0}C, range: 34.5-37.8^{0}C). The sensitivity and specificity of the hand touch method against the digital thermometer were 69% and 97%, respectively, while the positive predictive value and negative predictive value were 93% and 84%, respectively. The likelihood ratio for hypothermia was 22, while the likelihood ratio for non-hypothermia was 0.3 only as shown in Table 3.

VIII. DISCUSSION

A clinically useful diagnostic tool for detection of neonatal hypothermia should be simple, rapid, inexpensive, and, most importantly, accurate. The use of hand touch method in determining neonatal hypothermia easily fulfills the criteria of simplicity, rapidity and its being inexpensive. This study focused on the validity and accuracy of hand touch method in detection of hypothermia among full term neonates delivered at the Obstetric Admitting Section of a tertiary hospital.

According to this study, detection of neonatal hypothermia has a high specificity (97%), but low sensitivity (69%). This shows that with hand touch method, if a baby were determined to be non-hypothermic, there is a 97% chance that the baby is really non-hypothermic, however due to its low sensitivity it is likely that hand touch method may miss one-third of those neonates who are truly hypothermic if used as a screening tool. On the other hand, once a baby is detected to be hypothermic, there is 93% probability that the baby is truly hypothermic, and because of its high likelihood ratio for hypothermia, there is a 22-fold increase in the odds of detecting hypothermia among those who are truly hypothermic, while only 0.3 or 3 out of 10 neonates will be detected to be non-hypothermic by hand touch method among those who are truly not hypothermic.

The possibility to easily, rapidly, and reliably detect hypothermia is very important for the clinician. Therefore, if a neonate were deemed to be not hypothermic, this would assure the clinician that they have not missed detection of hypothermia. Also, if the neonate were deemed to be hypothermic, further assessment and enhanced thermal care will be done to prevent neonatal morbidity and mortality.

The sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratios were comparable with the previous studies done on hand touch method in

detection of neonatal hypothermia. Although variability among studies exists, this study confirms that hand touch method is very specific in detection of neonatal hypothermia, but not very sensitive. Of the studies mentioned earlier done at Nepal and Indian slum dwellings, all of them have a higher sensitivity and lower specificity which are opposite to the data of this study, which has a low sensitivity and higher specificity in detection of neonatal hypothermia. These differences may be due to the subjective findings of the health care workers who did the hand touch method. These may also be due to the differences of the location and equipment used in temperature determination. One study used low-reading thermometer as compared to the use of digital thermometer in this study, and one study placed the thermometer in the axillary area in contrast to the rectal area as the location for placement of the thermometer in this study (8, 9). Ambient temperature can also affect the results of this study and another variable which has caused the difference in the result is the number of participants in this study. Hence it is emphasized that the data of this study were based on a relatively small sample and larger series are needed for verification of the results.

IX. CONCLUSION

Hand touch method is a rapid, simple, and inexpensive diagnostic tool for detection of neonatal hypothermia. Although hand touch method can reliably determine those who are truly hypothermic, its use for the detection of neonatal hypothermia is limited due to its low sensitivity. Despite this, its clinical use for the determination of neonatal hypothermia is very important so that appropriate measures for thermoregulation can be instituted to prevent neonatal morbidity and mortality. In this regard, hand touch method can be recommended as an easy, inexpensive, and feasible tool to detect hypothermia among newborn babies especially in areas of the community where thermometer is scarce after giving adequate training to health care workers.

X. BIBLIOGRAPHY

1. http://www.countdown2015mnch.org/documents/countryprofiles/Countdown_2015_Philippines_8_20080604_revised.pdf

2. Sobel HS, Silvestre MA, Mantaring JB 3rd, Oliveros Y, Nyunt-U S. Immediate newborn care practices delay thermoregulation and breastfeeding initiation. *Acta Pediatrica* 2011.

3. Costeloe K et al. The EPICure study. *Pediatrics* 2000;106:659–71.

4. Mullany LC, Katz J, Khatry SK, LeClerq SC, Darmstadt GL, Mullany J, et al. Research article on hypothermia and associated risk factors among newborns of southern Nepal. *BMC Medicine* 2010;8:43.

5. Essential Newborn care. DOH-WHO protocol.PPS Southern Tag.pdf

6. http://www.newbornwhocc.org/pdf/teaching-aids/hypothermia.pdf.

7. Department of Reproductive Health Research, World Health Organisation. Thermal protection of the newborn: a practical guide. Geneva: World Health Organisation, 1997.

8. Tuitui RL, Suwal SN, Shrestha S. Hand-touch method for detection of neonatal hypothermia in Nepal. *Journal of Tropical Pediatrics* 2010;Vol.0,NO.0.

9. Ellis M, Manandhar D, Hunt L, Barnett S, Azad K. Touch detection of neonatal hypothermia in Nepal. *Arch Dis Child Fetal Neonatal Ed* 2006;91:F367–F368.

10. Agarwal S, Sethi V, Srivastava K, Jha P, Baqui AH. Human touch to detect hypothermia in neonates in Indian slum dwellings. *Indian J Pediatr* 2010;77(7):759-762).

11. Kumar, V. et al. Journal of Perinatology (2009) Neonatal hypothermia in a low resource settings: a review www.nature.com/jp

XI. APPENDIX

Appendix I

Table 1. Characteristics of Neonates Born at the Obstetric Admitting Section of a tertiary hospital

Characteristics:	N=300
Mean Age of Gestation	39 weeks (range: 37-41 weeks)
Number (%) of males/females	Males 47% Females 53%
Developed Clinical Signs of Illness	None
Mean Birth Weight	2,969 grams (range: 2,500 – 4,150 grams)
Maternal Illness/Risk Factors	
Urinary Tract Infection	14 (18.2%)
Premature rupture of membranes	10 (13%)
Pre-eclampsia	9 (11.7%)
Bronchial Asthma	6 (7.8%)
Hypertension	5 (6.4%)
Young Primigravid	4 (5.2%)
Gestational Diabetes Mellitus	4 (5.2%)
Placenta Previa	4 (5.2%)
Gestational Hypertension	3 (3.9%)
Chronic Hepatitis B Infection	3 (3.9%)
Upper Respiratory Tract Infection	3 (3.9%)
Elderly Primigravid	2 (2.6%)
Diffuse non-toxic goiter	2 (2.6%)
Gravidocardiac	1 (1.3%)
Hypothyroidism	1 (1.3%)
Condyloma Acuminata	1 (1.3%)
Neurofibromatosis Type I	1 (1.3%)
Rheumatic Heart Disease	1 (1.3%)
Parkinson's Disease	1 (1.3%)
Beta-Thalassemia	1 (1.3%)
Epilepsy	1 (1.3%)

Table 2. Distribution of Neonates with Hypothermia and Non-Hypothermia Detected by Hand Touch Method and Digital Thermometry

Hand Touch Method	Digital Thermometer < 36.5^{0}C	Digital Thermometer >/= 36.5^{0}C	Total
Hypothermic	76	6	82
Non-hypothermic	34	184	218
Total	110	190	300

Table 3. Diagnostic Validity of Hand Touch Method Versus Digital Thermometry in Temperature Determination

Diagnostic Validity of Hand Touch Method in Detecting Neonatal Hypothermia Compared to Digital Thermometry (N=300; 95% CI)	
Sensitivity	69% (54-77%)
Specificity	97% (93-99%)
Positive Predictive Value	93% (84-97%)
Negative Predictive Value	84% (78-89%)
Likelihood Ratio (Hypothermia)	22
Likelihood Ratio (Non-hypothermia)	0.3

Appendix II

INFORMED CONSENT

I, _____, mother/father/guardian of _____, do fully understand that my child will be included in the study of 'The Validity of using Hand Touch Method Compared to Digital Thermometry in Detection of Hypothermia among Full Term Neonates Delivered at the Obstetric Admitting Section of a tertiary hospital." The study is being done to determine the diagnostic validity of using hand touch method in detection of neonatal hypothermia as compared to digital thermometer among full term neonates delivered at the Obstetric Admitting Section of a tertiary hospital.

Procedure of the study

The study will be carried out in the delivery area of the Obstetric Admitting Section of a tertiary hospital. 300 full-term neonates will be selected who fulfil the inclusion criteria; such as, delivered within 24 hours, birth weight of at least 2.5 kilograms and with consent from the mother. Those who are preterm, less than 2.5 kilograms, with congenital anomalies, and who are clinically ill will be excluded in the study. Informed consent will be obtained from the neonate's mother/ father/guardian prior to examination either before the delivery or after the delivery of the baby. The neonate's body temperature will be assessed first by hand touch followed by rectal digital thermometer. The health care worker will palpate the baby's trunk using the dorsal surface of the right hand to feel the coldness or warmth of the newborn. Neonates will be classified as hypothermic (< 36.5^{0}C) and not hypothermic (>/= 36.5^{0}C).

Rectal temperature will be taken using the digital thermometer (SANITAS Fieberthermometer 01/1, Germany; accuracy ±0.1^{0}C). The temperature probe will then be placed in the rectal area until there is temperature recorded on the digital thermometer (this is determined when an acoustic sound is heard few minutes after placing the digital thermometer inside the rectum of the patient). Neonates will be classified as hypothermic (<36.5^{0}C) or not hypothermic (>/= 36.5^{0}C).

The sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratios of the hand touch method for temperature assessment will be calculated against digital thermometer readings.

Possible complications and risks from the study

As a participant in this study, your child will not be exposed to any serious risk. Determination of temperature will not disturb the routine care being provided to the neonates at the neonatal resuscitation area.

The use of a digital thermometer for temperature determination has no record of any risk.

Benefits from the study

The benefits to your child will be that he/she will be provided close monitoring for hypothermia by the investigator during their stay at the neonatal resuscitation area. Once patient is determined to be hypothermic, warmth will be provided for the neonate by giving warm linen or placing a droplight near the baby's bed. The results of this study might not benefit your child directly but will benefit future patients by providing information that may justify the use of hand touch method in assessing for hypothermia among neonates.

Refusal to participate

Your participation in the study is voluntary. You may withdraw your child anytime without penalty and this will not affect the present and future treatment of your child.

Payment as a result of the complications of the study

There are no medications in this study. No payment will be given to the child as a result of participation in the study.

Rights of the participants

Participation in the study is voluntary. Refusal to participate will not influence the care of your child in the hospital in any way. Though we would like all participants to complete the study, you are free to withdraw any time. If at any time you have any questions or concerns related to the study, you may contact the ethics review board of the tertiary hospital.

Confidentiality

All information collected in this study will be kept strictly confidential, except as may be required by law. Your child or family will not be identified by name when the results of the study are published. You have a right to know the results of the study at the end of the trial. Any additional information about the study results will be provided to you at its conclusion, upon your request. The results of this study will be presented in local and international conferences and will be written for possible publication in a scientific journal.

Alternatives to participation in the study

If you do not want your child to participate in this study, your child will still be seen every day by the doctors and health care workers in the hospital and provided treatment according to the regular treatment protocol of the hospital.

Should you agree to participate, please sign your name below, indicating that you have read and understood the nature of the study, and that all your inquiries concerning the activities have been answered to your satisfaction.

Consent

I have had the study explained to me and have read the contents of this form/had the contents of this form read to me. I have been given the opportunity to ask questions and have them answered to my satisfaction. I understand that my child's temperature will be determined using hand touch method and digital thermometer. I am willing for my child to be enrolled in this study.

_____	_____
Signature of parents/guardian	Hospital personnel who explained consent
_____	_____
Date/time	Date/time
_____	_____
Signature of witness	Signature of witness
_____	_____
Date/time	Date/time