



**THE PREVALENCE AND FACTORS ASSOCIATED WITH
GASTROESOPHAGEAL REFLUX RELATED SYMPTOMS IN
INFANTS AT THE MATERNAL CHILD HEALTH CLINIC,
KENYATTA NATIONAL HOSPITAL.**

**A DISSERTATION SUBMITTED IN PARTIAL FULFILMENT FOR THE FOR THE
DEGREE OF MASTERS OF MEDICINE (PAEDIATRICS AND CHILD HEALTH),
UNIVERSITY OF NAIROBI.**

DR. YVONNE WAIGUMO (MBChB)

H58/80957/2015

The University of Nairobi

2018

DECLARATION

This dissertation is submitted as my original work and has neither been published elsewhere nor been presented for the award of a degree in any other university.

Signed.....Date.....

Dr. Yvonne Waigumo (MBChB).

Department of Paediatrics and Child Health, University of Nairobi

APPROVAL

This dissertation has been presented to the University of Nairobi with our full approval as University supervisors:

Signed.....Date.....

Prof. Dalton C. Wamalwa (MBChB, M.Med, MPH).

Associate Professor,

Department of Paediatrics and Child Health, University of Nairobi.

Signed..... Date.....

Dr. Ahmed Laving (MBChB, M.Med (Paediatrics))

Senior Lecturer / Paediatric Gastroenterologist,

Department of Paediatrics and Child Health, University of Nairobi.

DEDICATION

This dissertation is dedicated to my dear mother Muthoni Thiongo, my loving and supportive husband Maina Ngechu, and my family. Thank you all for your continuous prayers, love, patience, words of encouragement and constant support through this journey.

ACKNOWLEDGEMENTS

I would like to thank God for seeing me through this journey.

I wish to express my sincere appreciation to:

- My supervisors Dr. Ahmed Laving and Prof. Dalton Wamalwa for their continuous guidance and support during this study
- The faculty members of Department of Paediatrics and Child Health, University of Nairobi for their contribution in making this study a success.
- Prof. Njuguna Ngethe and Mary Wamuyu for their continued support.
- Statistician Mr. Francis Njiiri, for his assistance in data entry and data management.
- Kenyatta National hospital management and maternal child health clinic staff.
- All the infants and their guardians who agreed to participate in this study.

TABLE OF CONTENTS

DECLARATION	ii
DEDICATION	iii
ACKNOWLEDGEMENTS	iv
LIST OF TABLES	vii
LIST OF FIGURES	vii
ABBREVIATIONS:	viii
DEFINITIONS:.....	ix
ABSTRACT.....	x
CHAPTER ONE: INTRODUCTION AND LITERATURE REVIEW	1
1.1 Background.....	1
1.2 Pathophysiology.....	1
1.3 Clinical Features	2
1.4 Diagnostic modalities.....	2
1.5 Epidemiology and Prevalence.....	4
1.6 Management.....	6
1.7 Study Justification.....	8
1.8 Study utility.....	8
CHAPTER TWO: RESEARCH QUESTIONS AND STUDY OBJECTIVES.....	10
2.1 Research Question	10
2.2 Study Objectives	10
CHAPTER THREE: RESEARCH METHODS.....	11
3.1 Study Design.....	11
3.2 Study Period.....	11
3.3 Study Location	11
3.4 Study Population.....	11
3.4.1 Inclusion Criteria:.....	11
3.4.2 Exclusion Criteria:.....	11
3.5 Sample Size Determination:	12
3.6 Study Outcomes:	13
3.7 Study Tools	13
3.8 Study Procedure:	15
3.8.1 Study personnel	15

3.8.2 Patient recruitment procedure	15
3.9 Data Management and Analysis	16
3.9.1 Control of Bias and Errors	16
3.10 Ethical considerations	16
3.10.1 Ethical approval.....	16
3. 10.2 Confidentiality.....	17
3.10.3 Study risk.....	17
3.10.4 Benefit from the study.....	17
CHAPTER FOUR: RESULTS	18
4.1 Sociodemographic Characteristics of the Study Participants	18
4.2 Caregivers Sociodemographic characteristics	19
4.3 Infant Gastroesophageal reflux symptoms.....	20
4.4 Prevalence of infant regurgitation.....	22
4.5 Infant Gastroesophageal Reflux Questionnaire Revised Score	22
4.6 Multivariate Analysis.....	24
4.7 Management of gastroesophageal reflux symptoms.....	25
CHAPTER FIVE: DISCUSSION.....	26
5.1 Strengths of Study.....	30
5.2 Study Limitation	30
CHAPER SIX: CONCLUSIONS AND RECOMMENDATIONS.....	31
6.1 Conclusions.....	31
6.2 Recommendations.....	31
REFERENCES.....	32
APPENDICES:.....	36
Appendix 1: Questionnaire	36
Appendix 2: Consent form.....	41
Appendix 3: Dodoso (Questionnaire translated to Kiswahili).....	44
Appendix 4: Fomu ya Idhini (Consent form translated to Kiswahili)	49
Appendix 5: KNH-UON/ERC RESEARCH APPROVAL LETTER AND TURNITIN REPORT	52

LIST OF TABLES

Table 1: Clinical Manifestations in Gastroesophageal Reflux and Gastroesophageal Reflux Disease.	2
Table 2: The Infant gastroesophageal reflux questionnaire revised (IGERQ-R) score scale. .	14
Table 3: Summary of parameters of Infants recruited.	19
Table 4: Summary of median Z scores for the study population.	19
Table 5: Caregivers sociodemographic characteristics	20
Table 6: Summary of Infants' gastroesophageal reflux symptoms.	21
Table 7: Summary of Infant Gastroesophageal Questionnaire Revised Score Parameters	23
Table 8: Summary of bivariate analysis of median I-GERQ-R Score and factors associated with gastroesophageal reflux symptoms.	23
Table 9: Logistic regression of factors associated with gastroesophageal reflux symptoms. .	24

LIST OF FIGURES

Figure 1: Sociodemographic characteristics of the infants (n=414)	18
Figure 2: Prevalence of Regurgitation.	22
Figure 3: Summary of management of gastroesophageal reflux symptoms.	25

ABBREVIATIONS:

GER- Gastroesophageal Reflux

GERD- Gastroesophageal Reflux Disease

GI- Gastrointestinal

H2RA- Histamine 2 Receptor Antagonists

I-GERQ- Infant Gastroesophageal Reflux Questionnaire

IGERQ –R- Infant Gastroesophageal Reflux Questionnaire Revised

KNH – Kenyatta National Hospital

LES- Lower Esophageal Sphincter

MCH Clinic- Maternal Child Health Clinic

PPI- Proton Pump Inhibitor

SIDS- Sudden Infant Death Syndrome

TLESR- Transient lower Esophageal Sphincter Relaxations

UON- University of Nairobi

WHO– World Health Organization

DEFINITIONS:

Gastroesophageal reflux: This is the passage of gastric contents into the oesophagus with or without regurgitation and vomiting. GER is a normal physiologic process occurring several times per day in healthy infants, children, and adults. Most episodes of GER in healthy individuals lasts <3 minutes, occur in the postprandial period, and cause few or no symptoms.

Gastroesophageal reflux disease: This is when the reflux of gastric contents causes ‘troublesome’ symptoms and/or complications. “Troublesome “is defined as having an adverse effect on the wellbeing of the patient

Regurgitation: This is the passage of refluxed gastric contents into the pharynx or mouth and sometimes expelled out of the mouth. Regurgitation is generally assigned as effortless and non-projectile, although it may sometimes be forceful in infants. It is also referred to as spitting up or spilling.

In this study, Rome III criteria for Infant regurgitation was used. Diagnostic criteria included both of the following in otherwise healthy infants 3 weeks to 12 months of age:

- Regurgitation two or more times per day for 3 or more weeks.
- No retching, hematemesis, aspiration, apnea, failure to thrive, feeding or swallowing difficulties, or abnormal posturing.

ABSTRACT

Background

Gastroesophageal reflux (GER) occurs when there is passage into the oesophagus or oropharynx, of stomach contents. It may be accompanied by vomiting. This occurrence is physiological among infants. Regurgitation is a prominent clinical manifestation of gastroesophageal reflux. Rome III diagnostic criteria for infant regurgitation was used in this study. Infant regurgitation has a worldwide prevalence range of 3-87%. Epidemiological studies suggest the prevalence of gastroesophageal reflux varies amongst different ethnic groups. There is currently no information on the prevalence of gastroesophageal reflux among Kenyan infants or the factors associated with these symptoms.

Objectives

The primary objective was to determine the prevalence of gastroesophageal reflux related symptoms among infants aged 1-12 months, attending the maternal child health clinic, Kenyatta National Hospital. The secondary objectives were to identify the factors associated with gastroesophageal reflux related symptoms in these infants, and describe the management of these symptoms in these infants.

Methods

This was a cross-sectional hospital based descriptive study, in infants aged 1 to 12 months, presenting at the maternal child health clinic (Clinic 66), Kenyatta National Hospital. Infants presenting at the clinic were screened and there was sequential enrollment of those who met inclusion criteria. A validated, structured pre-tested questionnaire, the Infant Gastroesophageal Reflux Questionnaire Revised, (IGERQ-R) was administered to assess gastroesophageal reflux symptoms. (IGERQ-R Score of 0 -No reflux, Score>15 – Gastroesophageal reflux disease). Factors associated with these symptoms and management of these symptoms was also assessed. Statistical package for Social Sciences (SPSS) ver. 24, was utilized for data entry and analysis. Categorical data was summarized as frequency distributions and tabulated. Proportions were represented graphically as pie charts and bar graphs. Bivariate and multivariate analysis was undertaken to establish variables statistically associated with symptom severity of gastroesophageal reflux.

Results

Four hundred and fourteen (414) infants were enrolled into the study, 269(65%) infants were aged 1-6 months and 145 (35%) 7 -12 months of age, with a male-to-female ratio of 1:1. Prevalence of regurgitation according to Rome III diagnostic criteria amongst our study

population was 72.9%. Infants aged 1-6 months had a prevalence of 84%, while those 7-12 months of age had a prevalence of 52.4%.

The association between infant age as a demographic variable and gastroesophageal reflux related symptoms was significant ($p= 0.003$). Complementary feeding was associated with decreased gastroesophageal symptoms, however this was not found to be significant. There was no significant association found with regards to gastroesophageal reflux symptoms and gender of the infant, care giver age and level of education or number of children within the household. There was no infant found to have a score of 16 or greater which is a positive score, for gastroesophageal reflux disease.

Only 25 (6.03%) infants were reported to have received treatment for GER symptoms. Of these 72% received non-pharmacological treatment compared to pharmacological treatment (28%), 90% reported improvement of symptoms.

Conclusion

The prevalence of regurgitation in infants aged 1-12 months according to Rome III diagnostic criteria was 72.9%. Infant age was significantly related to gastroesophageal reflux symptoms. Frequency and severity of these symptoms decreased with age as evaluated by IGERQ-R. No infant was found to have gastroesophageal reflux disease (IGERQ-R Score >15). There was improvement of gastroesophageal reflux symptoms with non-pharmacological treatment.

Recommendations

We recommend education of caregivers on resolution of gastroesophageal reflux symptoms with increase in age and efficacy of non-pharmacological treatment as condition is physiological. Encourage utilization of the Infant gastroesophageal reflux questionnaire revised (I-GERQ-R) to screen infants who present with gastroesophageal reflux symptoms, and assess severity of these symptoms

CHAPTER ONE: INTRODUCTION AND LITERATURE REVIEW

1.1 Background

Gastroesophageal reflux (GER) occurs when there is passage into the oesophagus or oropharynx, of stomach contents. It may be accompanied by vomiting. Among infants this occurrence is physiological. Common visible symptoms observed by parents and care givers include spitting up or regurgitation, which occurs every day in approximately 50% of infants aged less than 3 months. In most healthy infants there is resolution of regurgitation by 12-14 months of age.(1)

Gastroesophageal reflux disease occurs when the wellbeing of a patient, is adversely affected by clinical symptoms or complications of the reflux of stomach contents. These symptoms may be due to frequent or persistent GER, producing esophagitis related symptoms or extraesophageal symptoms.(1)

1.2 Pathophysiology

Normal intraabdominal pressure augmentations occur during day to day life. Increased reflux episodes may occur due to insufficient lower oesophageal sphincter tone, increased recurrence of lower oesophageal sphincter relaxations and by hiatal herniation. Normal intraabdominal pressure augmentations may be worsened by straining or respiratory efforts.(2)

The lower oesophageal sphincter forms the anti-reflux barrier. It is a high pressure zone by manometry. It performs valve like functions through support by the crura of the diaphragm at the gastroesophageal junction together with the oesophagogastric junction anatomy.(2)

Transient lower oesophageal sphincter relaxations (TLSERS) a physiological process that enables the stomach to release gas, is the primary mechanism allowing gastroesophageal reflux among children. It involves lower oesophageal sphincter relaxing concurrently with the surrounding crura. It is induced spontaneously independent of swallowing. This mechanism prevents accumulation of gas in the stomach or duodenum. The main stimulus for TLSERS is gastric distension which may be postprandial or from abnormal gastric emptying or air swallowing.(2)

Physiological reflux may progress to gastroesophageal reflux disease with alterations in anti-reflux protective processes. These include poor gastric emptying, inadequate clearance of

refluxate, abnormalities in epithelial repair and decreased neurological protection of aero digestive tract.(2,3)

1.3 Clinical Features

Reflux in healthy infant presents frequently with regurgitation (40%), with or without vomiting (especially postprandially). Other symptoms of reflux include hiccups (36%), crying duration of greater than an hour in a day (17%), arching of the back (10%) and mild respiratory symptoms. (1,4)

Clinical symptoms in infants may demonstrate differences between gastroesophageal reflux and gastroesophageal reflux disease as shown in the Table 1.(5)

Table 1: Clinical Manifestations in Gastroesophageal Reflux and Gastroesophageal Reflux Disease.

Gastroesophageal Reflux	Gastroesophageal Reflux Disease
Normal weight curve in a regurgitating infant	Stationary weight curve or weight loss in a regurgitating infant
No esophagitis symptoms	Refusal of food, difficulty swallowing, melena stools, haematemesis, anaemia, repeated irritability, hyposideremia
No critical respiratory symptoms	Chronic cough, stridor, wheezing, aspiration, apnea, sleep disorders, episodes of cyanosis, recurrent pneumonia, dysphonia
No neurobehavioural symptoms	Abnormal arching of the back (Sandifer syndrome)

1.4 Diagnostic modalities

Diagnosis of GER and GERD is often made through clinical symptoms or signs. These subjective descriptions are considered nonspecific and inaccurate in children less than 8-12 years of age.(6,7)

Investigations are important in evaluation of the presence of symptoms or complications of reflux, demonstrate an association among various symptoms and reflux episodes, assess treatment and rule out alternative conditions that may present in a similar way. Tests must be carefully selected as no individual test can attend to all these questions.(6)

History and physical examination is used in gastroesophageal reflux to assist in the exclusion of other conditions that may present with comparable symptoms such as vomiting, and to recognize complications of the disease.(7)

Individual symptoms do not accurately correspond with objective findings amongst the paediatric population and as such, parent or patient reported questionnaires based on groups of symptoms have been established. The Infant gastroesophageal reflux questionnaire (I-GERQ) and Infant gastroesophageal reflux questionnaire revised (I-GERQ-R) are infant based questionnaires that have been used as diagnostic tool for infant gastroesophageal reflux disease. It is an important diagnostic tool in countries with restricted economic and technological resources.(4,7,8)

The I-GERQ was developed by Orenstein et al in 2005, and approved as tool to collect relevant baseline clinical data and also for diagnosis. Abnormal esophageal biopsies and/or pH probe studies were used as reference standards in its validation as a diagnostic tool for GERD in infants, 1-14 months of age. It is not approved as a tool to assess response to various treatment modalities.(4)

Kleinman et al, revised the I-GERQ to develop a short 12 item questionnaire, the I-GERQ-R. It was based on feedback reports from parents and paediatricians, and in keeping with best practice of questionnaire development. It has been shown to provide an accurate evaluation of GERD symptoms in infants, to differentiate cases of GERD from those with inadequate clinical manifestations for the diagnosis, assessing disease severity and monitoring therapeutic intervention outcomes. It can also be used for appraisal in clinical trials.(8)

Esophageal manometry evaluates pressure of the upper and lower esophageal sphincter, esophageal peristalsis and the structures' synchronized activity during swallowing. Manometry studies cannot diagnose GERD. However, it is crucial in identifying esophageal sphincter relaxations (TLESRS) as the causative mechanism for gastroesophageal reflux disease.(6,7,9)

Upper gastrointestinal series (Barium contrast radiography) is not a precise investigation for diagnosis of GER and GERD, and as such, there is no rationale for its routine use. **Esophageal and gastric ultrasonography** has no role in diagnosis of GERD in children and infants. Gastroesophageal junction ultrasonography however, can reveal non acid reflux through identification of fluid motion over a brief time period. **Nuclear scintigraphy** assesses postprandial reflux episodes unaided by the gastric pH. It also provides knowledge on duration of gastric emptying. It is not justified for routine use in management of GERD.(7,10)

Esophageal pH monitoring is a quantifiable assessment of frequency and duration of acid exposure in the esophagus with determined standard ranges. Intensity of symptoms or complications does not usually correspond to the severity of pathologic reflux. It is however, a beneficial tool in assessing the efficiency of gastric antisecretory treatment. It may also be valuable in linking acid reflux events with clinical manifestations such as cough, wheeze or chest pain and thus identify children whose symptoms are aggravated by gastroesophageal reflux.(7)

Episodes of acid and non-acid reflux can be detected through **combined multiple intraluminal impedance and pH monitoring test**. In comparison to esophageal pH monitoring only, it is valuable in the assessment of sequential association of symptoms and gastroesophageal reflux. Its use among the paediatric population to detect severity of disease or treatment response has not been determined.(7)

There is lack of data to support **continuous monitoring of esophagus for bilirubin**, or use of histology obtained through **endoscopy and biopsy** to diagnose or exclude reflux disease. Diagnosis of this condition by **empiric trial of acid suppression** through pharmacotherapy among infants and children is not recommended.(6,7)

1.5 Epidemiology and Prevalence

Studies among paediatric and adult population indicate that the prevalence of this condition may differ among various ethnic groups(11)

Vandeplas et al reviewed published evidence and clinician opinion on the prevalence and long-term health consequences of functional gastrointestinal symptoms in infants younger than 12 months. Infant regurgitation was the most common functional gastrointestinal symptoms in infants, with a wide prevalence range of 3-87%. The expert consensus on

prevalence of infant regurgitation worldwide according to Rome III criteria, was estimated to be approximately 30%. (12)

In the United States, a study was done by Nelson et al to determine the prevalence of symptoms of gastroesophageal reflux during the first year of life and describe when most infants outgrew these symptoms. They also assessed the prevalence of parental reports of various symptoms associated with GER and percentage of infants treated for GER. It was a cross-sectional study done in nineteen paediatric practice research group practices in Chicago Illinois. The tools used included the Infant Gastroesophageal reflux questionnaire shortened and revised form (I-GER-SF) and Children's Eating Behaviour inventory (CEBI). They found that 'at least one episode a day' of regurgitation was reported in 50% of infants aged 0-3 months. Peak regurgitation was reported at 4 months at 67%. The symptoms decreased to 21% at 6-7 months and reached 5% at 10-12 months. Infants with at least 4 episodes daily of regurgitation showed a similar pattern, though peak regurgitation reported as a "problem" was at 6 months and this prevalence decreased to 14% at 7 months of age. Parents considered regurgitation a problem when associated with increased frequency and volume, increased crying or fussiness, discomfort with spitting up, and frequent back arching. Treatment for regurgitation reported included a change in formula in 8.1%, thickened feedings in 2.2%, termination of breast-feeding in 1.1%, and medication in 0.2%.(13)

In rural Michigan, Van Howe et al, undertook a prospective cohort study to determine the degree of GER associated symptoms amongst healthy infants aged 0-6 months of age. They used the Infant Gastroesophageal reflux Questionnaire-Revised, I-GERQ-R. Their study concluded that in otherwise healthy infants, gastroesophageal reflux symptoms as determined by the I-GERQ-R, reduced with age in the first 6 months of life. At least one episode of regurgitation was reported in the previous day in 82% in the first month, 77% in the second month, and 83% in the fourth month and decreased to 67% by the sixth month. There was no relation between breastfeeding and GER symptoms in this study.(14)

In Adelaide, Australia, Martin et al, carried out a study to determine natural history of infant spilling (regurgitation/vomiting) during first 2 years of life. Peak prevalence of regurgitation in infants was 41% at 3-4 months, decreasing to 35% in 6-7 month old infants, 15% in 8-9 month old infants and 10% in 10-11 month old infants. Factors such as gender, breastfeeding and environmental tobacco smoke exposure were not significantly associated to spilling.(15)

In Italy, a study to evaluate the prevalence and natural history of infant regurgitation in Italian children during first 2 years of life was carried out by Campanozzi et al. Infant regurgitation was according to Rome II criteria and they used a modified I-GERQ questionnaire completed by primary care paediatricians, at an interval of 2 months for a period of 24 months. They concluded that 12% of Italian infants had infant regurgitation according to the Rome II diagnostic criteria. 88% of the infants in the study had improved by 12 months. No significant difference was observed in prevalence amongst breastfed and formula fed infants, however, formula fed infants stopped regurgitating later than breastfed infants.(16)

The prevalence of GER related symptoms and complications among Japanese infants visiting healthy baby checkups was studied by Miyazawa et al. Infants with one or more regurgitation or vomiting episode per day was at 47.1% at 1 month, 28.8% at 4 months and 6.4% at 7 months. Those with 3 or more episodes per day showed a similar pattern. The prevalence of regurgitation between breastfed and formula fed infants was not shown to be significantly different in this study.(17)

Prevalence of gastroesophageal reflux symptoms amongst Thai infants contrasts that of Western infants. A study done by Osatakul et al found that peak prevalence was 86.9% at 2 months of age, it gradually reduced to 69.7% at 4 months of age, 66% at 6 months with a significant decrease to 7.6% at 12 months. The prevalence of infants who regurgitated daily also decreased from 33.1% at 1 month to only 2.1% at 6 months, from 6-12 months of age, almost all infants with GER regurgitated only 1-3 days a week. The type of feeding, breastmilk or formula had no impact on the prevalence of regurgitation.(11)

In northern India, a study on the prevalence of gastroesophageal reflux in infants and children was done by De et al. They used the I-GERQ questionnaire designed by Orenstein et al. Prevalence of regurgitation in this study was 55% at 1-6 months, 15% at 7-12 months and 10% at 12-24 months.(18)

1.6 Management

Infants with physiologic gastroesophageal reflux are often sufficiently managed through lifestyle changes such as parental education, guidance and support, feeding and positional modifications. Surgery is done in severe or chronic cases of gastroesophageal reflux disease.(7)

Several studies have shown comparable prevalence in physiologic GER, amongst breastfed and formula fed infants', despite duration of reflux episodes being shorter in breastfed infants as assessed by pH probe. This may be due to peristalsis stimulated by lower esophageal pH in breastfed infants, thus shorter period of reflux.(7,11,19)

Exclusion of cow milk from maternal and infant diet has been shown to reduce vomiting and regurgitation in infants with cow milk protein allergy, whose symptoms are often indistinguishable from those of physiologic GER. Trial use of extensively hydrolyzed or amino acid formula for about 4 weeks, has been recommended by several studies, for management of vomiting and regurgitation in formula fed infants.(7,20–26)

Reduced feeding volume has also been established to decrease the number of reflux episodes in a study by Khoshoo V et al. Large volume feeds were postulated to increase regurgitation by increasing frequency of TLESR. The study concluded that vomiting and reflux episodes in healthy infants may be reduced by use of rice cereal to thicken formula, decreasing the volume of feed but maintaining nutritional balance.(7,27)

Studies show that placing the infant in prone position reduces exposure to esophageal acid in terms of frequency and volume as assessed by pH probe. It is therefore associated with less reflux symptoms and longer uninterrupted sleep periods compared to supine position which has more frequent arousals and crying episodes. However, the Nordic Epidemiological SIDS Study demonstrated that prone and lateral positioning is associated with increased incidence of sudden infant syndrome (SIDS). The risk of SIDS therefore exceeds the benefit of prone or lateral sleep position for GER. Therefore, supine position during sleep is recommended in infants.(7,28–34)

Several pharmacologic agents are used for treating GERD in children. These include gastric acid buffering agents, mucosal surface barriers, and gastric antisecretory agents. Commonly used agents include histamine 2 receptor antagonists and proton pump inhibitors. Histamine-2 receptor antagonists (H2RAs) decrease acid secretion by inhibiting histamine-2 receptors on gastric parietal cells. Proton pump inhibitors (PPIs) inhibit acid secretion by blocking Na⁺K⁺ ATPase, the final common pathway of parietal cell acid secretion, often called the proton pump. Decreased 24 hour intragastric volumes due to efficacious acid suppression by PPIs, also promotes gastric emptying which results in decreased reflux volumes.(7,35)

PPI therapy prescriptions for infants have increased recently although their use in this age group is not recommended. In majority of these infants, there was no evidence of acid related disease. Several studies have also shown that acid suppression therapy in infants is associated with many risks.(36–40)

1.7 Study Justification

From the literature, it is evident that a number of issues are highly relevant to the study and some of them serve as good justifications for this study. Studies show that prevalence of GER is not the same amongst diverse racial groups and also varies with age of the infant. Several factors such as gender, smoke exposure and feeding practice (breastfeeding and formula feeding) have also been studied with regards to gastroesophageal reflux. The prevalence of gastroesophageal reflux and factors associated with these symptoms in infants in Kenya is not known.

Gastroesophageal reflux disease impacts negatively on the health related quality of life. Underdiagnoses of this disease exposes infants to the risk of severe complications such as bronchospasm, esophagitis, esophageal stricture, Barrett's esophagus or adenocarcinoma, whereas over diagnosis may lead to unsuitable treatment. No pharmacological agent is permitted for use among infants. However, prescriptions of PPIs for infants have increased recently despite current guidelines reporting that they are not beneficial in the management of this condition and lack of evidence of acid related disease in the majority. This study will establish the prevalence of GER, using a standardized tool of gastroesophageal reflux in our population and thus highlight the need to curb pharmacological treatment for physiological reflux symptoms.(7,41)

1.8 Study utility

This study will provide new knowledge on current prevalence rates of gastroesophageal reflux symptoms amongst healthy infants in our setting. This will offer a reference point for further studies on this subject and related issues such as gastroesophageal reflux disease in our region.

Gastroesophageal reflux is very common in infancy worldwide and although symptoms are physiological in this age group up to 20% of caregivers have been shown to seek medical attention. The initial goal of most health care providers evaluating infants with gastroesophageal reflux symptoms is to exclude serious disease. This study will provide information on

prevalence of these symptoms among infants and as such reduce overtreatment of physiological symptoms and promote identification and early referral to specialist clinic of those with severe symptoms, and thus enhance patient care in our setting (42)

This study will also enable health policy makers and specialists in this field to create guidelines for management of this condition in our country and region.

CHAPTER TWO: RESEARCH QUESTIONS AND STUDY OBJECTIVES

2.1 Research Question

1. What is the prevalence and the factors associated with gastroesophageal reflux related symptoms among infants at the Maternal Child Health clinic in Kenyatta National Hospital?

2.2 Study Objectives

Primary Objective

1. To determine the prevalence of gastroesophageal reflux related symptoms among infants (age 1-12 months), at MCH clinic, Kenyatta National Hospital.

Secondary Objective

1. To identify the factors associated with gastroesophageal reflux related symptoms in infants aged 1-12 months old, at MCH clinic, Kenyatta National Hospital.
Factors of interest include infants and caregiver demographic details and feeding practices.
2. To describe the management of infants with gastroesophageal reflux related symptoms.

CHAPTER THREE: RESEARCH METHODS

3.1 Study Design

This was a hospital based cross-sectional study.

3.2 Study Period

The study was carried out between the months of October and December 2017.

3.3 Study Location

The study site was the Maternal Child Health clinic, Kenyatta National Hospital.

Kenyatta National Hospital, one of the two main public referral hospitals in Kenya, is located in the Upper Hill area about 3.5km from Nairobi City Centre. It is a teaching hospital engaged in training of many cadres of health professionals. Maternal child health clinic is one of the outpatient clinics situated in clinic 66, and this is the point where immunization, nutrition and growth monitoring services are offered daily on weekdays.

3.4 Study Population

The population of this study was drawn from infants aged 1- 12 months, who attended the Kenyatta National Hospital MCH clinic, during the data collection phase of the study.

The Maternal Child health clinic is served by 10 qualified nursing staff. It provides services to approximately 1600-2500 infants and children every month of which about 700-800 are regular clients (Kenyatta National Hospital, Health Information department). The clinic has an urban catchment area with a population of about 3.1 million of which 22% live below the poverty line.

3.4.1 Inclusion Criteria:

- Infant age 1-12 months

3.4.2 Exclusion Criteria:

Infants meeting any of the following were excluded from the study:

- Those born prematurely (less than 37 weeks completed gestation).
- Those with neurologic conditions such as cerebral palsy, muscle hypotonia or spasticity.

- Severely malnourished infants (<-3 SD of the "weight to length z-score of the WHO 2006 growth chart").
- Infants who had previously undergone gastrointestinal surgery.
- Caregiver who declined to consent.

3.5 Sample Size Determination:

The study population was stratified into two, 1-6months of age and 7-12months of age. Studies have shown that prevalence rates for the 2 groups differ, and as such sample size was determined for the 2 strata, using Daniel's Formula for Sample Size Determination in Prevalence studies and population correction factor was then applied for finite –population. This is shown below;

$$n = \frac{z^2 p(1-p)}{d^2} = \frac{1.96^2 \times 0.55 \times 0.45}{0.06^2} = 264$$

$$n_o = \frac{n}{1 + \left(\frac{n-1}{\text{total population}}\right)} = \frac{264}{1 + \left(\frac{264-1}{7000}\right)} = 254$$

$$n_{1-6\text{months}} = 254$$

$$n = \frac{z^2 p(1-p)}{d^2} = \frac{1.96^2 \times 0.15 \times 0.85}{0.06^2} = 136$$

$$n_o = \frac{n}{1 + \left(\frac{n-1}{\text{total population}}\right)} = \frac{136}{1 + \left(\frac{136-1}{7000}\right)} = 133$$

$$n_{7-12\text{months}} = 133$$

- n = Sample Size
- z = Normal Standard Deviation taken with a 95% Confidence Interval; set at 1.96.
- p = Expected Prevalence of gastroesophageal reflux-De et al study, Prevalence for 1-6 months-55%, 7-12 months- 15%.
- d = Study Precision taken as 6%.

Calculated sample size for 1-6 months is 254, and that for 7-12 months is 133.

Total sample size is 387.

3.6 Study Outcomes:

The study achieved the following outcomes:

- Determined the prevalence of regurgitation among infants at the Maternal and Child Health Clinic at Kenyatta National Hospital.
- Determined the factors affecting gastroesophageal reflux related symptoms and described management of these symptoms, among infants presenting at the Maternal Child Health Clinic at Kenyatta National Hospital.

3.7 Study Tools

Participant Interviews and Questionnaires:

The questionnaire included the following:

1. The study subjects socio-demographic details such as age, gender, gestation at birth, birth order and anthropometric measures. Caregiver's relationship to infant, age and level of education.
2. Age of onset of spitting up (regurgitation). According to Rome III diagnostic criteria, regurgitation should have occurred for 3 or more weeks.
3. A validated structured Pretested Questionnaire, the Infant gastroesophageal reflux questionnaire revised (IGERQ-R), which assessed details of the following;
 - Infant's spitting up- frequency of spitting up, volume spit up, whether it is uncomfortable to the child.
 - Infant's feeding habits-refusal to feed, irritability during feeding.
 - Infant's crying or fussiness, hiccups and back arching.
 - Any acute life threatening events in the past week.

The questionnaire included questions that had a specific recall period and 2-5 scaled possible responses with total point score of 42. A score of 16 or greater was a positive score, for GERD.

Table 2: The Infant gastroesophageal reflux questionnaire revised (IGERQ-R) score scale.

Question summary	Maximum Point
1. Spit up frequency	3
2. Spit up volume	4
3. Spit up uncomfortable	4
4. Refuse feeding	4
5. Stop eating even if hungry	4
6. Cry during or after feeding	4
7. Cry more than usual	4
8. Cry duration	3
9. Hiccups frequency	4
10. Arching frequency	4
11. Stop breathing while awake or struggle to breath	2
12. Turn blue or purple	2
Total possible	42 cutoff >15

3.8

3.9 Study Procedure:

3.8.1 Study personnel

The study personnel included: the principal investigator (myself) and one research assistant. The research assistant was a nursing officer with experience in the maternal child health clinic and paediatric wards. The research assistant was trained on how to recruit patients, collect data and proper documentation.

3.8.2 Patient recruitment procedure

Stratified sampling was carried out. A separate sampling frame was used for the two strata 1 to 6 months and 7 to 12 months. Within each sampling frame consecutive sampling was done until desired sample size achieved.

Patients are attended to one after the other, on a first come, first serve basis at the Maternal Child Health Clinic. A waiting bay with seats is provided for patients, outside the growth monitoring and immunization room, as they await their turn.

Recruitment of study participants was done in the waiting bay after patient registration and prior to growth monitoring and immunization. Recruitment did not interfere or delay service provision to clients who chose to participate in the study.

The investigator and trained assistant screened the infants at the clinic to identify eligible infants. Once eligible infants were identified, the caregiver (parent or guardian) was adequately informed of the study and consent taken. This was through a pre-designed written consent form which provided information on the purpose of the study, study procedure as well as potential benefits and risks of study participation. Before signing the consent form, the investigator or trained assistant checked that the caregiver understood the information provided and any questions regarding the study were answered. Consent was voluntary and free of coercion. Caregivers' who agreed to take part in the study signed the consent form and the investigator or trained assistant countersigned the form.

Data was collected by administration of a structured pre-tested questionnaire. The forms were collected at the end of each day and reviewed for omissions and errors.

3.10 Data Management and Analysis

Statistical package for Social Sciences (SPSS) ver. 24, was used for data entry and analysis.

Univariate statistics was used to summarize the socio-demographic data for mothers and infants. Descriptive analysis was done for continuous variables and presented in terms of mean, median and mode when appropriate. The frequency was reported in terms of numbers tables, graphs and pie charts.

Bivariate and multivariate analysis was undertaken to establish variables statistically related to severity of gastroesophageal reflux. The variables in case were factors thought to be associated with GER symptoms.

The prevalence of gastroesophageal reflux related symptoms among the different age groups was calculated and presented as percentages. Statistical significance was based on an alpha level of 0.05.

3.9.1 Control of Bias and Errors

Measures taken to reduce bias and errors include:

1. To reduce measurement bias, the IGERQ-R questionnaire was pretested to ensure questions were appropriately phrased and easily understood. The study assistant was also thoroughly trained.
2. To reduce recall bias, symptom frequency was assessed for a short time frame of the preceding week.
3. The Principal investigator assessed the questionnaires filled at the end of each day to check for errors and omissions. Data entry was monitored to ensure validity of collected data.

3.10 Ethical considerations

3.10.1 Ethical approval

Ethical consent was granted by Kenyatta Hospital /University of Nairobi Ethics Research Committee to collect and analyze data before conducting the study. The purpose of the study was carefully explained to the caregiver with an aim to obtain voluntary participation. Caregiver was required to give informed written consent before enrolling infants in the study. No experimental investigations or products were used in this study.

3.10.2 Confidentiality

The principal investigator and research assistant ensured strict confidentiality was maintained during the study period. No personal identification data of study participants was recorded, study identification numbers were used. The filled questionnaires were stored safely under lock and key to ensure confidentiality.

3.10.3 Study risk

The participants were not exposed to any risk during the study.

3.10.4 Benefit from the study

Dissemination of study research findings will be availed to the primary health team at the maternal child health clinic and paediatric units Kenyatta National Hospital, thereby contributing to the improvement of care delivered to this group of infants.

The study findings will also be availed to the University of Nairobi (UON) Department of Pediatrics and Child Health academic staff and students in fulfillment of the requirements of the M.Med Program.

CHAPTER FOUR: RESULTS

During the study period between October and December 2017, a total of 425 infants were screened for recruitment into the study. Eleven (11) infants were excluded. Therefore 414 infants were enrolled and included in the final analysis.

4.1 Sociodemographic Characteristics of the Study Participants

The descriptive analysis of the basic characteristics of the infants enrolled in this study and summary of infants' parameters is shown in Figure 1 and Table 3 respectively:

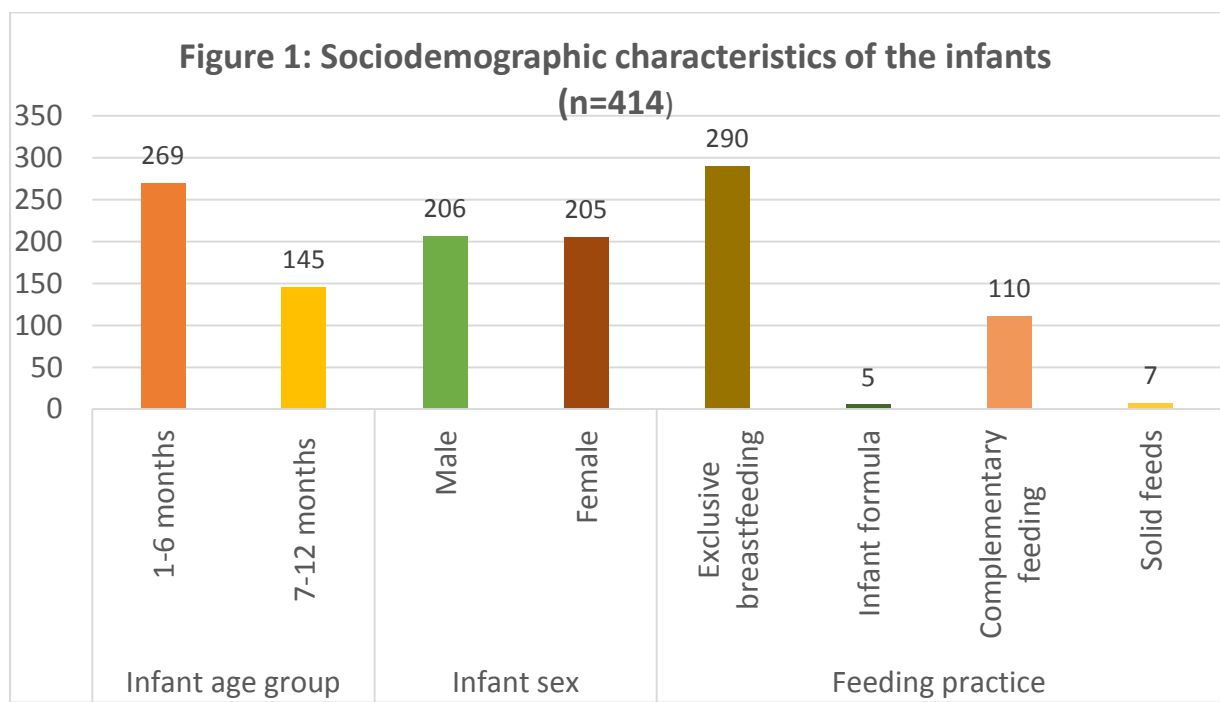


Figure 1: Sociodemographic characteristics of the infants (n=414)

Of the 414 infants, 269 (65%) infants were aged 1-6 months and 145 (35%) infants were 7-12 months of age. There were 206 (50.2%) male infants and 205 (49.8%) female infants, with a male-to-female ratio of 1:1.

290 (70.4%) infants were exclusively breastfed, 110 (26.7%) infants were complementary fed. Only 5 (1.2%) infants were reported to be formula fed.

Table 3: Summary of parameters of Infants recruited.

Infant characteristic	Median(IQR)
Infant age (months)	4(2-7)
Birth weight (kg)	3.2(3.0-3.6)
Gestation at birth (weeks)	40(39-40)
Current weight (Kg)	6.4(5.0-7.5)
Length (cm)	61(57-67)

The median age of onset of spitting up amongst the study population was 3 months (IQR 1-5).

The median age of infants enrolled in the study was 4 months (IQR 2-7).The median birth weight was 3.2 kilograms (IQR 3.0-3.6) with a median gestation at birth was 40 weeks (IQR 39-40)

Using the WHO reference ranges, the weight for length z-scores (WHZ), the height for age z-scores (HAZ) and weight for age z-scores (WAZ) for the study population were determined and are summarized in Table 4.

Table 4: Summary of median Z scores for the study population.

	Median (IQR)
WHZ	0 (-1.0-1.0)
HAZ	0(-1.0-1.0)
WAZ	0(-1.0-1.0)

4.2 Caregivers Sociodemographic characteristics

The descriptive analysis of the characteristics of the caregivers who participated in the study is summarized in Table 5:

Table 5: Caregivers sociodemographic characteristics

Characteristic	Category	n=414	%
Relationship to infant	Mother	410	99.0
	Other caregiver (Father Grandmother, Aunt)	4	1.0
Gender	Male	2	.7
	Female	412	99.3
Level of education	< Secondary school	57	13.8
	≥ Secondary school	357	86.2
Number of children in household	1	127	30.8
	2	149	36.1
	>2	137	33.2

Majority of the infants (99%) were under the care of their mothers. The age of caregivers ranged from 17 to 48 years with a median age of 29 years (IQR 26-31). Most caregivers had attained at least secondary school level of education 357(86.2%), three (0.7%) caregivers did not attend formal school.

4.3 Infant Gastroesophageal reflux symptoms

The Infant Gastroesophageal Reflux Questionnaire Revised (IGERQ-R) was used to determine the presence and frequency of these symptoms. Table 6 summarizes the various symptoms assessed and difference in symptom frequency amongst the 2 age groups.

Table 6: Summary of Infants' gastroesophageal reflux symptoms.

Symptom	Characteristic	Infant age group			
		1-6 months		7 -12 months	
		N	%	N	%
Regurgitation frequency	<1	45	16.7	73	50.3
	1-3	169	62.8	58	40.0
	4-6	42	15.6	11	7.6
	>6	13	4.8	3	2.1
Regurgitation volume	Did not spit up	45	16.7	73	50.3
	Less than 1 tablespoonful	159	59.1	43	29.7
	1 tablespoonful to 2 ounces (1/4 cup)	61	22.7	26	16.9
	More than 2 ounces(1/4 cup) to half the feeding	4	1.5	3	2.1
Refuse feed when hungry	Yes	16	5.9	12	8.3
	No	253	94.1	133	91.7
Stop feed when hungry	Yes	11	4.1	13	9.0
	No	258	95.9	132	91.0
Cry during/after feed	Yes	14	5.2	6	4.1
	No	255	94.8	139	95.9
Cry greater than usual	Yes	22	8.2	12	8.3
	No	245	91.1	133	91.7
Cry duration	At least 10 minutes	29	10.8	17	11.7
	Less than 10 minutes	238	88.5	128	88.3
Hiccups during feeding	Yes	164	61.0	57	39.3
	No	104	38.7	88	60.7
Arching of back	Yes	53	19.7	11	7.6
	No	216	80.3	134	92.4

296 (71.5%) infants were reported to have spit up more than once over the past week. Majority of infants aged 1-6 months were reported to spit up 1-3 times a day and quantity spit up was less than a table spoon. Most of those 7-12 months of age spit up less than once a day in the past week.

Only 3.4 % of infants were reported to spit up more than 6 times in the past week. Majority 13 (4.8%) were 1-6 months of age. No infants were reported to spit up more than half the feed.

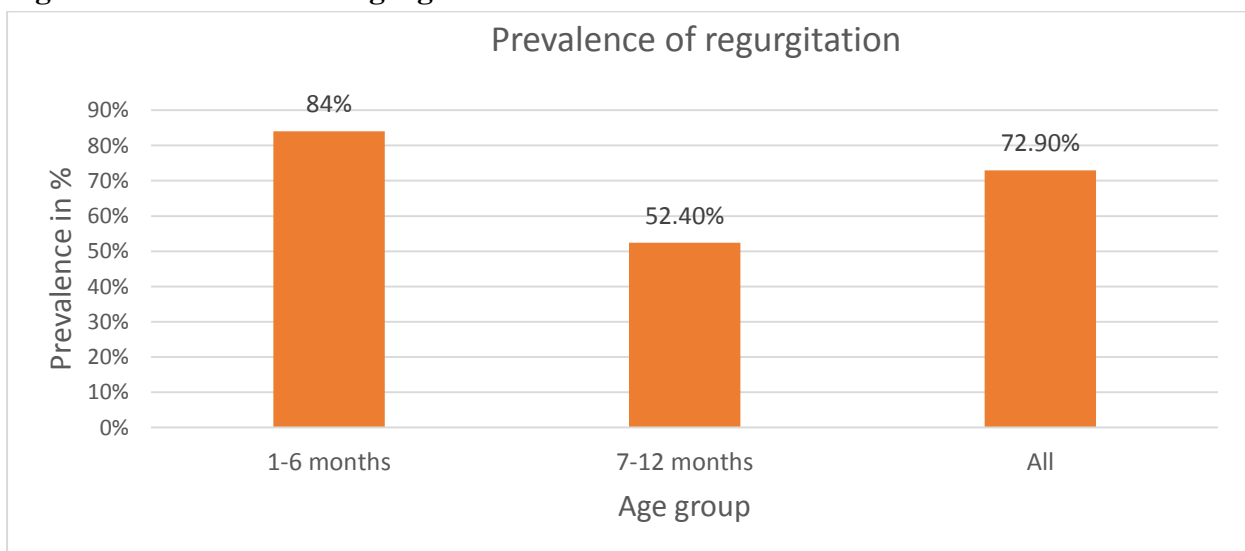
Hiccups was a commonly reported gastroesophageal reflux symptom amongst the study population. 221 (53.4%) infants were reported to have hiccups. It was more amongst those 1-6 months of age (61.05%) compared to those 7-12 months of age (39.3%).

No infants were reported to have acute life threatening events such as apnea (cessation of breathing or struggling to breathe) and cyanosis in the past week.

4.4 Prevalence of infant regurgitation

The prevalence of regurgitation according to Rome III diagnostic criteria amongst our study population was 72.9% (95% CI 72.707-73.093). Infants aged 1-6 months had a prevalence of 84% (95%CI 83.76-84.24) and for those 7-12 months of age it was 52.4% (95%CI 52.074-52.726). This is summarized in Figure 2:

Figure 2: Prevalence of Regurgitation.



4.5 Infant Gastroesophageal Reflux Questionnaire Revised Score

The score was determined from scaled responses given in the Infant gastroesophageal Reflux Questionnaire, which was used to establish severity of gastroesophageal reflux symptoms in each infant enrolled in the study.

Table 7 is a summary of the IGERQ-R score parameters for the 2 infant age groups.

Table 7: Summary of Infant Gastroesophageal Questionnaire Revised Score Parameters

		Infant age group				
		Mean	Standard Deviation	Median	Percentile 25	Percentile 75
IGERQ-R Score	1-6 months	5.9	3.1	5.0	4.0	8.0
	7-12 months	4.3	3.4	4.0	2.0	6.0
	Total	5.4	3.3	5.0	3.0	7.0

1. The IGERQ-R score ranges from 0-42. A higher IGERQ-R score indicates increased severity of symptoms.
2. A score of 16 or greater is a positive score, for gastroesophageal reflux disease.

The mean Infant Gastroesophageal Reflux Questionnaire Revised Score (I-GERQ-R) for the study population was 5.4 (SD 3.3), while the median was 5 (IQR 3.0-7.0). No infants had a score of 16 or greater, which is a positive score, for gastroesophageal reflux disease.

In most infants the 2 questions that determined the score was frequency and volume of regurgitation and frequency of hiccups.

Table 8: Summary of bivariate analysis of median I-GERQ-R Score and factors associated with gastroesophageal reflux symptoms.

		I-GERQ-R score group				OR [95%CI]	p-value
		Score \leq median(5)		Score $>$ median(5)			
		N	%	n	%		
Infant age group	1-6 months	138	51.3	131	48.7	Ref	<0.0001
	7-12 months	104	71.7	41	28.3	2.4 [1.6-3.7]	
Infant sex	Male	118	57.3	88	42.7	Ref	0.576
	Female	123	60.0	82	40.0	1.1 [0.8-1.7]	
Relationship to infant	Mother	240	58.5	170	41.5	Ref	0.730
	Other	2	50.0	2	50.0	0.7 [0.1-5.1]	
Mean age in years		29.64		29.51		1.0[1.0-1.03]	0.821
Level of	< Secondary	34	59.6	23	40.4	Ref	0.844

education	≥ Secondary	208	58.3	149	41.7	0.9 [0.5-1.7]	
Feeding practice	Exclusive breastfeeding	158	54.5	132	45.5	Ref	
	Infant formula	1	20.0	4	80.0	0.2 [0.02-1.9]	0.161
	Complementary feeding	75	68.2	35	31.8	1.8 [1.1-2.8]	0.013
	Solid feeds	7	100.0	0	.0	-	-

The proportion of infants aged 1- 6 months with an I-GERQ-R score greater than 5(median) compared with infants 7-12 months of age with I-GERQ-R score of greater than 5(median) was, 131 (48.7%) vs 41(28.3%), and this was significant statistically $p<0.0001$.

The proportion of infants exclusively breastfed with an I-GERQ-R score greater than 5 (median) compare with infants complementary fed with an I-GERQ-R score greater than 5 (median) was 132(45.5%) vs 35 (31.8%), and this was statistically significant $p=0.013$.

Infant gender, Caregiver age, relationship to infant and level of education was not found to be significant.

4.6 Multivariate Analysis

In order to eliminate confounders, infant age group and complementary feeding were assessed and put in the logistic regression model shown in Table 9.

Table 9: Logistic regression of factors associated with gastroesophageal reflux symptoms.

Parameter		Odds Ratio [95% CI]	p-value
Infant age group	7-12 months	3.0 [1.5-6.1]	0.003
	1-6 months	ref	
Feed practice	Complementary feeding	1.4 [0.7-2.9]	0.410
	Exclusive breastfeeding	ref	

Infants aged 1-6 months had a 3 fold significant increase in odds of having gastroesophageal reflux symptoms compared to those aged 7-12 month. OR 3.0 (95%CI 1.5-6.1), p=0.003. This finding was statistically significant.

Exclusively breastfed infants had a 1.4 fold increase in odds of having gastroesophageal reflux symptoms compared to those complementary fed. This finding was not statistically significant.

4.7 Management of gastroesophageal reflux symptoms

Additional information on whether treatment was received for gastroesophageal reflux symptoms was collected in the study. Only 25 (6.03%) infants were reported to have received treatment for gastroesophageal symptoms such as spitting up, hiccups, excessive crying or fussing, and arching back. Of these infants, 72% are reported to have received non pharmacological treatment, while 28% are reported to have received pharmacological treatment. This is summarized in Figure 3.

Most common pharmacological treatment reported to have been received for gastroesophageal reflux symptoms was colic drops such as Infacol and Bonisan.

Most common non-pharmacological treatment received was feed modification at 28%. Caregiver education was received by 24% and position modification by 20% of the infants. Almost all (90%) infants were reported to have improvement of symptoms.

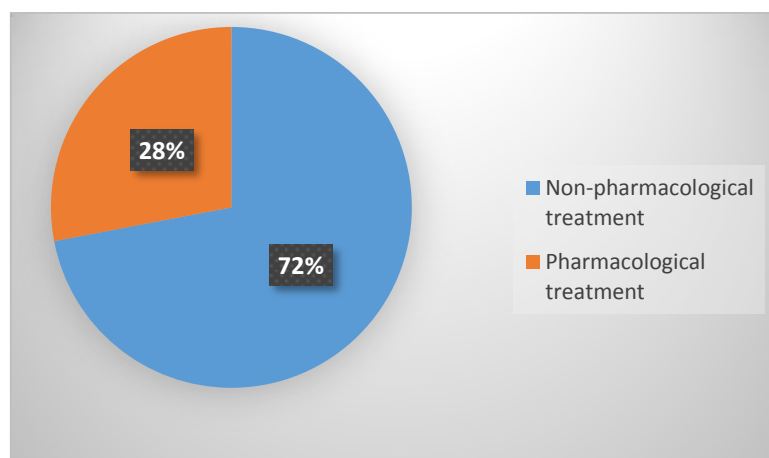


Figure 3: Summary of management of gastroesophageal reflux symptoms.
n=25 (6.03%)

CHAPTER FIVE: DISCUSSION

This study sought to establish the prevalence of gastroesophageal reflux symptoms and describe the factors related to this symptoms, among infants at the maternal child health clinic in Kenyatta National Hospital. We recruited 414 infants who were attended to at the maternal child health clinic between October-December 2017. Of these, 269 infants were 1-6 months in age while 145 were 7-12 months of age, with a female to male ratio of 1:1.

Regurgitation is one of the most noticeable clinical manifestations of gastroesophageal reflux in infants (43). The prevalence of regurgitation according to Rome III criteria was 72.9% (95% CI 72.707-73.093) among infants 1-12 months of age. In infants 1-6 months of age, it was 84% (95%CI 83.76-84.24) and 52.4% (95%CI 52.074-52.726) amongst infants 7-12 months of age.

The prevalence of regurgitation among infants aged 1-12 months of 72.9% found in this study is in keeping with the prevalence range of 3-87% found in the Vandenplas et al study. This was after review of published evidence and clinician opinion on prevalence and long term health consequences of functional gastrointestinal symptoms in infants. The wide range in the prevalence rate of regurgitation may be explained by the use of different study methodology in various studies either observational or prospective cohort type of research studies. Diagnostic criteria for infant regurgitation also differs in various studies because prior to the development of Rome criteria for functional disorders in children, there was no standardized diagnostic definition of infant regurgitation.(11,12,16)

The expert consensus on worldwide prevalence of infant regurgitation according to Rome III criteria was estimated to be approximately 30%. Rome III criteria was used in this study and the prevalence rate was higher at 72.9%. This may be attributed to study methodology differences and possible epidemiological differences in our population. Some studies have suggested that GER symptoms may be genetically determined and as such the prevalence and severity may vary depending on ethnic background. No prevalence rates on infant regurgitation have been reported from Africa from which we can compare this study findings to. The quantity of feed given per feeding session was also not assessed in this study, and thus unable to establish whether the higher prevalence rate of reflux regurgitation may be due to overfeeding.(12,44)

There was a concomitant decrease in gastroesophageal reflux symptoms frequency and prevalence and with increase in age, in this study. This finding compares closely to several other studies. In the USA, Nelson et al reported that 'at least one episode a day' of regurgitation was reported in 50% of infants aged 0-3 months. Peak regurgitation was reported at 4 months at 67%. The symptoms decreased to 21% at 6-7 months and reached 5% at 10-12 months. Van Howe et al in Michigan study concluded that the symptoms of gastroesophageal reflux as measured by the I-GERQ-R decreased with age in the first 6 months of life in otherwise healthy infants. Martin et al, reported prevalence of regurgitation in infants in Adelaide Australia, reaching peak at 3-4 months at 41%, decreasing to 35% in 6-7 month old infants, 15% in 8-9 month old infants and 10% in 10-11 month old infants. Miyazawa et al. studied the prevalence of GER related symptoms and complications among Japanese infants visiting healthy baby checkups. Infants with one or more regurgitation or vomiting episode per day was at 47.1% at 1 month, 28.8% at 4 months and 6.4% at 7 months. Those with 3 or more episodes per day showed a similar pattern.(13,14,17,45)

In Thai infants, Osatakul et al found that at 2 months of age the prevalence of regurgitation peaked at 86.9%, gradually decreased to 69.7% at 4 months, 66% at 6 months with a significant decrease to 7.6% at 12 months. In northern India, a study on the prevalence of gastroesophageal reflux in children done by De et al, using the I-GERQ questionnaire, demonstrated the prevalence of regurgitation was 55% at 1-6 month , 15% at 7-12 months.(11,18)

The decrease in prevalence and frequency of gastroesophageal reflux symptoms with increase in age is physiological and attributed to progressive development in the infant. Anatomically there is maturity of the lower esophageal sphincter as the infant grows older. Other factors include the increase in length of the lower esophageal pressure zone and intra-abdominal portion of esophagus. The progressive development of the crural fibres of diaphragm, also augments generation of an adequate lower esophageal pressure zone. All these enhance the anti-reflux barrier capability of the gastroesophageal junction. The infant is also able to sit up and later stand and walk from a primarily supine position. There is also introduction of solid foods, with weaning being initiated at 6 months. All these are related to reduced TLESRS, which is the primary process which allows gastroesophageal reflux, thus less reflux symptoms.(13,46-48)

Most infants in our study regurgitated 1-3 times a day, and had a regurgitation volume of less than 1 tablespoon, each episode. This was higher amongst infants 1-6 months of age (159, 59.1%), compared to those 7-12 months of age (43, 29.7%). Greater than 4 episodes of regurgitation in a day was found to be two fold higher amongst infants 1-6 months old (20.4%), compared to those 7-12 months of age (9.7%). This findings are similar to Nelson et al study which found 20% of American infants aged 1-6 months of age were reported to have 4 or more episodes of regurgitation. However, fewer Thai infants had 4 or more episodes of regurgitation, 14% at 1 month of age, with decline to 3% at 6 months of age as reported in the Osatakul study.(11,13)

The mean Infant Gastroesophageal Reflux Questionnaire Revised (I-GERQ-R) score, for all infants in this study was 5 (SD 3). The median score was also 5 with an interquartile range from 3 to 7. The mean IGERQ-R score in infants 1-6 months (5.9) was higher than that of infants 7-12 months (4.3). This is similar to the Michigan study which showed a decrease in IGERQ-R score with increase in age of infant. In most infants the 2 questions that determined the score was frequency and volume of regurgitation and frequency of hiccups.

Gastroesophageal reflux related complications include Sandifer syndrome, which is arching of the back, apneic and cyanotic episodes. In this study no infants were reported to have apnea or cyanosis, 15.5% of infants were however reported to have arching of the back. A larger proportion of these infants were in the 1-6 month old age group. Despite this, no infants had a positive score for gastroesophageal reflux disease. This is similar to the Osatakul study on Thai infants attending a well-baby clinic.(11)

In this study we looked into several factors that may be related to gastroesophageal reflux symptoms, using the IGERQ-R score as an evaluation tool. Infant age as a demographic variable was found to be significantly associated with gastroesophageal reflux symptoms. Infants aged 1-6 months had a 3 fold significant increase in odds of having gastroesophageal reflux symptoms compared to those aged 7-12 month. OR 3.0 (95%CI 1.5-6.1), p=0.003. This is clearly shown in the differences in prevalence of reflux regurgitation symptoms amongst infants of different age groups in various countries discussed previously.

Feeding practice among infants has also been assessed in several studies. Some studies such as Hegar et al study of Indonesian infants showed regurgitation was higher amongst formula fed infants compared to breastfed infants. (49)

Regurgitation was not associated to exclusively breastfeeding in the Martin et al, Osatakul et al and Miyazwa et al studies. Campanozzi et al also did not find a significant difference in regurgitation amongst formula fed infants and breastfed infants, however their study showed that cessation of regurgitation was earlier in breastfed infants. In this study, a larger proportion of formula fed infants (80%) had IGERQ-R score above the median compared to exclusively breastfed infants (45.5%). However this was not found to be statistically significant ($p=0.161$). We however note that the number of infants reported to be formula fed was quite small at 1.2% of the study population. Complementary feeding was associated with decreased gastroesophageal symptoms. However, after elimination of confounders in a logistic regression model table, this was not found to be statistically significant ($p=0.410$). There was no significant association found with regards to gastroesophageal reflux symptoms and gender of the infant, care giver age and level of education or number of children within the household.(11,16,17,45,50)

The paediatric clinical practice guidelines on gastroesophageal reflux, recommend caregiver education and guidance, feed modification and positioning therapy as initial therapeutic approach in the management of infant GER symptoms. This is because it is most likely physiologic gastroesophageal reflux. Pharmacological treatment is not recommended for infants and studies have shown that acid suppression therapy in infants is associated with many risks.(7,39,40)

In this study only 25 (6.03%) infants are reported to have received treatment for GER symptoms. Majority (72%) received non-pharmacological treatment compared to pharmacological treatment (28%). Almost all (90%) reported improvement of symptoms. Hegar et al study reported similar findings, in that reassurance and non-pharmacologic treatment was effective and had a 50% better outcome.(7,50)

5.1 Strengths of Study

This study highlights the presence of gastroesophageal reflux symptoms amongst healthy infants aged 1-12 months in our population and its associated morbidity. Another strength of this study is the large sample size used, which enabled us to give good estimates of the prevalence of these symptoms in this age group.

5.2 Study Limitation

The following study limitations were encountered:

1. Recall bias, some caregivers were not able to recall details of the infants feeding habits or reflux symptoms over the past week. The study also relied on self-reported data with no accompanying measures of data accuracy.
2. Selection bias, as data collected was confined to one maternal child health clinic at a referral hospital, and may not be generalizable to the population.
3. The study was a cross-sectional descriptive study, and as such unable to demonstrate temporal sequence between the factors studied and gastroesophageal reflux symptoms.

CHAPTER SIX: CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

- The prevalence of regurgitation in infants (1-12 months) according to Rome III criteria was 72.9 % (95% CI 72.707-73.093). In infants 1-6 months of age, it was 84% (95%CI 83.76-84.24) and 52.4% (95%CI 52.074-52.726) amongst infants above 7-12 months of age.
- Infant age was found to be significantly associated with gastroesophageal reflux related symptoms. Frequency and severity of these symptoms decreased with age as evaluated by IGERQ-R.
- There was no significant association was found between gastroesophageal reflux symptoms and gender of the infant, feeding practice, caregiver age and level of education or number of children within the household.
- No infant was found to have gastroesophageal reflux disease. (IGERQ-R Score >15).
- Management for gastroesophageal reflux symptoms was received by 6.03%. Of these 72% received non pharmacological treatment and 90% reported improvement of symptoms.

6.2 Recommendations

Therefore:

- We recommend education of caregivers on resolution of gastroesophageal reflux symptoms with increase in age and efficacy of non-pharmacological treatment as this condition is physiological.
- Encourage utilization of the Infant gastroesophageal reflux questionnaire revised (I-GERQ-R) to screen infants who present with gastroesophageal reflux symptoms, and assess severity of these symptoms.

REFERENCES

1. Sherman P, Hassall E, Fagundes-Neto U, Sherman P, Hassall E, Fagundes-Neto U, Gold BD, Kato S KS et al. A global evidencebased consensus on the definition of gastroesophageal reflux disease in children. *Am J Gastroenterol* 2009;104:1278–95.
2. Vandenplas Y, Hassall E. Mechanisms of gastroesophageal reflux and gastroesophageal reflux disease. *J Pediatr Gastroenterol Nutr*. 2002 Aug;35(2):119–36.
3. Jadcherla SR, Hogan WJ, Shaker R. Physiology and pathophysiology of glottic reflexes and pulmonary aspiration: from neonates to adults. *Semin Respir Crit Care Med*. 2010 Oct;31(5):554–60.
4. Orenstein SR, Shalaby TM, Cohn JF. Reflux symptoms in 100 normal infants: diagnostic validity of the infant gastroesophageal reflux questionnaire. *Clin Pediatr (Phila)*. 1996;35(12):607–14.
5. Jung AD. Gastroesophageal reflux in infants and children. *Am Fam Physician*. 2001 Dec;64(11):1853–60.
6. Hegar B, Vandenplas Y. Gastroesophageal reflux in children. *Paediatr Indones*. 2011;51(6):361–71.
7. Vandenplas Y, Rudolph CD, Di Lorenzo C, Hassall E, Liptak G, Mazur L, et al. Pediatric gastroesophageal reflux clinical practice guidelines: joint recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) and the European Society for Pediatric Gastroenterology, Hepatology, a. *J Pediatr Gastroenterol Nutr*. 2009;49(4):498–547.
8. Kleinman L, Rothman M, Strauss R, Orenstein SR, Nelson S, Vandenplas Y, et al. The Infant Gastroesophageal Reflux Questionnaire Revised: Development and Validation as an Evaluative Instrument. *Clin Gastroenterol Hepatol*. 2006;4(5):588–96.
9. Omari TI, Barnett C, Snel A, Goldsworthy W, Haslam R, Davidson G, et al. Mechanisms of gastroesophageal reflux in healthy premature infants. *J Pediatr*. 1998 Nov;133(5):650–4.
10. Papaila JG, Wilmot D, Grosfeld JL, Rescorla FJ, West KW, Vane DW. Increased incidence of delayed gastric emptying in children with gastroesophageal reflux. A prospective evaluation. *Arch Surg*. 1989 Aug;124(8):933–6.
11. Osatakul S, Sriplung H, Puetpaiboon A, Junjana C, Chamnongpakdi S. Prevalence and natural course of gastroesophageal reflux symptoms: a 1-year cohort study in Thai infants. *J Pediatr Gastroenterol Nutr*. 2002;34(1):63–7.
12. Vandenplas Y, Abkari A, Bellaiche M, Benninga M, Chouraqui JP, Çokura F, et al. Prevalence and Health Outcomes of Functional Gastrointestinal Symptoms in Infants From Birth to 12 Months of Age. *J Pediatr Gastroenterol Nutr*. 2015 Nov;61(5):531–7.
13. Nelson SP, Chen EH, Syniar GM, Christoffel KK. Prevalence of symptoms of gastroesophageal reflux during infancy. A pediatric practice-based survey. Pediatric Practice Research Group. *Arch Pediatr Adolesc Med*. 1997 Jun;151(6):569–72.
14. Van Howe RS, Storms MR, Mittal R, Holloway R, Penagini R, Sherman P, et al. Gastroesophageal reflux symptoms in infants in a rural population: longitudinal data

- over the first six months. *BMC Pediatr.* 2010;10(1):7.
15. Martin AJ, Pratt N, Kennedy JD, Ryan P, Ruffin RE, Miles H, et al. Natural history and familial relationships of infant spilling to 9 years of age. *Pediatrics.* 2002 Jun;109(6):1061–7.
 16. Campanozzi A, Boccia G, Pensabene L, Panetta F, Marseglia A, Strisciuglio P, et al. Prevalence and Natural History of Gastroesophageal Reflux: Pediatric Prospective Survey. *Pediatrics.* 2009 Mar;123(3):779–83.
 17. Miyazawa R, Tomomasa T, Kaneko H, Tachibana A, Ogawa T, Morikawa A. Prevalence of gastro-esophageal reflux-related symptoms in Japanese infants. *Pediatr Int.* 2002 Oct;44(5):513–6.
 18. De S, Rajeshwari K, Kalra KK, Gondal R, Malhotra V, Mittal SK. Gastroesophageal reflux in infants and children in north India. *Trop Gastroenterol.* 2006;22(2):99–102.
 19. Heacock HJ, Jeffery HE, Baker JL, Page M. Influence of breast versus formula milk on physiological gastroesophageal reflux in healthy, newborn infants. *J Pediatr Gastroenterol Nutr.* 1992 Jan;14(1):41–6.
 20. Hill DJ, Cameron DJ, Francis DE, Gonzalez-Andaya AM, Hosking CS. Challenge confirmation of late-onset reactions to extensively hydrolyzed formulas in infants with multiple food protein intolerance. *J Allergy Clin Immunol.* 1995 Sep;96(3):386–94.
 21. Iacono G, Carroccio A, Cavataio F, Montalto G, Kazmierska I, Lorello D, et al. Gastroesophageal reflux and cow's milk allergy in infants: a prospective study. *J Allergy Clin Immunol.* 1996 Mar;97(3):822–7.
 22. Orenstein SR, McGowan JD. Efficacy of Conservative Therapy as Taught in the Primary Care Setting for Symptoms Suggesting Infant Gastroesophageal Reflux. *J Pediatr.* 2008 Mar;152(3):310–314.
 23. Nielsen RG, Bindslev-Jensen C, Kruse-Andersen S, Husby S. Severe gastroesophageal reflux disease and cow milk hypersensitivity in infants and children: disease association and evaluation of a new challenge procedure. *J Pediatr Gastroenterol Nutr.* 2004 Oct;39(4):383–91.
 24. Farahmand F, Najafi M, Atae P, Modarresi V, Shahraki T, Rezaei N. Cow's Milk Allergy among Children with Gastroesophageal Reflux Disease. *Gut Liver.* 2011 Sep;5(3):298–301.
 25. Semeniuk J, Kaczmarek M. Gastroesophageal reflux in children and adolescents. clinical aspects with special respect to food hypersensitivity. *Adv Med Sci.* 2006;51:327–35.
 26. Vance GHS, Lewis SA, Grimshaw KEC, Wood PJ, Briggs RA, Thornton CA, et al. Exposure of the fetus and infant to hens' egg ovalbumin via the placenta and breast milk in relation to maternal intake of dietary egg. *Clin Exp Allergy.* 2005 Oct;35(10):1318–26.
 27. Khoshoo V, Ross G, Brown S, Edell D. Smaller volume, thickened formulas in the management of gastroesophageal reflux in thriving infants. *J Pediatr Gastroenterol Nutr.* 2000 Nov;31(5):554–6.

28. Vandenas Y, Sacre-Smits L. Seventeen-hour continuous esophageal pH monitoring in the newborn: evaluation of the influence of position in asymptomatic and symptomatic babies. *J Pediatr Gastroenterol Nutr.* 1985 Jun;4(3):356–61.
29. Tobin JM, McCloud P, Cameron DJ. Posture and gastro-oesophageal reflux: a case for left lateral positioning. *Arch Dis Child.* 1997 Mar;76(3):254–8.
30. Corvaglia L, Rotatori R, Ferlini M, Aceti A, Ancora G, Faldella G. The Effect of Body Positioning on Gastroesophageal Reflux in Premature Infants: Evaluation by Combined Impedance and pH Monitoring. *J Pediatr.* 2007 Dec;151(6):591–596.
31. Vandenas Y, Hauser B. Gastro-oesophageal reflux, sleep pattern, apparent life threatening event and sudden infant death. The point of view of a gastro-enterologist. *Eur J Pediatr.* 2000 Oct;159(10):726–9.
32. Oyen N, Markestad T, Skaerven R, Irgens LM, Helweg-Larsen K, Alm B, et al. Combined effects of sleeping position and prenatal risk factors in sudden infant death syndrome: the Nordic Epidemiological SIDS Study. *Pediatrics.* 1997 Oct ;100(4):613–21.
33. Skadberg BT, Morild I, Markestad T. Abandoning prone sleeping: Effect on the risk of sudden infant death syndrome. *J Pediatr.* 1998 Feb;132(2):340–3.
34. Adams EJ, Chavez GF, Steen D, Shah R, Iyasu S, Krous HF. Changes in the epidemiologic profile of sudden infant death syndrome as rates decline among California infants: 1990-1995. *Pediatrics.* 1998 Dec;102(6):1445–51.
35. Champion G, Richter JE, Vaezi MF, Singh S, Alexander R. Duodenogastroesophageal reflux: relationship to pH and importance in Barrett’s esophagus. *Gastroenterology.* 1994 Sep;107(3):747–54.
36. Barron JJ, Tan H, Spalding J, Bakst AW, Singer J. Proton pump inhibitor utilization patterns in infants. *J Pediatr Gastroenterol Nutr.* 2007;45(4):421–7.
37. Orenstein SR, Hassall E. Infants and proton pump inhibitors: tribulations, no trials. *J Pediatr Gastroenterol Nutr.* 2007 Oct;45(4):395–8.
38. Khoshoo V, Edell D, Thompson A, Rubin M. Are We Overprescribing Antireflux Medications for Infants With Regurgitation? *Pediatrics.* 2007 Nov;120(5):946–9.
39. Orenstein SR, Hassall E, Furmaga-Jablonska W, Atkinson S, Raanan M. Multicenter, Double-Blind, Randomized, Placebo-Controlled Trial Assessing the Efficacy and Safety of Proton Pump Inhibitor Lansoprazole in Infants with Symptoms of Gastroesophageal Reflux Disease. *J Pediatr.* 2009 Apr;154(4):514–520.
40. Moore DJ, Tao BS-K, Lines DR, Hirte C, Heddle ML, Davidson GP. Double-blind placebo-controlled trial of omeprazole in irritable infants with gastroesophageal reflux. *J Pediatr.* 2003 Aug;143(2):219–23.
41. Hassall E, Dimmick JE, Magee JF. Adenocarcinoma in childhood Barrett’s esophagus: case documentation and the need for surveillance in children. *Am J Gastroenterol.* 1993 Feb;88(2):282–8.
42. Sandler RS, Everhart JE, Donowitz M, Adams E, Cronin K, Goodman C, et al. The

- burden of selected digestive diseases in the United States. *Gastroenterology*. 2002 May;122(5):1500–11.
43. Hegar B, Alatas FS, Kadim M, Putri ND, Wardhani WI. Natural Evolution of Regurgitation in Children Aged 12-24 Months: A 1-year Cohort Study. *Indones J Gastroenterol Hepatol Dig Endosc*. 2013;14(1):13–8.
 44. Trudgill NJ, Kapur KC, Riley SA. Familial clustering of reflux symptoms. *Am J Gastroenterol*. 1999 May;94(5):1172–8.
 45. Martin AJ, Pratt N, Kennedy JD, Ryan P, Ruffin RE, Miles H, et al. Natural History and Familial Relationships of Infant Spilling to 9 Years of Age. *Pediatrics*. 2002;109(6).
 46. BOTHA GSM. The gastro-oesophageal region in infants; observations on the anatomy, with special reference to the closing mechanism and partial thoracic stomach. *Arch Dis Child*. 1958 Feb;33(167):78–94.
 47. Boix-Ochoa J, Canals J. Maturation of the lower esophagus. *J Pediatr Surg*. 1976 Oct;11(5):749–56.
 48. Orenstein SR. Gastroesophageal reflux. *Pediatr Rev*. 1999;20(1):24–8.
 49. Hegar B, Rantos R, Firmansyah A, De Schepper J, Vandenplas Y. Natural Evolution of Infantile Regurgitation Versus the Efficacy of Thickened Formula. *J Pediatr Gastroenterol Nutr*. 2008 Jul;47(1):26–30.
 50. Hegar B, Dewanti NR, Kadim M, Alatas S, Firmansyah A, Vandenplas Y. Natural evolution of regurgitation in healthy infants. *Acta Paediatr*. 2009 Jul;98(7):1189–93.

APPENDICES

Appendix 1: Questionnaire

THE PREVALENCE AND FACTORS ASSOCIATED WITH GASTROESOPHAGEAL
RELUX RELATED SYMPTOMS IN INFANTS AT THE MATERNAL CHILD HEALTH
CLINIC, KENYATTA NATIONAL HOSPITAL.

Questionnaire No: _____

Date: _____

Information on the infant

1. Date of birth: _____ Age: _____ months _____ days

2. Birth weight: _____ (Kg)

3. Infant's sex:

Male

Female

4. Gestation at birth: _____ weeks.

5. Current weight (Kg) _____ Length(cm) _____

(Indicate Weight and Length measurements taken at the clinic, on the day questionnaire is administered)

6. Birth order: _____ born.

Information on the Caregiver

(Record details of the care giver present at the clinic, on the day questionnaire is administered)

7. Relationship to Infant:

8. Age in years:

9. Gender: Male Female

10. Level of education:

None Primary Sch. Secondary Sch. University/
College. Others

11. Feeding practice

Exclusively breastfeeding Infant formula Cow milk Complementary
feeds Solid feeds

12. Age of onset of spitting up _____

Infant Gastroesophageal Reflux Questionnaire (I-GERQ-R)

1. During the past week, how often did the baby usually spit-up (anything coming out of the mouth) during a 24-hour period?
 - Less than once
 - 1 to 3 times
 - 4 to 6 times
 - More than 6 times

2. During the past week, how much did the baby usually spit-up (anything coming out of the mouth) during a typical episode?
 - Did not spit up
 - Less than 1 tablespoonful
 - 1 tablespoonful to 2 ounces (1/4 cup)
 - More than 2 ounces to half the feeding
 - More than half the feeding

3. During the past week, how often did spitting up (anything coming out of the mouth) seem to be uncomfortable for the baby, for example, crying, fussing, irritability, etc.?
 - Never
 - Rarely
 - Sometimes
 - Often
 - Always

4. During the past week, how often did the baby refuse a feeding even when hungry?
 - Never
 - Rarely
 - Sometimes
 - Often
 - Always

5. During the past week, how often did the baby stop eating soon after starting even when hungry?
- Never
 - Rarely
 - Sometimes
 - Often
 - Always
6. During the past week, did the baby cry a lot during or within 1 hour after feedings?
- Never
 - Rarely
 - Sometimes
 - Often
 - Always
4. During the past week, did the baby cry or fuss more than usual?
- Never
 - Rarely
 - Sometimes
 - Often
 - Always
5. During the past week, on average how long did the baby cry or fuss during a 24 hour period?
- Less than 10 minutes
 - 10 minutes to 1 hour
 - More than 1 hour but less than 3 hours
 - 3 or more hours
6. During the past week, how often did the baby have hiccups?
- Never
 - Rarely

Sometimes

Often

Always

7 During the past week, how often did the baby have episodes of arching back?

Never

Rarely

Sometimes

Often

Always

8 During the past week, has the baby stopped breathing while awake or struggled to breathe?

No

Yes

9 During the past week, has the baby turned blue or purple?

No

Yes

Treatment

1) Has treatment been sought for the symptoms discussed above-spitting up, hiccups, excessive crying or fussing, arching back or difficulty breathing?

Yes

No

If Yes

a .Which symptoms in particular made the care giver seek medical attention:

b. What treatment was provided?

i) Pharmacological-Medication

Name of medication _____

ii) Non Pharmacological

Caregiver education

Positional modification

Feed modification

c. Did the symptoms improve?

Yes No

Appendix 2: Consent form

Questionnaire No.:

Date

Study Title: **PREVALENCE AND FACTORS ASSOCIATED WITH GASTROESOPHAGEAL REFLUX SYMPTOMS AMONG INFANTS AT THE MATERNAL CHILD HEALTH CLINIC, KENYATTA NATIONAL HOSPITAL.**

Investigator: **Dr. Yvonne Waigumo (MB ChB)**
Paediatric Resident, University of Nairobi
Tel Number: - 0722-917143

Supervisors: **Prof. Dalton Wamalwa**
Senior Lecturer,
Department of Paediatrics and Child Health, University of Nairobi.

Dr. Ahmed Laving
Senior Lecturer, Paediatric Gastroenterologist,
Department of Paediatrics and Child Health, University of Nairobi.
Mobile Number: 0724644122

Investigator's Statement:

I am Dr. Yvonne Waigumo, a postgraduate student at the University of Nairobi. I am conducting a study as part of the requirement for the degree of Master of Medicine in Paediatrics. The purpose of the study is to evaluate the frequency and factors associated with gastroesophageal reflux symptoms among infants below the age of 1 year. The study is being conducted out at the Maternal Child Health Clinic in Kenyatta National Hospital.

We would like to request you to participate in the study, by providing us with some information about yourself and your child regarding your experience with gastroesophageal reflux symptoms. The purpose of this consent form is to provide you with the information you will need to help you decide whether to participate in the study. Kindly read the consent information provided and ask any questions on any issue concerning the study.

Introduction:

Gastroesophageal reflux refers to the passage of gastric contents into the oesophagus or oropharynx; with or without vomiting. It is a normal event especially in infants. Common symptoms observed by parents and care givers include regurgitation or spitting up. Gastroesophageal reflux disease occurs when the reflux of stomach contents causes 'troublesome' symptoms and/or complications. These symptoms include excessive crying, back arching, regurgitation, and irritation around feedings. This study aims to establish the frequency and factors affecting gastroesophageal reflux symptoms among infants in our population.

Procedure

If you agree to participate in the study, you will be requested to fill in a questionnaire with the assistance of a trained interviewer. It will take approximately 15-20 minutes. The questionnaire will have no personal identifiers to protect your confidentiality.

Voluntariness:

The study will be fully voluntary. There will be no financial rewards to you for participating in the study. One is free to participate or withdraw from the study at any point. Refusal to participate will not compromise your child's care in any way.

Confidentiality:

The information obtained about you and your child will be held in confidence. Your name will not appear in any report of publication of the research. Your data will be handled with high level of confidentiality, and will be stored in a secure facility, that only the principal investigator and supervisors will have access to.

Benefits:

There will be no direct benefit of participating in the study. However should you have questions regarding gastroesophageal reflux symptoms the interviewer will readily assist you.

The results of the study will also be used by the health care providers in this clinic to provide better care for infants with gastroesophageal reflux symptoms.

Risks:

There will be no risks or discomfort to you or your child, associated with participating in this study. Refusal to participate will in no way jeopardize the care of your child.

Problems or Questions:

If you ever have any questions about the study or about the use of the results you can contact the principal investigator, **Dr Yvonne Waigumo** by calling **0722-917143**.

If you have any questions on your rights as a research participant you can contact the **Kenyatta National Hospital Ethics and Research Committee (KNH- ESRC)** by calling **2726300 Ext. 44355**.

Consent Form:

PREVALENCE AND FACTORS ASSOCIATED WITH GASTROESOPHAGEAL
REFLUX SYMPTOMS AMONG INFANTS AT THE MATERNAL CHILD HEALTH
CLINIC, KENYATTA NATIONAL HOSPITAL.

Investigator: Dr. Yvonne Waigumo (MB ChB)
Paediatric Resident, University of Nairobi
Mobile Number: - 0722-917143

Lead Supervisor: Dr. Ahmed Laving
Senior Lecturer, Paediatric Gastroenterologist,
Department of Paediatrics and Child Health, University of Nairobi.
Mobile Number: 0724644122.

KNH- UON ERC secretariat, Telephone: 2726300 extension 44355

Kenyatta National hospital

Nairobi

I _____ agree to participate in the study .I
have received adequate information regarding the study research, risks and benefits. I
understand the nature of the study, that participation is fully voluntary and that I am free to
withdraw at any time. I have received answers to all questions and adequate clarification on
the study by the researcher.

Participant's Signature: _____ Date _____

Interviewer's Signature _____ Date _____

Appendix 3: Dodoso (Questionnaire translated to Kiswahili)

KIWANGO CHA KUENEA NA SABABU ZINAZOHUSIANA NA UGONJWA WA GASTROESOPHAGEAL REFLUX, MIONGONI MWA WATOTO WACHANGA KATIKA KLINIKI YA AFYA YA UZAZI NA MTOTO, HOSPITALI YA KITAIFA YA KENYATTA.

Dodoso nambari:

Tarehe:

A.Taarifa juu ya mtoto mchanga

1. Tarehe ya kuzaliwa : Umri:Miezi_____Siku_____

2. Uzito wa kuzaliwa:(Kilo)

3. Jinsia ya mtoto mchanga:

Kiume Kike

4. Mtoto alizaliwa akiwa na miezi mingapi kwa tumbo:

5. Uzito wa sasa:(Kilo) Urefu wa sasa(Sentimita)
(Andika vipimo vya uzito na urefu zilizochukuliwa kliniki, wakati wa kujaza dodoso hili)

6. Mtoto wa ngapi:

Taarifa juu ya mlezi

(Andika taarifa juu ya mlezi aliyekuja kliniki, siku ya kujaza dodoso hili)

7. Uhusiano na mtoto mchanga:

8. Umri wa mzazi au mlezi:

9. Jinsia MumeMke

10. Kiwango cha elimu cha mlezi:

Hakuna Shule ya msingi Shule ya sekondari. Chuo/Chuo kikuu

Nyingine_____

11. Mazoea ya kulisha:

Kunyonyesha pekee Fomula ya watoto wachanga Maziwa ya ngombe

Chakula kizito Kunyonyesha pamoja na vyakula vingine

12. Umri wa kuanza kutema juu_____

B. Infant Gastroesophageal Reflux Questionnaire (I-GERQ-R)

1. Wiki iliopita, mtoto alitema (chochote kutoka kinywa) mara ngapi wakati wa kipindi cha saa 24
 - Chini ya mara moja
 - Mara 1 hadi 3
 - Mara 4 hadi 6
 - Zaidi ya mara 6

2. Wiki iliyopita, mtoto alitema kiasi gani (chochote kutoka kinywa), kila kipindi?
 - Hakutema kitu chochote juu
 - Chini ya kijiko kikubwa 1
 - Kijiko kikubwa kimoja hadi robo kikombe
 - Zaidi ya robo kikombe hadi nusu ya alichokula
 - Zaidi ya nusu alichokula

3. Wiki iliyopita, ni mara ngapi kutema (chochote kutoka kinywa) kilimletea wasiwasi mtoto, kwa mfano kulia, kuzozana au kutokuwa na raha?
 - Kamwe (Hata mara moja)
 - Mara chache (kidogo)
 - Wakati mwingine
 - Mara nyingi
 - Kila mara

4. Wiki iliyopita, ni mara ngapi mtoto alikataa chakula hata akiwa na njaa?
 - Kamwe(Hata mara moja)
 - Mara chache (kidogo)
 - Wakati mwingine
 - Mara nyingi
 - Kila mara

5. Wiki iliyopita, ni mara ngapi mtoto aliacha kula mara baada ya kuanza hata wakati wa njaa?

- Kamwe (Hata mara moja)
- Mara chache (kidogo)
- Wakati mwingine
- Mara nyingi
- Kila mara

1. Wiki iliyopita, mtoto alilia sana wakati wa kula ama baada ya saa 1 ya kula?

- Kamwe (Hata mara moja)
- Mara chache(kidogo)
- Wakati mwingine
- Mara nyingi
- Kila mara

7. Wiki iliyopita, mtoto alilia au kuzozana kuliko kawaida?

- Kamwe (Hata mara moja)
- Mara chache(kidogo)
- Wakati mwingine
- Mara nyingi
- Kila mara

8. Wiki iliyopita, kwa wastani, mtoto alilia au kuzozana kwa muda gani, katika kipindi cha saa 24?

- Chini ya dakika 10
- Dakika 10 hadi saa 1
- Zaidi ya saa 1 lakini chini ya masaa 3
- Masaa 3 na zaidi

9. Wiki iliyopita, ni mara ngapi mtoto alikuwa na kwikwi?

- Kamwe(Hata mara moja)

Mara chache(kidogo)

Wakati mwingine

Mara nyingi

Kila mara

10. Wiki iliyopita,, ni mara ngapi mtoto alikuwa na matukio ya kupina nyuma/ mtoto amepindana?

Kamwe(Hata mara moja)

Mara chache(kidogo)

Wakati mwingine

Mara nyingi

Kila mara

11. Wiki iliopita, kuna wakati wowote mtoto ameacha kupumua akiwa macho au kupata shida ya kupumua?

La

Ndio

12. Wiki iliyopita, mtoto amegeuka rangi ya samawati au rangi ya zambarau?

La

Ndio

C.Matibabu

1. Mtoto amepata matibabu yoyote kwa dalili zozote ambazo zimejadiliwa hapo juu kama kutema juu, kufanya kwikwi, kulia au kuzozana zaidi ya kawaida, upinde au kushindwa kupuma?

Ndio

La

Kama Ndio,

a. Ni dalili gani haswa zilikufanya kama mlezi kutafuta matibabu_____

b. Ni matibabu gani (mtoto mchanga) alipewa:

i) Matibabu yanayohusu dawa

Jina ya dawa _____

ii) Matibabu yasiyohusu dawa:

Kuelimisha mlezi

Jinsi ya kumlaza mtoto

Jinsi ya kumlisha mtoto

c. Mtoto alipata nafuu baada ya matibabu:

Ndio

La

Appendix 4: Fomu ya Idhini (Consent form translated to Kiswahili)

Nambari ya Dodoso:

Tarehe:

Swala kuu la utafiti:

KIWANGO CHA KUENEA NA SABABU ZINAZOHUSIANA NA UGONJWA WA GASTROESOPHAGEAL REFLUX, MIONGONI MWA WATOTO WACHANGA KATIKA KLINIKA YA AFYA YA UZAZI NA MTOTO, HOSPITALI YA KITAIFA YA KENYATTA.

Mpelelezi: Dr. Yvonne Waigumo (MB ChB)
Paediatric Resident, University of Nairobi
Tel Number: - 0722-917143.

Wasimamizi wakuu:

Prof. Dalton Wamalwa
Senior Lecturer,
Department of Paediatrics and Child Health, University of Nairobi
Mobile number: 0774350699

Dr. Ahmed Laving
Senior Lecturer, Paediatric Gastroenterologist
Department of Paediatrics and Child Health, University of Nairobi
Mobile Number: 0724644122

Kumbusho la mpelelezi:

Mimi Daktari Yvonne Waigumo ni mwanafunzi wa uzamili katika Chuo Kikuu cha Nairobi. Nafanya utafiti kama sehemu ya masomo yangu ya uzamili ya Udaktari Bingwa wa Watoto. Madhumuni ya utafiti huu ni kuthamini kiwango cha kuenea na sababu zinazohisiana nakutema miongoni mwa watoto wachanga chini ya umri wa mwaka moja.

Tungependa kukuomba kushiriki katika utafiti kwa kutupatia baadhi ya taarifa kuhusu wewe mwenyewe na mtoto wako na pia kuhusu uzoefu wako na dalili za kutema. Madhumuni ya fomu hii ya idhini ni kukupa habari unayohitaji kukusaidia kuamua kama utashiriki katika utafiti huu. Tafadhali soma taarifa hii ya ridhaa na jisikie huru kuuliza maswali yoyte juu ya swala lolote kuhusiana na utafiti huu

Utangulizi

Kutema inahusu kupita kwa yaliomo tumbo katika koo; bila au pamoja na kutapika. Ni tukio la kawaida kwa watoto wachanga. Dalili inayoonekana kwa kawaida na wazazi au walezi ni cheu au kutema baada ya kula. Ugonjwa wa kutema, hutokea wakati kupita kwa yaliomo tumboni, kusababisha matatizo. Hizi ni baadhi ya shida zinazoleta athari mbaya kwa ustawi wa mgonjwa. Dalili hizi ni pamoja na wingi wa kilio, kupinda nyuma na kulia wakati wa

kula. Malengo ya utafiti huu ni kuonyesha kiwango cha kuenea na mambo yanayoathiri kutema miongoni mwa watoto wachanga katika idadi yetu.

Utaratibu

Ukikubali kushiriki katika utafiti huu, utaombwa kujaza dodoso (fomu) na msaidizi aliyefunzwa. Kujaza dodoso hilo litachukua kwa makisio baina ya dakika 15 na 20. Dodoso utalopewa kujaza halina vielelezo vyako binafsi ili kutunza siri za taarifa zako.

Kushiriki Kwa Hiari

Kushiriki kwa utafiti huu utakuwa kikamilifu kwa hiari yako. Hakutakuwa tuzo ya fedha kwa kushiriki katika utafiti. Uko huru kushiriki au kujitoa na utafiti katika hatua yoyote. Kukataa kushiriki haitatatiza huduma kwa mtoto ako kwa njia yoyote.

Usiri

Taarifa zitakazopatikana kuhusu wewe na mtoto wako binafsi zitakuwa siri . Jina lako halitaonekana katika taarifa yoyote au uchapishaji wa utafiti hu. Taarifa binafsi inayokuhusu itabebwa na kiwango cha juu cha siri, na itahifadhiwa katika kituo salama ambayu tu mkuu wa uchunguzi na wasimamizi wataweza kufikia.

Faida

Hakutakuwa na faida za moja kwa moja kwa kushiriki kwako katika utafiti huu. Hata hivyo ukiwa na maswali yoyote, mtafiti mhusika atakuwa tayari kukusaidia.

Matokeo ya utafiti yataweza kutumiwa na watoa huduma za afya katika hospitali hii kutoa huduma bora zaidi kwa watoto wachanga waliona ugonjwa wa kutema

Athari

Hakuna athari zozote zitakazotokana na kushiriki kwako katika utafiti huu. Kukataa kushiriki kwa utafiti huu, hakutahatarisha kupata huduma ya mtoto wako

Matatizo au Maswali

Ukiwa na maswali yoyote kuhusu utafiti huu au juu ya matumizi ya matokeo unaweza kuwasiliana na mpelelezi mkuu **Dr. Yvonne Waigumo** kwa kupitia nambari ya simu ya mkononi **0722-917143**.

Kama una maswali yoyote kama mshiriki wa utafiti unaweza kuwasiliana na **Kamati ya Utafiti Hospitali ya kitaifa ya Kenyatta** kwa kupiga simu **2726300 Ext. 44355**.

omu ya Ridhaa:

KIWANGO CHA KUENEA NA SABABU ZINAZOHUSIANA NA UGONJWA WA GASTROESOPHAGEAL REFLUX, MIONGONI MWA WATOTO WACHANGA KATIKA KLINIKA YA AFYA YA UZAZI NA MTOTO, HOSPITALI YA KITAIFA YA KENYATTA

Mpelelezi: Dr. Yvonne Waigumo (MB ChB)
Paediatric Resident, University of Nairobi
Mobile Number: - 0722-917143.

Msimamizi mkuu: Dr. Ahmed Laving
Senior Lecturer, Paediatric Gastroenterologist,
Department of Paediatrics and Child Health, University of Nairobi.
Mobile Number: 0724644122.

Mimi _____nakubali kushiriki katika utafiti huu. Nimepokea habari za kutosha juu ya utafiti huu, na kuhusu athari na faida ya utafiti huu. Naelewa hali ya utafiti na kwamba kushiki kwangu ni kwa hiri yangu kikamilifu. Naelewa pia ya kwamba mimi niko huru kujiondoa kutoka utafiti huu wakati wowote. Nimepokea majibu ya maswali yote na ufafanuzi wa kutosha juu ya utafiti huu kutoka mtafiti.

Sahihi ya Mshiriki: _____ Tarehe: _____

Sahihi ya Mtafiti: _____ Tarehe: _____

Appendix 5: KNH-UON/ ERC RESEARCH APPROVAL LETTER AND TURNITIN REPORT



UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P.O. BOX 19576 Code 01202
Telegrams: varsity
Tel: 254-020-2725300 Ext 14355

KNH-UON ERC
Email: unh@erc.uonbi.ac.ke
Website: <http://www.erc.uonbi.ac.ke>
Facebook: <https://www.facebook.com/uonbi.erc>
Twitter: @UONNH-ERC <https://twitter.com/UONNH-ERC>



KENYATTA NATIONAL HOSPITAL
P.O. BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: KN 10304, Nairobi

Ref: KNH-ERC/A/257

4th September 2017

Dr. Yvonne Waiguna
Reg. No. H56/00957/15
Dept. of Paediatrics and Child Health
School of Medicine
College of Health Sciences
University of Nairobi



Dear Dr. Waiguna

RESEARCH PROPOSAL – THE PREVALENCE AND FACTORS ASSOCIATED WITH GASTROESOPHAGEAL RELUX SYMPTOMS IN INFANTS AT THE MATERNAL CHILD HEALTH CLINIC, KENYATTA NATIONAL HOSPITAL, (P357/072017)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and approved your above proposal. The approval period is from: 4th September, 2017 – 3rd September 2018.

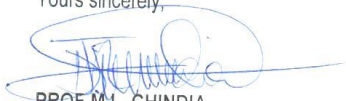
This approval is subject to compliance with the following requirements:

- Only approved documents (informed consent, study instruments, advertising materials etc) will be used.
- All changes (amendments, deviations, variations etc) are submitted for review and approval by KNH-UoN ERC before implementation.
- Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
- Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
- Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period (Attach a comprehensive progress report to support the renewal)
- Submission of an executive summary report within 30 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism

For more details consult the KNH- UoN ERC website: <http://www.erc.uonbi.ac.ke>

Protect to discover

Yours sincerely,



PROF M.L. CHINDIA
SECRETARY, KNH-UoN ERC

- c.c. The Principal, College of Health Sciences, UoN
 The Director, CS, KNH
 The Chair, KNH- UoN ERC
 The Assistant Director, Health Information, KNH
 The Dean, School of Medicine, UoN
 The Chair, Dept. of Paediatrics and Child Health, UoN
 Supervisors: Prof. Dalton Wamalwa, Dr. Ahmed Laving

Protect to discover

THE PREVALENCE AND FACTORS ASSOCIATED WITH GASTROESOPHAGEAL REFLUX RELATED SYMPTOMS IN INFANTS AT THE MATERNAL CHILD HEALTH CLINIC, KENYATTA NATIONAL HOSPITAL

DR. YVONNE WAIGUMO

ORIGINALITY REPORT

HSB/80.057/2015

14%

SIMILARITY INDEX

9%

INTERNET SOURCES

12%

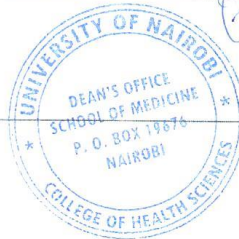
PUBLICATIONS

3%

STUDENT PAPERS

PRIMARY SOURCES

1	archpedi.jamanetwork.com Internet Source	1%
2	www.naspghan.org Internet Source	1%
3	www.nice.org.uk Internet Source	1%
4	bmcpediatr.biomedcentral.com Internet Source	1%
5	Badriul Hegar, Debora Hindra I. Satari, Damayanti R. Sjarif, Yvan Vandenplas. "Regurgitation and Gastroesophageal Reflux Disease in Six to Nine Months Old Indonesian Infants", Pediatric Gastroenterology, Hepatology & Nutrition, 2013 Publication	1%
6	www.science.gov Internet Source	1%



Wamahu