ASSOCIATION BETWEEN HELICOBACTER PYLORI INFECTION AND NUTRITIONAL STATUS OF CHILDREN AGED 1 TO 5 YEARS AT KENYATTA NATIONAL HOSPITAL.

A DISSERTATION SUBMITTED IN PARTIAL FULFILMENT FOR THE AWARD OF THE MASTERS OF MEDICINE IN PAEDIATRICS AND CHILD HEALTH UNIVERSITY OF NAIROBI.

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DECLARATION

This dissertation is my original work and has not been presented before for the award of a degree in any university

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DEDICATION

This study is dedicated to all health workers who treat children across the country. May they think out of the box when the children are not growing well and explore all possible causes of childhood under nutrition.
ACKNOWLEDGEMENT

I give glory God for giving me the wisdom to write this dissertation

Special thank you to my study group members Dr Agweyu A, Dr Opondo G, Dr Munge R, Dr Okara P and Dr Baya E for their support.

My greatest appreciation to Dr Ambrose Agweyu for the assistance with result interpretation and guidance in the presentation of the results and to Dr Opondo Gabbriel for standing with me in all times during the final write up.

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Last and not least special thanks to my husband, Dr Shibona, my daughter Neema and my son Abba for their support, patience and understanding during the Study period.
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LIST OF ABBREVIATION

H.pylori  Helicobacter pylori
WHO       World Health Organization
MUAC      Mid upper arm circumference
HAZ       Height for age Z score
WAZ       Weight for age Z score
WHZ       Weight for height Z score
KDHS      Kenya democratic health survey
UNICEF    United Nations Children’s Fund
ABSTRACT

**Introduction and background information:** H. Pylori is the most common chronic bacterial infection in humans worldwide with 50% of the world’s population thought to be infected. The infection is mostly acquired before 10 years of age and persists for decades with a very low rate of spontaneous recovery. The main route of transmission is person to person through either faeco-oral or oral-oral route. The infection causes hypochlohydria. The impaired gastric acid production interferes with digestion and absorption of nutrients. Increased metabolic requirement associated with the infection affects the nutritional status in children. H. pylori infection has been thought to be associated with slower growth in children. The prevalences of H. pylori and undernutrition in Kenyan children are high. The current treatment guidelines indicate that H. pylori infection should only be treated in patients who are symptomatic. There are many asymptomatic children living with H. pylori infection for a long time. There is, therefore, a need to find out the effect of this chronic infection with H. pylori on height and weight of children.

**Objective:** The main aim of this study was to determine the association between H. pylori infection and the nutritional status among the 1-5-year-old children attending outpatient clinic at Kenyatta National Hospital.

**Study population:** The study population included 1-5-year-old children attending the paediatric emergency clinic at Kenyatta National Hospital.

**Methodology:** This was a hospital based cross sectional study. The study was carried out after obtaining informed consent from the parent/care taker who then provided information on the age of the child, socioeconomic status and any recent history of antibiotic use. A fresh stool sample was taken from each child and stool H.pylori antigen test done. Weight, height and MUAC of all children involved in the study were measured using standard methods.

**Data analysis:** The outcome measures of interest were weight, height and MUAC and the exposure of interest was H.pylori infection. These measures were compared between infected and uninfected children using the statistical programme for social sciences (SPSS) version 18 software. Age was stratified to allow for comparison because all the outcomes were age dependent.
Chi square statistics was conducted for the categorical variable and univariate analysis of variance was used to evaluate further associations between H. pylori infection and the anthropometric measurements

**Results:** 153 children were enrolled in the study 64 tested positive for H pylori and 89 were the negative controls. There were no statistically significant differences in the height, weight and MUAC between infected and uninfected children with the mean, heights 86.87v/s 89.87 cm p=0.097, weight 11.37v/s 12.04kg p= 0.149 and MUAC 15.12 v/s 15.44 p= 0.195 respectively. 34.4% of the infected children were stunted compared to 22.5% of the uninfected children p= 0.104. Among the infected children, 11.2% were underweight versus 10.7% of the uninfected p=0.582. Wasting was at 2.4% among the positive compared to 0.7% among the negative children p= 0.346. There was no association between socioeconomic factors and H.pylori infection.

**Conclusion:** There was a difference in anthropometric measurements between H.pylori infected children and non-infected but this was not statistically significant.
1.0 CHAPTER ONE

1.1 INTRODUCTION AND BACKGROUND INFORMATION

Helicobacter pylori is a spiral shaped microaerophilic gram negative bacteria measuring approximately 3.5 microns in length and 0.5 microns in width. It has 2-7 unipolar sheathed flagella which enhances its motility through viscous solution. It produces urease which together with the flagellae enable the organism colonize the gastric mucosa. There are two important genes of H pylori that is VACA and CAGA. The VACA gene codes the Vac-A cytotoxin, a vacuolating toxin and the CAGA gene codes for Cag A protein which seems to stimulate the production of chemotactic factors for the neutrophils by the gastric epithelium of the host.

H pylori was first cultured by Marshall and Warren in 1982 and named Campylobacter pyloridis which was later renamed H. pylori. Since then many studies have been done to understand the pathogenesis potential of H. pylori infection. Peptic ulcer disease is the most studied disease caused by H pylori. The bacterium is also seemingly involved in the pathogenesis of several extra gastric diseases such as coronaritis, gastro-oesophageal reflux disease, iron deficiency anaemia, mucosa-associated lymphoid tissue lymphoma, rheumatologic conditions and even growth retardation in children.

Transmission is thought to be from person to person through either faeco-oral or oral-oral routes. Intrafamilial spread has been observed in developing countries\(^1\). Humans are the major reservoir but infection has also been found in primates. If the environment is less than ideal the, bacteria form colloids that help them to survive in faeces and drinking water outside the human body.

1.1.1 Pathogenesis.

H. pylorus has been associated with the development of extragastric disorders including iron deficiency anaemia, chronic idiopathic thrombocytopenic purpura, growth retardation, and diabetes mellitus\(^2\). The postulated role of H. pylori in the pathogenesis of extragastric disorders is based on the fact that local inflammation has systemic effects. H. pylori is a chronic infection that lasts for several decades. The persistent infection induces a chronic inflammatory and immune response that is able to induce lesions both locally and in organs remote from the primary site of infection\(^3\).

Biochemically, H. pylori are classified according to their ability to produce catalase, oxidase or urease. The urease hydrolyses the gastric luminal urea to ammonia and bicarbonate that in
turn neutralize gastric acid and form a protective cloud around the bacteria. Other physical properties like flagellae, spiral shape, and mucolytic enzymes allow H. pylori to survive in the stomach environment. H. pylori infection is associated with inflammation mainly in the non acid secreting antrum. This inflammation causes increased gastrin release which in turn induces excess acid secretion from the fundus mucosa and associated damage in form of ulceration of the duodenum and stomach in up to 80% of patients.

H. pylori infection may produce partial loss of the gastric acid barrier and this may result in chronic diarrhoea and malnutrition due to impaired nutrient absorption, direct nutrient losses or increased metabolic requirements\(^4\). The infection has also been associated with iron deficiency and growth retardation in children\(^5\).

There is no disease staging of H. pylori infection but its progression through some stages has been observed. The first stage is the chronic gastritis. The second stage is atrophic gastritis with ulceration. The third stage is the interstitial metaplasia and dysplasia. The last stage is the development of gastric adenocarcinoma. The progression is a very slow process and can stop at any stage because the development of gastric cancer requires several other predisposing factors beside H Pylori infection. The organism can be cultured from the vomitus or diarrheal stool. The diagnosis of the infection is based on stool antigen test, carbon 13 urea breath test or serological test.

H. pylori faecal antigen test is based on monoclonal antibody immunochromatography of the stool samples. This test has 98% specificity and 94% sensitivity. The result is positive in the initial stages of infection and is used to confirm eradication after treatment. The carbon 13 urea breath test is based on the detection of the products created when urea is split by the organism. In this test, patients are given urea that is labelled with carbon isotope orally. The concentration of the labelled carbon is then measured in the breath. The concentration is only high when urease is present in the stomach and because humans don’t produce urease, such a reaction is possible only with H pylori infection. The serological tests involve detection of immunoglobulin G antibodies against H. pylori by means of enzyme linked immunosorbent assay. It is more than 90% both sensitive and specific. It is a good test for detecting a newly infected patient but it is not good for follow up of the treated patients because antibody titre may remain elevated for a long time after H Pylori eradication. The number of false positive result is age related and increases with age.
2.0 CHAPTER TWO

2.1 LITERATURE REVIEW

2.1.1 Prevalence of H. pylori in children

Helicobacter pylori is regarded as the most widespread chronic infection in man. It has a worldwide distribution and it is estimated that half of the human population is infected\(^6\). \textit{Helicobacter pylori}(H. pylori) infection has been recognized as one of the most common chronic bacterial infections in humans with prevalence of 20\% in European studies, 60\% in South American studies and 50\% among Asian populations\(^7\). This highly prevalent, serious and chronic infection that has been associated causally with a diverse spectrum of extragastric disorders including iron deficiency anaemia, chronic idiopathic thrombocytopenic purpura, growth retardation, and diabetes mellitus\(^2\). The infection is most frequently acquired during childhood in both developed and developing countries and the children are more likely to develop clinical sequelae\(^8\).

H. pylori affect approximately 50\% of the population in developed and developing countries. In general, in developing countries more than 50\% of children are infected by age of 10 years and the prevalence rises to more than 80\% in young adults unlike in developed countries where children become infected at a rate of less than 1\% per year\(^9, 10\). H.pylori is the most common bacterial infection in Africa\(^10\). Most infections acquired during childhood persists for decades unless the child is treated with appropriate antibiotics\(^7\) and intrafamilial spread is now beyond controversy\(^11\).

H. pylori prevalence varies from one region to another. In Kampala, Uganda, a total prevalence of 44.3\% was found with early colonization of children below one year and an increase in prevalence with age in a population based cross sectional study done among children\(^12\). A study in Egypt in 2008 among school children found a prevalence of 72.4 \%\(^13\). Locally the prevalence is high as demonstrated in cross sectional study by in Trans-Nzoyia that found a prevalence of H pylori infection in Kenyan school children 3-15years to be up to 80\% with most of the affected being below the age of 3 years\(^14\). In another study in Nairobi (Dagoreti), Langat found a prevalence of 45.6\% in children below 3 years of age\(^15\).

The prevalence of H.pylori increases with age. Across section population based study in Czech Republic found a positive association with increasing age\(^16\) a finding that was
demonstrated in the world gastroenterology organization global initiative 2010 that indicated an increase in prevalence with age in different countries as shown in the table below\textsuperscript{17}.

**Table 1 : prevalence of H.pylori according to age in different countries**

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>AGE GROUP IN YEARS</th>
<th>PREVALENCE %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethiopia</td>
<td>2-4</td>
<td>48</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>Adults</td>
<td>More than 95</td>
</tr>
<tr>
<td>Nigeria</td>
<td>5-9</td>
<td>82</td>
</tr>
<tr>
<td></td>
<td>Adults</td>
<td>70-90</td>
</tr>
<tr>
<td>Gambia</td>
<td>5</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td>Adults</td>
<td>More than 95</td>
</tr>
</tbody>
</table>

In an article “H. pylori – an African perspective”, it is indicated that in sub Saharan Africa, the majority of subjects are infected with H pylori, 61-100\% having antibodies to H.pylori. In Ivory Coast, 55\% of children aged less than 10 years have been reported to be infected with H Pylori. These findings apply to Nigeria and Gambia but this is in children under 5 years. A study in Soweto South Africa found that 46\% of children at 1 year and 100\% of children at 12 years were infected with H Pylori\textsuperscript{9}. Thus prevalence of H pylori varies widely by geographical area, age, race, ethnicity, and socioeconomic status.

**2.1.2 Factors associated with H. pylori infection.**

Infection rates are high in the developing countries and seem to be decreasing with improvement in hygiene practices. Overall inadequate sanitation practices, low social class and crowded or high density living conditions seem to be related to a higher prevalence of H pylori infection\textsuperscript{17}. A descriptive study in Spain in 2005 conducted among 264 children showed that there was a high prevalence of H pylori infection in children from families with a low socioeconomic (p<0.001) status, higher rates of overcrowding (p<0.005) and in immigrants (p<0.001)\textsuperscript{18}. In Russia, Tkachenko demonstrated a dramatic decline in H pylori infection in children over 10 years of improved socioeconomic status. In this study the infection rate was at 44\% in 1995 and reduced to 13\% after 10 years\textsuperscript{19}. Josef Syokora in Czech Republic demonstrated that the independent risk factors for acquiring H. pylori
infection include number of children per household, low level of education of parents and institutionalization of children\textsuperscript{16}.

Studies in Africa have demonstrated similar associations. In Egypt, the major risk factors for H pylori infection were attending school in a socially deprived area and residing in an overcrowded home\textsuperscript{13}. In urban Uganda, congestive living, low level of education of the female care taker, poor hygienic status and low wealth index were the major risk factors for infection with H. Pylori\textsuperscript{12}. Locally, Langat in Dagoreti, Nairobi and Nabwera in Transnzoia found that low socioeconomic status, crowding in the homes and poor sanitation were associated with H Pylori infection\textsuperscript{14, 15}.

\subsection*{2.1.3 The effect of H. pylori infection on nutritional status in children.}
H. pylori infection and its effect on growth in children remain controversial. Acute and chronic infections may impair linear growth by interfering with micronutrient absorption, appetite, metabolism, and related factors. However, human growth is also dictated by factors such as diet, socioeconomic status, other infections, and genetics\textsuperscript{20}. In Colombia, a study on effects of H Pylori infection on growth velocity of school age children who were followed-up for an average length of 3.7 years demonstrated that persistence of H. pylori infection leads to reduced growth velocity. After nearly 4 years of observation, a multivariate height-based growth model analysis showed that the children with H. pylori infection grew at 0.022cm/month slower than the uninfected children. Children who were always \textit{H. pylori}-positive were 1.76 cm shorter by the end of the observation period than those who were always negative, and 1.45 cm shorter than those who cleared the infection, after adjustment for initial values and all other covariates\textsuperscript{21}. In a publication on “H. pylori infection and growth impairment in developing countries: a vicious cycle”, it is hypothesized that infection with H. pylori in children in developing countries is the initiator of a vicious cycle of events that result ultimately in malnutrition and growth impairment. Acute infection with H. pylori is accompanied by hypochlohydria which facilitates the acquisition of other enteropathogens because of removal of the acid barrier which allows occurrence of multiple co-infections. The synergistic impact of the diarrheal diseases and micronutrient deficiency on growth and cognitive functions in children has a significant public health implication\textsuperscript{22}. In Scotland, growth in height between 7-11 years diminished in infected children by a mean of 1.1 cm over four years. In the developing world, the height to age ratio is significantly lower in children infected with H. pylori than the uninfected and recent reports show that over half of the children being investigated for short stature were infected with H. pylori\textsuperscript{23}. 


A cross sectional study by Richter demonstrated that height of the children infected with H.pylori was 117.6+/- 5.5cm vs. 118.9+/- 5.7cm among children without H.pylori infection (p<0.001). The infected boys were 2.06cm smaller than uninfected boys but there was no significant differences were found in girls. He concluded that H.pylori infection is associated with growth delay, growth retardation or both in infected children\textsuperscript{24}. In a cohort of 347 children in Colombia, Mera looked at the effect of H pylori infection on height and weight in preschool children and demonstrated a decrease in growth velocity during the first 4 months of infection with H. pylori, and lack of height catch-up in infected children with an accumulative difference of 0.24cm over 8 months less in infected compared to uninfected children. Newly infected children experienced a smaller decrease in weight which became less significant after the second visit\textsuperscript{25}. In a prospective longitudinal survey, the potential effects of new \textit{H. pylori} infection on linear and ponderal growth in low socioeconomic status young children living in poor suburbs of Quito, Ecuador, were assessed. Six height and weight measurements were collected during one year. The main finding of this study was that new \textit{H. pylori} infections were associated with reduced linear growth in young children. The estimated deficit in the average growth velocity during one year of follow-up in children with new infections was 1 cm/year. There was no evidence of catch-up growth in children with \textit{H. pylori} infection\textsuperscript{26}.

Sub-Saharan Africa has the highest burden of disease but very few studies have been done to determine the association of the high H. pylori prevalence and under-nutrition in children. In the Egyptian study\textsuperscript{13}, Mohammad demonstrated differences in height and weight in the infected and uninfected children. The mean weight of the infected children was 39.5+/-1.0 kg while the mean weight of the uninfected children was 44.6 +/- 1.8kg p<0.05. The mean height of infected children was 139.9+/-1.3cm compared to the mean height of 144.2+/-2.1 cm among the uninfected children, p<0.009. The number of children falling below the 5\textsuperscript{th} percentile of height for age was significantly higher in the infected than in the uninfected children. Chi-square tests indicated that the prevalence of stunted growth was significantly higher in the infected children than in children free of H. pylori: 23.67% of infected children (odds ratio54.59, 95% confidence interval 1.66–13.68) had the height for age percentile below the 5th percentile compared with only 6.33% among the children without infection, p<0.001. Mohammad concluded that the adverse effects of H.pylori infection extend beyond the stomach\textsuperscript{13}. 

\textsuperscript{6}
In two consecutive prospective longitudinal-cohort studies in Gambia\textsuperscript{27}, Thomas assessed the effects of early H. pylori colonization on growth. They demonstrated that children with early colonization became significantly lighter, shorter and thinner than their peers in late infancy. No socioeconomic or demographic confounders were identified to explain that finding and the weight deficit was no longer detectable when the children were five to eight years old\textsuperscript{27}.

The effect of H. pylori infection on growth parameters is still not fully understood. Some studies have demonstrated minimal differences in the anthropometric parameters of the infected compared to uninfected peers. This was demonstrated by a study done in Guatemala USA that concluded that H. pylori infection appeared to have no effect on nutritional status of the studied children and that the differences detected were small and likely due to Sociodemographic factors\textsuperscript{28}.

\textbf{2.1.4 H. pylori testing.}

Both invasive methods like endoscopy with biopsy and non invasive methods like serology, stool antigen and urea breath tests are available for diagnosis of H. pylori infection in children. Ideally a diagnostic test for H. pylori in children should be non invasive, highly sensitive and specific, inexpensive and easy to perform. Because H. pylori and/or its macromolecules such as proteins and DNA are shed in the faeces, stool based tests have become acceptable techniques for diagnosis of non invasive infection\textsuperscript{29}. Stool culture for isolation of H. pylori has limitations because the organism is usually already dead or present in a nonviable colloid form\textsuperscript{30}. This leaves stool H. pylori DNA and antigen detection tests as more suitable diagnostic tools\textsuperscript{31}.

Several enzyme linked immunosorbent assays (ELISA) tests are available. Some use a polyclonal anti H. pylori capture antibody while others use monoclonal antibodies\textsuperscript{32, 33}. A Meta-analysis of H. pylori stool antigen test involving 43 studies reported an overall sensitivity of 92.4\% with a specificity of 91.9\% using the urea breath test criterion\textsuperscript{34}. Another Meta-analysis using 22 studies reported a sensitivity of 94\% and a specificity of 97\%\textsuperscript{35}.

In systematic reviews of studies on the accuracy of the noninvasive test for diagnosis of H. pylori infection, the following conclusion was made\textsuperscript{36}. 

7
### Table 2: H.pylori diagnostic tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity for active infection</th>
<th>Specificity for active infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stool antigen</td>
<td>96.1%</td>
<td>95.7%</td>
</tr>
<tr>
<td>Urea breath test</td>
<td>95.2%</td>
<td>89.7%</td>
</tr>
<tr>
<td>Serum antibody serology</td>
<td>85.6%</td>
<td>79%</td>
</tr>
</tbody>
</table>

### Table 3: Summary of the relevant literature review

<table>
<thead>
<tr>
<th>Author</th>
<th>Title</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Richter T, Richter T, List S, et al.2001</td>
<td>Five- to 7-year-old children with <em>Helicobacter pylori</em> infection are smaller than <em>Helicobacter</em>-negative children.</td>
<td>H.pylori infection is associated with growth delay, growth retardation or both in infected children.</td>
</tr>
<tr>
<td>Mahmoud.A.Mohammad, Laila Hussein, Andy Coward and Sarah J Jackson (2008).</td>
<td>Prevalence of <em>Helicobacter pylori</em> infection among Egyptian children: impact of social background and effect on growth</td>
<td>The number of the children falling below the 5th percentile of height for age was significantly higher in children infected with H.pylori.</td>
</tr>
</tbody>
</table>
2.2 STATEMENT OF THE RESEARCH PROBLEM
Helicobacter pylori is the most common chronic infection in mankind worldwide. In developing countries, the prevalence of H. pylori infection is very high and it is now known that infection is acquired early in life and lasts for decades. A lot known about the pathogenesis and treatment of the gastric infection by the H. pylori but there is very little known about the extragastric effects of this chronic infection especially in children. The gastric manifestations of the infection are known and guidelines have been developed to guide on when to test and treat. Studies done in the developed countries, where H. pylori prevalence is lower, have indicated that there is an association between H pylori infection with slower growth in children. Studies done in Kenya have shown that there is a high prevalence of H. pylori infection in children of up to 45.6% by three years of age and of up to 80% by fifteen years. However, there are no studies done to look at the association between H. pylori infection and the nutritional status in children in such high prevalence zones.

2.3 JUSTIFICATION
According to the Kenya Demographic Health Survey 2014, 26% of children under the age of 5 years are stunted, 11% are underweight and 4% are wasted. This calls for aggressive measures to eradicate all the possible causes of this poor health in children. One of the main contributors is chronic infections. H. pylori is one of the most common human bacterial infections in the world and children in developing countries acquire it early in life and the prevalence of H. pylori infection is very high. Studies done in Kenya have mainly dwelt on the prevalence of H pylori infection in both adults and children and have revealed a high prevalence without any studies on the effects of this high prevalence in the individuals.

This study thus aimed at determining the association of H. pylori infection on the level of nutrition in children since it is biologically plausible that this infection affects digestion, nutrient absorption and nutrient loss because of the altered acid environment. The studies that have been done on the effect of the infection on growth did not compare groups of children with and without H. pylori infection. In this study, anthropometric parameters of children with infection were compared with those of the children with infection.
2.4 STUDY OBJECTIVE.

2.4.1 PRIMARY OBJECTIVE
To determine the association between H. Pylori infection and the nutritional status of children aged 1-5-years-old at Kenyatta National Hospital.

2.4.2 SECONDARY OBJECTIVES
To compare the difference in the weight, height, weight for age Z scores, height for age Z scores, weight for height Z scores and MUAC of children whose H. pylori antigen test was positive compared with those whose test is negative

To assess the association of socioeconomic factors on H.pylori outcome.
3.0 CHAPTER THREE

3.1 METHODOLOGY

3.1.1 STUDY DESIGN
This was a hospital based cross sectional study.

3.1.2 STUDY POPULATION
The study population included 1-5-year-old children who attended the paediatric emergency clinic, children whose parents/care takers gave consent for their children to participate in the study and children who gave a fresh stool sample. The children whose H. pylori test was positive formed the cases while those with a negative test result formed the controls.

3.1.3 STUDY AREA
This study was carried out at the outpatient paediatric department at Kenyatta National Hospital. At the paediatric outpatient unit, all children up to 12 years of age are seen except those with surgical conditions and those with burns.

3.2 ELIGIBILITY CRITERIA

3.2.1 INCLUSION CRITERIA
Eligible for inclusion in the study were 1-5-year-old children seen at the paediatric emergency clinic, children whose parents gave consent for their children to participate in the study and children who gave a fresh stool sample.

3.2.2 EXCLUSION CRITERIA
Excluded from the study were very sick children who required admission the study as they were unstable for taking the physical growth parameters, children who had used antibiotics in the last two weeks prior to the interview day because antibiotic use was likely to interfere with H. pylori test result and children with chronic medical conditions like diabetes, congenital heart disease, chronic lung conditions, cancers, and sickle cell disease because these conditions interfere with growth in children.
3.3 SAMPLE SIZE

Sample size calculation was based on the formula for comparisons of two proportions\(^{38}\)

\[
n = \frac{\left(\frac{Z_{\alpha} + Z_{\beta}}{2}\right)^2 \left[\pi_1 (1 - \pi_1) + \pi_2 (1 - \pi_2)\right]}{\pi_1 - \pi_2^2}
\]

Where

- \(n\) = the sample size required in each group
- \(\pi_1\) = First proportion (stunting in H pylori infected children at 0.24) Mohammad et al. 2008
- \(\pi_2\) = Second proportion (stunting in non-infected children at 0.06) Mohammad et al. 2008
- \(\pi_1 - \pi_2\) = size of difference of clinical importance (0.18)
- \(Z_{\alpha}\) = Desired significant level (1.96)
- \(Z_{\beta}\) = Desired power at 80% (0.84)

Substituting the values in the formula above,

\[
n = \frac{[1.64 + 1.28]^2 \times [0.24(1 - 0.24) + 0.06(1 - 0.06)]}{(0.24 - 0.06)^2} = 58
\]

The total sample size is thus 116. The sample size will be increased by 10% to 128. To account for laboratory errors and lost stool samples therefore \(n = 64\).

3.4 STUDY SAMPLING PROCEDURE

Written consent was obtained from the parents/care takers of the children who met the eligibility criteria after the study procedure was explained to them.

Recruitment of the children into the study was by consecutive sampling with those whose stool antigen test was positive as cases and those whose stool test was negative as controls. Consecutive sampling of the eligible children into the study was done until a minimum of 64 cases were obtained in each group. All the children recruited had a stool antigen test done and their anthropometric measurement taken. With the stool antigen test result, categorization
into positive or negative group was done. There being many children testing negative, sampling was continued until a minimum of 64 positives were obtained.

Two research assistants were selected and trained on the administration of questionnaire and on measuring the weight, height and mid upper arm circumference (MUAC) accurately. The tools/instruments were pretested with a selected sample of the target population. After pretesting, appropriate adjustment/corrections of the research tools/instruments were made. Upon selection of the subjects, the study aim and procedure was explained to the parent/guardian and a written consent obtained. With the help of the research assistant, a fresh stool sample was obtained either voluntarily in the older children or by doing a rectal swab for the ones who could not pass stool at that point and the young ones.

A semi structured questionnaire was administered to the parent/guardian to assess the socioeconomic status. Height, weight and MUAC of the children were taken by the chief investigator with children wearing minimal clothing and without footwear. Weight was measured to the nearest 0.1 kg using a lightweight Portable electronic scale with a taring capability calibrated to 0.1 kg with a digital screen. Length and height was measured to the nearest 0.1 cm using the WHO/UNICEF height/length measuring board. The measuring boards were specially produced by Shorr Productions (Olney, MD, USA). The length of children less than two years of age were measured using the measurement board put horizontally on a flat surface with two research assistants to position the child on the board. The height of children more than two years old who could stand was taken using the same measuring board but the board put in a vertical position to allow the child to stand. The children without shoes and in wearing minimum clothing were assisted to stand with the feet together, hands on the sides and with the head, buttocks and heels touching the vertical surface of the board, with the child looking straight ahead. The height was taken to the nearest 0.1 cm. The MUAC was measured using the MUAC tape to the nearest 0.1 cm. All measurements were done twice and an average obtained. The stool sample was taken to the laboratory within an hour of collecting.

**H. pylori stool antigen test procedure.**

Stool antigen test was done at the University of Nairobi Paediatric Laboratory using the one step H.pylori faeces test kit, (I chek) from Chem Laboratories Limited. The stool sample was taken to the laboratory within one hour of collecting and the H. pylori antigen test done immediately.
The one step H.pylori test kit has a test cassette that contain monoclonal H.pylori antibody coupled to red coloured colloid gold and a sample bottle that contains 1 milliliter of a buffer solution. A fresh stool sample was diluted in the sample bottle and an aliquot of the diluted stool sample added to the sample well of the test cassette. The result were read within 15 minutes and recorded.

3.5 DATA COLLECTION
Data was collected on H pylori test outcome using the stool antigen test kit. Weight, height and upper mid arm circumference was measured and recorded for all the children.

The interviewer administered semi-structured questionnaire was used to collect data on demographic parameters, the socioeconomic status, and number of children in the family, washing of hands of parent before preparing food and after visiting the toilet, washing of hand of the child before feeding and prior use of antibiotics.

3.6 DATA ANALYSIS
Data was collected, cleaned and checked before entry into Epi info and transferred into statistical programme for social sciences (SPSS) software version 18 which was used to analyse the data. Quantitative data, i.e. height, weight, MUAC were expressed as means with standard error. Differences between means were evaluated using independent t-tests. The $\chi^2$ test was used in the analysis of contingency tables to establish any association between H.pylori results and the socio-demographic characteristics and washing of hands. The effects of H. pylori infection on growth was evaluated by using univariate analysis of variance using weight, height, WAZ, HAZ, and MUAC as per the WHO standards as dependent variables. The age was stratified during analysis to allow for comparison of the dependent variables as per age.

The dependent variables were analysed individually to determine which variable was most affected by the H pylori infection. The parental social class was analysed as both continuous and categorical variables. A p-value of 0.05 or less was taken to signify statistical significance.

3.7 MINIMIZATION OF BIAS
Completeness of the data was checked every day by the principal investigator to minimise information bias. Training of research assistants was done for 4 days and followed by pre-testing of the research tools/instruments with a selected sample of the target population not from the actual targeted study facilities. The pre -testing was done prior to conducting the
actual main study and necessary adjustments/corrections of the research tools were made accordingly.

3.8 ETHICAL CONSIDERATIONS
Ethical clearance was sought from, Kenyatta National hospital, and University of Nairobi Ethical Committee. Informed consent was obtained from the parents/care giver because the children were very young to assent. Confidentiality was observed and unauthorized persons did not have access to the data collected. The data was kept by the principal investigator under key and lock. Each subject was assigned a study identification number, and these subject identifiers were not released outside the research group. Codes were used and no identification was made for the responders. Data was only accessed by the research group. Respondents were informed that their data will be used anonymously. The parents/ care takers whose children tested positive were informed and referred to the paediatric outpatient gastroenterology clinic where children were evaluated for treatment.
4.0 CHAPTER FOUR

4.1 RESULTS PRESENTATION

One hundred and fifty three (153) children aged one to five years were enrolled into the study after meeting the eligibility criteria and the following are results.

Sixty four (42%) of the children tested H. pylori positive (cases) on stool antigen test with eighty nine (58%) testing negative (controls) as illustrated in the figure below.

Figure 1: H. pylori results

Stratification of age in months was done to allow comparison between different age groups because the dependent variables were all age dependent. The age groups were 12 to 23, 24 to 35, 36 to 47 and 48 to 59 months. As illustrated in the table below, (49.7%) of the children were aged 12-23 months with the least number being children aged 48-59 months. 88 (58%) of the study participants were males with 65 (42%) being females. There were more males than females in all the age groups except in the group 48 to 59 months where females were more than males though the numbers in the positive and negative groups were comparable. All the children were accompanied by either a parent or a care giver.
Table 4: Baseline Characteristics of Enrolled Participants and H.pylori results

<table>
<thead>
<tr>
<th>Age in months</th>
<th>%</th>
<th>gender</th>
<th>H.pylori negative n=89</th>
<th>H.pylori positive n=64</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-23</td>
<td>49.7</td>
<td>M 45</td>
<td>28</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td></td>
<td>F 31</td>
<td>17</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total</td>
<td>76</td>
<td>45</td>
</tr>
<tr>
<td>24-35</td>
<td>21.6</td>
<td>M 21</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>F 12</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total</td>
<td>33</td>
<td>17</td>
</tr>
<tr>
<td>36-47</td>
<td>16.3</td>
<td>M 16</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>F 9</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total</td>
<td>25</td>
<td>14</td>
</tr>
<tr>
<td>48-59</td>
<td>12.4</td>
<td>M 6</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>F 13</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total</td>
<td>19</td>
<td>13</td>
</tr>
</tbody>
</table>

Table 4 outlines the distribution of the children according to age and gender with their H.pylori outcomes.

The family's socio-economic characteristics were derived from the questionnaires administered to the parents / care givers. Majority of the respondents were married (92%) with seventy two percent of the parents having attained secondary level education. 55% of the parents of the children who tested positive were self-employed. Of the infected children 48% were from families with income of less than 2500 Kenya shillings per month and this was almost equal proportion of the uninfected children 52% from families with similar income. Among the respondents (36%) who had an income of more than 10000 shillings per month, 39% had a positive result and 61% had a negative test result. The two groups of children were comparable as far as socioeconomic factors were concerned. This is illustrated in the table 4.
Table 5: Socioeconomic characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>H.Pylori Outcome</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive n=89 (%)</td>
<td>Negative n=64 (%)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>37 (42)</td>
<td>51 (58)</td>
</tr>
<tr>
<td>Female</td>
<td>27 (42)</td>
<td>38 (58)</td>
</tr>
<tr>
<td><strong>Parental marital status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>57 (40)</td>
<td>84 (60)</td>
</tr>
<tr>
<td>Single</td>
<td>5 (56)</td>
<td>4 (44)</td>
</tr>
<tr>
<td>Separated</td>
<td>2 (67)</td>
<td>1 (33)</td>
</tr>
<tr>
<td><strong>Parental level of education</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>0 (0)</td>
<td>1 (100)</td>
</tr>
<tr>
<td>Primary</td>
<td>14 (48)</td>
<td>15 (52)</td>
</tr>
<tr>
<td>Secondary</td>
<td>29 (40)</td>
<td>43 (60)</td>
</tr>
<tr>
<td>Tertiary</td>
<td>21 (41)</td>
<td>30 (59)</td>
</tr>
<tr>
<td><strong>Parental employment status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not employed</td>
<td>26 (43)</td>
<td>34 (57)</td>
</tr>
<tr>
<td>Casual</td>
<td>2 (45)</td>
<td>4 (55)</td>
</tr>
<tr>
<td>Self employed</td>
<td>27 (55.1)</td>
<td>33 (44.9)</td>
</tr>
<tr>
<td>Permanent employment</td>
<td>9 (33)</td>
<td>18 (67)</td>
</tr>
<tr>
<td><strong>Parental level of income</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2500</td>
<td>25 (48)</td>
<td>27(52)</td>
</tr>
<tr>
<td>2501-5000</td>
<td>7 (35)</td>
<td>13 (65)</td>
</tr>
<tr>
<td>5001-7500</td>
<td>1 (50)</td>
<td>1 (50)</td>
</tr>
<tr>
<td>7501-10000</td>
<td>9(39)</td>
<td>14 (61)</td>
</tr>
<tr>
<td>&gt;10000</td>
<td>22 (39)</td>
<td>34 (61)</td>
</tr>
</tbody>
</table>

Parents were also asked to indicate whether they washed their hands before preparing food and after changing the children and whether they washed their children’s’ hands after the children came from the toilets. 95% of the parents reported that they washed hands all the
time before preparing food and 86% reported washing the child’s hands after the child visits the toilet. Of the positive children only 5% did not wash hands before handling food and 20% did not wash hands after visiting a toilet.

Chi square statistics was performed to assess the effect of age and socioeconomic status on H. pylori outcome and the results are summarized in the tables below.

### Table 6: Relationship between age and H. pylori result

<table>
<thead>
<tr>
<th>Variable</th>
<th>H. pylori outcome</th>
<th>Total</th>
<th>$\chi^2$ statistic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in months</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-23</td>
<td>Positive 31 (41)</td>
<td>Negative 45 (59)</td>
<td>76</td>
<td>1.503</td>
</tr>
<tr>
<td></td>
<td>24-35</td>
<td>16(48)</td>
<td>17(52) 33</td>
<td></td>
</tr>
<tr>
<td></td>
<td>36-46</td>
<td>11(44)</td>
<td>14(56) 25</td>
<td></td>
</tr>
<tr>
<td></td>
<td>48-59</td>
<td>6 (32)</td>
<td>13 (68) 19</td>
<td></td>
</tr>
</tbody>
</table>

Age did not affect the H. pylori status as illustrated in the table above. The sex of the children did not have an effect on the H. pylori status with none of the socioeconomic factors having effect on the H. pylori infection.

As noted below, (table 6) despite the fact that 40% of the parents of the infected children were unemployed and 39% had income of less than 2500 Kenya shillings per month no statistical significant was noted between the two groups on the H. pylori infection. Parental marital status did not have any effect on H. pylori infection neither did parental level of education change the H. pylori outcome. There was almost a uniform distribution of the children across all the categories with no single socioeconomic factor significantly affection H. pylori outcome. Table 4.4 has the summary.

The majority of the parents reported washing hands before handling food and washed their child’s hands after visiting the toilet (95% and 84% respectively). However hand washing did not have any significant effect on the H. pylori outcome, $p=0.955$ and $p=0.260$ respectively.

Family size which ranged between 1-9 children per respondent was not significantly associated

With H. pylori infection (positive outcome), $X^2=4.436$, $P=0.618$. 

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Table 7: Relationship between socio-demographic characteristics and H.pylori test outcome

<table>
<thead>
<tr>
<th>Variable</th>
<th>H.Pylori Outcome</th>
<th>Total</th>
<th>$\chi^2$ statistic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive</td>
<td>Negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>37 (42)</td>
<td>51 (58)</td>
<td>88</td>
<td>0.004</td>
</tr>
<tr>
<td>Female</td>
<td>27 (42)</td>
<td>38 (58)</td>
<td>65</td>
<td></td>
</tr>
<tr>
<td><strong>Marital Status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>57 (40)</td>
<td>84 (60)</td>
<td>141</td>
<td>1.572</td>
</tr>
<tr>
<td>Single</td>
<td>5 (56)</td>
<td>4 (44)</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Separated</td>
<td>2 (67)</td>
<td>1 (33)</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td><strong>Education level</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>0 (0)</td>
<td>1 (100)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>14 (48)</td>
<td>15 (52)</td>
<td>29</td>
<td>1.295</td>
</tr>
<tr>
<td>Secondary</td>
<td>29 (40)</td>
<td>43 (60)</td>
<td>72</td>
<td></td>
</tr>
<tr>
<td>Tertiary</td>
<td>21 (41)</td>
<td>30 (59)</td>
<td>51</td>
<td></td>
</tr>
<tr>
<td><strong>Employment status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not employed</td>
<td>26 (43)</td>
<td>34 (57)</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>Casual</td>
<td>2 (45)</td>
<td>4 (55)</td>
<td>6</td>
<td>1.283</td>
</tr>
<tr>
<td>Self employed</td>
<td>27 (55.1)</td>
<td>33 (44.9)</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>Permanent</td>
<td>9 (33)</td>
<td>18 (67)</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>level of income(Ksh)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2500</td>
<td>25 (48)</td>
<td>27 (52)</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>2501-5000</td>
<td>7 (35)</td>
<td>13 (65)</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>5001-7500</td>
<td>1 (50)</td>
<td>1 (50)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>7501-10000</td>
<td>9 (39)</td>
<td>14 (61)</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>&gt;10000</td>
<td>22 (39)</td>
<td>34 (61)</td>
<td>56</td>
<td></td>
</tr>
</tbody>
</table>
One way analysis of variance (ANOVA) was conducted to assess if there were significant differences in anthropometric parameters among the 1-5-year-old children who were categorized in different age groups in months namely 12-23, 24-35, 36-47 and 48-59.

The results showed that the anthropometric parameters were better in those who were negative on H.pylori test than those who had the infection as depicted in the summarized tables below. The results showed that children infected were shorter and lighter than the negative controls. There were minimal differences in the means of MUAC in the two groups.

**Table 8: Anthropometric measures and H.pylori status**

<table>
<thead>
<tr>
<th>H.Pylori result</th>
<th>Negative</th>
<th>Positive</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height</td>
<td>89.87</td>
<td>86.87</td>
<td>0.097</td>
</tr>
<tr>
<td>Weight</td>
<td>12.04</td>
<td>11.33</td>
<td>0.149</td>
</tr>
<tr>
<td>MUAC</td>
<td>15.44</td>
<td>15.12</td>
<td>0.195</td>
</tr>
</tbody>
</table>

The children with H.pylori infection were shorter 86.87v/s89.87 cm p=0.097, lighter 11.33v/s12.04kg p=0.149 than the uninfected children. Though these differences were noted, there was no statistical difference between the two groups. The MUAC was almost equal in the two groups p=0.195(table 8)

**Table 9: Gender, Anthropometric measures and H.pylori status**

<table>
<thead>
<tr>
<th>Sex</th>
<th>H.Pylori result</th>
<th>H.Pylori result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>variable</td>
<td>Negative</td>
</tr>
<tr>
<td>Male</td>
<td>Height(cm)</td>
<td>88.61</td>
</tr>
<tr>
<td></td>
<td>Weight(kg)</td>
<td>11.79</td>
</tr>
<tr>
<td></td>
<td>MUAC(cm)</td>
<td>15.37</td>
</tr>
<tr>
<td>Female</td>
<td>Height (cm)</td>
<td>91.57</td>
</tr>
<tr>
<td></td>
<td>Weight (kg)</td>
<td>12.38</td>
</tr>
<tr>
<td></td>
<td>MUAC (cm)</td>
<td>15.53</td>
</tr>
</tbody>
</table>
By gender, there were notable differences in weight and height with negligible differences in the MUAC between the infected and the uninfected children. The difference in mean height was more in the infected females than infected males 85\text{cm} \text{v/s} 92\text{cm} \ p=0.053 \text{ and } 88\text{cm} \text{v/s} 89\text{cm} \ p=0.735 \text{ respectively (table 9).}

In the individual age categories, anthropometric measures were better in the uninfected children than the infected ones. The differences in the absolute measures seemed to be more in the older children though this was not statistically significant as illustrated in table 4.7

**Table 10: Anthropometric measures, age and H.pylori status**

<table>
<thead>
<tr>
<th>Age in Months</th>
<th>Anthropometric measure (mean)</th>
<th>H.Pylori result</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-23</td>
<td>Height (cm)</td>
<td>80.96</td>
<td>79.75</td>
</tr>
<tr>
<td></td>
<td>Weight (kg)</td>
<td>9.75</td>
<td>9.58</td>
</tr>
<tr>
<td></td>
<td>MUAC (cm)</td>
<td>14.93</td>
<td>14.77</td>
</tr>
<tr>
<td>24-35</td>
<td>Height (cm)</td>
<td>90.96</td>
<td>88.87</td>
</tr>
<tr>
<td></td>
<td>Weight (kg)</td>
<td>12.65</td>
<td>12.12</td>
</tr>
<tr>
<td></td>
<td>MUAC (cm)</td>
<td>15.81</td>
<td>15.44</td>
</tr>
<tr>
<td>36-47</td>
<td>Height (cm)</td>
<td>100.39</td>
<td>95.32</td>
</tr>
<tr>
<td></td>
<td>Weight (kg)</td>
<td>14.97</td>
<td>13.27</td>
</tr>
<tr>
<td></td>
<td>MUAC (cm)</td>
<td>16.06</td>
<td>15.44</td>
</tr>
<tr>
<td>48-59</td>
<td>Height (cm)</td>
<td>107.98</td>
<td>102.77</td>
</tr>
<tr>
<td></td>
<td>Weight (kg)</td>
<td>16.04</td>
<td>14.67</td>
</tr>
<tr>
<td></td>
<td>MUAC (cm)</td>
<td>16.06</td>
<td>15.47</td>
</tr>
</tbody>
</table>
Z scores for height for age, weight for age and weight for height were computed to help classify children in different nutritional categories. The table below (Table 11) shows the mean z scores of height for age, weight for age and weight for height with the standard deviation of the mean. The infected children had a lower height z score than the uninfected children except for children in the category of 12 to 23 months whose mean height z score was the same for positives and negative children. Infected children in the aged groups 12 to 23 and 36 to 47 had lower mean weight for age z scores (-2 versus -1 and -2 versus 0 respectively) than the uninfected children. Weight for age z scores means in the other two age groups were similar for the infected and uninfected children.

Mean weight for height z scores were the same in the infected and uninfected children. There were however differences in the individual z scores with the infected children being more malnourished but this was not statistically significant.

Table 11: HAZ, WAZ, WHZ and H.pylori status

<table>
<thead>
<tr>
<th>Age in Months</th>
<th>H.Pylori outcome</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Negative</td>
<td>Positive</td>
</tr>
<tr>
<td>12-23</td>
<td>Mean</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Standard Deviation</td>
<td>2</td>
</tr>
<tr>
<td>Height for Age z score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight for Age z score</td>
<td>Mean</td>
<td>-1</td>
</tr>
<tr>
<td></td>
<td>Standard Deviation</td>
<td>2</td>
</tr>
<tr>
<td>Weigh for Height z score</td>
<td>Mean</td>
<td>-2</td>
</tr>
<tr>
<td></td>
<td>Standard Deviation</td>
<td>2</td>
</tr>
<tr>
<td>24-35</td>
<td>Mean</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Standard Deviation</td>
<td>2</td>
</tr>
<tr>
<td>Height for Age z score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight for Age z score</td>
<td>Mean</td>
<td>-1</td>
</tr>
<tr>
<td></td>
<td>Standard Deviation</td>
<td>2</td>
</tr>
<tr>
<td>Weigh for Height z score</td>
<td>Mean</td>
<td>-1</td>
</tr>
<tr>
<td></td>
<td>Standard Deviation</td>
<td>2</td>
</tr>
<tr>
<td>36-47</td>
<td>Mean</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Standard Deviation</td>
<td>2</td>
</tr>
</tbody>
</table>
Z scores computed were used to classify the nutritional status of the children. The percentages of children in the stunted, underweight and wasted were higher among the infected children than uninfected. 34% of the infected children were stunted compared to 23% in the uninfected group. Of the 64 children who had a positive test result, 7 (11.2%) were underweight. Two of the infected children were wasted as compared to one in the negative group. Though these differences were not statistically significant, there was a trend that the infected children had lower anthropometric measures. Table 12 summarizes these findings.

Table 12: HAZ, WAZ, WHZ classification and H.pylori status

<table>
<thead>
<tr>
<th>H.Pylori result</th>
<th>Negative(n=89)</th>
<th>Positive(n=64)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Height for age z category</td>
<td>Stunted</td>
<td>20</td>
<td>22.5%</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>69</td>
<td>77.5%</td>
</tr>
<tr>
<td>Weight for age z category</td>
<td>Underweight</td>
<td>10</td>
<td>10.7%</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>73</td>
<td>82.3%</td>
</tr>
<tr>
<td></td>
<td>Overweight</td>
<td>6</td>
<td>7.0%</td>
</tr>
<tr>
<td>Weight for Height z category</td>
<td>Wasted</td>
<td>1</td>
<td>0.7%</td>
</tr>
<tr>
<td></td>
<td>Not wasted</td>
<td>88</td>
<td>99.3%</td>
</tr>
</tbody>
</table>
5.0 CHAPTER FIVE

5.1 DISCUSSION

The stool antigen test was positive in 64 (42%) of 153 children. This point prevalence of 42% is lower than that of recent unpublished study by Mwangi and laving at Kenyatta national hospital where they reported a prevalence of H.pylori of 59% among children who had chronic sinusitis and dyspepsia. Similarly Langat documented that the prevalence of H.pylori in children less than three years of age was 45.6 %. There was no significant difference in H.pylori status by gender. This finding is similar to all studies done on H.pylori in children that have shown that male and females are infected equally, as noted by Mohammad that there was no gender differences among children infected with H. pylori13, 15.

In this study, 48% of the children positive for H.pylori were in the age group one to two years. This finding that most of the children with infection were young is in agreement with finding by Langat that infection occurred in children between six to thirty six months attending well baby clinic15. However, this finding is contrary to the report by Robertino that the prevalence of H.pylori infection increased with increasing age. It is possible that the older children who tested positive have been living for long with the infection as described by that the infection is acquired during childhood and persists for decades7. There were no differences in rates of H.pylori infection by gender. There were more males in each age category but this did not have any influence on the H.pylori status.

The distribution of the socioeconomic factors among infected and uninfected children did not differ. Children 5with H.pylori infection did not fall in any distinct category but rather fell in all groups of parental level of income, education and employment.34% of the children with H. pylori infection were from families with a monthly income of more than ten thousands shillings. This finding is different from those of Leandro and Mohammad who demonstrated a high H.pylori prevalence in children from families with low socioeconomic status and who live in socially deprived regions13, 18.

In this study, 45% and 32% of those with H. pylori infection were children of parents who had attained secondary and tertiary level of education respectively. This finding is contrary to those of Hestivik and Langat who found that the risk factors for infection with H.pylori in children were congestive living, low level of education, poor hygienic status and low wealth index. Langat showed that high rates of H.pylori infection were associated with low socioeconomic status, crowding in homes and poor sanitation12, 15.
Most of the parents washed hands before food preparation and after visiting the toilet. This may explain why the prevalence of H. pylori was not high as expected and therefore there was no statistically significant difference in the prevalence of H. pylori infection among those who washed the hands and among those who did not wash the hands. Similar findings have been reported in studies that looked at the effect of improved hygienic standards and the prevalence of H. pylori. Tkachenko demonstrated a 30% reduction in the prevalence of H. pylori infection over 10 years of improved sanitation and socioeconomic level\textsuperscript{19}. On contrary In Gambia Thomas ruled out low socioeconomic factors and demographic factors as confounders for the H. pylori outcome\textsuperscript{27}.

This observation can be explained by the fact that there has been health education on hand washing and proper waste disposal in the recent past in Kenya. There has been documented improvement in the economy and therefore improvement in the living standards. There is also a possibility that this result was influenced by the fact that the study was carried out in Nairobi which is a city with most people having access to health education.

Most of the children with H. pylori (40%) were from families with only two children with only one family reporting a total of nine children in a household. Other studies have documented overcrowding as an associated risk factor for H. pylori infection. Hestivik in Uganda concluded that congestive living was associated with the infection\textsuperscript{12}.

Lack of any association between H. pylori infection and the socioeconomic factors in this study can be explained by the fact that, the study was carried out in an urban setup where most people have access to clean water and health education. In the urban areas most family practice family planning and therefore have fewer children. The other explanation could be that the study was a hospital based and may not reflect the true picture of the population.

**Effect of H. pylori infection on growth parameters**

The infected children were shorter than the uninfected children 86.87\text{cm}$/89.87\text{cm}$. This difference was not statistically significant $p=0.097$. This finding is similar to that Goodman who showed that children with H. pylori infection were 1.76\text{cm} shorter than those without the infection\textsuperscript{21}. The same effect was demonstrated in the individual age categories. The difference in the height was more marked in the older children. This may be explained by the fact that these children must have acquired the infection earlier and lived with it longer and
therefore the effect of the chronic infection on height was apparent. Robertino et al demonstrated long term effect of H.pylori in children and he demonstrated that the children who stayed positive for long were shorter than the uninfected children. The effect of H.pylori infection on height was more marked in females than males p=0.053. This has been demonstrated in other studies that the females with H.pylori infection are shorter than uninfected counterparts. Quiñonez demonstrated that infected girls had lower height for age p=0.008. Similarly Mohammad noted that differences between infected and non-infected children were significant with regard to height 139.9 +/- 1.3 vs. 144.2 +/- 2.1 cm; P = 0.009. Robertino et al demonstrated that children who were treated for H. pylori infection demonstrated a significantly faster linear growth than those who remained with the infection.

The infected children were more stunted than uninfected children 11.2% and 10.7% respectively. This demonstrated a finding similar to that of Mohammad that 24% of the infected and only 6% of the uninfected children had height for age percentile below 5%.

This study demonstrated that children infected with H.pylori are lighter 11.33 v/s 12.04 kg. although this was not statistically significant p= 0.149 there was a trend indicating that the weight differences were greater in the older children. The possibility of the effect of chronic infection on weight can be entertained. Mohammad did however demonstrated that infected children were lighter p=0.05 than uninfected ones. We found that 11.2% of the infected children were underweight on weight for age Z score, a finding Mohammad also demonstrated in infected children in Egypt. Other studies have reported controversial findings as far as effect of the infection on weight is concerned with some reporting no effect at all. Quiunonez reported that neither height nor weight, differed by H. pylori infection status.

The adverse effect of H. pylori infection on the weight in this study was more evident in the older children than in the younger ones despite the fact that more of the younger children tested positive (31 of the 64 were less than 2 years old). This is in keeping with the finding in several studies that the longer the duration of exposure to the infection, the more negative effect on both height and weight are evident.

Weight for height Z score for the children in the study were computed and it was noted that 2.4% of the infected children were wasted compared to 0.7% of the negative children. Thomas presented results suggesting that H pylori colonization in early infancy predisposes
to the development of malnutrition and growth faltering, although the effect did not persist into later childhood but the infected children were more malnourished than uninfected ones\textsuperscript{27}.

The effect of the H. pylori infection on the MUAC was not statistically significant $p=0.195$. However MUAC was higher in the uninfected children compared to infected children. Similarly the difference was greater in the older children. No other study has used MUAC as the outcome measure and therefore there are no comparisons that can be done.

The overall nutritional status of the infected children on the basis of rate of stunting, and underweight (34%, and 11.2%) were worse than the Kenyan national figures for stunting currently at 26%, underweight at 11% respectively\textsuperscript{38}. 
6.0 CHAPTER SIX

6.1 LIMITATIONS, CONCLUSIONS AND RECOMMENDATIONS STUDY

LIMITATIONS

One measure of anthropometric parameters may not give a true reflection of the effect of the H. pylori infection on nutritional status.

Weight, height and upper arm circumference are determined by genetics, socioeconomic status, nutritional status and infections and therefore it is not possible to control for all these confounders and accurately conclude that the effect noted in the growth parameters is purely due to H. pylori infection.

The study design cannot be used to look for causal relationship and therefore we can not demonstrate if H. pylori actually caused the effect on the anthropometric measure.

6.2 CONCLUSION

There were no differences in nutritional status between infected and uninfected children.

Socioeconomic status has no effect on H. pylori infection

6.3 RECOMMENDATIONS

Studies with a higher power are recommended to determine if there is any association between H. pylori infection and nutritional status.
REFERENCES.


12. Elin Hestvik, Thorkild Tylleskar, and James K Tumwine *Helicobacter pylori* in apparently healthy children aged 0-12 years in urban Kampala, Uganda: a community-based cross sectional survey.


37. Kenya Demographic Health Survey 2013-2014


APPENDICES

APPENDIX I: QUESTIONNAIRE

Questionnaire Id No ---------------Date of interview-------------------

Height------------------------cm
Weight----------------------Kg
MUAC------------------------cm

Residence -------------------------------Mobile number-----------------------------

H.pylori test result-------------------------

Instructions
Please fill in the required information in the blank spaces or tick against the responses given.

A. DEMOGRAPHIC DATA

2. Date of birth      -----/---------/-------
                      Day/Month/Year

3. Sex
   1. Male
   2. Female

4. Marital status of parent (Please tick one)
   0. Married
   1. Single
   2. Separated
   3. Divorced
   4. Widowed

5. Highest level of education attained by the parent (Please tick one)
   0. None
   1. Primary
   2. Secondary
   3. Tertiary

6. Employment status of the parent
   0. Not employed
   1. Casual
   2. Self employment
   3. Permanent employment
7. Level of income of the parent per month in Kenya Shillings (Please tick one)
   0. <2500
   1. 2500-5000
   2. 5001-7500
   3. 7501-10000
   4. > 10000

8. Number of children in the family ------------------------

9. Antibiotic use in the last two weeks
   0. No
   1. Yes which one?

11. Do you wash hand every time you are preparing food?
   0. Yes
   1. No

12. Do you wash your child’s hands after he/she visits the toilet and before eating ?
   0. Yes
   1. No
APPENDIX II: CONSENT FORM - parent

Study Identification Number: --------------------------parent’s mobile number---------------------

Date: -------------------------------------

Study Title: ASSOCIATION BETWEEN HELICOBACTER PYLORI INFECTION OF CHILDREN BETWEEN 1 YEAR TO 5 YEARS ATTENDING OUT PATIENT CLINIC AT KENYATTA NATIONAL HOSPITAL AND THEIR NUTRITIONAL STATUS.

Investigator: Dr. Judith Awinja Andati. (MBChB)

     Paediatric Resident, University of Nairobi
     Tel Number:-0721257896

Supervisors:

Prof Ezekiel Wafula,

     Professor, Paediatrics and Child Health,
     Department of Paediatrics and Child Health, University of Nairobi

Dr Ahmed Laving,

     Consultant Paediatrician and Gastroenterologist, Lecturer Department of Paediatrics and Child Health, University of Nairobi.

Dr Daniel Njai,

     Senior Lecturer Department of Paediatrics and Child Health School of Medicine, University of Nairobi.
**Investigator’s Statement:**
We are requesting you to kindly participate in this research study. 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. This process is called ‘Informed Consent’. Please read this consent information carefully and ask any questions or seek clarification on any matter concerning the study with which you are uncertain.

**Introduction:**

H pylori infection is the most common chronic bacterial infection in the world. It is most commonly acquired during childhood. The infection is associated with impaired digestion and absorption of nutrients which can affects the nutritional status in children.

**Study procedure:**

We intend to recruit children at the aged one to five years old at the paediatric outpatient emergency clinic at Kenyatta national hospital. We will ask for your consent for your child to participate in this study. Weight, height and MUAC will be measured for all the children recruited in the study. You will be asked to help your child get a fresh stool sample on which the H pylori antigen test will be done in the paediatric laboratory at the University of Nairobi. If your child will not pass stool at the time of interview then we will request you to allow us to do a rectal swab to get a stool sample. This will involves us putting a small swab made of cotton in your child’s rectum and collecting a stool sample. The weight, height and MUAC of the children with H pylori infection will be compared with the ones of the children without infection to determine if there is any difference.

**Benefits:**

The results of the study will help us to know if there is an association between H pylori infection and undernutrition in children and if so then preventive and eradication programmes will be recommended.

**Risks:**

There will be no risks to your child during the study. There will be no invasive procedures carried out in the study that may harm your child. Refusal to participate will in no way lead to victimization or discrimination.
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 lead to victimization or discrimination in any way.

Confidentiality:

The information obtained about you will be kept in strict confidence. No specific information regarding you will be released to any person without your written permission. I will, however, discuss general overall findings regarding the findings but nothing specific will be discussed regarding you. We will also not reveal your identity or your child’s identity.

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 Judith Awinja by calling 0721257896.

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: PARTICIPANT’S STATEMENT:

I having received adequate information regarding the study research, risks, benefits hereby
AGREE / DISAGREE (Cross out as appropriate) to participate in the study. I understand that
my participation is fully voluntary and that I am free to withdraw at any time. I have been
given adequate opportunity to ask questions and seek clarification on the study and these
have been addressed satisfactorily.

Parent’s Signature……………………………………………… Date…………………………

I declare that I have adequately explained to the above participant, the study procedure, risks,
and benefits and given him /her time to ask questions and seek clarification regarding the
study. I have answered all the questions raised to the best of my ability.

Investigator’s Signature: ……………………………………………… Date………………
APPENDIX III: KNH/UON-ERC LETTER OF APPROVAL

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
(254-020) 2726089 Ext 44355

KHN/UON-ERC
Email: uonkh_eac@uonbi.ac.ke
Website: www.uonbi.ac.ke

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 725360-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/368
Link: www.uonbi.ac.ke/activities/KNHuOn

13th November 2014

Dr. Judith Awinya Andati
Dept. of Paediatrics & Child Health
School of Medicine
University of Nairobi

Dear Dr. Andati

Research proposal – Association between Helicobacter Pylori infection of children between 1 year to 5 years attending Out-patient clinic at Kenyatta National Hospital and their nutritional status (P448/07/2014)

This is to inform you that the KNH/UoN-Ethics & Research Committee (KNH/UoN-ERC) has reviewed and approved your above proposal. The approval periods are 13th November 2014 to 12th November 2015.

This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH/UoN ERC before implementation.
c) Death and life threatening problems and severe 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.
d) 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.
e) 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)
f) Clearance for export of biological specimens must be obtained from KNH/UoN-Ethics & Research Committee for each batch of shipment.
g) Submission of an executive summary report within 90 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 www.uonbi.ac.ke/activities/KNHuOn.

Protect to discover