PREVALENCE OF HELICOBACTER PYLORI IN CHILDREN LESS THAN THREE YEARS OF AGE AS SEEN IN HEALTH FACILITES IN NAIROBI PROVINCE. fr

A DISSERTATION PRESENTED IN PART FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF MEDICINE IN PAEDIATRICS AND CHILD HEALTH OF THE UNIVERSITY OF NAIROBI.

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DECLARATION

I declare that this dissertation is my original work and has not been published elsewhere or presented for a degree in any other university.

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DEDICATION

This work is dedicated to my daughter Anne Jemutai and my husband Dan Kiptoon.

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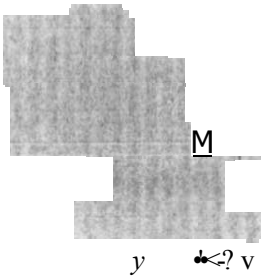

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LIST OF ABBREVIATIONS

H. Pylori..... *Helicobacter Pylori*

HPS A..... *Helicobacter Pylori* stool antigen test

SPSS..... Statistical Package for Social Sciences

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ABSTRACT

Background: Helicobacter pylori (H. pylori) is among the most common infections in humans and has been recognized as a cause of gastroduodenal diseases. Data on prevalence in children is mainly from industrialised countries and ranges from less than 5 % in the under fives to about 10% in the adolescent group. The data available from the African region report a prevalence ranging from 40% to 50% in the under fives. In Kenya a prevalence of 60% by the age of 10 years and 80% by the age of 15 years has been reported.

Objectives: To determine the prevalence of Hpylori in children less than 3 years of age and to determine socio-demographic correlates of H.pvlori infection in these children

Setting Nairobi Province, The well baby clinics.

Subjects: Children less than 3 years of age

Design: Cross sectional study.

Methodology: Random selection of the well baby clinics in Nairobi province was done and consecutive sampling of the children and mothers who gave consent and met the inclusion criteria were recruited into the study. Data was entered into a questionnaire. A stool sample was obtained from the child and finger prick whole blood from the mother was obtained. The stool was tested using a rapid test for H.Pylori antigen and the mother's blood was tested using a rapid test for H Py lori antibody.

Results: A total of 195 children were analysed in the study. There were 103 (52.8%) males and 92(47.2%) females giving a male to female ratio of 1.1: 1. The mean age was 17.7 months and the median age was 16 months(range 2weeks to36months).

H.Pylori antigen was found in stool of 89(45.6%) of the children. Low socioeconomic status, crowding in the homes and poor sanitation were associated with H.Pylori infection.

Conclusion: There is a high prevalence rate of H.Pylori infection in children less than three years as found in this study which is in agreement with studies done in other developing countries. Family income is associated with H.Pylori infection and families with low income are at higher predisposition to H.Pylori infection when compared to families with high income,

INTRODUCTION AND LITERATURE REVIEW

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Helicobacter are gram-negative, spiral, flagellate bacilli which were first described by Warren and Marshall in 1983 (1). *Helicobacter pylori* naturally infects humans and monkeys and has been recently described in domestic cats (2).

The bacterium was first called *Campylobacter pyloridis* but was subsequently differentiated from Campylobacter by among other properties, the presence of multiple flagellae. A new genus "Helicobacter" was devised in 1989(3). Since then many strains have been identified with variable virulence (3).

In colonised subjects, *Helicobacter pylori* is present within the gastric mucus layer and on the gastric mucosa. The bacterium does not invade the epithelium. *Helicobacter pylori* is usually found on the antral mucosa but may also be present in other parts of the stomach (2). The spiral structure and flagellae render *Helicobacter pylori* motile in the mucus environment and it produces urease which hydrolyzes urea into carbon dioxide and ammonia, hence ensuring its survival in the acidic milieu of the stomach. It binds tightly to epithelial cells by multiple bacterial surface components and secretes an exotoxin, which is a vacuolating cvtotoxin (Vac A) (2),

It is now recognized that infection with H. pylori is associated with some of the most common clinical problems in medicine including chronic active gastritis, peptic ulcer disease, non-ulcer dyspepsia and duodenitis. Colonization is currently classified as a premalignant condition for MALT lymphoma (mucosal associated lymphoid tissue) and gastric adenocarcinoma by the World Health Organisation (4,5),

It is now recognized that H. pylori is mainly acquired in childhood (6). Studies have demonstrated that H. pylori infection is worldwide with approximately 50% of the population being infected (6). However, the prevalence, timing of acquisition, symptoms, and sequelae of infection differ in developed compared to developing countries. In developed countries infection during childhood is uncommon. It is estimated that less than 5% of children under 5 years of age in United states are infected with H.pvlori and by adolescence only about 10%, and this peaks to about 50 -60 % by 60 years of age in a study reported in 1995 (6,7).

In contrast. H.pvlori infection in the developing world occurs earlier in life with a higher frequency. Approximately half of the children living in developing countries are seropositive by 5 years of age and seroprevalence rates as high as 90% have been reported in early adulthood (6, 7).

In Nigerian children aged 2 years the seroprevalence rate was 57% rising to 82% in 5 year olds (8). In Gambian children aged 0-60 months the prevalence of Hpylori in a rural set up was 15 - 46% (9). An age-specific increase in the prevalence was also observed in South Africa where the prevalence was 50% by the age of 10 years and 94% by the age of 30years (10).

In Thailand. H.pvlori infection in the rural areas is acquired early in life with seroprevalence rate of 17.5% in children aged 5-9 years. At a Bangkok orphanage, where enteric infections were hyperendemic, 74% of children 1-4 years of age were seropositive for H.pvlori (10).

In a large cross-sectional seroprevalence study conducted in Southern China, the overall prevalence of Rpylori infection was **44.2%. A** higher prevalence was **found** in the urban areas (52**.4%)** than in the rural areas (38.6%), and this was attributed to crowding. The prevalence increased with age, and by the age of 5years 23% of children were infected with Rpylori (10).

In a poor peri-urban community in Bangladesh, prevalence of H. pylori was found to be 85%. In another Bangladeshi study on asymptomatic healthy adult volunteers, 52% were found to be H.pviori positive and in a cross-sectional study conducted in the same area. 42% of asymptomatic infants younger than 1 year of age were positive for Rpylori (11).

A study in Chile revealed increasing prevalence of Rpylori antibodies with age (12). In Peru, children acquired H.pylori infection early in life, with an overall prevalence of 48%. This finding was confirmed in a later report on a seroepidemological survey of children predominantly from lower socioeconomic strata, which demonstrated that H.pviori infection begins in the first years of life; by the age of 4-5 years, 60% of these children are seropositive (13).

In Kenya, a study on school going children from age 3 - 1 5 years by Nabwera et al. found a prevalence of 80.7% H.Pylori infection (14),

Effect of socioeconomic status and environmental factors

A lower socioeconomic status is associated with a higher prevalence of H,**pylori** infection (15). H.pylori tends to cluster in families and in people living in crowded conditions (16,17).

Studies have demonstrated an inverse relationship between H.pylori prevalence and the educational level of the population studied (17). Environmental factors such as general level of hygiene, source of water supply and sanitation have been linked to seroprevalence of H.Pylori(16).

Transmission of H.pvlori

H.pylori is believed to be a strictly human pathogen, although it or similar organisms have been isolated from several non-human mammals including primates, pigs and cats (18). The extensive clustering of H.pylori cases in families, the higher seroprevalence of H.pylori among persons living in institutions or in other crowded conditions, and the lack of plausible environmental reservoir of H.pylori all point to the fact that person-to-person spread is the primary mode of transmission (19). The two modes of transmission that have been proposed are faecal-oral and oral-oral transmission (19).

H.pylori can be detected in the gastric juices and thus can pass down into the intestines. Successful isolation of H.pylori from faeces of Gambian children proved that Hpylori can survive in the intestinal tract and be shed in the environment along with the faeces (20). In Peru, a case control study found that children using

municipal water were three times more likely to acquire H.pylori than are children using water from wells at home(21).

H.pylori can reach the oral cavity via regurgitation of gastric contents. The oral cavity can act as a reservoir and saliva as the vehicle of transmission. A study done in India isolated H.pylori in dental plaque in 100% of H.pylori positive subjects. A case control study in Burkina Faso reported that premastication of food by H.pylori positive mothers to feed their infants constitutes a three-fold greater risk of spread to the infants compared to controls (10).

Okuda confirmed that breastfeeding protects from H.pylori infection in early childhood. He speculated that breastfeeding offers some form of natural protection from H.pylori infection in early childhood due to high levels of lactoferrin in human milk (22, 23, 24).

There was no literature demonstrating any seasonal variation in the transmission of H.Pylori.

Diagnosis

Diagnostic tests currently used for the detection of H.pylori fall into two categories: invasive and non-invasive. The invasive methods require endoscopy and biopsy, and include culture, rapid urease test and histology'. The non-invasive tests for H.pylori include the urea breath test, serology, and the analysis of materials such as faeces, urine and saliva for antigens of H.Pylori (25).

Serology has a low sensitivity in younger children given that immunological response to H.pylori is immature (26). In addition serum antibodies, both IgG and JgA, continue to be positive for several months after the organism has been eradicated leading to decreased specificity (27).

Urea breath test has high diagnostic accuracy in children, however it is not easy to perform the test in children who do not ingest 13C urea or in whom the collection of exhaled breath is difficult because of age or because of mental or physical disturbance **(28).**

The H. pylori stool antigen (HpSA) test is inexpensive and requires no specialized test equipment. Consequently, it is possible to perform the test at any medical center. Furthermore, as stool samples can be stored frozen the test is also suitable for epidemiological studies. As a non-invasive test, the HpSA could be used in all age groups (29, 30). This test has undergone testing in the initial diagnosis of H. Pylori and in the confirmation of eradication and has been extensively evaluated and compared against the gold standard Urea breath test (25). In the studies performed in 1999, 3419 patients were evaluated with the stool antigen test in the pre-treatment clinical settings and the mean for sensitivity was 93.2% and for the specificity was 93.2%. These studies suggest that the test is comparable to the Urea Breath Test (sensitivity of 94.7% and specificity of 95.7%) in the initial detection of H. Pylori infection (25,31,32,33).

Clinical Impact

H. Pylori is a common factor in the pathogenesis of many gastroduodenal diseases. When the age at first infection with H.Pylori is less than five years, the inflammation usually occurs throughout the stomach damaging the acid producing cells. This leads to a low acid production which is insufficient for the formation of a duodenal ulcer (34, 35). Chronic inflammation persists for decades and in the presence of genetic or inflammatory instability of oncogenes there is a possibility' of gastric cancer developing later in life (34, 36).

When the age at acquisition of H. Pylori is greater than five years, the acid producing cells have matured and are not inflamed. If gastric metaplasia occurs in the duodenum, then H.Pylori infection could cause duodenitis and because of the increased acid production, duodenal ulcers could develop (34, 37).

Although the incidence of gastric cancer has fallen rapidly in developed countries in recent decades, gastric cancer still occurs frequently in developing countries and shows remarkable variation in incidence both between and within countries (38). Prospective case-control studies have shown a clear association between H.Pylori infection and the subsequent development of gastric cancer (39). In recent decades the frequency of H.Pylori infection has decreased at the same time that gastric cancer cases have declined in developed countries (40).

Over 90 % of duodenal ulcer and 70 % of gastric ulcer patients are infected with H. Pylori. The incidence of duodenal ulcers has declined in recent years in developed countries and seems to parallel the falling prevalence of H. Pylori infection (38).

Ogutu et al in a prospective study looking at patients with dyspepsia found that peptic ulcer was the most prevalent pathological finding and all the cases had evidence of H.Pylori. However this was in patients aged 12 years and above (41). Lule et al found antral gastritis, closely followed by duodenitis, as the most common endoscopic features associated with H.pylori isolation. The number of H.Pylori isolated increased with age reaching a peak at 51 to 60 years of age (42).

H.Pylori infection is a major cause of type B gastritis and was found in 90% of children with duodenal ulcers and in 25% with gastric ulcers (43, 44). In most children the presence of H. Pylori infection does not usually lead to symptomatic disease even when the organism colonizing the mucosa causes chronic active gastritis (45). A study done in Finland which followed children who had H.Pylori by use of endoscopy for two years found that there was progressive inflammatory changes (nodular gastritis) with deterioration in histological features of the gastric mucosa of infected children (30% -100%) despite stable R pylori colonization and absence of symptoms (46).

However even though the infected individuals develop chronic gastritis of variable severity, the reasons why only 10% - 20% of those infected individuals develop clinical disease (peptic ulcers and gastric carcinoma) is not well understood. Individual differences and also difference in virulence among strains of H. Pylori may affect clinical risk of acquiring the clinical disease (47).

Acquisition of H. Pylori has been shown to occur in all age groups (6, 7). Mucosal inflammatory changes seen in early childhood has an impact on the type of

gastroduodenal disease one develops in later in adulthood(31,33).The most effective approach to reducing the incidence of gastroduodenal disease secondary to HPylori would then be the prevention of childhood H.Pylori acquisition This could then be achieved by determining the age at which children become infected, the associated factors of infection and the possible modes of transmission. Armed with this epidemiologic knowledge it may be possible to develop effective strategies in the public health sector to reduce the transmission of infection (40).

STUDY JUSTIFICATION

Helicobacter Pylori is among the most common infection in humans and has been recognised as a major cause of gastroduodenal disease. There is increasing evidence that H.pvlori is acquired in early childhood and infects more people in developing countries than industrialized countries.

Acquiring the infection early in childhood causes chronic inflammation throughout the stomach w hich may lead to development of chronic gastritis, peptic ulcers and gastric tumours later on in life.

Knowledge of the prevalence of H Pylori in children less than 3 years will help our understanding of how early this infection is acquired locally. It will also alert health workers to the possibility of H. pylori infection when faced with young children with dyspeptic symptoms. These children may then be evaluated further for H. Pylori with the background knowledge of the prevalence in this geographical region. On a wider scale such knowledge can lead to better planning of health sen ice provision specifically making available the diagnostic tests used to identifying H. pylon at the regional health referral facilities and also prov iding H Pylori eradication drugs for those who are sy mptomatic. Public health measures can also be instituted to prevent the transmission of H. Pylori once the associated factors are known and hence reduce the disease burden.

There is no local data on the prev alence of H Pylori in children less than 3 years of age. nor is there any data on associated factors of H. pylori infection in our population. This study aims to obtain this information.

RESEARCH QUESTION

What is the prevalence of RPylori in children less than 3 years of age in health facilities in Nairobi Province?

OBJECTIVES

Primary objective

To determine the prevalence of H. pylori infection in children less than 3 years of age in health facilities in Nairobi Province.

Secondary objective

To determine if the following are correlated with H.Pylori infection: - age, socio economic status, household crowding and H. Pylori seropositivity of the mother.

METHODOLOGY

- Study Area

  The study was conducted in well baby clinics in the health facilities in Nairobi Province.

  Study Population

  This comprised of children less than 3 years of age (36 months inclusive) presenting to the well baby clinic for immunization or regular weighing and satisfying the inclusion criteria.

Inclusion Criteria

- All children less than 3 years.
- All mothers of the children recruited into the study. The mothers were not subjected to other eligibility criteria independently.

Exclusion Criteria

- Children with watery stool (a stool sample that takes the shape of the container), a watery specimen was inappropriate for testing.
- Children who had been on the following drugs within two weeks to the test: antimicrobials, proton pump inhibitors, bismuth preparation. These drugs are known to suppress H. Pylori and ingestion of these prior to H. Pylori testing may give false negative result.
- Children whose mothers did not give consent.

Study Design

This was a cross sectional-descriptive study.

Sample Size

The prevalence of *HelicohacterPylori* in Gambia in the 0-36 months age group was 15% (9). Kenya and Gambia are both developing countries in Africa. This prevalence was used to determine the sample size using the following formula:

Andrew Fisher et al [1983]:

$$n \qquad \frac{Z^2(\text{-}a/2) \quad PH\text{-}P)}{d^2}$$

_Where:

n = Estimated sample size.

Z^2 (1- a *12)* = The standard normal deviation corresponding to a confidence interval of 95%(= 1.96).

p = The estimated prevalence of Helicobacter Pylori from one study expressed as a proportion as a decimal percent (0.15).

d = The desired precision level set at ± 0.05

Substituting in the above formula:

$$n = \frac{1.96^2 \text{ x } 0.15(1 - 0.15)}{(0.05)^2}$$

n = 195

- Sampling method

All the well baby clinics in Nairobi were listed dov\n in each of the eight divisions and then random sampling was done for each division using a computer programme -SPSS- selecting one health facility per division. From the eight centres so obtained a further random selection was done to get four study centres and these were Amref Kibera. Mater Hospital. Kayole health centre and Dagoretti health centre.

Consecutive sampling of clients meeting the inclusion criteria was done until the sample size was achieved. The clients were recruited as they walked in without categorizing them into age groups so long as they fulfilled the inclusion criteria Forty eight clients were selected from each of the four centres named above. Approximately sixty five subjects were selected from the following age groups: - birth to 12months, 13months to 24months. and 25 months to 36 months, where possible This was to ensure an adequate representation across the categories.

Study group definition

Children less than 3 years of age

- Data Collection

The investigator recruited those children presenting to the well baby clinic who fulfilled the inclusion criteria. Their parents were given information on the study and signed consent obtained. Demographic data was recorded in a coded closed questionnaire (Appendix II)

A physical examination was done on the child and stool samples were collected in plastic polypot containers provided to the parent. The pohpots were carried in a cooler and transported to the department of paediatrics laboratory where they were stored frozen (at -20°C to -80°C) until tested. Children who were unable to provide the stool specimen at the site were allowed to go home with the polypot and mother asked to bring a stool

specimen to the health center the next day so long as the specimen was collected within 24 hours(the antigen was v iable for 24 hours).

Whole blood from a prick on the left hand middle finger tip of the mother was used to do the test at the site of data collection for those w ho accepted.

Laboratory Procedure:

a} Stool antigen test for the child.

The Rapid Strip HPSA (Meridian Diagnostics, Ohio) test utilises a monoclonal anti-H. Pylori antibody. It's based on a lateral flow chromatography technique that detects H. Pylori antigens in stool. The specimen was thawed and mixed as thoroughly as possible prior to sampling. The test kit used in this study had a sensitivity of 96.1% and a specificity of 90.6 %(25).

1. One ml. of sample diluent was transferred into a test tube or vial (diluent provided in the kit).
2. With a wooden applicator a stool sample portion of approximately 5-6mm size was added into the 1ml. of diluent and shaken gently.
3. When the solid particles had settled for about three minutes. 500 microliters of supernatant was transferred to another test tube with a pipette.
4. The reaction strip was dipped in the second test tube with the arrow pointing to the bottom
5. The results were read after exactly 5 minutes in the white area.

Negative test result: Only one blue coloured band (control line) appeared across the white central area of the reaction strip. H.Pylori antigens are absent or below the level of detection.

Positive test result: In addition to the blue band, a distinguishable Pink-Red band (test-line) also appeared across the white central zone of the reaction strip A positive line indicates that there are detectable H. Pylori antigens in the specimen.

Invalid test result: The blue band (control line) was absent, with or without a visually detectable pink-red band (test line).

b) Serology test: Acu-check H. Pylori test for the mother.

This was a rapid chromatographic immunoassay test for the detection of Helicobacter Pylori antibodies in whole blood.

The test strip, specimen, buffer, and/or controls were allowed to equilibrate to room temperature (15-30°C) prior to testing.

The tape was peeled off from the test card, and stuck to the test strip in the middle of test card w ith arrows pointing down on the test card.

Using a lancet the client's skin on the left hand middle finger tip was punctured and allowed 2 hanging drops of whole blood to fall onto the "specimen pad" of test strip, then 1 drop of buffer was added and the timer was started.

Results were read at 10 minutes after starting the test.

Negative: Only one red line appeared in the test region

Positive: Two distinct red lines appeared. One line was in the control region and another line was in the test region.

The test kit used in this study had a sensitivity of 93.0%, a specificity of 89.2 % (4S).

Data Analysis

Data collected from the study was entered in the computer database for management. The data was analysed using the standard software package SPSS (Statistical Package for Social Sciences).

Data was summarised into frequency tables, charts and graphs. The prevalence of H. pylori was computed according to the age. Correlates of H.pvlori were evaluated by a comparison of proportions of children with and without infection using chi-square test and Fischer's exact test as appropriate.

Ethical Considerations

1. A written approv al from the Ethical and Research committee of the Kenyatta National Hospital was obtained before embarking on the study.
2. A written consent from the Ministry of Health. Nairobi City Council and from the Private institutions was also obtained before starting the study.
3. A signed consent from the parent after full disclosure of the study protocol was obtained (Appendix I).
4. All the information and results obtained remained confidential.
5. Patient specimens may contain infectious agents and thus were handled and disposed of as potential biohazards (glov es w ere worn when

handling the specimens and the stool samples were then disposed with other immunology laboratory infectious waste).

6. The parents of the children who had H.Pylori in stool were advised that in this age group the bacteria was less pathogenic but as the child grew older and should he/she develop chronic(recurrent) abdominal pain they should visit the paediatric gastroenterology clinic in Kenyatta National Hospital.
7. Mothers found to be positive for H.Pylori and had symptoms of gastroduodenal disease were referred to the adult gastroenterology clinic at Kenyatta National Hospital. However those without symptoms had the natural history of the infection explained to them.

STUDY RESULTS

Description of study population

The study was carried out between 1st October and 3 I st December 2004 both dates inclusive. The clinics were visited between 8 am and 9 am during the weekdays. Out of a total of 375 children given polypots only 215 returned stool samples. Twenty samples were rejected due to various reasons: nine had watery stool, six had missing labels and five had indeterminate results on the test strip. Therefore only 195 children were analysed in the study.

Table 1. Age distribution of the study population (n=!95)

Age group (months)	No.of cases	(%)
0 - 6	34	(17.4)
7 - 12	46	(23.6)
13 - 18	33	(16.9)
19 - 24	39	(20.0)
25 - 30	7	(3.6)
31 - 36	36	(18.5)
TOTALS	195	(100)

Of the study subjects males were 103/195 (52.8%) while the females were 92/195 (47.2%), giving a male to female ratio of 1.1: 1. The mean age was 17.7 months, median 16months (range 2 weeks to 36 months).

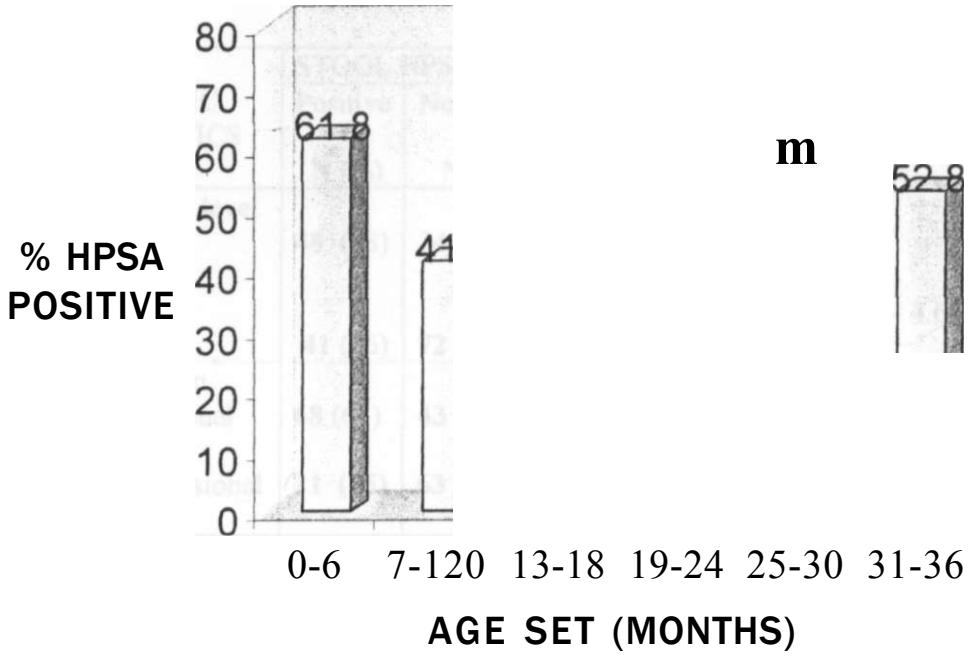
Prevalence of Helicobacter Pylori

Of the 195 children recruited for the study 89/195 were found to have the antigen for Helicobacter pylori positive in their stool. The prevalence of H.Pylori in children less than three years was 45.6% (95% CI= 40.6 - 50.6).

Table 2 : Prevalence of Helicobacter Pylori by age

Age group (months)	NO. of cases	HPSA Positive	
	N	N	(%)
0 - 6	34	21	(61.8)
7 - 12	46	19	(41.3)
13 -18	33	9	(27.3)
19-24	39	16	(41.0)
25 - 30	7	5	(71.4)
31-36	36	19	(52.8)
TOTALS	195	89	(45.6)

Fig 1. Prevalence of Helicobacter Pylori by age



The mean age for the children with HPSA was 17.7 months with a median of 15 months (range 2 weeks to 36 months).

Prev alence among the male subjects was 46/103 (45%) and that among the females was 43/92 (46%). The difference between the sex was not statistically significant (p = 0.776). There was also no difference in the age.

Associations of Helicobacter Pylori and some correlates

Table 3. Association of Helicobacter Pylori and socio-economic status

SOCIOECONOMIC CHARACTERISTICS	STOOL HPSA Positive N (%)	Negative N (%)	Total N %)	P - value	OR (confidence interval)
Mothers education level					
Primary	**48** (58)	34 (42)	**82**(100)		
				0.001	2.48 (1.33-4.64)
Post-primarv	**41** (36)	72 (64)	**113**(100)		
Mothers occupation					
Unemp loved/manual	**68 (61)**	**43** (39)	**111**(100)		4.74
				0.001	(2.43-9 32)
Whitecollar/professional	**21** (25)	**63** (75)	**84** (100)		
Family income / month					
< 50.000 ksh	**72** (61)	47 (39)	**119**(100)		5.32
				<0.001	(2.64- 10.80)
> 50.000 ksh	**17**(22)	**59** (78)	76(100)		

Measures of social economic status that were determined were mother's education, their occupation and family income per month.

In this study 58% of the children whose mothers had only primary education or less were HPSA positive as compared to 36% whose mothers had post-primary education, This was statistically significant (p=0.001). A child whose mother had a lower level of education had a two fold increased risk of getting H. pylori infection as compared to one whose mother had post-primary education

Children whose mothers were unemployed 68(61%) had a 4.7 fold increased risk of having positive stool results as compared to mothers who had white collar jobs (p=0.001, OR=4.74 (2.43-9.32).

The range of family income per month was very wide (KShs 1,000- 250,000) and when stratified those who had low income had a five fold increased risk of getting the infection.

Table 4. Association of Helicobacter Pylori and household characteristics

HOUSEHOLD CHARACTERISTICS	STOOL HPSA		Totals N (%)	P=value	OR (CI 95%)
	Positive N (%)	Negative N (%)			
Place of residence					
Slum*	**63** (62)	**38** (38)	**101** 100)	0.001	4.34 (2.27-8.33)
Other	**26** (28)	**68** (72)	**94** (100)		
Type of house					
Semi-permanent	**62** (62)	**38** (38)	**100**(100)		4.11 (2.16-7.86)
Permanent	**27** (28)	**68** (72)	**95** (100)	0 001	
Sharing of bed*					
Own bed	**17** (24)	**56** (77)	**73** (100)	0.001	0.22 (0.11-0 44)
Shared bed	**71** (58)	**51** (42)	**122** 100)		
Number of rooms in the house Excluding bathrooms/kitchen					
1	**59** (58)	**42** (42)	**101**(100)	0.001	3(1.60-5.64)
> 1	**30** (32)	**64** (68)	**94** (100)		

Children living in the slums 63/101 (62%) (p= 0.001, OR =4.34 (2.27-8.33)) and living in semi permanent houses 62/100 (62%) (p=0.001, OR = 4.11(2.16-7.86) had a four fold increased risk of getting the infection and this w as statistically significant

Most children shared their beds w ith their mother and 71/122 (58%) of them had H.pylon in stool and this was statistically significant (p = 0.001),

We found that of those children liv ing in crowded houses (1 room per house) 59/101 (58%) had H.Pylori in stool as compared to those who stayed in a house w ith more than one room 30/94 (32%). This was statistically significant (p = 0.001),

slum: a heavily papula/eel urban area characterised bv substandard, poor housing and squalor

sharing of bed: mother sharing bed with child

Table 5; Associations between Helicobacter Pylori and method of stool disposal

SANITARY TOILET FACILITIES	STOOL HPSA		TOTALS	P value	OR (CI= 95%)
	Positive N (%)	Negative N (%)			
Toilet facilities					
Inside house	**21** (25)	**62** (75)	**83** (100)	0.001	0.22 (0.11-0.43)
Outside house	**68** (61)	**44** (39)	**112** (100)		
If outside is it:					
Flush toilet	**23** (43)	**30** (57)	**53** (100)	0.007	0.24 (0.10 -0.43)
Pit latrine	**45** (76)	**14** (24)	**59** (100)		
Where do you dispose of the Childs excreta					
Flush toilet	**38** (34)	74 (66)	**112** (100)		
Pit latrine	**26** (61)	17 (40)	**43** (100)	0.001	
Other*	**25** (63)	15 (38)	**40** (100)		

Majority of the children who had the H. Pylori in stool 68/112 (61%) had toilet facilities which were outside as compared to those who had toilet facilities inside 21/83 (25%) and this was statistically significant (p = 0.001). Of those who had toilet facilities outside 45/59 (76%) of the children used pit latrines while 23/53 (43%) used flush toilets and this was also statistically significant (p = 0.007).

When ev aluating where the child's excreta was disposed, pit latrine and flush toilet were compared and the OR = 0.34 (0.15 - 0.74) while looking at flush toilet and •other" the OR = 0.54 (0.38 - 0.77).

- ***Other: places like into the sewer, a nearby river or Just on the grass.***

Table 6: Associations between Helicobacter Pylori and Childs feeding pattern

CHILD FEEDING HABITS	Stool HPSA		TOTALS	P value	OR (CI=95%)
	Positive N (%)	Negative N (%)			
Is child still breastfeeding					
Yes	**58** (50)	**59** (50)	**117**(100)	0.114	1.49 (0.8-2.78)
No	**31** (40)	**47** (60)	**78** (100)		
If yes duration of exclusive breastfeeding:					
< 4 months	**45** (52)	**41** (48)	**86** (100)		1.78 (0.61 -
> 4 months	**8** (38)	**13** (62)	**21** (100)	0.166	5.30)
Premastication of child's food by mother;					
Yes	**13** (52)	**12** (48)	25 (100)	0.525	1.34 (0.54-3.36)
No	**76** (45)	**94** (55)	**170**(100)		

Breastfeeding, duration of breastfeeding and premastication were not associated with H.Pylori infection

The mothers who were still breastfeeding at the time of the study were 55% (107/195) of those recruited into the study. This was to assess if breastfeeding exclusively was protective. For the children who had stopped breast feeding it was assumed that they were already on the family diet where by the preparation of the food was influenced by a number of hygienic factors and also there was increased risk of fecal oral route transmission.

Table7: Association between Helicobacter Pylori and Mothers serology for H. Pylori

MOTHER'S H. PYLORI SEROLOGY	STOOL HPS A		
	Positive N (%)	Negative N (%)	Total **N (%)**
Positive	**48** (49)	**49** (51)	**97** (100)
Negative	**16**(55)	**13** (45)	**29** (100)
Total	**64** (51)	**62** (49)	**126**(100)

P value = 0.373 OR (CI 95%) = 0.80 (0.32 - 1.98)

Out of the 195 mothers who had their children recruited into the study only 66%(126/195) consented to their H.Pylori status being checked. There was no significant association between mother's serology and their children's H.Pylori stool prevalence.

MULTIVARIATE ANALYSIS

Table 8: Logistic regression

Variable	p value	OR (CI = 95%)
mothers education	0.183	0.6(0.25-1.2)
Mothers occupation	0.873	0.9(0.7-1.6)
[r]amil\ income	1.008	: i> < i 6 -2.9)
Place of residence	0.314	3.0(0.3-28)
Type of house	0.83	0.8(0.1-6.4)
Sharing of bed	0.776	0.8 (0.3 -2.3)
Toilet facilities	0.410	1.5 (0.6-3.6)

Using logistic regression, family income was the only variable that remained significantly associated with the presence of H Pylori infection after controlling for the other variables in the model

DISCUSSION

This study revealed a very high prevalence rate of Helicobacter Pylori of 45.6% (89/195) in the under three years which mirrored that of many other countries in the developing world. A study carried out in Nigeria among children aged 6months - 2 years showed a seroprevalence of 57 % (8). In a study done in Gambia using serology among children less than five years of age the prev alence was between 15 -46% (9). At a Bangkok orphanage the prevalence was 74% among children aged 1 - 4 years (10). In contrast a study in the United States found that the prevalence of H. Pylori infection was much lower with only 5% of the the under 5 years old positive for H Pylori (6. 7)

Our study results compare favourably with a study done in Cameroon where they used the same method (stool H. Pylori antigen) in asymptomatic children and found a prevalence of 37.5% for those less than three years of age (49). In both studies the prev alence may have been low because the stool antigen test indicates active infection while the other studies (8,10) may hav e had a high prevalence because they used serology which test antibodies (immunoglobulin G) which continues to be positive for several months after the organism has been eradicated, leading to decreased snecificity(27).

We found that the prevalence in the age groups 0-6months (61.8%) and 7-12 months (41.3%) was high; and then declined in ages 13-18months (27.3%) and 19-24 months (41%); and then rose again in ages 25 -30months (71.4%) and 31-36 months (52.8%). Similar trends were found in Egypt when they studied children less than 3 years. Their ov erall prev alence was 10% with age specific prev alence ranging from

5% -15%. The prevalence of the age groups 6-1 lmonths(14%),12-17months(15%) was high and it declined in the age groups 18-23months(5%),24-29 months(7%) and rose again in the age group 30 -35 months to 12% (50). A cohort study in Peru looking at children less than 2 years and used the C13 Urea breath test, the prevalence rates were seen to decrease from 71% at 6 months to 48% at 18 months (13). In a study in Nicaragua looking at children with persistent diarrhoea and using the CI3 Urea breath test, a decline was seen from 91% in less than 12 months to 65% in those 13 - 65 months (51)

Many theories have been used to explain the trend that was observed in this study and other studies done on children. It is generally thought that following the acquisition of H Pylori in the absence of treatment, infection would persist through out life however based on the seroepidemiologic studies in adults and children in both the developing and developed countries it appears that spontaneous elimination of H. Pylori infection may occur (50). Loss of infection might be related to the widespread use of antimicrobials drugs that are used for other common infections (52).

It is also thought that in young children relative protection from the pathogenic effects of H.Pylon infection may be derived from a predisposition to T-helper cell type ,TH-2 rather than a T-helper cell type. TH-1 immune response. Relative to the TH-1 response which is associated with release of proinflammatory cytokines, the TH-2 response is dominated by anti-inflammatory effects. This vary ing immune response of the host may make the gastrointestinal tract less accommodating to the H.pylori

survival and this may lead to spontaneous clearance of H.Plori in young children, a rare event in the adults (47). This also explains decline that was seen in this study

This study showed that sex was not a significant factor in the prev alence of H. Pylori, which is similar to other findings in other studies done in the Gambia. Peru and Canada (9, 13. 52). This finding could be attributed to the fact that both the boy and girl child are exposed to the same environment.

Education and occupation are closely linked to socioeconomic status (53). This study showed that there was a high prevalence of H.Pylori in children whose mothers had a low education level and with mothers who were unemployed or were manual workers and this was statistically significant. Several studies have also shown an inverse relationship between the H.Pylori prevalence and educational level of the population studied (17). In Saudi Arabia H Pylori infection in college graduates was 54% and in non graduates 77% (10). Study in Bangladesh looking at children aged 1 -99 months concluded that maternal education may be protective and may operate through some undetermined proximate behav ioural determinants (54).

Low socioeconomic status has been associated w ith a high prev alence of H.Pylori in many studies worldw ide in North America, South America. Europe, Asia and also Africa (15. 51). The association between infection with H.Pylori and socioeconomic status in this study is demonstrated using the variables of mother's level of education, mother's occupation and family income. There is a strong relation between these variables and when put in a logistic regression model (multivariate analysis), family income was the only significant factor that influenced infection after controlling for

the other variables. Family income determines the level of education and also where one resides. Those living in the slums live in very crowded conditions and these places have poor sanitation facilities.

In this study there was an increased risk of acquiring the infection for those who shared beds. Though in this study the serostatus of the mother was not matched with that of the child, an association between bed sharing and H.Pylori infection was demonstrated by Duggan et al. in a study which showed a "dose-response" effect, as the risk of infection increased significantly with the length of time of childhood bed-sharing. This observation further supports the importance of close personal contact for the transmission of H.Pylori infection (55.56). Those who lived in a one roomed house, staved in the slums and in semi permanent houses also had an increased risk of acquiring the infection H Pylori infection tends to cluster in families and in people living in crowded close conditions (19). For this reason it is widely believed that impoverished children may acquire H.Pylori in this manner (3. 17, 19, 57).

This study did not show any association between prevalence of H. Pylori and the source of drinking water. This may have been because 99 % of subjects used tap water which all comes from one source, the Nairobi City council. Klein in a study in Peru demonstrated an association between the prevalence of H.Pylori in the children and the source of drinking water. He found that children in Peru using municipal water were three times more likely to acquire H Pylori infection than were the children using an alternative source of water and this was because studies on their municipal water indicated that it had been contaminated (faecal) with H.Pylori (21)

Having a toilet outside, a pit latrine or communal toilets were all associated with a higher prevalence of H. Pylori infection and these were all statistically significant. This could be explained by the poor state of hygiene. It is harder to keep a communal pit latrine clean at all times. Poor hygiene which includes poor fecal matter disposal contributes to the spread of diseases especially those that are spread through the fecal - oral route. In Kenya most communities have believed that the young child's fecal matter is safe, consequently not much effort is made to ensure safe disposal of the child's faeces.

Breastfeeding was found not to be statistically significant nor was the duration of exclusive breastfeeding. This was not in keeping with some of the other studies that had been done Okuda in his study showed that breastfeeding protects from H. Pylori infection in early childhood. He found that the mean period of breast feeding of those who were H.Pylori positive was 5.3 mo while that for the negative group was 7.8 mo ($p=0.02$). He speculated that breastfeeding offers some protection from H.Pylori infection in early childhood due to the high levels of lactoferrin in the human milk (22. 23. 24). In this study most mothers' did not practise exclusive breast feeding for six months as recommended by the Kenyan Minislv of Health guidelines on infant feeding. In this study though the adequacy of water was not assessed, water supply in the slums is usually limited and clean running water to always wash hands before breast feeding may be a problem. Kitvvaga et al in his study showed that if mothers did not w ash their nipples and hands prior to breastfeeding, horizontal transfer of infection may occur (58.59).

This study showed that majority of the mothers did not premasticate the food for their children .Most of the mothers mashed the food or passed it through a sieve before giving it to the babies. They considered premastication to be an outdated activity. The prevalence of H. Pylori compared to the premastication of food was not statistically significant. A study in Bolivia found that consumption of premasticated food was not statistically significant in the transmission of H.pylori from mother to child (60). A maternal -child transmission via an oral-oral route was inferred by one study in West Africa where the mothers did premasticate the food for their babies (54) A case control study in Burkina Faso reported that premastication of food by H.Pylori positive mothers to feed their infants constitutes a 3-fold greater risk to the infants as compared w ith the risk for the controls (54)

H.Pylori occurs in clusters and it is for this reason that it is widely believed that impoverished children may acquire H.Pylori through contact with their mothers (16.17) H Pylori serology status of the mothers of children recruited in this study w as compared to that of their child's H.Pylori status.

Most mothers in our study declined to have their blood taken to test for H.Pylon despite adequate explanation. They feared that their HIV status was being evaluated and hence many declined the test. The sample size (66% of expected) was not statistically powerful to conclude that mother's serology status was not an associated factor. So our results were inconclusive.

In a study in Brazil. Mitchell found no correlation between the seropositivity of the mother and that of the child (16). In a study in Japan, they found that the prevalence of seropositivity in children Ii\ing with infected mothers was five times higher than in

children living with negative mothers. This confirmed that infection occurs in clusters in families and also that there was evidence of transmission of infection from mother to child (61).

CONCLUSIONS

1. The prevalence of Helicobacter Pylori is 45.6% in children less than three years as seen in Nairobi Province among children attending the health facilities.

2. Family income is associated with H.Pylori infection. Low income families have a higher predisposition to H.pylori infection as compared to the high income families.

RECOMMENDATIONS

1. Improving environmental sanitation(improving the toilet facilities) and providing better housing standards at the community level would help in the reduction of acquisition of H Pylori infection in childhood.

2. The children with H.Pylori infection should be followed up so as to further describe the natural history of the disease in our set up (the characteristics of the children who end up having gastroduodenul disease).

STUDY LIMITATIONS

1. Many mothers declined to have their blood drawn for the serology test for H. Pylori. This decreased the number of the mothers analysed in the study and thus did not have statistical power to truly say that mothers' H.Pylori status was not associated with the child's H. Pylori status.

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APPENDIX I

CONSENT FORM FOR STUDY PARTICIPATION.

PREVALENCE OF HELICOBACTER PYLORI IN CHILDREN LESS THAN THREE YEARS OF AGE.

Study Number:

Hospital Number:

Investigator

Dr. Langat Agnes

24 hour contact telephone number: Dr. Langat Agnes 0722871602

Ethical Rev iew Committee Chairperson: Professor K.M. Bhatt 726300 Nairobi.

We are requesting you and your child to participate in a research study. The purpose of this consent form is to giv e you the information you will need to help you decide whether to participate in this study or not. You are free to ask questions about what we will do. your rights as a volunteer, the risks or benefits or anything else about the study or this form that is not clear. When all your questions have been answered, you can then decide whether to participate in the study or not.

Introduction

Helicobacter Pylori is among the most common infection in humans and has been recognised as a major cause of various gastroduodenal diseases. There is increasing evidence that H.pylori is acquired in early childhood and infects more people in dev eloping countries than industrali/ed countries.

The purpose of this study is to investigate H.pviori infection among children who have not yet started going to school. This will help us see how the bacteria are transmitted and how to prevent this infection in future.

Procedure

I will get some stool from your child with your help for the detection of Helicobacter Pylori.

I will take a drop of blood from a finger prick done on you (the mother) to test it for antibodies against Helicobacter P\lori.

Risks and discomforts of participating in the study.

There is no risk for those who participate in the study. You (the mother) shall undergo some slight discomfort during the finger prick procedure. Your child shall undergo no discomfort at all.

Benefits of participating in the studv

If you and/or your child are found to have any symptoms of peptic ulcer disease or dyspepsia you shall be offered free consultation and advice on treatment.

V oluntary participation

Your participation in this study is voluntary. You are free to decline consent or withdraw from the study at any time without any adverse effects. Participation in this studv entails no financial benefit.

Confidentiality

All of the information obtained will be held in the strictest confidence and no information of any kind by which you or your child may be identified will be released or published.

Ethical Consideration

This study has been approved by the Ethical Review Committee of the Kenvatta National Hospital and by the Ministry of Health.

Do you have any questions? Do you agree to participate[9]

Si "nature of Investigator Printed Name Date

Participant

The study described above has been explained to me. I agree to participate in the study. I have had a chance to ask questions. I have been told that if I have any further questions about the research or about my rights as a subject I can ask the inv estigator listed above. I understand that I am free to withdraw from the study at am time.

Signature of mother Printed Name Date

Signature of w itness:

If thumbprint used Printed Name

APPENDIX II

QUESTIONNAIRE

SOCIO- DEMOGRAPHIC DATA

ID NO STUDY NO

Age (months)

Sex

1. Fathers education: i. primary (0)
ii. Secondary (I) ( )
iii. post-secondary (2)

2 Mothers education : i. primary (0)
n. secondary (1) ( )
iii. post-secondaiy (2)

3 FATHERS OCCUPATION:_____( )

4 MOTHERS OCCUPATION:_____( )

5. FAMILY MONHTLY INCOME
KSH

6. PLACE OF RESIDENCE: SLUM(O) OTHER (1) ( )

7. TYPE OF HOUSE : SEMI-PERMANENT (0) PERMANENT (1) ( )

8. (a) SHARING OF BEDROOM: OWN BEDROOM (0)
SHARED BEDROOM (1) ( )
(b) SHARING OF BED: OWN BED (0)
SHARED BED(l) ( )

9. HOUSEHOLD SIZE (PEOPLE PER ROOM)
NO OF PPLE IN HSE
NO OF ROOMS IN HSE EXCLUDING BATHROOMS/KITCHEN

10. NUMBER OF CHILDREN: ONE(O) TWO (1) THREE (2)>FOUR (3) ( )

11. NUMBER OF ADULTS : ONE(O) TWO (1)THREE(2)> FOUR (3) ( )

12. WATER SUPPLY: TAP (0) WELL(l) BOREHOLE(2) RIVER (3) ( )

13. TOILET FACILITIES: INSIDE HSE (0) OUTSIDE HSE(1) ( )
If outside is it: FLUSH TOILET (1) PIT LATRINE (2) ( )
Where do you dispose of the childs excreta: FLUSH TOILET(1)
PIT LATRINE (2) ( )
OTHER (specify)

14. TOILET FACILITY : COMMUNAL(O) FOR FAMILY ONLY(1) ( )

15. IS CHILD STILL BREASTFEEDING : YES (0) NO(1) ( )
IF YES. DURATION OF EXCLUSIVE B/FEEDING IN MONTHS

16. PREMASTICATION OF CHILDS FOOD BY MOTHER YES(0) NO (1) ( )

CLINICAL DATA

I. STOOL HPSA : POSITIVE (0) NEGATIVE (1) ( )

2 MOTHER S H. PYLORI SEROLOGY : POSITIVE (0) NEG(1) ( )

C35KJ

KENYATTA NATIONAL HOSPITAL
Hospital Rd. along, Ngong Rd.
P.O. Box 20723, Nairobi.

Tel: 726300-9
Fax: 725272
Telegrams: "MEDSUP", Nairobi.
Email: **KNHplan@Ken.Heaithnet.org**

Ref: KNH-ERC/01/2354 **Date: 22 July 2004**

Dr. Agnes Langat
Dept. of Paediatrics
Faculty of Medicine
University of Nairobi

Dear Dr. Langat

RESEARCH PROPOSAL "THE PREVALENCE OF HELICOBACTER PYLORI IN CHILDREN LESS THAN THREE YEARS OF AGE AS SEEN IN NAIROBI PROVINCE" (P76/6/2004)

This is to inform you that the Kenyatta National Hospital Ethics and Research Committee has reviewed and **approved** the revised version of your above cited research proposal for the period 22 July 2004 - 21 July 2005. You will be required to request for a renewal of the approval if you intend to continue with the study beyond the deadline given.

On behalf of the Committee, I wish you fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of database that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Yours sincerely,

PROF. A N GUANTAI
SECRETARY. KNH-ERC

Cc Prof. K M Bhatt, Chairperson, KNH-ERC
The Deputy Director (C/S), KNH
The Dean, Faculty of Medicine, UON
The Chairman, Dept. of Paediatrics, UON
CMRO
Supervisors: Prof. E Ogutu, Dept. of Medicine, UON
Dr. D Simiyu, Dept. of Paediatrics, UON
Dr. R Kamenwa, Dept. of Paediatrics, KNH

MEDICAL OFFICER OF HEALTH
TELEGRAMS: "MUNICIPALITY" NAIROBI
CITY HALL
Tel: 224281 Ext. 2108

Public Health Department

P.O BOX 30108
NAIROBI.

REF: PHD/MOH/R.l VOL 1 (19) **DATE:** 25th August 2004

DR. AGNES LANGAT
DEPARTMENT OF PAEDIATRICS
UNIVERSITY OF NAIROBI
P. O. BOX 19676
NAIROBI.

RE: RESEARCH STUDY

This is in reference to your letter dated 3rd August 2004. I am pleased to inform you that your request to carry out research in the following sites has been accepted.

1. Kayole Health Centre
2. Karen Health Centre
3. Nairobi South B Clinic
4. Ngong Road Health Centre
5. Dagoretti Health Centre
6. Loco dDspensary
7. Kibera Health Centre

Note that this is however, subject to payment of Ksh. 1200/= (one thousand two hundred) research fee.

By a copy of this letter, the District Medical Officer of Health of the concerned districts are requested to accord you the necessary assistance.

DR. D.M. NGUKU
MEDICAL OFFICER OF HEALTH

CC. District Medical Officer of Health - Embakasi
Dagoretti
Central
Langata
Makadara

i i I h e
Mater Hospital
we care more

PO.Box 30325 00100-Dunga Road, Nairobi, Kenya
Telephone: (254) (020) 531199,556010,558179,554780,557552
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Emergency Hotline: 351269
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Website: www.raaterkenya.com

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12th October 2004

Dr. Langat
Senior House Officer
Dept. of Paediatrics
UNIVERSITY OF NAIROBI

Dear Dr. Langat,

The Standards and Ethics Subcommittee of the hospital sat and reviewed your research proposal.

I am glad to notify you that your research proposal titled ***"The prevalence of Helicobacter Pylori in Children less than 3 years of age as seen in Nairobi Province" was*** approved without amendments.

You are now at liberty to commence your recruitment at the hospital.

The hospital anticipates to receive a copy of your research at completion.

Tbank

DR. C. F. OTIENO
For: Chairman
MEDICAL ADVISORY COMMITTEE

CC 1 Acting CEO - Mrs Juma
2 Medical Director - Dr. Dolan
3. Acting Matron - Sr. Gachathi