

PREVALENCE OF HELICOBACTER PYLORI IN CHRONIC
RENAL FAILURE PATIENTS WITH DYSPEPSIA


BY

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DECLARATION

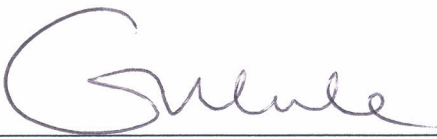
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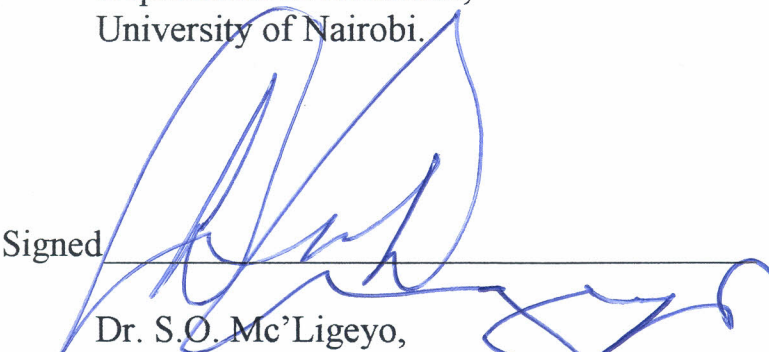
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DEDICATION

- To my husband Hosea who stood with me throughout the M. Med program and to our children Timothy and James.
- To my parents James and Phyllis who taught me the value of hard work.

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LIST OF ABBREVIATIONS

- CLOtest - *Campylobacter* like organism test
- CRF - Chronic renal failure
- HLA-DR - Human leukocyte antigen-DR
- H₂ receptor - Histamine 2 receptor
- KNH - Kenyatta national hospital
- IL-1 - Interleukin 1
- IL-2 - Interleukin 2
- MALT - Mucosal associated lymphoid tissue
- PUD - Peptic ulcer disease
- TNF α - Tumor necrosis factor alpha
- UON - University of Nairobi

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ABSTRACT

Background: The aim of the study was to determine the prevalence of *H. pylori* in dyspeptic patients with chronic renal failure.

Methods: One hundred and fifty four patients with dyspepsia, in two groups of seventy-seven patients each were studied. The patients were divided on the basis of presence or absence of CRF. *H. pylori* was tested for using the biopsy urease test and histology. Patients were considered to have *H. pylori* if they tested positive on both tests.

Results: The prevalence of *H. pylori* in CRF was 53.2%. There was no statistically significant difference between the prevalence of *H. pylori* in CRF patients from that observed in the controls. Patients with endoscopically proven PUD had a very high prevalence of *H. pylori* (87.3%) regardless of their renal function.

Conclusion: Dyspepsia in patients with or without CRF is due to multiple causes and just over 50% is attributable to *H. pylori*. The prevalence of *H. pylori* in dyspeptic CRF patients is similar to that in dyspeptic patients with normal renal function. We recommend that all patients with dyspepsia should routinely undergo endoscopy and *H. pylori* studies before treatment for the dyspepsia is started.

INTRODUCTION AND LITERATURE REVIEW

Dyspepsia is a common problem in patients with chronic renal failure (CRF) and is due to multiple factors including uraemia and/or various forms of peptic ulcer disease (PUD). Dyspepsia secondary to uremia usually improves with dialysis but that due to PUD does not (1).

Peptic ulcer disease (PUD) occurs in up to one fourth of patients with chronic renal failure (1). The predisposition for uraemic patients to peptic ulceration has been well studied. In 1934 Jaffe and Lanig (2) reviewed 196 autopsies of patients dying of CRF and reported an incidence of gastrointestinal lesions in 20% of these patients. Hampers and Schupak (3) reported an ulcer incidence of 11% in a study of 48 patients on haemodialysis. Margolis et al (4) in a prospective study of 45 CRF patients reported duodenitis in 60%, gastritis in 20%, oesophagitis in 13% and Mallory Weiss tear in 2%. Joshi (5) in a local (Kenyatta National Hospital [KNH], Kenya) study found gastritis in 27.5%, duodenitis in 20%, bile reflux in 17%, Oesophagitis in 5% distorted duodenal bulb in 17% and duodenal ulcer in 5% in forty patients with CRF.

Life time PUD prevalence in the general population is estimated to range between 4 – 20% (6), with most studies reporting figures below 10% (7,8). Obviously, this is much lower than that reported in CRF patients.

The pathogenesis of PUD in renal failure is thought to be multi-factorial. Some of the factors implicated in its causation include hypergastrinemia, secondary hyperparathyroidism, drugs and recently *Helicobacter pylori* (*H. pylori*) infection. *H. pylori* is known to be associated with peptic ulcers in the general population (9,10) and there are studies to show that it may be associated with the severe gastritis seen in CRF (11).

Reduced renal clearance and hypersecretion of gastrin lead to a state of hypergastrinemia, which leads to increased production of gastric acid, an aggressive factor in the pathogenesis of peptic ulcer. Although the level of gastrin in these patients tends to be high, their gastric PH is raised as urea is converted to ammonia in the stomach. Hypergastrinemia therefore cannot by itself explain the increased incidence of PUD in CRF. The high gastric urea may be a predisposing factor for colonisation by *H. pylori*, an organism that splits urea to ammonia and carbon dioxide providing a more alkaline microenvironment that protects it from the effects of gastric acid.

Secondary hyperparathyroidism is the other factor thought to play a role in the development of PUD in CRF. In primary hyperparathyroidism, PUD is mediated through hypercalcemia (12), which stimulates gastrin secretion. The gastrin then stimulates gastric acid production. It is worth noting that most

patients with CRF have low calcium levels making it difficult to explain how secondary hyperparathyroidism contributes to the development of PUD in CRF.

H. pylori has been associated with 100% cases of type B gastritis, 95% of duodenal ulcer and over 80% of gastric ulcers in the general population (9,10). Most studies on *H. pylori* have involved patients with normal renal function and little has been done in patients with CRF despite the high incidence of PUD in these patients. The few studies on *H. pylori* in CRF have been inconclusive.

The first study reported in the literature on this subject was by Shousha et al (13) in 1990. They found the prevalence of *H. pylori* in CRF to be 24% compared to 42% in patients with normal renal function. The major draw back with this retrospective study was that the CRF group (n = 50) had endoscopies as a routine pre-transplant requirement and only 17% had dyspepsia while all the controls (n = 120) had dyspepsia. The groups were therefore not comparable and no conclusions can be made from their observations.

In 1991 Davenport et al (14) found the prevalence of *H. pylori* in haemodialysis patients to be 34%. They observed that this did not differ significantly from that they found in healthy age-matched controls, which was 30%.

Conz et al (11) [1992] examined biopsy specimens from 38 haemodialysed patients who had undergone endoscopy for various gastrointestinal symptoms. Forty eight percent tested positive for *H. pylori* and all those who had active chronic gastritis had *H. pylori* infection. They concluded that gastritis in CRF is associated with *H. pylori*. Unfortunately there were no controls in this study and we do not know whether non CRF controls would behave differently.

In 1993, Gladziwa et al (15) investigated 164 patients with different degrees of renal function (group 1—normal function, group 2—CRF with creatinine clearance $> 5 < 90$ ml/min, group 3—CRF on haemodialysis). In this study *H. pylori* prevalence ranged from 34% to 54% and there was no statistically significant difference between the three groups. They concluded that the high urea levels in gastric juice did not seem to be a risk factor for colonisation with *H. pylori*.

Jaspersen et al (16) suggested that uraemic patients seem to be protected against the infection after finding a prevalence of 22.6% in CRF compared to 37% in patients with normal renal function patients. Subsequent studies found the prevalence of *H. pylori* in CRF to be quite high ranging from 50% to 60% (17-19).

The foregoing clearly show that there is need for more work to be done in this area. This study was therefore carried out with an aim to determine the prevalence *H. pylori* in CRF patients and to compare it with that in non-CRF subjects, with the aim of providing a basis for management of dyspepsia in CRF patients at KNH.

HELICOBACTER PYLORI

HISTORICAL BACKGROUND

Curved and spiral organisms have been observed in the stomachs of human and *other* animals for more than a century. Bizzozero (20) found them incidentally in dogs in 1893, later they were found in cats and dogs by Solomon (21). The earliest human study was by Doenges (22) in 1933, who found the bacterium in 43% of stomachs during post-mortem examinations. Infiltration by polymorphs, lymphocytes and plasma cells was seen in association with the bacteria. Doenges was however unable to detect the relationship between the presence of the organism and various gastric diseases. In 1975 Colin-Jones (23) observed spiral gram negative bacilli in 80% of patients with gastric ulcer at endoscopy. In 1979, Warren (24) a pathologist in Perth, Western Australia, noted the appearance of spiral bacteria overlying the gastric mucosa especially over inflamed tissue. He also noted that these organisms were similar to *Campylobacter* and together with Marshall (24) used campylobacter specific methods to attempt isolation. They cultured the first of these organisms in 1982 from 11 patients with gastritis (24). A prospective study was undertaken in which 100 consecutive patients undergoing endoscopy had biopsies taken with correlation of findings with clinical and endoscopic data. During the study, a gram-negative, microaerophilic and catalase positive bacterium was isolated. It was observed that 95% of patients with active chronic gastritis had the

bacterium including all 13 with duodenal ulcer and 14 of 18 with gastric ulcers (25). It is now well known that these organisms are motile gram-negative rods that are oxidase, catalase and urease positive. Originally known as *Campylobacter pyloridis*, the name was changed to *Campylobacter pylori* (26). In 1989, a number of significant morphologic, structural, biochemical and genomic features indicated that these organisms should be placed in a new genus named *Helicobacter* (27).

EPIDEMIOLOGY

H. pylori is now regarded as one of the most common bacterial infections in human beings (28). In studies of healthy blood donors the incidence of antibodies to *H. pylori* appears to be about 20-30%. Patients with symptoms of PUD have higher rates (29). Its prevalence is higher in developing countries than in developed ones. In both situations there is an increase of its prevalence with age so that healthy persons less than 30 years have prevalence rates of approximately 10%, while those over 60 years have rates approaching 60% (28, 30). In a local study by Ogutu et al (31) the prevalence of *H. pylori* was found to be 81.7% in 125 patient with dyspepsia at KNH. A previous study by Lule et al (32) at the same hospital had found a prevalence of 57% in 50 patients with dyspepsia. Maende (33) found the prevalence of *H. pylori* to be 70.5% in adult dyspeptic Kenyan patients with sickle cell disease and 78% dyspeptic controls.

The geographic and social patterns of *H. pylori* are most consistent with faecal-oral transmission although other means such as oral-oral and endoscopy related transmission are also known. No significant non-human reservoir of *H. pylori* has been identified indicating that person to person spread is almost certainly the mode of transmission of the infection. Risk factors include increasing age, socio-economic deprivation, ethnic factors, over crowding and poor hygiene (34,35). Intra-familial clustering of the infection is well recognised and the same strain of organism has been identified in parents and their offspring (36,37). Infection is acquired early in childhood and the high levels in adults reflect childhood infection rates. Risk factors for infection in children include overcrowding, single parent families, attending school in deprived areas, and bed sharing (35,38-40). Acquisition of primary infection is rare in adults but some groups may be at increased risk. These include gastroenterologists and spouses of infected persons, evidence for endoscopic and oral to oral transmission (41-43).

ammonia that provides a more alkaline microenvironment, thus protecting the organism from the effects of gastric acid (55). It also enhances bacterial adherence (58), damages the gastric epithelium by the hydroxyl ions generated by the equilibrium of water and ammonia, and it is proinflammatory (54).

Most *H. pylori*-infected patients do not develop clinical sequelae (59). This may be due to bacterial factors, host factors (including age at infection), and environmental factors. Bacterial factors appear to be most important in that patients with ulcers are more likely to be infected with strains elaborating a cytotoxin, Vac A which is known to cause vacuolation of cultured epithelial cells and gastric damage in mice. All *H. pylori* strains possess the gene encoding for the cytotoxin (vac A) but only 50% have demonstrable cytotoxin activity in vivo. Infected patients with ulcers and or gastric adenocarcinoma are also more likely to be infected with Cag A-positive *H. pylori* strains. Cag A is a protein of unknown function associated with *H. pylori* infection (59).

MICROBIOLOGY

H. pylori is a motile gram negative rod that is oxidase, catalase and urease positive. It measures 2.5 μm by 0.5 μm with short spirals of 1-2 wavelengths. It has 4 unipolar sheathed flagella that show bulbous tips and may show bipolar flagella when dividing (60). The organism requires supplementation with

haematin, starch, serum or charcoal to grow on artificial culture (61). It grows best on chocolate agar under microaerophilic conditions at 37⁰C to produce small smooth transparent colonies in 3–4 days. It produces oxidase, catalase, alkaline phosphatase and hydrogen sulphide (62). Losing its spiral form it assumes coccoid forms in old colonies.

DIAGNOSIS

There are two groups of diagnostic tests:

1. Invasive: Gastric tissue is obtained at endoscopy and used to identify *H. pylori* by culture (63), histology (64) or biopsy urease test (65).
2. Non invasive: These include the urea breath tests (66,67) and serology (68). The use of polymerase chain reaction is being investigated (69).

A gold standard for determining *H. pylori* status has been hard to establish (9).

While culture is 100% specific for infection, sensitivity can be low if optimal conditions are not obtained. Use of at least two techniques selected from culture, histology and biopsy urease test gives high sensitivity and specificity for infection. Excretion of the enzyme urease is the basis of the biopsy urease test and urea breath tests. Serology is ideal for use in epidemiological studies but performance may be reduced in the elderly and cut-offs vary per population.

It is recommended that stated specificities and sensitivities of a commercial kit

should not be relied on unless the kit has been validated in a similar population (70).

DISEASE ASSOCIATIONS

H. pylori has been implicated in the pathogenesis of several gastric disorders e.g type B gastritis, gastric ulcer, duodenal ulcer, duodenal gastric reflux, non-ulcer dyspepsia, gastric adenocarcinoma and gastric mucosal associated lymphoid tissue (MALT) B cell lymphoma. Although *H. pylori* infection is often asymptomatic essentially all infected persons have gastric inflammation. Some patients develop transient infection after exposure to the organism, while others develop chronic superficial gastritis. In the absence of anti-microbial therapy, this process persists for life. Some patients then go on to develop some of the conditions mentioned above.

***H. pylori* and gastritis:** It is now generally accepted that *H. pylori* causes type B gastritis (9,28,71). Many studies have confirmed the presence of *H. pylori* in type B gastritis (72-76). Two human subjects who intentionally ingested *H. pylori* reportedly had an intense inflammatory response with abundant neutrophils, first in the antrum and then in the body of the stomach (77,78). In one, the infection and inflammation resolved spontaneously while the second subject went on to develop chronic gastritis (77). Strong indirect evidence that

the organism causes gastritis comes from studies in which antimicrobial agents were administered to subjects with *H. pylori* gastritis. There was a clear relation between the suppression or eradication of the organism and the resolution of the gastritis (79-82). Type A gastritis has not been causally associated with *H. pylori* and studies have reported very low prevalence rates (83,84).

***H. pylori* and duodenal ulcer:** There is a strong link between *H. pylori* and duodenal ulcer. The bacterium has been isolated in 95-100% of patients with duodenal ulcer (9, 71). A number of studies have shown an increase in basal and maximal gastric acid output following *H. pylori* infection (84-87) while *H. pylori* eradication reverses the process (87,88). The increased acid mediates duodenal ulceration and gastric metaplasia. Spread of the organism to the duodenum leads to duodenitis and eventually ulceration. Eradication of infection results in high cure rates and very low recurrence rates of duodenal ulcer (89-94).

***H. pylori* and gastric ulcer:** *H. pylori* is associated with over 80% of gastric ulcers, the rest being related to non-steroidal anti-inflammatory drugs (NSAID) use (9,71). Cure has been reported after eradication of infection (95). The role of *H. pylori* in pathogenesis of gastric ulcer is still unclear but its urease activity

might be a factor that breaks down the mucosal barrier, initiating the ulcerative process.

***H. pylori* and non-ulcer dyspepsia:** Non ulcer dyspepsia is a condition whereby patients present with classical symptoms of PUD but there is no definite ulcer crater. It is a diagnosis of exclusion after pancreatic and gall bladder diseases have been ruled out. Its pathogenesis is poorly understood and treatment has often been disappointing. A high incidence of *H. pylori* has been reported (96-99) and it has also been noted to coexist with chronic antral gastritis in some reports with rates of up to 70% (100, 101). Some clinical trials have reported improvement after eradication of the infection (102).

***H. pylori* and gastric carcinoma:** *H. pylori* is frequently found in association with gastric carcinoma and pre-cancerous lesions (103-107). Early reports of gastric spiral organisms actually concerned patients with gastric cancer (108,109). Marshall and associates (110) found 4 patients with *H. pylori* in biopsies of 5 patients with gastric cancer. In Kenya, Lachlan et al (111) documented association of the organism in rural patients with chronic gastritis some of whom were also found to have gastric cancer. Long term studies have shown evidence of a progression from *H. pylori* gastritis through atrophic gastritis to intestinal metaplasia and dysplasia (112-115). Chronic and atrophic

gastritis are two independent risk factors for cancer of the stomach. Other studies (116-119) have shown that *H. pylori* infection increases proliferation of gastric epithelial cells and this process is significantly reduced once the infection is treated. This effect is either a direct effect of *H. pylori* or an immune/ inflammatory response. It suggests that this bacterium may be an initiating step in gastric carcinogenesis and an important co-carcinogenic factor in subjects with the infection. *H. pylori* has also been shown to induce bile reflux (120). Bile induced injury to gastric epithelium contributes to gastritis and may initiate carcinogenesis.

***H. pylori* and gastric MALT- B cell lymphoma:** Normally, gastric mucosa is free of inflammatory cells. *H. pylori* colonisation stimulates acquisition and proliferation of organised lymphoid tissue in the stomach (mucosal associated lymphoid tissue-MALT). This is through production of chemotactic factors and cytokines discussed above. MALT is a precursor for MALT B-cell lymphoma and many studies have reported the association between *H. pylori* and development of this lymphoma (121-126). It is thought that persistent infection leads to organised lymphocyte proliferation, which can become autonomous and progress to a lymphoproliferative neoplastic disease.

AIMS AND OBJECTIVES

The main objective of the study was to determine the prevalence of *H. pylori* in dyspeptic patients with chronic renal failure. The specific objectives were:

1. To determine the prevalence of *H. pylori* in patients with dyspepsia and CRF.
2. To determine the prevalence of *H. pylori* in patients with dyspepsia and normal renal function.
3. To compare the prevalence of *H. pylori* in patients with CRF and dyspepsia to that in patients with normal renal function and dyspepsia.

PATIENTS AND METHODS

This was a hospital based comparative study carried out at KNH between June 1998 and January 1999. Patients with dyspepsia were screened and those that fulfilled the inclusion criteria were recruited into the study. A total of 154 patients were studied. This was the desired sample size (appendix 3). They were divided into two equal groups where the first group (CRF group) comprised patients with established renal failure and the second group (controls) had patients whose renal function was normal. Consecutive sampling was used for both groups. Patients in both groups had dyspepsia. Patients were enrolled from the KNH outpatient renal clinic and renal unit (CRF group), and the medical outpatient clinic (controls). Dyspepsia was defined as presence of at least three

of the following symptoms for a period not less than two weeks; regurgitation, belching, nausea, vomiting, post-prandial fullness or drowsiness, epigastric pain or bloating (99). Any patient taking, or who had taken proton pump inhibitors, H₂ receptor antagonists, bismuth salts, antibiotics, NSAIDs, or antacids in anti-ulcer dosages (140 Meq of antacid 1hr, 3hr after meals and at bedtime) within four weeks prior to endoscopy was excluded from the study. Patients with history of heavy alcohol ingestion before developing symptoms or patients already known to have pancreatic, liver or biliary diseases were also excluded.

Demographic data including name, sex, date of birth, occupation and place of residence were recorded for the study patients (Appendix 1). An attempt was made to match the patients for age and sex. Five milliliters of blood was obtained from each patient in a plain bottle for estimation of serum creatinine levels (CX5 BECKMAN). Those with normal creatinine levels (< 133 μ mol/l) were enrolled in the non-CRF group. Those with serum creatinine levels above 133 μ mol/l were enrolled in the CRF group if the patient was already known to have CRF as evidenced by records in the renal clinic. We did not endeavor to make a diagnosis of CRF, therefore only patients already known to have CRF were recruited in the CRF group. A cut off point of serum creatinine of 133 μ mol/l helped confirm the renal status of those previously thought to be normal. For those in the CRF group, duration of haemodialysis was recorded.

Each patient recruited underwent upper gastrointestinal endoscopy after local pharyngeal anaesthesia by a qualified endoscopist assisted by the investigator.

During endoscopy, six biopsies were routinely taken 2 from the antrum, 2 from the incisura and 2 from the fundus for subsequent *H. pylori* studies. For patients found to have masses, 2 biopsies of the mass were taken over and above the biopsies mentioned above. All lesions found at endoscopy were described and recorded (appendix 1).

H.PYLORI STUDIES

The biopsy urease test: The CLOtest was used. Three of the biopsies one from each region were pushed into the gel until completely covered. The CLOtest kit was then resealed and patient's name, date and time recorded on the label. The sample was then examined at 3 and 24 hours and the results recorded as positive or negative. A positive test constituted a color change from yellow to red.

Histology: The remaining biopsy specimens were placed in 10% formalin and fixed for 6 hours before processing and staining with haematoxylin and eosin for histological diagnosis. Modified Giemsa stain was used for detection of *Helicobacter pylori*. A qualified pathologist who was blinded to the results of the CLOtest examined all the three specimens from each patient.

ETHICAL CONSIDERATIONS

This study was performed following the approval of the Department of Medicine, Faculty of Medicine of the University of Nairobi and the KNH research and ethical committee. The investigator ensured that every patient understood the nature and purpose of the study before a freely given informed consent was obtained (appendix 2). Patients were advised on their rights to withdraw from the study without prejudice to their future treatment.

STATISTICAL METHODS

The desired sample size was calculated as shown in appendix 3. Data was collected using a standard questionnaire (appendix 1) and coded before being entered in to a computer. It was cleaned and verified before analysis was done using SSPS software. For discrete variables frequencies and percentages were calculated and data summarised in tables. The mean, standard deviation and range were worked out for age. The prevalence of *H. pylori* in each group was calculated as the proportion of the study population that had *H. pylori*. The values were expressed as percentages and their significance in determining the patient's likelihood of having *H. pylori* tested using the chi square contingency test. P values were calculated using two by two or two by three tables. Statistical significance was taken at p value below 0.05.

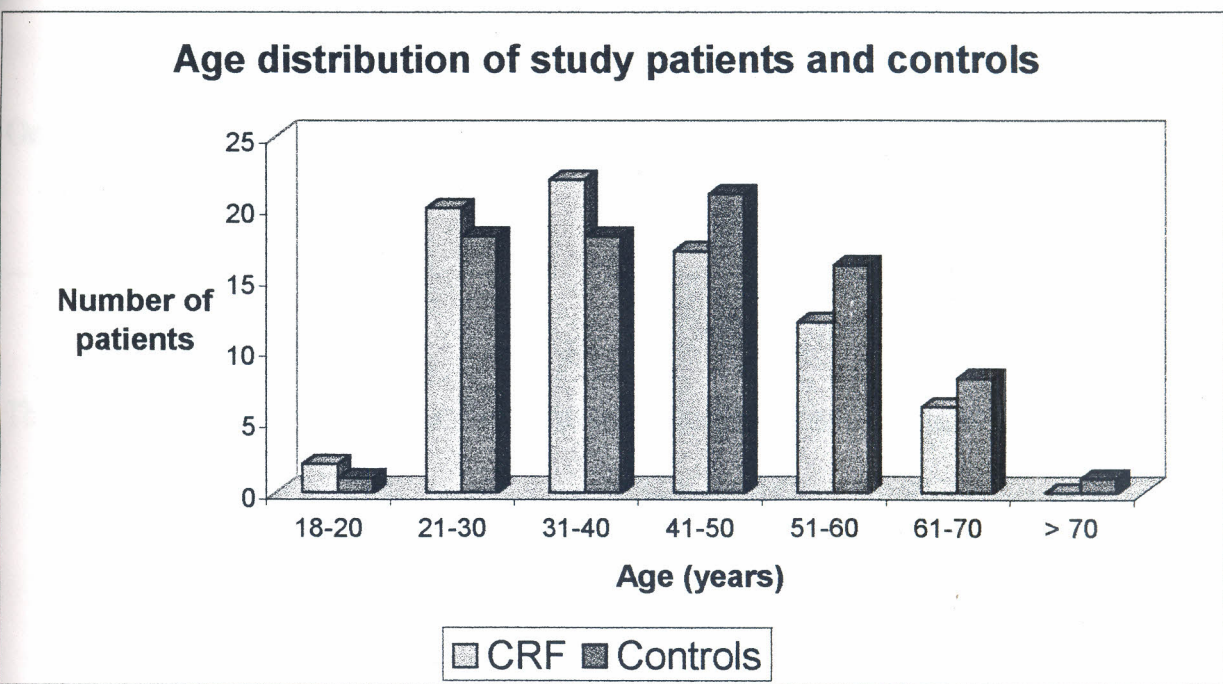
RESULTS

A total of 154 patients with dyspepsia (90 males and 64 females) were studied between June 1998 and January 1999. Their mean age was 40.3 (+/- 14.3) years, with a range of 18 to 87. Eighty-two (53.2%) of the patients lived in the rural areas. The rest lived in urban towns, 18 (11.6%) in the slums and 54 (35.1%) in non-slum areas. Sixty (39%) were unemployed, 18 (11.7%) worked at the level of subordinate staff while 76 (49.3%) were employed in other job groups. Other job groups included clerks, professionals in various professions such as teachers, doctors, nurses, officers in various offices etc and those involved in business. The patients were divided into 2 groups on the basis of presence or absence of CRF.

The mean age for the CRF patients was 38.71 (+/- 14.16) years with a range of 18 to 70. Forty-five (58.4%) were males and 32 (41.6%) were females. Six (7.7%) resided in high density urban centers, 46 (59.0%) in rural areas and 25 (33.3%) lived in low density urban centers. Thirty (39%) were unemployed, 8 (10.4%) worked at the level of subordinate staff while the rest 41 (53.2%) worked in other job groups. Forty-nine (62.6%) were on conservative management for the renal failure while 28 (36.4%) were on regular haemodialysis.

The mean age for the control patients was 41.9 (+/- 14.95) years with a range of 18 to 87. There were 45 (58.4%) males and 32 (41.6%) females. Twelve (15.6%) lived in high density urban centers, 29 (37.6%) lived in low density urban centers while 36 (46.8%) in rural areas. Thirty (39%) were unemployed, 10 (13%) worked at the level of subordinate staff and 37 (48%) worked in other job groups.

Figure 1



On average the CRF patients were slightly younger than the controls but the difference was not statistically significant.

Table 1: Demographic characteristics of study patients

Characteristic		Overall (%) N=154	CRF (%) N=77	Controls (%) N = 77	P value
Sex	Male	58.4	58.4	58.4	1.000
	Female	41.6	41.6	41.6	
Residence	Urban (high density)	11.6	7.8	15.6	0.349
	Urban (low density)	35.1	33.2	37.2	
	Rural	53.2	59.0	46.8	
Occupation	Unemployed	39.0	39.0	39.0	0.871
	S/Staff	11.8	10.3	13.0	
	Others	49.3	50.7	48.0	

The two groups were well matched for sex, residence and occupation.

Table 2: Endoscopic findings in the study patients

Endoscopic finding	Overall – n* (%)	CRF – n* (%)	Controls – n* (%)
Inflammatory lesions (gastritis, duodenitis)	69 (42.0)	29 (37.1)	40 (43.9)
Duodenal Ulcer	30 (18.4)	10 (14.1)	20 (20.8)
Normal findings	20 (12.2)	08 (10.2)	12 (15.5)
Oesophagitis	15 (09.1)	08 (10.2)	07 (07.7)
Gastric Ulcer	08 (04.9)	02 (02.5)	06 (06.5)
Gastric mass	02 (01.2)	00 (00.0)	02 (02.2)
Hypertrophic rugae	20 (12.2)	20 (25.6)	00 (0.0)

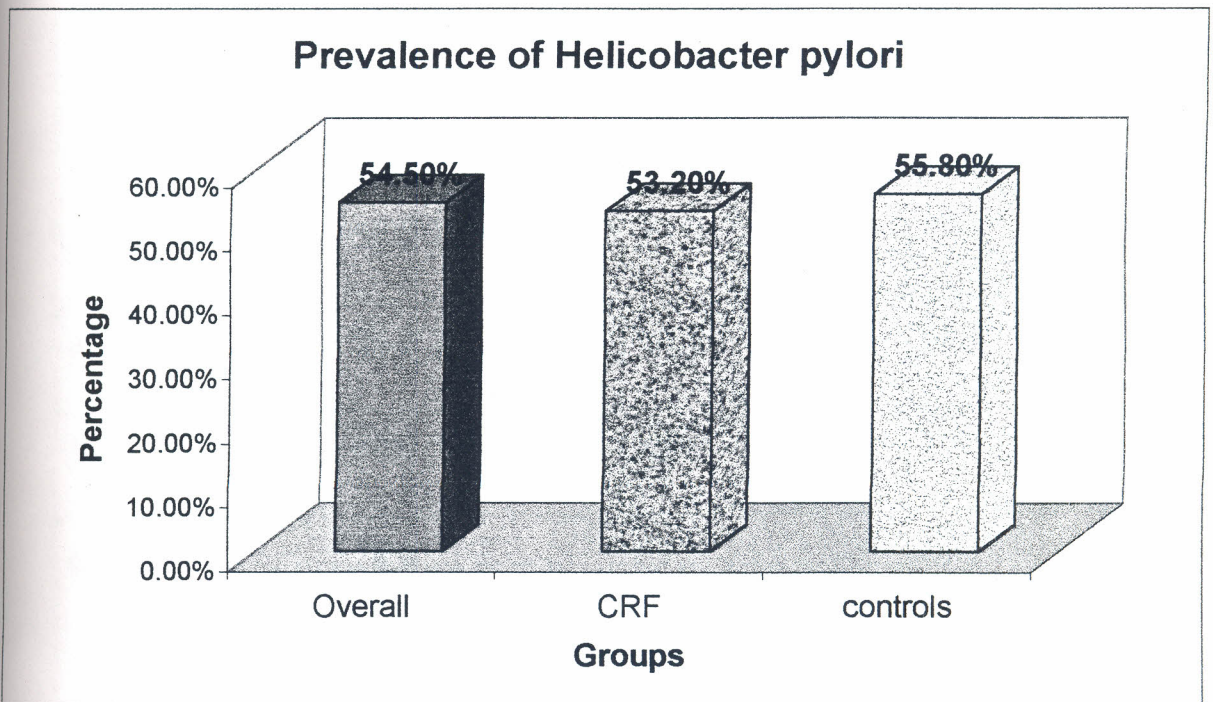
Note: n* refers to number of times a lesion was seen at endoscopy.

One hundred and sixty-four endoscopic diagnoses were made in 154 patients. Ten patients had more than one diagnosis. Inflammatory lesions were the commonest lesions seen at endoscopy in both groups. Of these antral gastritis occurred in 40 patients, duodenitis in 20 patients, fundal gastritis in 6 patients and generalised gastritis in 3 patients. Duodenal ulcer was the second commonest lesion seen. Normal endoscopic findings were more prevalent in the controls than in the CRF group. Hypertrophic rugae consistent with uraemic gastropathy was exclusively seen in the CRF patients and occurred in 25.6 %.

PREVALENCE OF *HELICOBACTER PYLORI*

Overall, *H. pylori* was detected in 84 patients by both biopsy urease test and histology. In the CRF group, 41 patients had *H. pylori* in the control group 43 patients had *H. pylori*.

Figure 2



There difference between the prevalence of *H. pylori* in the study patients and that in the controls was not statistically significant, p value = 0.746.

We assessed the prevalence of *H. pylori* by age, sex, endoscopic findings, residence and occupation with the following results.

Table 3: Prevalence of *H. pylori* by age in the study patients

Age in years	Overall (%)	CRF (%)	Non-CRF (%)
<20	33.3	0.0	50.0
21-30	50.1	45.8	55.0
31-40	51.0	50.0	56.4
41-50	56.0	62.1	58.0
51-60	60.0	58.8	62.5
61-70	78.6	67.7	87.5
>70	100.0	00.0	100.0

The prevalence of *H. pylori* increased with age in both groups. CRF patients aged between 60 and 70 years had a significantly lower prevalence of *H. pylori* compared to the controls in the same age bracket.

Table 4: Prevalence of *H. pylori* by sex in the CRF patients and controls.

	Male(%) n =45	Female(%) n = 32	P value
CRF	46.7	62.5	0.033
Controls	60.0	50.0	0.155

Significantly less females than males had *H. pylori* in the CRF group. This was not replicated in the controls, nor was it so when the two groups were combined.

Table 5: Prevalence of *H. pylori* by endoscopic findings

Endoscopic finding	Overall % (n)	CRF % (n)	Controls % (n)
Inflammatory lesions (gastritis, duodenitis)	87.3 (69)	88.9 (29)	86.1 (40)
Duodenal Ulcer	86.7 (30)	90.0 (10)	85.0 (20)
Normal findings	35.0 (20)	00.0 (08)	58.3 (12)
Oesophagitis	06.7 (15)	00.0 (08)	14.2 (07)
Gastric Ulcer	50.0 (08)	50.0 (02)	50.0 (06)
Gastric mass	50.0 (02)	00.0 (00)	50.0 (02)
Hypertrophic rugae	00.0 (20)	00.0 (20)	00.0 (0)

Note: n = number of times a particular lesion was seen at endoscopy.

The prevalence of *H. pylori* was very high in patients who had duodenal ulcers or inflammatory lesions. None of the CRF patients with only hypertrophied rugae had *H. pylori*.

Table 6: Prevalence of *H. pylori* by residence in the CRF patients and controls.

Residence	Overall (%)	CRF (%)	Controls (%)
Urban (high density)	58.7	56.5	58.3
Urban (low density)	51.2	48	60.1
Rural	49.1	50.5	50

Overall the patients living in high density urban centers had a higher prevalence of *H. pylori* compared to those residing in low density urban centers or rural areas. The difference was however not statistically significant, p value 0.634.

A sub analysis within the individual groups did not reveal any statistically significant association between residence and prevalence of *H. pylori*.

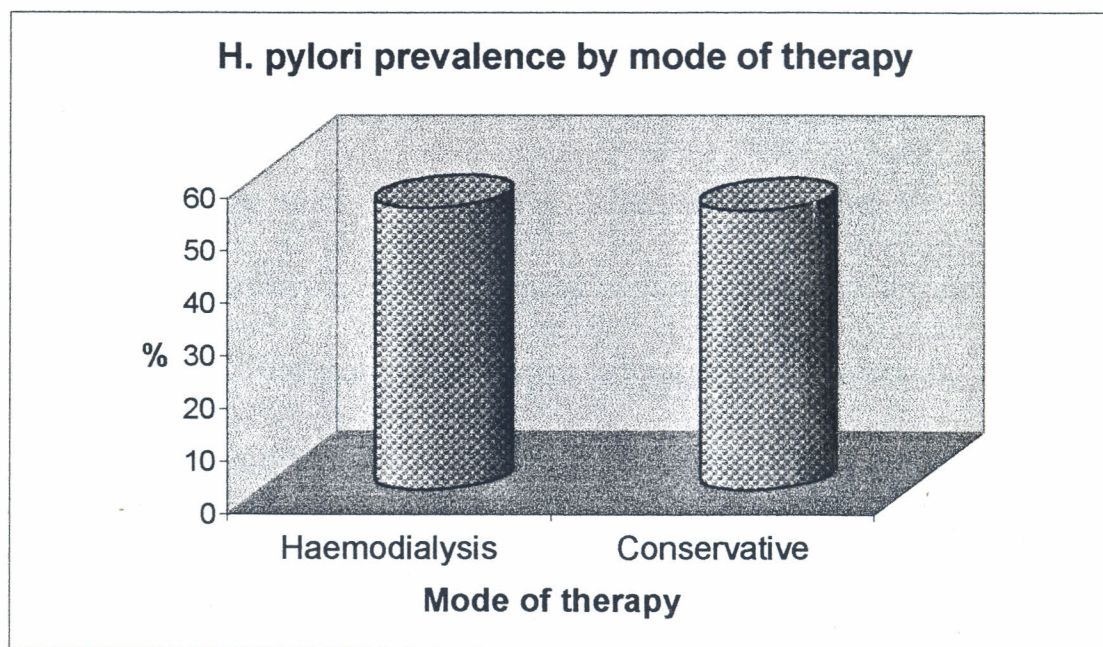
Table 7: Prevalence of *H. pylori* by occupation in CRF patients and controls.

Occupation	Overall (%)	CRF (%)	Controls (%)
Unemployed	58.0 (n=60)	56.5 (n=30)	57 (n=30)
S/Staff or equivalent	50.0 (n=18)	25.0 (n=8)	70 (n=10)
Other	53.5 (n=76)	56.0 (n=39)	51 (n=37)

The prevalence of *H. pylori* among patients employed at the level of subordinate staff in the CRF group was significantly lower than that in patients in other work strata, p value = 0.00. Of note is that the opposite was observed in the non-CRF group where the prevalence of *H. pylori* was significantly higher in a similar group of patients.

The prevalence of *H. pylori* in patients with CRF was not influenced by the mode of therapy for the renal failure as shown in the figure below.

Figure 3



DISCUSSION

The overall prevalence of *H. pylori* in patients with dyspepsia study was 54.5%. Reports from studies done elsewhere indicate that prevalence of *H. pylori* in dyspeptic patients varies widely from place to place, with a range of 10 % to 70% (13,15-19,30).

Previous studies at KNH have reported a range of 57% -81.7% (31-33). The study by Ogutu found a prevalence of 81.7%, that by Maende found a prevalence of 70.5% while that by Lule found a prevalence of 57%. In the studies by Ogutu and Maende (31,33), three methods (culture, histology and biopsy urease test) were used to detect *H. pylori*. A patient was said to have *H. pylori* if any of the tests was positive. This could explain the much higher prevalence of *H. pylori* reported in these studies compared to our results. We used two methods (histology and biopsy urease test) to detect *H. pylori* and a patient was only said to have *H. pylori* if both tests were positive. Lule whose results were comparable to ours performed only culture in the study.

The prevalence of *H. pylori* in CRF patients in our study was 53.2%. Studies performed elsewhere on prevalence of *H. pylori* in CRF patients have yielded a wide range of results. This may be explained by different study methods used in the various studies and the fact that some studies involved dyspeptic patients while others involved a mixed group. The prevalence of *H. pylori* is known to vary from place to place and this may partly explain the differences observed.

Conz et al (10) in a study performed in Italy studied 38 haemodialysed patients with dyspepsia and found the prevalence of *H. pylori* to be 48%. Ozgur (19) et al found the prevalence of *H. pylori* in CRF patients with dyspepsia to be 60%. These studies found the prevalence of *H. pylori* in the CRF patients to be quite high. This is comparable to our findings. Of note is the fact that all patients in the three studies had dyspepsia and this could explain the fairly high prevalence of *H. pylori* they reported compared to other studies discussed below.

The study by Davenport et al (14) found the prevalence of *H. pylori* to be 34% in haemodialysed patients. In their study, only 18% of the patients had dyspepsia, and although patients who had been on antibiotics one month prior to blood sampling for *H. pylori* (they used serological methods to detect *H. pylori*), those on H₂ receptor antagonists were not excluded. These factors could account for the low figures reported. Shousha (13) et al reported an even lower

prevalence of *H. pylori* in CRF patients (24%). They excluded patients with gastric ulcers (on endoscopic examination) from the study and only 17% of the patients had dyspepsia, the endoscopies having been done as routine pre-transplant procedure. This most probably explains the low prevalence of *H. pylori* in CRF patients that they found.

The prevalence of *H. pylori* in dyspeptic CRF patients in our study did not differ significantly from that we found in dyspeptic patients with normal renal function. Similar results have reported elsewhere (13,14,19). All the studies that failed to show a difference in prevalence of *H. pylori* in CRF and that in patients with normal renal function, involved dyspeptic patients and dyspeptic controls. It appears that patients with dyspepsia have a similar prevalence of *H. pylori* regardless of their renal function.

Some studies have reported a difference in prevalence of *H. pylori* in CRF and that in patients with normal renal function. Shousha et al (13), found the prevalence of *H. pylori* in CRF patients to be 24%, compared to 42% in controls. All controls in their study had dyspepsia, while the renal failure patients underwent endoscopy as a routine pre-transplant requirement and only 17% of the CRF patients had dyspepsia. This could explain the higher prevalence of *H. pylori* in the control group compared to the prevalence of *H.*

pylori in the CRF group. Jaspersen (16) and colleagues found a significant difference between prevalence of *H. pylori* in CRF patients versus that in patients with normal renal function despite controlling for dyspepsia. This however seems to be an isolated finding as no other study has reported similar findings.

The foregoing clearly indicate that there does not seem to be a significant difference between the prevalence of *H. pylori* in dyspeptic patients with CRF and that in dyspeptic patients with normal renal function. This implies that CRF patients are not protected from *H. pylori* infection nor are they at an increased risk of acquiring the infection. It is therefore reasonable to postulate that the risk of acquiring *H. pylori* in CRF is similar to that in the general population. This probably reflects the fact that *H. pylori* infection is acquired during childhood with minimal infection being acquired in adulthood (35). Therefore those CRF patients with *H. pylori* infection are likely to have become infected before they developed CRF. However this study only involved adult patients and we do not know whether children with CRF are at an increased risk of becoming infected with *H. pylori*. A similar study conducted among paediatric subjects would help answer this question. The mode of therapy for CRF does not seem to affect *H. pylori* status.

The prevalence of *H. pylori* was very high in patients who were found to have either inflammatory lesions or duodenal ulcer at endoscopy whether their renal function was normal or not. Similar results been reported in many studies (9,29,70, 71-75, 88-94) although none of these studies involved patients with CRF. This implies that the role of *H. pylori* in causing PUD in renal patients is similar to that in normal individuals.

The prevalence of *H. pylori* increased with age regardless of renal function. This is in keeping with what has been reported elsewhere (29). It is thought that this observation is due to a cohort effect, those older than 60 years having acquired the infection in their childhood much more than those under 30 years. There was no association between prevalence of *H. pylori* and sex. This was an expected finding as no study has so far reported such an association.

Patients living in high density urban centers had a higher prevalence of *H. pylori* compared with those living in other residential areas though the difference was not statistically significant. This was an expected outcome given the many studies that have shown an association between overcrowding and acquisition of *H. pylori*. A larger sample size would probably demonstrate this well.

Occupation did not seem to influence *H. pylori* status in our study. One would have expected prevalence of *H. pylori* to be higher in the unemployed patients based on the assumption that unemployment is an indicator of poor living conditions. Occupation correlated poorly with social economic status of our study patients as it turned out that most of the patients who were unemployed were dependants, mainly students. Their social economic status really was that of their parents or guardians details of which were not inquired in to.

LIMITATIONS

- Virulence factors for *H. pylori* were not studied. It is therefore difficult to draw any conclusions as to whether the *H. pylori* detected in these patients is linked to their dyspepsia or not.
- This study looked at CRF patients in general regardless of their level of uraemia. There was no sub-analysis of *H. pylori* status with regard to serum creatinine levels, as the study was not empowered to do so due to the number of patients recruited. We do not know from this study, whether for instance patients with serum creatinine above 1000 μ mol/l would be at a higher risk of acquiring *H. pylori* than those with levels below 500 μ mol/l and yet it is known that such patients are different in terms of symptomatology and complications. A similar study involving larger sample size would help answer that question.

CONCLUSION

The prevalence of *H. pylori* in dyspeptic CRF patients does not differ from that in dyspeptic controls, but it is high in patients with endoscopically proven peptic ulcer.

RECOMMEDATIONS

1. CRF patients presenting with dyspepsia at KNH should routinely undergo *H. pylori* studies before therapy for the dyspepsia is given, especially if dyspepsia has persisted despite adequate dialysis.
2. A study on the prevalence of *H. pylori* in children with CRF may help answer the question whether CRF patients are at an increased risk of acquiring *H. pylori*. We recommend that should such a study be done the correlation between *H. pylori* and level of uraemia should be assessed.
3. A study looking at virulence factors of *H. pylori* detected in patients in our environment would help relate the presence of *H. pylori* to observed disease processes.

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APPENDIX 1

STUDY PROFORMA

A SERIAL NUMBER _____

NAME: _____

1. DATE OF BIRTH: _____

2. SEX

Male = 1 Female = 2

3. OCCUPATION

Unemployed = 1

Subordinate Staff

or equivalent = 2

Others (Clerks, professionals,

business persons etc) = 3

4. RESIDENCE IN CHILDHOOD

urban (high density) = 1

Urban (low density) = 2

Countryside = 3

5. BED SHARING

Yes = 1 No = 2

6. CHRONIC RENAL FAILURE

Yes = 1 No = 2

Regular Haemodialysis = 3

7. DURATION OF HAEMODIALYSIS

0-1 year = 1 1-5 years = 2

>5years = 3

7. UREA AND ELECTROLYTES

Potassium = _____

Sodium = _____

Calcium = _____

Blood urea nitrogen = _____

Serum creatinine = _____

B. ENDOSCOPIC FINDINGS

Mouth: _____

Oesophagus: _____

Stomach: _____

Duodenum: _____

C. HISTOLOGICAL FINDINGS:

D. BIOPSY UREASE TEST

Positive = 1

Negative = 2

E. HELICOBACTER PYLORI STATUS

Positive = 1

Negative = 2

APPENDIX 2

INFORMED CONSENT

This is to confirm that I have agreed to participate in the research on "*The prevalence of Helicobacter pylori in patients with chronic renal failure with dyspepsia*". This will involve my undergoing upper gastrointestinal endoscopy with mucosal biopsy. If I find the procedure uncomfortable, I still have the right to refuse to participate in the study and my doing so will not hamper any further treatment I am likely to receive for my condition. I have also been assured that the results could be given to me but remain confidential property of the investigator.

Signed:----- patient.

----- Investigator.

APPENDIX 3

The sample size was calculated using the formula;

$$n = \frac{\{z_{1-\alpha}\sqrt{2p(1-p)} + z_{1-\beta}\sqrt{p_1(1-p_1) + p_2(1-p_2)}\}^2}{(p_1 - p_2)^2}$$

n = sample size, calculated to be 77 per group.

$z_{1-\alpha} = 1.96$, corresponding to a level of significance of 0.05.

$z_{1-\beta}$ - corresponding to a power of the test of 80%.

The following assumptions were made based on previous studies;

p_1 = anticipated prevalence in the CRF group = 60%.

p_2 = anticipated prevalence in the control group = 40%.

The formula is recommended for use to estimate the sample size required to compare two proportions for a one sided test.