RESEARCH ARTICLE

PREVALENCE OF HELICOBACTER PYLORI IN CHRONIC RENAL FAILURE PATIENTS AND ITS CORRELATION WITH UPPER GASTROINTESTINAL ENDOSCOPIC FINDINGS-A CASE CONTROL STUDY

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ABSTRACT

Background: The gastrointestinal symptoms of anorexia, hiccups, nausea and vomiting are common early manifestations of CRF. Peptic ulcer disease is common in CRF patients, whether the high incidence is related to altered gastric acidity, hyper-secretion of gastrin or enhanced colonization by Helicobacter pylori (H.pylori) is still unknown.

Aims: To study the prevalence of Helicobacter pylori in chronic renal failure patients as compared to a group of control subjects with normal renal function and to correlate the prevalence of Helicobacter pylori infection to upper gastrointestinal endoscopic findings.

Setting and Design: Hospital based prospective Case-Control study.

Materials & Methods: The patients were selected from the gastroenterology and Nephrology units Christian Medical College & Hospital, Ludhiana a tertiary care hospital to whom all subjected for endoscopy and for H. Pylori testing.

Results: The presence of endoscopic antral gastritis showed significant association with H.pylori prevalence (57.6%) and (p<0.005), however, H.pylori infection was not related significantly to any other form of gastritis. Antral pattern of gastritis was the most common endoscopic lesion observed in both groups. The presence of duodenal ulcer or gastric ulcer did not show any increased prevalence of H.pylori. The combination of antral gastritis and duodenal ulcer showed 100 percent prevalence of H.pylori. There was no association found between H.pylori and reflux esophagitis. Gastric ulcer was seen in 3.2 percent cases and 3.6 percent controls. Duodenal ulcer was seen in 1.6 percent CRF patients and 20.4 percent controls. The commonest pattern of antral histology was active chronic superficial gastritis and was found in 33.3 percent cases and 44.9 percent controls. Both, controls and patients with CRF showed a similar pattern of histological gastritis. There was good correlation between endoscopic and histological gastritis.

Conclusion: Gastrointestinal symptoms in patients with end stage kidney disease are due to multi-factorials, however high prevalence of H. Pylori infection is common in developing country like India where symptomatic patients need evaluation by doing U.G. I. Scopy where one should test and treat to alleviate the patients symptoms.

INTRODUCTION

Chronic Renal Failure (CRF) is a devastating disease for patients, their families and the nation's financial resources besides being a therapeutic challenge to the physician. As the kidneys play a central role in maintenance of homeostasis, a decline in their function leads to alteration in most systems of the body. The gastrointestinal symptoms of anorexia, hiccups, nausea and vomiting are common early manifestations of CRF. Peptic ulcer disease is common in CRF patients, whether the high incidence is related to altered gastric acidity,

Hype-rsecretion of gastrin or enhanced colonization by Helicobacter pylori (H.pylori) is still unknown. Helicobacter pylori is one of the most common bacterial infections in humans and is causally linked with gastritis, peptic ulcer disease, gastric B-cell lymphoma and Gastric adenocarcinoma. In the present study, it is our Endeavour to investigate patients with established CRF for upper gastrointestinal symptoms to evaluate the cause of these symptoms by an upper gastrointestinal endoscopy and to evaluate whether H.pylori infection has a significant contribution in producing the upper gastrointestinal symptoms commonly manifested by CRF patients and also histopathological correlation of gastroduodenal lesions caused by H. pylori. By this study, we aim to assess the need for gastrointestinal endoscopy in CRF patients with significant gastrointestinal symptoms and value of H. pylori eradication therapy in alleviating these symptoms.

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REVIEW OF LITERATURE

Upper gastrointestinal endoscopy of stable dialysis patient reveals abnormalities in upto 61 percent of cases. Gastritis, duodenitis and mucosal lesions were commonly seen. Also seen on oesophagogastroduodenoscopy (OGD) are osophagitis, brunner gland hyperplasia, gastric fold thickening, angiodysplasia and nodular duodenitis (Kang *et al.,* 1988). Pathogenesis of uremic lesions is not well understood. Fasting serum gastrin levels are commonly elevated in CRF patients since it is clear from serum by renal cortex (Gur *et al.,* 1999). Levels of gastrin relate with gastric acidity suggesting that elevated gastrin level may represent a response to hypochlorhydria rather than a cause of gastroduodenal lesions (Ala-Kala *et al.,* 1989). There is a lack of correlation between acid secretion and presence of upper gastrointestinal lesions and both basal and stimulated acid output can be normal, high or low. These findings suggest that neither hyperacidity nor hypergastrinemia play a major role in pathogenesis of uremic gastroduodenal lesions. Impaired mucosal cytoprotection has been postulated but not proven to cause gastroduodenal lesions in CRF patients (Rantala *et al.,* 1996).

The clinic-pathological conditions causing upper gastrointestinal symptoms commonly with CRF are: Gastroesophageal reflux disease (GERD), Peptic ulcer disease (including gastric and duodenal ulcers), gastritis and non-ulcer dyspepsia.

Peptic Ulcer Disease (PUD)

PUD is characterized by burning epigastric pain exacerbated by fasting and improved by meals. An ulcer is defined as disruption of mucosal integrity of the stomach/duodenum leading to a local defect or excavation due to inflammation.

Epidemiology of PUD

Data from National Health and Nutrition Examination Survey (NHANES) collected from 1976 to 1980, yielded a life time prevalence of peptic ulcer of 9.4 percent for adults between ages 20 and 74 and male life time prevalence of 11.3 percent and female life time prevalence of 7.7 percent (Kurata, 1991). Age is an important factor in peptic ulcer prevalence and trends of ulcer occurrence reflect declining rates, particularly for younger men and increasing rates particularly for older women reflecting an age coort phenomenon (Sonnenberg, 1984).

The diagnosis of peptic ulcer disease can done by Barium radiography and endoscopy. Endoscopy with flexible instruments provides a sensitive, specific and safe method for diagnosing peptic ulcers. Endoscopy allows direct inspection and biopsy. Endoscopists detect 85 to 95 percent of gastroduodenal lesions, failing to detect 5-10 percent of lesions found on radiography or at surgery (Kahn and Greenfield, 1986). The classical definition of an erosion is a break in the mucosa that does ot penetrate the muscularis mucosa into the submucosa. Haemorrhage refers to an appearance of discrete petechiae or bright red streaks and patches that are not associated with any visible breaks in the mucosa (Laine and Weinstein, 1991). The antral pattern is the most common of

gastritis, it is generally diffuse and is the type associated with H.pylori, duodenal and gastric ulcers. some case of severe atrophic gastritis in which prominent blood vessels and thin fold of mucosa are visible at endoscopy (Meshkintour *et al.,* 1979).

Specific Gastritis and Gastropaties

The designation specific or distinctive gastritis refers to histological and sometimes endoscopic features that markedly narrow the differential diagnosis or are occasionally pathognomonic. Examples, Crohn's disease of the stomach (Wilfren, 1993).

Helicobacter pylori

The discovery of Helicobacter pylori (H.Pylori) and its role in gastroduodenal disease has been one of the most significant discovery in the field of bacteriology and gastroenterology in the past 20 years. Nevertheless, histologists have described spiral shaped bacteria in the stomach of animals since last quarter of 19th century. Marshal developed this concept which led to the isolation of campylobacter like organisms. Finally, in 1989 Goodwin et al showed that the bacterium did not belong to the genus Campylobacter and renamed it. Helicobacter pylori. A consensus on the major role of H.pylori in gastroduodenal disease was reached in 1994 (Moran and Morain, 1997).

H. pylori's Role in Pathogenesis of Duodenal Ulcer (DU)

Patients with DU have several fold increase in acid secretion, both basally and in response to gastrin stimulation compared to true normal controls, i.e. H.pylori negative patients. This increase in acid secretion is predominantly due to H.pylori infection as it resolves following eradication of H.pylori (El omar *et al.,* 1993, 1995). The increased acid secretion in DU patients is caused by increased in hormone gastrin from G-cells and this increased of gastrin may be largely due to infection by H.pylori impairing release of somatostatin by D-cells as somatostatin normally exerts paracrine inhibitory control upon the releaseof gastrin from antral cells (Levi *et al.,* 1989; Moss *et al.,* 1992). The increased acid secretion stimulated by H.pylori infection in DU patients results in increased duodenal acid load and also gastric metaplasia. H.pylori are able to colonie thee patches of gastric metaplasia within duodenum. The duodenal mucosa subsequently subjected to increased acid load and damaging effects of bacterium leads to ulceration (Khulusi *et al.,* 1996).

Methods of detection of H.Pylori

Non-Invasive

1. **Serology:** Enzyme linked immunosorbent assay (ELISA) is the most commonly used method to measure H.pylori antibodies. Today the best IgG test available show sensitivity and specificity of over 90 % (Feldmen *et al.,* 1995).
2. **Urease Breath Test:** If an H.pylori infected individual ingests urea labeled with C13 or C14, the bacterial urease generates labeled CO_2 which is absorbed in blood and exhaled in breath in 5 minutes. The detection of

radiolabelled CO2, therefore, indicates H.pylori infection. It is more than 90 % sensitive and specific (Graham, 1987). Both these tests are of value in following patient to evaluate eradication of H.pylori following therapy and for screening, rather than primary diagnosis of infection.

Invasive

1. **Urease Test:** This test involves placing one or several biopsy specimens in contact with medium containing urea. If H.pylori is present, it would breakdown urea to ammonia and the ammonia liberated raises the pH of the medium and causes the pH indicator to change colour. These are 87 to 90 %sensitive and about 100 percent specific (Deltenre, 1989).

2. **Microscopic Examination**
   Specimens can be examined directly using dark field or phase contrast microscopy for morphological characteristics and motility. Gram stain, Giemsa, Warthin-Starry or Acridine Orange can be used or immunocytochemical staining with monoclonal anti H.pylori antibodies can be used. The specificity is between 95-100 % and sensitivity is low.

3. **Culture**
   It is the gold standard for detection of the bacteria, but requires lengthy incubation period (3-12 days). Biopsy specimens from antrum are used. Colonies are identified as small discrete, creamish growth on media upto 12 days of incubation. The organism can be identified by gram-staining and biochemical characteristics

4. **Polymerase Chain Reaction (PCR)**
   This method is highly sensitive and specific and gives rapid results without the need for strict transport conditions. Given sequences of H.pylori DNA are amplified using specific primers and H.pylori identified by analysis of amplified products (Monteirol, 1997).

AIMS OF THE STUDY

1. To study the prevalence of Helicobacter pylori in chronic renal failure patients as compared to a group of control subjects with normal renal function.
2. To correlate the prevalence of Helicobacter pylori infection to upper gastrointestinal endoscopic findings.

MATERIAL AND METHODS

The study was conducted in Gastroenterology and Nephrology Departments of Christian Medical College and Hospital, Ludhiana between April 2011 to June 2012 to study endoscopic findings in chronic renal failure (CRF) patients as compared to control subjects with normal renal function and also evaluate prevalence of Helicobacter pylori between the two groups. The study recruited a total of 112 patients (63 CRF patients and 49 control patients) who were age and sex matched. Both groups of patients had a similar symptom profile, therefore, they were also symptom matched.

Selection Criteria

Test Group

The test group comprised established chronic renal failure (CRF) patients and other features of CRF as anaemia,

hypocalcemia, hyperphosphatemia, hyperuricemia and/or bilateral reduction in renal size on ultrasound as well as urine renal failure indices suggesting intrinsic renal disease. These patients were screened for upper gastrointestinal symptoms as detailed in the characterized. Simultaneously, multiple biopsies were taken from the antrum. Two biopsies were sent for histopathological examination, two biopsies for rapid urease test and two for culture of H.pylori.

Histopathology

Histopathological evaluation of gastric antral biopsies specimens was done after processing, fixation and subsequent staining with hematoxylin and eosin stain. These biopsies were studied by a single pathologist and classified into different types of gastritis according to the type of inflammatory infiltrate, depth of mucosal involvement and features of atrophy. Normal histopathological specimens were the ones without any histo-pathological abnormalities detected on light microscopy. Also, histo-pathological screening for H. pylori was done as they also stain with hematoxylin and eosin stain (spiral shaped organisms with multiple flagella near the mucosa).

Rapid urease test

Rapid urease test was performed on antral biopsy specimens using urea broth and phenol red as indicator. Rapid urease test was termed positive if the indicator change colour within half an hour of incubation to pink.

Culture

Culture was performed on antral biopsy specimens. Antral biopsies were transported in 0.9 percent saline and cultured onto brain-heart infusion broth within 10 minutes and later subcultured onto a H.pylori selective media (blood agar base to Campylobacter supplement 1) The culture plates were incubated in microaerophilic chambers using appropriate concentrations of nitrogen, oxygen and carbon dioxide. These culture plates were studied for the growth of bacterial colonies up to 12 days of incubation. H.pylori was considered positive if the bacteria were spiral shaped and gram-negative and were also positive for urease catalase and oxidase test.

Data analysis

Statistical analysis of the above data was done using computer based statistical programme (EPI-INFO-6).

RESULTS

A total of 112 patients were enrolled for the study, in which 63 patients comprised the case group (i.e. patients with established chronic renal failure) and 49 comprised the control group (i.e. patients with normal renal function).
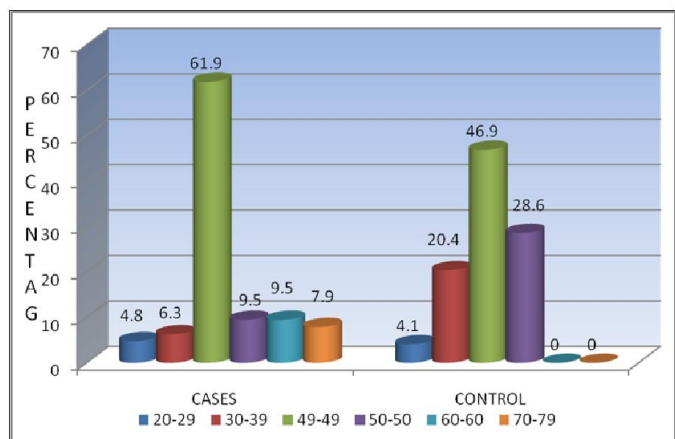
Age distribution

Age distribution in cases ranged from a minimum of 24 years to a maximum of 75 years and in control the range was 28 years to 56 years. The maximum number of patients in both the groups fell in the 40 to 49 years age group. There was no

statistical significant difference in age distributio9n between the two study groups (Table 1).

Table 1. Age Distribution

Age group (years)	Case (%)	Control (%)	Total (%)
20-29	3 (4.8)	2 (4.1)	5 (4.5)
30-39	4 (6.3)	10 (20.4)	18 (16.1)
40-49	39 (61.9)	23 (46.9)	62 (55.4)
50-59	6 (9.5)	14 (28.6)	16 (14.3)
60-69	6 (9.5)	0 (0.0)	6 (5.4)
70-79	5 (7.9)	0 (0.0)	5 (4.5)

AGE

P > 0.05

Sex Distribution

There were a total of 21 (33.3%) female patients and 42 (66.7%) male patients in the case group and 20 (40.8%) and 29 (59.2%) females and males, respectively in the control group. The two study groups were statistically similar in sex distribution (p=0.189) (Table 2)

Table 2.

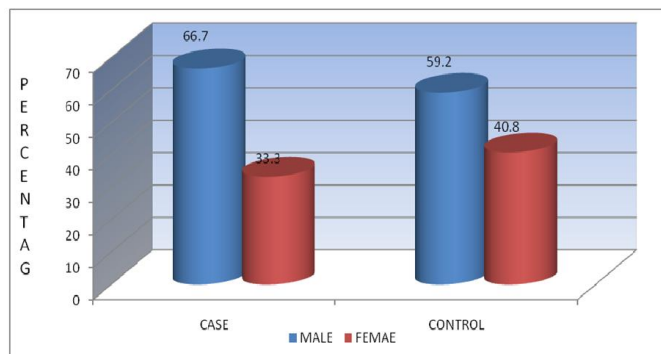| Sex	Case (%)	Control (%)	Total (%)
Females	21 (33.3)	20 (40.8)	41 (36.6)
Males	42 (66.7)	29 (59.2)	71 (63.4)
Total	63 (56.3)	49 (43.8)	112 (100.0)

Symptoms

The symptoms profile was similar in both the study groups. The nausea was universally present (100% in both cases and control followed by vomiting which was present in 100 percent of control and 94.8 percent in cases. Malena was the least common symptom and was present in only one control and no case. The study group was found to be symptom-matched and there was no statistically difference between any sympto9m in cases and control (p>0.05) (Table 3).
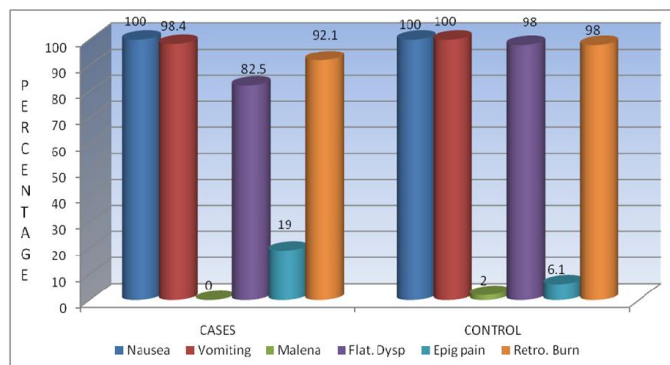
Table 3. Symptoms

Sex	Case (%)	Control (%)	Total (%)
Nausea	63 (100.0)	49 (100.0)	112 (100.0)
Vomiting	62 (98.4)	49 (100.0)	111 (99.1)
Malena	0 (0.0)	1 (2.0)	1 (0.9)
Flatulent dyspepsia	52 (82.5)	48 (98.0)	100 (89.3)
Epigastric pain	12 (19.0)	3 (6.1)	15 (13.4)
Retrosternal burning	58 (92.1)	48 (98.0)	106 (94.6)

Sex distribution

P > 0.05

Symptoms

P > 0.05

Endoscopic Findings

The endoscopic findings of the patients of the patients as studied by eosophagogastroduodenoscopy (OGD) were divided into three sub-groups:

Findings in the Esophagus

The esophageal findings on endoscopy showed reflux esophagitis in 3 (4.8%) cases and 4 (8.2%) controls.
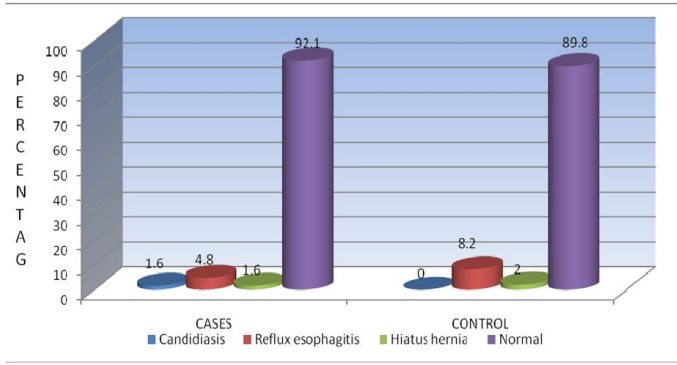
Esophageal candidiasis was observed in 1 patient of the case group and hiatus hernia was seen in 1 patient each of both the groups. The esophageal findings between cases and control did not vary significantly (Table 4)

Table 4.

Esophageal findings	Case (%)	Control (%)	Total (%)
Nausea	63 (100.0)	49 (100.0)	112 (100.0)
Candidiasis	1 (1.6)	0 (0.0)	1 (0.9)
Reflux esophagitis	3 (4.8)	4 (8.2)	7 (6.3)
Hiatus hernia	1 (1.6)	1 (2.0)	2 (1.8)
Normal	58 (92.1)	44 (89.8)	102 (91.1)

Findings in Stomach: The findings in the stomach were divided into different groups depending upon the topographical distribution of gastritis (i.e. antral, fundal or pangastritis) also multifocal atrophic gastritis and gastric ulcers were assigned separate groups.

Endoscopic Esophageal findings

P > 0.05

Gastritis was observed in 25 (39.7%) cases and 19 (38.8%) controls. Antral gastritis was the most common endoscopic pattern of gastritis seen, being present in 18 (28.6%) and 15 (13.6%) of cases and control, respectively. Gastric atrophy was seen in one patient in the case group. Pangastritis was observed in 7.9 percent of cases and 8.2 percent of controls. Gastric ulcer was seen in 2 (3.1%) cases and 8 (16.3%) controls.

The gastric endoscopic findings, therefore, showed a similar pattern in both the groups except the higher incidence of gastric ulcer in the control group (Table 5).
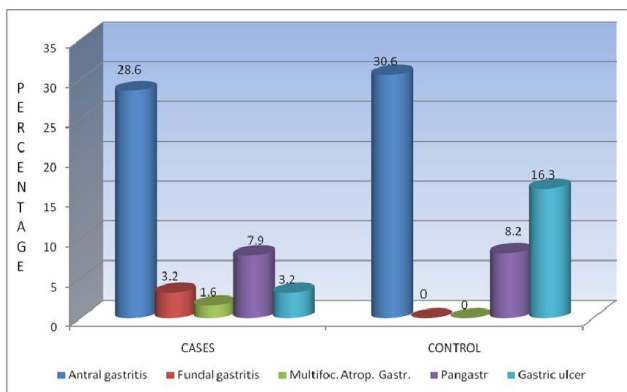
Table 5.

Gastric findings	Case (%)	Control (%)	Total (%)
Antral gastritis	18 (28.6)	15 (30.6)	33 (29.5)
Fundal gastritis	2 (3.2)	0 (0.0)	2 (1.8)
Multifocal atrophic gastritis	1 (1.6)	0 (0.0)	1 (0.9)
Pangastritis	5 (7.9)	4 (8.2)	9 (8.0)
Gastric ulcer	2 (3.2)	8 (16.3)	10 (8.9)

Findings in the Duodenum

In the duodenum endoscopy demonstrated duodenitis in 4 (6.3%) cases and no duodenitis was observed in controls. Duodenal ulcer was present in 1 (1.6%) case and 10 (20.4%) controls. The duodenal endoscopic findings showed a significant difference between the two study groups (p = 0.001) and duodenal ulcer was more common in control subjects as compared to case subjects (Table 6).
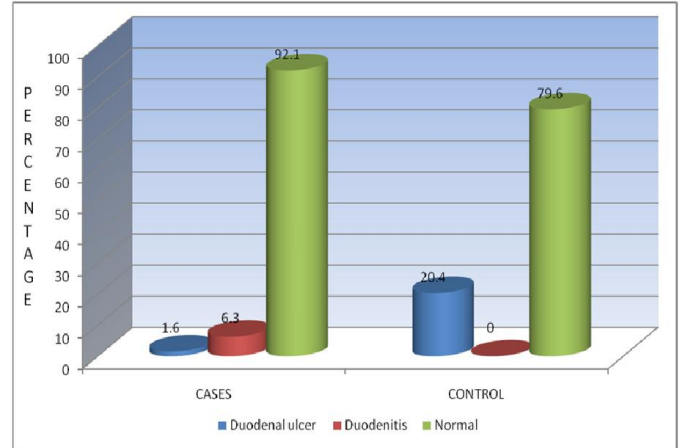
Endoscopic Findings of Stomach

P > 0.05

Table 6.

Duodenal findings	Case (%)	Control (%)	Total (%)
Duodenal ulcer	1 (1.6)	10 (20.4)	11 (9.8)
Duodenitis	4 (6.3)	0 (0.0)	4 (3.6)
Normal	58 (92.1)	39 (79.6)	97 (86.6)

Endoscopic Findings of Duodenum

P<0.05

HISTOLOGICAL PATTERN (from antral biopsies)

Histological examination was performed on antral biopsy specimens to study the pattern of inflammation. It was divided into three groups depending upon the nature of inflammatory infiltrate and depth of mucosal involvement or evidence of atrophy.

Active Chronic Superficial Gastritis: If the inflammatory infiltrate showed the presence of neutrophils along with lymphocytes and remained confined within muscularis mucosa.
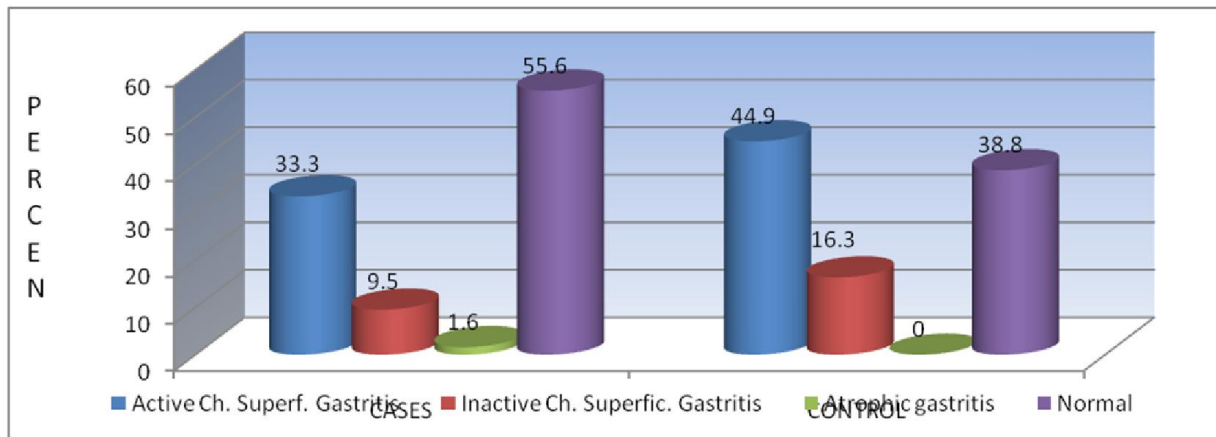
Infective Chronic Superficial Gastritis: If the inflammatory infiltrate showed the actions of neutrophils and remained confined to muscularis mucosa.

Atrophic Gastritis: The most common histological pattern of gastritis was active chronic superficial gastritis, being present in 21 (33.3%) of cases and 22 (44.9%) of controls. Inactive chronic superficial gastritis was observed in 6 (9.5%) cases and 8 (16.3%) controls. Atrophic gastritis was observed in one (1.6%) patient in the case group and no controls. The histology was normal in 35 (55.6%) cases and 19 (38.8%) controls (Table 7). There was no statistically significant difference in histopathological patterns between both the groups (p=0.0224).

Table 7.

Histopathology (Antral biopsy)	Case (%)	Control (%)	Total (%)
Active chronic superficial gastritis	21 (33.3)	22 (44.9)	43 (38.4)
Inactive chronic superficial gastritis	6 (9.5)	8 (16.3)	14 (12.5)
Atrophic gastritis	1 (1.6)	0 (0.0)	1 (0.9)
Normal	35 (55.6)	19 (38.8)	54 (48.2)

Histological Findings of Stomach (Antrum)

P > 0.05

Correlation between endoscopy and histopathology

To find out whether was a correlation between endoscopically and histologically demonstrable gastritis, we compared them statistically. Endoscopic gastritis was observed in 45 (40.2%) patients, out of which 38 (84.4%) also demonstrated histological evidence of gastritis. There was no gastritis on endoscopy in 67 (59.8%) patients, however, about 20 (29.9%) of these subjects demonstrated histological evidence of gastritis (Table 8). The correlation between endoscopic and histological gastritis was significant (p < 0.05).

Table 8.

Endoscopy	Histopathology		
	Gastritis (%)	Normal (%)	Total (%)
Gastritis	38 (84.4)	7 (15.6)	45 (40.2)
Normal	20 (29,9)	47 (70.1)	67 (59.8)

Correlation between histological gastritis and creatinine values

Creatinine Values in Patients of Each Category at Admission

In the case group, the minimum creatinine value was 2.6 mg% and maximum creatinine value was 22.3 mg%. The mean of creat being 5.47 mg% (standard deviation = 3.524) and median value was 4.6 mg%. In the case group, the range of creat was from 0.6 to 1.1 mg%, the mean being 0.765 (standard deviation = 0.133).

The mean values of creatinine were correlated with different patterns of gastritis (Table 9).

Table 9.

Pattern of histology	Mean creatinine value
Active chronic superficial gastritis	3.51
Inactive chronic superficial gastritis	3.10
Atrophic gastritis	4.60
Normal	3.38

There was no significant difference nor correlation between levels of creatinine and gastritis demonstrated on histopathology (p = 0.967).

Correlation of endoscopic gastritis and creatinine values

Also in the case group, the mean value of creatinine who demonstrated endoscopic gastritis was 6.165 and patients and patients who did not demonstrate endoscopic gastritis had mean creatinine value of 4.98. There was no correlation between levels of creatinine and presence of endoscopic gastritis.

Helicobacter pylori

Prevalence: Three methods were used for the detection of Helicobacter pylori (rapid urease test, histology and culture).
Rapid unease test: Using rapid urease test as an index of Helicobacter pylori positivity, it was found that the prevalence of helicobacter pylori I 14 (22.2%) cases and 19 (38.8%) controls. The difference in prevalence was not statistically significant (p=0.0566). Table 10.

Table 10.

Rapid urease test	Case (%)	Control (%)	Total (%)
Positive	14 (22.2)	19 (38.8)	33 (29.5)
Negative	49 (77.8)	30 (62.1)	79 (70.1)

Histology: Histology demonstrated Helicobacter pylori in only 2 (4.1%) of controls and no cases showed Helicobacter pylori (Table 11).

Table 11.

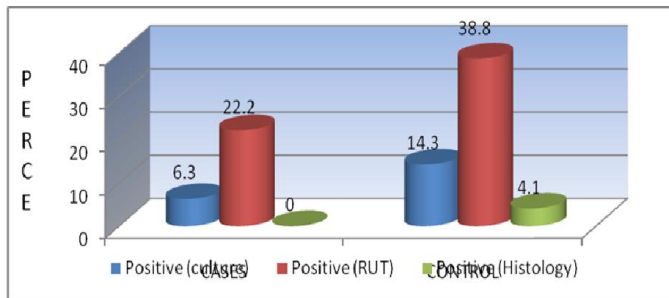| Histology	Case (%)	Control (%)	Total (%)
Positive	0 (0.0)	2 (4.1)	2 (1.8)
Negative	63 (100.0)	47 (95.9)	110 (98.2)

Culture: Culture demonstrated Helicobacter pylori in 4 (6.3%) cases and 7 (14.3%) of controls (Table 12).

Table 12.

Culture	Case (%)	Control (%)	Total (%)
Positive	4 (6.3)	7 (14.3)	11 (9.8)
Negative	59 (93.7)	42 (85.7)	101 (90.2)

As the rapid urease test was the most sensitive test, in our hospital setting, we have used it as the standard for further analysis.
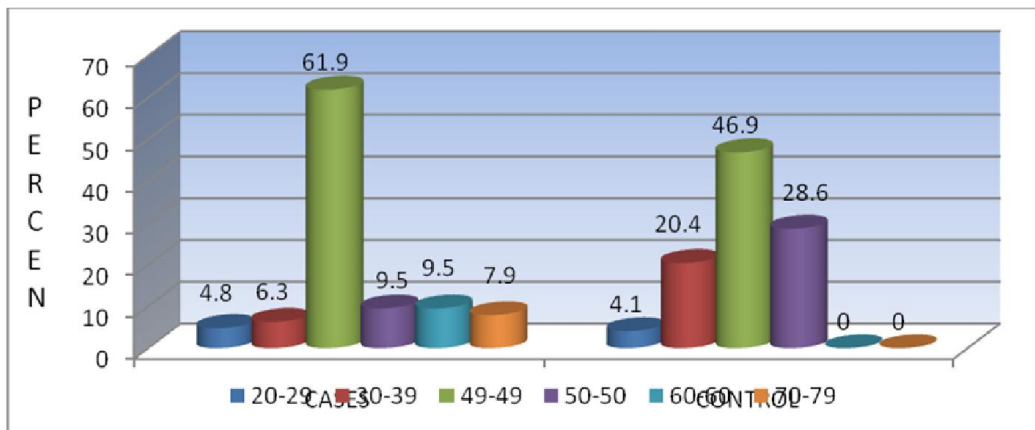
H.pylori prevalence by different methods

p value 0.062

Age Distribution of H. pylori: Helicobacter pylori was detected at the minimum age of 32 years and maximum age of 76 years. The mean age of H.pylori being positive was 47 years (standard deviation 9.31) and median age being 46 years. In H.pylori negative patients, mean age was 45.5 percent (standard deviation 10.72). The maximum age of H.pylori being positive was 40-49 years(Table-13). The age correlation between prevalence of Helicobacter pylori was not statistically significant (p = 0.478).

Sex Distribution of H.pylori

In the case group the females had 28.6 percent H.pylori positivity and males had 19.0 percent H.pylori positivity. The difference in prevalence between males and females was not statistically significant (p=0.291). In the control group, 30.0 percent of females were H.pylori positive and 44.8 percent males were H.pylori positive, the difference was not statistically significant (p=0.295).

Relationship of H.pylori to Creatinine Values

The mean value of creatinine in H.pylori positive patients was 3.63 (standard deviation 5.19) compared to mean creatinine values of 3.31 (standard deviation 2.57) in H.pylori negative cases. The prevalence of H.pylori did not seen to be influenced by levels of creatinine.

Histological Correlation of Helicobacter pylori

Different patterns of histological gastritis were compared to Helicobacter pylori prevalence.

Active chronic superficial gastritis: A total of 43 patients had active chronic superficial gastritis. Twenty six (60.5%) demonstrated H.pylori. The patients with no active chronic superficial gastritis had 10.1 percent prevalence of H.pylori. The result were statistically significant (p<0.05), therefore, there is a significant correlation between Helicobacter pylori prevalence and acute chronic superficial gastritis.

Inactive chronic superficial gastritis: Out of a total of 14 patients with inactive chronic superficial gastritis, 3 (21.4%)

Age distribution of H.pylori

P value 0.47

Table 13.

Age group (years)	Case (%)	Control (%)	Total (%)
20-29	3 (4.8)	2 (4.1)	5 (4.5)
30-39	4 (6.3)	10 (20.4)	18 (16.1)
40-49	39 (61.9)	23 (46.9)	62 (55.4)
50-59	6 (9.5)	14 (28.6)	16 (14.3)
60-69	6 (9.5)	0 (0.0)	6 (5.4)
70-79	5 (7.9)	0 (0.0)	5 (4.5)

were Helicobacter pylori positive as compared to 30.6 percent positivity in patients who did not have inactive chronic superficial gastritis. The difference in prevalence of H.pylori was not statistically related to presence of inactive chronic superficial gastritis.

Pangastritis

The total number of patients with pangastritis were 9, out of 55.5 percent were Helicobacter pylori positive and 44.4 percent H.pylori negative. There was no correlation between Pangastritis and H.pylori (p=0.083).

Atrophic Gastritis

There was one patient with atrophic gastritis who demonstrated .pylori. The number is too small for statistical comparison.

Endoscopic Correlation of Helicobacter pylori

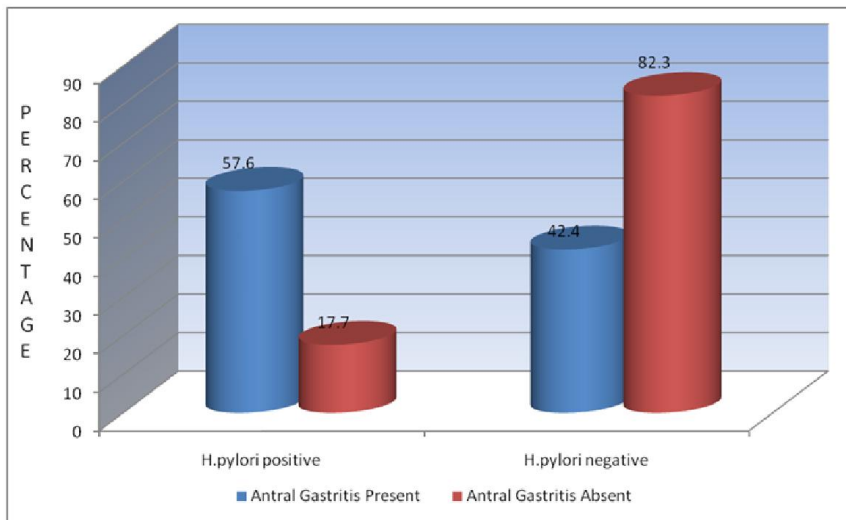Endoscopic findings were related to H.pylori as follows:

Antral Gastritis and Helicobacter pylori

A total of 33 patients had endoscopic antral gastritis, out of which 19 (57.6%) were Helicobacter pylori positive. The patients with no antral gastritis had 17.7 percent prevalence of H.pylori. The results are statistically significant (p<0.05). Therefore, there was a significant correlation between antral gastritis and H.pylori (Table 14).

Table 14.

Antral Gastritis	H.Pylori		
	Positive (%)	Negative (%)	Total (%)
Present	19 (57.6)	14 (42.4)	33 (29.5)
Absent	14 (17.7)	65 (82.3)	79 (70.5)

Antral Gastritis and H.pylori

p value < 0.05

Gastric Ulcer (GU)

P= value 0.13

Gastric Ulcer

A total of 10 patients had gastric ulcer, out of which 5 (50.0%) were H.pylori positive. Patients with no gastric ulcer showed 27.5 percent H.pylori positivity (Table 15). The difference in prevalence of H.pylori between the gastric ulcer and non-gastric ulcer group is not statistically significant (p=0.130).

Table 15.

Gastric Ulcer	H.Pylori		
	Positive (%)	Negative (%)	Total (%)
Present	5 (50.0)	5 (50.0)	10 (8.9)
Absent	28 (27.5)	74 (72.3)	102 (91.1)

Duodenal Ulcer

A total of 11 patients had duodenal ulcer, out of which 54.5 percent were Helicobacter pylori positive. Patients without duodenal ulcer showed 26.7 percent H.pylori positivity (p=0.62), therefore, there was no direct correlation between Helicobacter pylori prevalence and duodenal ulcer (Table 16).

Table 16.

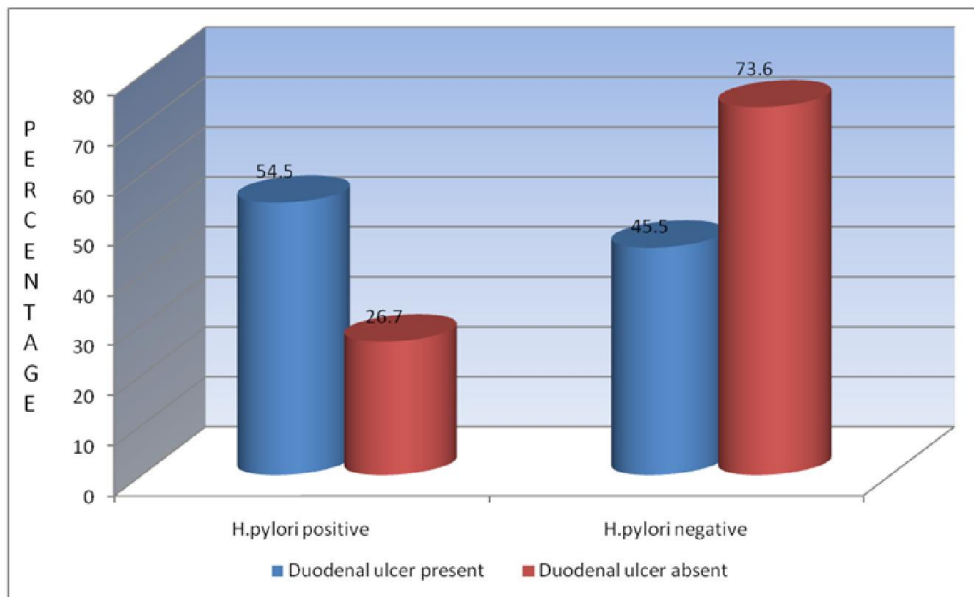| Duodenal Ulcer	H.Pylori		
	Positive (%)	Negative (%)	Total (%)
Present	6 (54.5)	5 (45.5)	11 (9.8)
Absent	27 (26.7)	74 (73.6)	101 (90.2)

H.pylori and Reflux Esophagitis

A total of 7 patients had reflux esophagitis, out of which 28.6 percent were H.pylori positive and 71.4 percent were negative. The difference in prevalence of H.pylori between patients with reflux esophagitis and no reflux esophagitis was not significant.

Complex Patterns of Upper Gastrointestinal Lesions Associated and their Correlation to Prevalence of H.pylori:
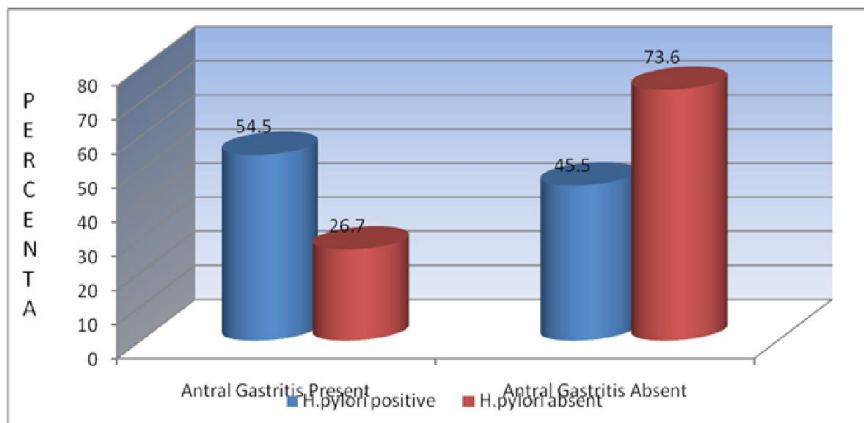
Antral Gastritis and Duodenal Ulcer

Antral gastritis and duodenal ulcer are usually associated with H.pylori. Therefore, we tried to find whether the combination of antral gastritis and duodenal ulcer were related to Helicobacter pylori prevalence.

Duodenal Ulcer

p value < 0.05

Antral Gastritis and Duodenal Ulcer together in relationship to H.pylori.

P <0.003.

In the case group, a total of 3 patients demonstrated antral gastritis and duodenal ulcer, out of which all patients had H.pylori.   Therefore, there is a statistically significant correlation of the presence of antral gastritis and duodenal ulcer with H.pylori.

Antral Gastritis and Duodenitis

A total of 6 patients had the combination of antral gastritis and duodenitis, out of which 5 were H.pylori positive.

Active Chronic Superficial Gastritis and Duodenitis

A total of 3 patients demonstrated active chronic superficial gastritis and duodenitis, out of which only one was H.pylori positive

DISCUSSION

Our study group included patients between ages 24 years to 75 years. The maximum number of patients fell in the age group between 40 to 49 years and patients in extremes of age were few. The case group (patients with established CRF) and the control group (patients with normal renal function) were age matched. Most patients with CRF fall in the ages beyond 40 years as diabetic nephropathy is the most common cause of CRF worldwide and was also the most common etiological factor for CRF in our study.

Sex distribution

In both cases and controls, there was male preponderance as compared to females and males represented 66.7 percent and 59.2 percent of cases and controls respectively. This pattern of sex distribution did not influence the statistical analysis of data.

Symptoms

All patients in both cases and control groups demonstrated a similar profile of symptoms. Although CRF patients to the general population with significant gastrointestinal symptoms. Since both our study groups are symptom matched, histopathological and endoscopic findings as well as H.pylori prevalence would not be biased on the basis of symptoms.

Endoscopic findings

We divided the endoscopic findings into three sub-groups:

Endoscopic Esophageal Findings

The endoscopic esophageal findings revealed reflux esophagitis in 3 (4.8%) cases and 4 (8.2%) controls. Esophageal candidiasis was observed in one patient of the case group. The prevalence of reflux esophagitis was similar in both groups of patients and comparable to the prevalence of reflux esophagitis observed in the general population which is about 3 to 5 percent (Tibbling *et al.,* 1987).

Findings in Stomach

Depending upon the topographical distribution of gastritis it was divided into three sub-groups: (i) Antral gastritis, (ii) Fundal gastritis, and (iii) Pan-gastritis.   On endoscopic appearance, multifocal atrophic gastritis and gastric ulcer were directly observed. Gastritis was observed in 39.7 percent of patients with chronic renal failure and 38.8 percent of controls. The commonest pattern of gastritis observed was antral gastritis, being present in 18 (28.6%) cases and 15 (30.6%) controls. Gastritis atrophy was observed in only one patient who was a CRF patient.   Pan-gastritis was observed in 7.9 percent cases and 8.2 percent controls.   Gastric ulcers were observed in 2 (3.2%) cases and 8 (16.3%) controls. The gastric endoscopic findings, therefore, showed a similar pattern between cases and control except relatively higher prevalence of gastric ulcer in control groups.

Findings in Duodenum

Duodenitis was observed at endoscopy in 4 (6.3%) cases and no duodenitis was observed in control subjects.   Duodenal ulcer was seen in 1 patient with CRF and 10 (20.4%) of the control subjects.   The difference between duodenal ulcer prevalence in control was significantly higher compared to CRF patients (p=0.001) (Table 17).

Comparison of endoscopic findings between different studies on CRF patients

Table 17.

Name of Study (n = No. of patients)	Gastritis (%)	Gastric ulcer (%)	Duodenal ulcer (%)
Our study (2001) (n=63)	39.7	3.2	1.6
Prakash *et al.* (1991) (n=182)	48.8	0.8	8.8
Abu Farsakh *et al.* (2001) (n=76)	71.0	1.67	1.67
Margolis *et al.* (1978) (n=85)	22.0	-	-
Teena *et al.* (2000) (n=88)	10.0	4.0	0.0
Ahmed *et al.* (2000) (n=101)	70.0	7.0	7.0

Histopathology

We studied the histopathological patterns of gastritis in the following sub-groups: (i) Active chronic superficial gastritis – if there was presence of neutrophils in the inflammatory infiltrate and it was restricted to the muscularis mucosa; (ii) Inactive chronic superficial gastritis – If the infiltrate did not demonstrate neutrophils and remain confined to the muscularis mucosa; (iii) Atrophic gastritis – If there was evidence of atrophy. We observed active chronic superficial gastritis as the most common pattern of gastritis in the antrum, being present in 21 (33.3%) of cases and 22 (44.9%) of controls. Inactive chronic superficial gastritis was observed in 6 (9.5%) cases and 8 (16.3%) of controls. Atrophic gastritis was observed in only one patient. There was no statistically significant difference in the patterns of histological gastritis observed in CRF patients and controls (Table-18).

Comparison of histopathological findings in CRF patients

Table 18.

Name of Study (n = No. of patients)	Histologial antral gastritis (%)	Normal antral mucosa (%)
Our study (2001) (n=112)	44.4	55.6
Margolis *et al.* (1978) (n=85)	46.0	54.0
Abu Farsakh *et al.* (2001) (n=76)	52.6	47.4
Mostafa *et al.* (1993) (n=70)	52.0	48.0
Ahmed *et al.* (2000) (n=101)	37.0	63.0

Correlation between endoscopy and histopathology

Endoscopic gastritis in the antrum correlated well to histological gastritis on biopsy. Endoscopic gastritis was observed in a total of 45 patients, out of which 38 (84.4%) also demonstrated histological evidence of gastritis.

Correlation between levels of creatinine and endoscopic gastritis

In CRF patients, the mean value of creatinine in patients of gastritis was not statistically different as compared to patients without gastritis. Therefore, mere rise in creatinine did not seem to contribute to gastroduodenal lesions in our study.

Helicobacter pylori

Prevalence between cases and controls

H.Pylori was demonstrable in only 2 (4.1%) of controls and no H.pylori was demonstrable histopathologically in cases. Culture demonstrated H.pylori in 4 (6.3%) of cases and 7 (14.3%) of controls. Considering RUT as the index of H.pylori positivity, the prevalence of H.pylori was evaluated. A total of 14 (22.2%) of case subjects were H.pylori positive and 19 (38.8%) controls had H.pylori infection (Table-19). This difference in prevalence between patients with CRF and patients with normal renal function did not differ significantly (p=0.0566).

Comparison of H.pylori prevalence in CRF patients and its comparison with controls

Table 19.

Name of Study (n=no.of patients)	Method of H.pylori detection	CRF patients (%)	Controls (%)	p-value (CRF vs. controls)
Our study (2001) (n=112)	RUT/Cult./HIST	22.2	38.8	0.056
Gladziwa *et al.* (1993) (n=164)	RUT/Cut.	34.0	54.0	>0.05
Jasperson *et al.* (1995) (n=220)	RUT/Cult.	25.0	56.0	<0.05
Davenport *et al.* (1997) (n=525)	ELISA	52.0	43.0	>0.05
Misra *et al.* (1999) (n=100)	RUT/HIST	56.0	78.0	<0.05
Shousha *et al.* (1990) (n=170)	RUT	24.0	42.0	<0.05
Ozgur *et al.* (1997) (n=201)	RUT	60.0	64.0	>0.05
Aa-Kaila *et al.* (1991) (n=153)	RUT/Cult	17.0	54.0	<0.05

RUT = Rapid urease test
Clut. = Culture on selective media
HIST = Histopathological direct staining

Age distribution of h.pylori

H.pylori was detected by RUT at a minimum age of 32 years and maximum age of 76 years. The mean age for H.pylori positivity was 47 years (standard deviation 10.7 years). There was no statistical significant correlation between the present of

H.pylori and the age of the patients. However, H.pylori was maximally observed in patients in the 40 to 49 years age group.

Sex distribution of h.pylori

In our study, a total of 36.4 percent females were H.pylori positive as compared to 63.6 percent H.pylori prevalence in males. The difference was not statistically significant (p=0.972).

Relationship of h.pylori prevalence to levels of creatinine

There is a theoretical possibility that raised creatinine levels leading to raised intra-gastric urea concentration would influence colonization of H.pylori which is a urea splitting organism. However, our study did not find any statistically significant difference in H.pylori prevalence in CRF patients with different levels of creatinine (p> 0.05).

H.pylori prevalence in relationship to antral gastritis

H.Pylori has been implicated to cause antral predominant gastritis in majority of patients. In our study, 19 out of 33 patients were H.pylori positive (57.6%) as compared to 17 percent H.pylori positivity without antral gastritis. The difference was statistically significant (p < 0.05). Therefore, we found a significant correlation between antral gastritis and H.pylori.

Histopathology in relationship to h.pylori

Our study showed that 26 out of 43 patients with active chronic superficial gastritis were H.pylori positive (60.5%) compared to 10.1 percent H.pylori prevalence in patients without active chronic superficial gastritis. The result was statistically significant (p < 0.05) and direct correlation between antral gastritis and H.pylori prevalence was found. Inactive chronic superficial gastritis did not correlate to H.pylori prevalence significantly (p>0.05). There was only one patient of atrophic gastritis in the study and he was H.pylori positive. However, statistical correlation was not possible due to low prevalence of possible due to the low prevalence of atrophic gastritis.

H.pylori and gastric ulcer

In our study, patients with gastric ulcer had 50 percent prevalence of H.pylori compared to 27 percent prevalence of H.pylori in the on-gastric ulcer group. The relationship between H.pylori and gastric ulcer was found to be statistically insignificant (p = 0.13).

H.pylori and duodenal ulcer

In our study, a total of 11 patients had duodenal ulcer, out of which 54.5 percent were H.pylori positive as compared to 26.7 percent H.pylori positivity in patients without duodenal ulcer. The association between duodenal ulcer and H.pylori was found to be statistically insignificant (p=0.062).

Summary and Conclusions

Helicobacter pylori prevalence as demonstrated by a positive rapid urease test was 38.8 percent in controls and 22.2 percent in patients with chronic renal failure.The difference in

prevalence between the two groups was not statistically significant.The prevalence of H.pylori was not related to increasing age of the patient and maximum H.pylori prevalence was seen in the age group between 40 and 49 years. H.Pylori prevalence did not seem to be influenced by the levels of creatinine. The presence of endoscopic antral gastritis showed significant association with H.pylori prevalence, however, H.pylori infection was not related significantly to any other form of gastritis. The presence of duodenal ulcer or gastric ulcer did not show any increased prevalence of H.pylori. The combination of antral gastritis and duodenal ulcer showed 100 percent prevalence of H.pylori. There was no association found between H.pylori and reflux esophagitis.

The endoscopic findings showed reflux esophagitis in 4.8 percent cases and 8.2 percent controls, which are comparable..In stomach, gastritis was observed in 39.7 percent of patients with chronic renal failure and 38.8 percent of controls. Antral pattern of gastritis was the most common endoscopic lesion observed in both groups. Gastric ulcer was seen in 3.2 percent cases and 3.6 percent controls. Duodenal ulcer was seen in 1.6 percent CRF patients and 20.4 percent controls. The endoscopic findings were similar in patients with CRF and controls and except a higher prevalence of duodenal ulcer in controls as compared to CRF patients. A total of 42.2 percent patients had some form of histological gastritis. The commonest pattern of antral histology was active chronic superficial gastritis and was found in 33.3 percent cases and 44.9 percent controls. Atrophic gastritis was present in only one patient. Both, controls and patients with CRF showed a similar pattern of histological gastritis. There was good correlation between endoscopic and histological gastritis. There was no correlation between levels of creatinine and severity and nature of histological lesions in the antral mucosa. Gastrointestinal symptoms in patients with end stage kidney disease are due to multi-factorials ,however high prevalence of H. Pylori infection is common in developing country like India where symptomatic patients need evaluation by doing U.G. I. Scopy where one should test and treat to alleviate the patients' symptoms as well as to avoid the feared complications associated with H. Pylori infection.

Abbreviations

OGD-Oesophagogastrduodenoscopy, H. Pylori-Helicobater Pylori, CRF-Chronic renal failure.

Competing interests

The authors declare that they have no competing interests.

Authors' contribution

K.C. Das, Sanatan Behera, Sumeet David were involved in the clinical assessment and writing the study.

All authors read and approved the final manuscript.

Consent

Full written consent was received for the manuscript to be published.

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