Observations and Results
A total of nine hundred and fifty five patients were included in this study.

These patients comprised the following four groups:

Group I  –  Asymptomatic adults and children (n=205),
           A – Children (n = 105)
           B – Adults (n = 100)

Group II – Upper gastrointestinal disorders (n=458),

Group III – Complicated duodenal ulcer other than perforated duodenal ulcer (n=142)

Group IV – Perforated duodenal ulcer (n=262).

ASYMPTOMATIC ADULTS AND CHILDREN (GROUP I):

Children – Group IA:

There were 105 children in group IA. The children belonged to different age groups as shown below:

i)  -  up to 5 Years  (n=37)
     Mean age ± SEM 2.59 ± 0.92 years

ii) -  6-10 years of age  (n=36)
       Mean age ± SEM 7.11 ± 0.21 years

iii) -  11-15 years of age  (n=32)
       Mean age ± SEM 11.47 ± 0.12 years

The overall prevalence rate of *H pylori* in children was 45% (47/105). It was 46% in the under fives, 44% in children between 6 and 10 years of age and 44% in
children between 11 and 15 years of age. There was no significant difference between children of different age groups (Table 1.1.1). It was seen that four out of eight children under one year of age showed anti-\textit{H pylori} IgG antibodies in their serum. The ability to mount an immune response at this age is uncertain and in the absence of maternal IgG levels, it cannot be said whether these antibodies have been transplacentally transferred to the infants. Although there was an apparent higher prevalence rate in female children under 5 years of age and male children between 6 and 10 years of age compared to the opposite gender, these differences were not significant (Table 1.1.2). Overall, in children, \textit{H pylori} prevalence in boys and girls at 47\% and 41\% was similar (P = 0.67). Comparison of IgG antibody titres in children of different age groups did not show any significant difference in the titres of antibodies in different age groups although the titres were slightly higher in older children (p = 0.53) (Table 1.1.3).

\textbf{Adults – Group IB:}

There were one hundred asymptomatic adults in group IB. There were 82 men and 18 women. The age of asymptomatic adults ranged from 18 to 75 years with a mean $\pm$ SEM of 41.05 $\pm$ 1.46 years. Sixty nine of these adults (69\%) were infected with \textit{H pylori}. The maximum colonization rate of 74\% was seen in young adults (21-40 years). Thereafter, there was a minimal decline in prevalence with advancing age. It was 69\% between 41-60 years and 67\% in patients beyond 60 years. The prevalence rate of \textit{H pylori} in asymptomatic men at 66\% (54/82) was not
significantly different from the prevalence rate of 83% (15/18) seen in women ($p = 0.24$). The prevalence rate in different age groups is shown in Table 1.2.1.

There was a significant difference in the prevalence rate of *H. pylori* between children and adults. Only 47/105 (45%) children below 15 years of age were positive for *H. pylori* as compared to 69/100 (69%) in adults ($p = 0.0007$). The odds ratio of having *H. pylori* infection at different ages is shown in Table 1.2.1. It is highest at 3.68 between 21-40 years of age and declines to 2.53 in adults over 60 years of age ($p = 0.0002$).

The anti-*H. pylori* antibody levels too followed more or less a similar pattern. The mean ± SEM titres in EU/ml of anti-*H. pylori* IgG were higher at 63.96 ± 6.03 between 41-60 years of age. It was 62.48 ± 5.58 EU/ml in the 21-40 year age group and 50.54 ± 9.75 EU/ml in those over 60 years of age. One way ANOVA showed the difference in IgG titres to be significant ($P = 0.0007$) (Table 1.2.2). The trends in *H. pylori* positivity and antibody titres at different age groups is shown in Fig.1.2.

**UPPER GASTROINTESTINAL DISORDERS (Group II):**

A total of four hundred and fifty eight patients with various upper gastrointestinal disorders were studied.
Prevalence rates:

The prevalence of *H pylori* infection in various upper gastrointestinal disorders is shown in Table 2.1.1. The prevalence rate was highest at 87% for duodenal ulcers followed by 80% for stomal ulcer, 77% for gastric ulcer, 74% for chronic gastritis, 72% for patients with non-ulcer dyspepsia, 59% for erosive gastritis and 57% for carcinoma stomach. These prevalence rates compare with the 69% rate in asymptomatic adults (Table 2.1.1). The difference in prevalence rates from controls was not significant for any of these disorders other than duodenal ulcer (p = 0.0008). The prevalence rate in increasing order is shown in Fig.2.1.1. Logistic regression analysis of prevalence rates in patients with duodenal ulcer as opposed to controls when adjusted for age and sex is shown in Table 2.1.1A. The difference in prevalence rates between duodenal ulcer and controls remained significant (p = 0.0004).

Serological titres:

The titres for anti-*H pylori* IgG antibodies in various upper gastrointestinal disorders is shown in Table 2.1.2. The titres were highest in patients with stomal ulcer. The titres in various diseases in ascending order (in EU/ml) is shown in Fig.2.1.2. One way ANOVA test did not show any significant difference in the titres of antibodies in various upper gastrointestinal disorders (p = 0.68). Although, patients with duodenal ulcer had a significantly higher prevalence rate of *H pylori*
compared to controls, the IgG titres at 64.24 ± 2.67 EU/ml were not significantly different from controls.

**Carcinoma stomach:**

There were 51 patients with carcinoma of the stomach. Of these, antral tumors accounted for 24, body 18 and fundic tumors for 5. In 4 patients the carcinoma was diffuse (Table 2.2.1). The *H pylori* prevalence was highest in patients with fundic tumors at 80%, followed by 67% in the antrum. The positivity was less with tumors of the body and diffuse lesions. However, there was no significant difference in positivity of *H pylori* for tumors of different sites (p = 0.36).

**Erosive gastroduodenitis:**

There were 58 patients with erosive gastroduodenitis. Of these, 23 had a history of NSAID use as defined in methodology and in 35 patients there was no history of use of NSAIDs. The prevalence rate in NSAID users was 52% (12/23) as opposed to 63% (22/35) in non-NSAID users. This difference was not significant.

Majority of patients (36/58) had erosions primarily involving the body. Other areas were less frequently involved (Table 2.3.1). The *H pylori* prevalence in patients with erosions at different sites is shown in the Table. It is seen that it was 100% for patients with fundal erosions followed by 67% for antral erosions and 50% for patients with erosions of the body. Although a trend towards higher positivity was seen for fundal erosions, it did not reach significance (p = 0.055).
Patients with erosive gastroduodenitis were classified into smokers and non-smokers and also into alcoholics and non-alcoholics as defined in methodology (Table 2.3.2). The prevalence rate in smokers at 78% was higher but not significantly different from the 55% seen in non-smokers. There was also no significant difference in prevalence between alcoholics and non-alcoholics although there was a trend to a higher positivity rate of 73% versus 55% in alcoholics.

**Gastric ulcer:**

There were 53 patients with gastric ulcer. Majority of patients (66%) with gastric ulcer had evidence of healed or active duodenal ulcer simultaneously. 29/35 (83%) patients in this group were infected with *H pylori*, while only 12/18 (67%) patients having gastric ulcers without evidence of duodenal ulcer were infected (Table 2.4.1). This difference was not significant although a trend towards higher positivity is apparent when gastric ulcer is associated with healed or active duodenal ulcer (*P* = 0.32). 36 patients (68%) presented with a solitary gastric ulcer and 17 (32%) with multiple gastric ulcers. When the number of gastric ulcers was related to *H pylori* status, 27/56 (75%) patients with a single ulcer were infected as opposed to 14/17 (82%) when multiple ulcers were present. There was no difference in prevalence between the two. The relationship of *H pylori* prevalence in patients with gastric ulcer when related to smoking and alcohol abuse is shown in Table 2.4.2. In patients with gastric ulcer the prevalence of *H pylori* was 70% in smokers compared to 79% in non-smokers (*P* = 0.40). It was 83% in alcoholics as opposed to 77% in
non-alcoholic patients ($p = 0.59$). 70% (14/20) of patients with analgesic intake and gastric ulcer had a positive *H pylori* status compared to 82% (27/33) of patients with gastric ulcer and no analgesic intake. This difference was not significant ($p = 0.51$).

**Duodenal ulcer:**

There were a total of one hundred and sixty six patients with active or chronic duodenal ulcer in this study. One hundred and nineteen patients had active visible duodenal ulcers and 47 had a cicatrised duodenum suggestive of healed ulcers. Of patients with active ulcers, 55 patients (46%) had ulcers ranging in size from 6-10 mm. There were 25 patients with ulcers larger than 10 mm in diameter and 39 whose ulcers were less than 5 mm in size (Table 2.5.1). When *H pylori* status was correlated with the size of the duodenal ulcer, 90% of patients with a 5 mm duodenal ulcer were infected, 95% were infected when the ulcer size was 6-10 mm and 88% were infected when the ulcer size was more than 10 mm. When more than one ulcer was present, the size of the largest ulcer was considered for size. No correlation was seen between size of ulcer and *H pylori* prevalence ($p = 0.54$). There were 85 patients who had single ulcers and 34 with multiple ulcers. 94% of patients (80/85) with a single ulcer and 85% patients (29/34) with multiple duodenal ulcers were infected ($p = 0.23$).

The prevalence of *H pylori* in patients with duodenal ulcer was related to smoking and drinking habits. Ninety one percent of smokers with duodenal ulcer were infected with *H pylori* compared to 86% of non-smokers ($p = 0.41$). Regarding
alcohol intake, 89% alcoholics with duodenal ulcer were *H pylori* positive compared to 86% of non-alcoholics \( (p = 0.50) \). Nine out of nine patients with analgesic intake and duodenal ulcer were infected with *H pylori* compared to 135/157 (86%) with no analgesic intake and duodenal ulcer. Due to small numbers these differences were not statistically significant (Table 2.5.2).

**COMPLICATED DUODENAL ULCER OTHER THAN PERFORATED DUODENAL ULCER (GROUP III):**

**Bleeding Duodenal Ulcer:**

Table 3.1.1 shows *H pylori* status in uncomplicated active duodenal ulcer, bleeding duodenal ulcer and asymptomatic controls. There were 54 patients with active duodenal ulcer and 30 with bleeding duodenal ulcer.

The positive *H pylori* status was higher at 93% in active duodenal ulcer compared to the 80% seen in bleeding duodenal ulcer and 69% in asymptomatic controls. However, in spite of this apparent trend, no statistically significant difference was present in positivity rate between active and bleeding duodenal ulcer \( (p = 0.09) \). There was also no significant difference in positivity between bleeding ulcers and controls \( (p = 0.35) \).

Of 30 patients with bleeding duodenal ulcer, in 20 the ulcer size was less than 10 mm. In others it was over 10 mm. No difference in positivity was seen
when ulcer size was correlated with prevalence (p = 0.69) since the percentage positivity for both sizes was 80%.

There was no correlation between \textit{H pylori} status and NSAID use in patients with bleeding duodenal ulcer (Table 3.1.2). The prevalence rates were more or less equal at 82% (9/11) and 79% (15/19) in NSAID users and non-users respectively (p = 0.62).

\textbf{Gastric Outlet Obstruction:}

Table 3.2.1 shows a comparison of \textit{H pylori} status in duodenal ulcer with and without gastric outlet obstruction. There were 54 patients with uncomplicated active duodenal ulcer (Subgroup A). 47 patients had gastric outlet obstruction as evidence of previous duodenal ulcer but no active ulcer at the time of examination (Subgroup C). In 65 patients although cicatricial gastric outlet obstruction was present, the patients also showed an active duodenal ulcer on endoscopy (Subgroup B). The \textit{H pylori} positivity rate was 93% in subgroup A (50/54) as compared to 91% in subgroup B (59/65) and 74% in subgroup C (35/47). The difference in positivity rate between subgroup A and B was not significant, i.e. in the presence of an active ulcer whether or not associated with gastric outlet obstruction, the positivity rate was similar. When patients in subgroups A and B were compared separately with subgroup C, the positivity rate was significantly different (Table 3.2.1). The same significant difference was maintained when adjusted for age and gender by logistic regression analysis (Table 3.2.1A).
A comparison of the anti-\(H\) pylori IgG antibody levels in patients with duodenal ulcer with and without gastric outlet obstruction is shown in Table 3.2.2. The same subgroups were taken for analysis as in Table 3.2.1. The titres were slightly higher in patients with an active ulcer whether or not it was associated with gastric outlet obstruction (Subgroups A and B) compared to patients who had no active ulcer (Subgroup C).

The titres were higher in patients with gastric outlet obstruction and active ulcer (Subgroup B). Statistical analysis revealed no significant difference in titres between subgroups A and B (i.e. patients with active ulcer with or without gastric outlet obstruction). The titres were significantly higher in patients with gastric outlet obstruction when there was an active ulcer as opposed to those with gastric outlet obstruction but no active ulcer (\(p = 0.024\)). Although a trend to higher titres was seen in subgroup A, this did not reach significance compared to subgroup C (\(p = 0.086\)).

PERFORATED DUODENAL ULCER (GROUP IV):

Age and \(H\) pylori positivity:

Age related serological \(H\) pylori status in patients with perforated duodenal ulcer (prospective group) is shown in Table 4.1.1 and Figure 4.1.1. The prevalence rate varied between 58% in patients between 51-60 years and 100% in those over 70 years of age although the numbers in the older age groups were fewer. Odds
ratio varied between 0.62 (51-60 years) to 1.91 (21-30 years). However, study of linear trend by Chi-Square did not show any significant difference between the various age groups (p = 0.12).

Corresponding prevalence rates in the retrospective group are shown in Figure 4.1.2 and Table 4.1.2. The prevalence rates varied between 17-87%, being highest in younger patients between 21-30 years of age. The difference between the various age groups was found to be significant when the Chi-Square test for linear trend was applied (P = 0.02). Discounting patients in older age groups due to small numbers, the positivity rate in both the prospective and retrospective group was highest in patients between 21-30 years of age. The overall positivity rate in the prospective group was 73% which was not significantly different from that seen in controls at 69% (p = 0.52). In the retrospective group, though H pylori status in controls was slightly more at 69% than in patients at 53%, the difference did not reach significance (p = 0.07).

Gender and Positivity:

Overall, there were only 7 women out of a total of 202 patients with perforated duodenal ulcer in the prospective group which is commensurate with the gender incidence seen in this disease in this part of the country. H pylori positivity was not related to gender, being 143/195 in men (73%) versus 5/7 in women (71%). Likewise, in the retrospective group also there were only 3 women out of a total 60 patients. In this group, H pylori positivity was 56% in men (32/57) and nil (0/3) in
women. Due to small numbers of women this difference did not reach significance (p = 0.09).

Size of Perforation and Positivity:

*H pylori* positivity status was assessed with respect to size of perforation (Table 4.2.1). Perforations were classified into less than 5 mm in diameter, 6-10 mm and over 10 mm in diameter. The *H pylori* status was 70% (106/151), 79% (30/38) and 92% (121/13) in the above 3 groups. These differences in the prospective group were not significant (p = 0.15). However, a trend towards a higher positivity status of 92% was seen in perforations over 10 mm in diameter (Table 4.2.1). In the retrospective group, however, this trend was not noticeable (Table 4.2.2) with the positivity rates varying between 50-59% in the three subgroups based on perforation size. It is likely, however, that being a retrospective group taken from old case records, the size of the perforation may not have been accurately recorded in all the case sheets.

Chronicity and *H pylori* Positivity:

The *H pylori* prevalence when related to pre-perforation duration of symptoms, whether or not over 3 months, is shown in Table 4.3.1. The prevalence rate was more or less equal at 74% (95/128) and 72% (53/74) showing that *H pylori* positivity rate was not different in perforation of acute or chronic duodenal ulcer (p = 0.81) as defined by duration of pre-perforation symptoms. This analysis was
not possible in the retrospective group since the duration of symptoms prior to perforation was not always found in the records.

The titres of anti-\(H\) \(pylori\) IgG antibodies did not show any difference between acute and chronic duodenal ulcer perforation (Table 4.3.2). The mean titre was \(62.05 \pm 2.80\) EU/ml in the acute group and \(66.95 \pm 4.12\) EU/ml in the chronic group \((p = 0.313)\).

**Relationship of \(H\) \(pylori\) Positivity to Smoking, Alcohol and NSAID use:**

The positivity status in both the prospective and retrospective group of perforated duodenal ulcer in relation to smoking and alcohol intake is shown in Tables 4.4.1 and 4.4.2. There was no statistical difference in positivity between smokers and nonsmokers and alcoholics and nonalcoholics in both the groups.

In the prospective group four patients gave history of NSAID intake for abdominal pain prior to perforation. Two of them were positive for \(H\) \(pylori\). In the retrospective group, only one patient had history of NSAID intake prior to perforation. He was \(H\) \(pylori\) negative. If the four NSAID users were excluded in the retrospective the overall prevalence of \(H\) \(pylori\) (74%) was similar to controls. Likewise if the single NSAID user was excluded from the retrospective group, the \(H\) \(pylori\) prevalence in this group would be 54% as compared to 69% in controls.
Eradication Rates with Therapy:

A comparison between the eradication rates achieved with ranitidine versus quadruple therapy is shown in Table 4.5.1. Only patients with positive *H pylori* status at presentation were included for this purpose. It was seen that at every interval of followup, eradication rates were higher with quadruple therapy as opposed to ranitidine alone. In the quadruple group the eradication rate dropped from 80% at 8 weeks to 33% at 2 years whereas in the ranitidine group it fell from 57% to 28% at corresponding periods (Table 4.5.1). However, the difference between ranitidine and quadruple therapy reached statistical significance only at 8 weeks (p = 0.01). This was probably due to the high rate of recrudescence with quadruple therapy and due to limited number of patients returning for follow up. The follow up percentage of patients with perforated duodenal ulcer in the prospective group at 8 weeks, 6 months, 1 year, 18 months and 2 years was only 88%, 78%, 55%, 23% and 10% respectively. The results are summarised in Table 4.5.2 and Fig.4.5.2.

Side Effects of Therapy:

Side effects of quadruple therapy were not very marked (Table 4.6.1 and Figure 4.6.1). Nausea and diarrhoea were most common at 37% and 21%. Other important side effects included abdominal pain (18%), a metallic taste (18%) and vomiting (13%). These, however, did not lead to discontinuance of therapy.
Serological Titres at Followup:

Serological positivity for anti-\textit{H pylori} IgG antibodies at various periods in the prospective group following therapy is shown in Table 4.7.1. The serological positivity dropped from 73% to 64% at 6 months and to 68% at one year. No significant change was seen in serological positivity as a whole (\( p > 0.05 \)) during the year's followup.

Table 4.7.2 shows serology titres at various intervals of followup in the prospective group. Patients were classified into those showing >20% fall in anti-IgG titres in EU/ml compared to titres at presentation and those with less than this value. It was seen that between 53% to 67% of patients had a fall below 20% when compared to basal values at different times, whereas 33% to 47% had a fall of more than 20% in comparison to basal titres. Since these titres pertain to the group as a whole without separating the eradicated from the non-eradicated, no statistical comparisons were done.

Overall serological positivity or absolute titre values do not convey any important information. Hence serological titres were studied in patients in whom \textit{H pylori} was eradicated as opposed to those in whom it was not eradicated. This was done at 6 months and at one year (Table 4.7.3 and Figure 4.7.3). It was seen that at 6 months 71% of the eradicated patients had a fall in titre of more than 20% compared to the basal titres as opposed to only 45% in the noneradicated group.
(P < 0.012). A similar difference was seen at one year also with corresponding figures of 72% and 17% (P < 0.0001). When a decline of ≥ 20% titre levels in EU/ml was used as a test of eradication, it was found to have a sensitivity of 71% at 6 months and 72% at 1 year with corresponding specificity of 55% and 83%. When the cut off of IgG titres altered to different percentages, e.g. 10%, 25%, 30% and 50% it was seen that with the increase in percentage decline in titre levels as a test of eradication, the sensitivity progressively decreased and the specificity increased (Table 4.7.4). The accuracy was ranging from 62% to 65% at 6 months and 75% to 78% at 1 year follow up (Fig.4.7.4). Urease test and histology were used as gold standards for this purpose as described in methodology.

**H pylori Positivity and Ulcer Recurrence:**

Tables 4.8.1 shows a correlation between the *H pylori* status with presence of recurrent or residual ulcer at various intervals of time after perforation closure. It was seen that *H pylori* positive status is significantly higher in all patients who have recurrent or residual ulcer compared to those in whom the ulcer has remained healed upto 1½ years. The difference was highly significant upto one year (P < 0.0001) and remained significant even at 1½ years. The positivity status varied between 76% to 94% in those who had persistent ulcer and between 11% to 38% only in those who had no residual ulcer. At two years, although the positivity rate in patients with ulcer was 86% as opposed to 42% in those without ulcer this did not reach significance due to small numbers but confirmed the same trend as described above. The *H pylori* status and residual recurrent ulcer presence was further
analysed with adjustment for age and sex by logistic regression. It was seen that
*H. pylori* state was significantly higher in all patients who had recurrent or residual
ulcer compared to those in whom the ulcer had healed as seen in Table 4.8.1 (Table
4.8.1A).

Fig.4.8.1 shows risk of residual/recurrent ulcer related to *H. pylori* status at
various intervals of followup in the prospective group. It is seen that in patients with
positive *H. pylori* status, the chance of having an ulcer ranges between 55-70% at
different time intervals. On the other hand, in patients with negative *H. pylori* status,
the risk of having an ulcer lay between 4-28%. Overall taking all *H. pylori* positive
patients and discounting the period of followup, residual / recurrent ulcers are found
in roughly two-thirds of patients (62%) whereas in *H. pylori* negative patients, the
corresponding figure is only 8%. *H. pylori* status is, therefore, more valuable as a
negative predictor of ulcer recurrence.

In the retrospective group also the positivity status was very much higher at
90% in those who had a recurrent ulcer compared to 19% only in those who had no
ulcer (P < 0.0001). This is shown in Figure 4.8.2 and Table 4.8.2. When adjusted
for age and sex the significantly higher prevalence of *H. pylori* in patients with
recurrent ulcer was maintained (Table 4.8.2A). In the retrospective group also, it
was seen that a positive *H. pylori* status was associated with 81% chance of residual
/ recurrent ulcers whereas a negative *H. pylori* status was associated with only 11%
risk of residual / recurrent ulcer.