DISCUSSION

In children, the prevalence of *H. pylori* ranges from less than 10% to greater than 80% in otherwise healthy individuals and is dependent upon age, socioeconomic class and country of origin [168]. Children present an ideal population for studying the interaction between *H. pylori* and gastric mucosa because pediatric age is free from common causes of secondary gastrointestinal disease (drugs, tobacco, and alcohol) [169]. Also the natural history of diseases related to *H. pylori* is conditioned by the early acquiring of the bacterium [170].

The present study was conducted over the period from June 2011 to June 2012 and included 95 selected patients who were planned to have upper GI endoscopy because of hematemsis, vomiting and/or abdominal pain. Multiple biopsy samples were taken from the esophagus, the fundus, the antrum, and the duodenum. Using stool antigen, urease test and PCR, *H. pylori* was detected in 50 symptomatic patients out of 95. These patients compared to 25 asymptomatic *H. pylori* positive children diagnosed by stool antigen.

In the present study we have examined the potential correlation between *H. pylori* virulence factors and clinical presentations, endoscopic and histopathological findings.

Hematemsis is the most common clinical manifestation in patient who referred to our pediatric gastroenterology clinic for upper gastrointestinal endoscopy (54.7%, 52 out of 95 children). This is similar to a study in Taiwan in which, there was 112 patients involved in the study and hematemesis patients were 77 cases (68.8%) [171].

H. pylori infection is the most important cause of primary duodenal ulcer in children. Since duodenal ulcer and the use of nonsteroidal anti-inflammatory drugs are the most common etiologies of upper gastrointestinal bleeding during childhood, *H. pylori* infection should be sought in children with acute upper gastrointestinal bleeding[172].

Our study reveals statistically significant association between *H. pylori* and hematemsis. In Russian study, hematemsis was present in the children with *H. pylori* infection only and in no patients without *H. pylori*[173].

The most common ulcer symptom in *H. pylori* positive children is burning pain in the epigastrium, which typically occurs when the stomach is empty, between meals, and in the morning hours, although it can also occur at other times. It may last from minutes to hours and may be relieved by eating or by taking antacids[174, 175].

In the present study, a detailed examination of the characteristics of abdominal pain in the symptomatic children showed that night- time pain with nocturnal awakening and fasting pain relieved by food are significantly associated with *H. pylori* infection ($p<0.05$). The abdominal pain associated with meals is less common in children with *H. pylori* than in children without the infection ($p<0.05$). Lamireau et al [176] suggested that epigastric location of the pain and vomiting were equally frequent in both groups.. Alternatively, Gremse and Sacks stated that nocturnal pain, a positive family history of peptic ulcer, and pain in periumblical region were not associated with *H. pylori* gastritis in childhood[177].

While estimating the relationship between *H. pylori* strains and clinical presentations, neither of abdominal pain nor vomiting are associated with H. pylori.

There are several studies investigating the association between recurrent abdominal pain (RAP) and *H. pylori* infection, but no association has been identified [178,179]. Authors suggests that abdominal pain was not more frequent in H. pylori-positive than in H. pylori-negative children submitted to endoscope.[47,180,181]

In contrast, some investigators have demonstrated that *H. pylori* are common finding among children suffering from RAP [74,182,183]. In study in USA, it suggests that the RAP complaints found in children with *H. pylori* are caused by secondary gastroduodenal pathology, rather than by *H. pylori* infection itself [184].

Several consensus statements and guidelines have suggested that children with RAP should be investigated for *H. pylori* only when upper gastrointestinal endoscopy is required to look for an organic disease such as peptic ulcer or esophagitis [132,137,185]. In the revised guidelines regarding the management of *H. pylori* infection, RAP is not an indication for a "test and treat" strategy for *H. pylori* infection in children [132,137].

The important cause of non specific RAP can be the gastrointestinal motor function abnormalities associated with gastrin hyperproduction [186,187]. The fasting gastrin concentrations were significantly higher in *H. pylori* positive children than in negative children, but there was no difference between RAP positive and RAP- negative children[187].

In 1982, Warren and Marshal described *H. pylori* in gastric mucosa and reported the presence of endoscopic nodular gastritis in positive cases [188]. Later, Czinn et al [189] and Cadranel et al[190] reported the same endoscopic finding in children. Nodularity was associated with lymphoid follicles seen with histological examination in some of their patients. More recent studies have also reported a significant association between endoscopic nodular gastritis and *H. pylori* infection [62,176,191-193].

Existence of antral nodularity can be assigned as an endoscopic sign of infection in children [194]. Our study establishes the importance of antral nodularity finding during endoscopic examination of children. At endoscopic examination of the 50 symptomatic affected children, nodular antrum seemed to be the most common finding, we also found a significant association between endoscopic nodular gastritis and symptomatic *H. pylori* infection (as seen in 82% of the patient with *H. pylori* and not seen in patient without infection $p<0.05$).

Lame L, ET [195] observed that antral nodularity had a high specificity for *H. pylori* 96% with positivity predictive value of 90%. Also, Sbeih, et al[196] described that all observed of his patients with endoscopic antral nodularity had *H. pylori* in their antral biopsy specimens (100%). While, our study revealed that the sensitivity, the specificity, the PPV, NPV and accuracy of antral nodularity for *H. pylori* infection are 82, 100, 100, 83.33, 90.53% respectively. These figures suggest that antral nodularity is a significant predictor of *H. pylori* infection.

Recently, Grellierl, et al[197] suggested that the nudularity of gastric antrum is a specific marker of mucosal colonization by *H. pylori* with the sensitivity of 74.1% and specificity of 100%. He advised that in the presence of antral nodularity *H. pylori* colonization may be assumed, thus avoiding the need for an additional biopsy.

A study in Australia suggested that nodularity in children is more conspicuous than in adults with three possibilities (1) nodularity is the response of an immature immune system to initial antigenic stimulation by *H. pylori* (2) nodularity relates to the dose of *H. pylori* at initial infection, a large initial inoculums initiating an exaggerated immune response, (3) nodularity is a characteristic of the early stage of infection with *H. pylori* [(198)].

Antral predominant gastritis is the main pattern of gastritis in our samples histologically 92% (46out of 50). This is in agreement with a study which suggested that antral predominant nonatrophic gastritis is more common in children[(199)].

In the present study, duodenal erythema was the second most common finding after nodularity in *H. pylori* infected patients. Significant relation between *H. pylori* and duodenal erythema was present ($p<0.05$). 35.6 %of our *H. pylori* non infected cases had duodenal abnormality endoscopically, while in *H. pylori* infected patient the percent reach 68% ($p<0.05$). Histologically, 78% (39 out of 50) symptomatic *H. pylori* positive cases had duodenitis in comparison to 66.7% (30 out of 45) symptomatic *H. pylori* negative cases had duodenitis($p>0.05$).

We observed a significant negative correlation between *H. pylori* infection and esophageal erythema by endoscopic picture ($p<0.05$). Esophageal erythema is seen in (91.1%) of the non infected group in comparison to 52% of the *H. pylori* positive cases. While histologically, 78% (39 out of 50) of the symptomatic h pylori positive cases had picture suggestive of reflux esophagitis in comparison to 68.9% (31 out of 45) of the symptomatic h pylori negative cases with the same picture ($p>0.05$).

In adults, the majority of data suggest a negative association between *H. pylori* infection and reflux esophagitis [(174,175)] and with Barrett esophagus [(200)]. This topic is still controversial in the pediatric population, with few studies, some demonstrating similar inverse correlation in children[(201)], and other a positive correlation[(202,203)]. And other no relationship[(204)].

Some investigators suggested that the presence of *H. pylori* may protect against the development of GERD by suppressing gastric acidity via the neutralizing effect of bacterial ammonia production and corpus gastritis induced by persisting *H. pylori* infection [(205-208)].

In our study, the histopathological parameters were assessed using the criteria as described in the modified updated Sydney classification[(116)] with addition of other parameters. There is a statistically significant difference between *H. pylori* positive and negative cases as regard the severity, depth and presence of lymphoid follicles.

Our findings are in agreement with the studies from Peru[(205)], Colombia[(210)], Japan[(211)] and Greece[(212)], which have reported a high prevalence of *H. pylori* infection associated with severe inflammation in gastric mucosa.

Although *H. pylori* cause chronic gastritis in virtually all patients, not all individuals develop more severe gastric pathology. Thus, there is a marked discrepancy between the number of individuals colonized and those with clinical symptoms[(213)]. The gross endoscopic finding was nodularity in (90.9%) of patients complaining of hematemsis. Most of the children with RAP (83.9%) had antral nodularity in their endoscopy. In our study, 66.7% of *H. pylori* infected cases who complain of hematemsis has duodenal

erythema endoscopically, however, there was a negative association between hematemsis in *H. pylori* positive cases and erythema of the esophagus.

In our study, the histopathological picture of symptomatic *H. pylori* positive cases reveals a significant relation between hematemsis and the severity of inflammation in comparison to those not complaining of hematemsis ($p<0.05$). Also, there is a significant relation between abdominal pain and severity of inflammation ($p<0.05$).

There have been reports correlating between different *H. pylori* genotypes and the severity of the disease in adults and children[214-216].Our aim in the present study is to correlate the main bacterial virulence factors comprise adhesions (babA2), the vaculating cytotoxin (vacA), and the products of the cag pathogenicity island (cag PAI) with the histopathological parameters of *H. pylori* related gastritis, the endoscopic picture and with the clinical presentations. This will be important for the future policies for the eradication of *H. pylori* in order to prevent severe diseases in children and adults. Our study adds new pieces of information in this respect.

The relation between the genotypes of causative strain and clinical outcome should be considered in different geographic regions in order to make a true estimation of prognosis. The geographic distribution of distinct *H. pylori* genotypes remain largely unknown, and the prevalence of virulent bacterial genotypes in certain regions may have important epidemiological consequences [6,7,89,217]. Also, Nomura et al suggested that, the pathogen, a genetically diverse species with a high DNA recombination rate may be involved in the complex variety of diseases in infected patients [128].

The cytotoxin associated gene A (cagA) being a marker for the presence of the cag pathogenicity island (cag PAI) was the first recognized virulence gene in the *H. pylori* genome in both adults and children.[216,217] In the present study, more than half of the *H. pylori* positive cases are cagA positive (52%),. The prevalence of the cagA gene in children among European countries varies from 22.4% to 76 %[219,220]. Earlier studies performed in Turkish children showed the prevalence of the cagA gene was 55%-74.4%[221,222]. In a study from Iran, 68.7% of the adults patients were infected with cagA – positive strains [223]. As to the Middle East, a wide range of cagA distribution has been identified in adults [224]. The lowest has been from Jordan, (26.4%), and the highest from Kuwait (87%). Such difference in the prevalence of cagA positivity could not be explained precisely, however, they have been attributed to the genetic heterogenicity or to difference in the geographic locations [225-227].

In our study, 70% of the symptomatic *H. pylori* positive patients were infected with cagA-positive strains (35 0ut of 50) in comparison to 16% in *H. pylori* positive asymptomatic group ($p<0.05$). The cagA positivity was significantly correlated with hematemsis and abdominal pain ($p<0.05$). Recently, it has been shown that children with a cagA + strain more often complained about abdominal pain and vomiting [228]. The authors explain this phenomenon by claiming that cagA positive strains may favor the local release of neuromediator [229].

According to, Nogueira et al, Persistent infection by *H. pylori* leads to infiltration of neotrophils and lymphocyte in gastric epithelium, causing severe inflammatory activity, which can result in atrophic gastritis with development of intestinal metaplasia and dysplasia[230].

With respect to our study, cag positivity showed significant association with severity of inflammation and with the activity of inflammation ($p<0.05$). Deep inflammation was present in our study, in more than half of the cagA positive cases (51.4%). This is in accordance with Demirturk et al, suggested that cagA positivity is associated with more severe glandular atrophy, inflammation, and activity [(231)].

Also, this is in concordance with a study in North America, which observed that presence of gene cagA presented high degrees of colonization, inflammation, and neotrophilic activity when compared to absence of cagA[(232)]. Whereas other studies in children [(233-236)] have not emphasized this association.

Several genes of the cag pathogenicity island encode proteins that enhance the virulence of the strain, e.g., by increasing the production of interleukin-8 by gastric epithelial cells[(237)], causing infiltration of polymorphonuclear neotrophils, resulting in more severe inflammatory activity of the gastric epithelium[(237)]. Our significant relation between cagA positivity and the severity and the activity of inflammation is consistent with this theory

In our study, there is a significant relation between cag positivity and antral erythema) (57.1% of the cases) also the antral nodularity (94.3%), ($p= 0.002$). This is in concordance with Selimoglu, Mukadder A.[a] who suggested that antral nodularity was more common in cagA-positive patients ($P<0.05$).[(238)]

On other hand, there is a negative or insignificant relation between cagA genotype and normal antrum ($p=0.02$) in macroscopic picture (e.g., the genotype is rarely present in normal samples) which further substantiate the role of cagA as a marker for increased virulence of pylori. In children, many studies suggested that, cagA was shown to be related to the pathogenicity[(239,240)].

There may be a several distinct forms of cagA gene with uneven geographical distribution and these differences in cag genotypes may provide a marker for differences in the virulence among cag-positive *H. pylori* strains and that only some forms of cag gene are associated with severe gastroduodenal disease[(241)].

Gastric epithelial cell injury is caused by a vaculating cytotoxin, encoded by the vacA gene, which induces host cell vacuolation and, finally cell death. The vacA signal (s) region encodes the signal peptide and the N terminus of the processed vacA toxin: the vacA s1 genotype is fully active but the type2 genotype has a short N-terminus extension that blocks vacuole formation[(103)] On other hand, the vacA middle (m) region also has two genotypes (m1 and m2), and the m1 genotypes causes stronger vacuolating activities than the m2 genotype [(103).]

Analysis of *H. pylori* isolates from diverse geographic locations also showed high variability in the vacA gene [(227,242,243)]. In the present study, 72% of the *H. pylori* positive cases were vacA positive. The most common s allele is s2 (64.4%, 29 out of 45 cases) this is similar to previous study from North Africa including Egypt which reported the prevalence of vacA s2 genotype in adults [(244)]. This is in contrary with a study in Kuwait reported that vacA s1 and s2 types were detected in approximately equal numbers in biopsies obtained from patients of Middle –Eastern origin[(245)].

Heterogenicity among vacA alleles may be an important factor in understanding variations in clinical manifestations among *H. pylori* –infected subjects. Our study has shown that 30% of symptomatic *H. pylori* infected children were s1 positive in gastric samples in comparison to 4% of asymptomatic children ($p<0.05$). Also, children with abdominal pain have more frequent association with *H. pylori* strains with s1 allele compared to the children without pain abdomen($p<0.05$). Moreover, there is a significant association between hematemsis and s1 positivity ($p<0.05$).

When we subtyped the vacA gene, we found a strong association between vacA s1-positive status and the erythema in the esophagus as well as the antral nodularity endoscopically ($p<0.05$). This finding is supported by a study in *H. pylori* infected Greek children which found a positive correlation between vaculating vacA s1 genotype and presence of nodular gastritis. [246]

Also, in our study, the vacA s1 genotype is not present in normal antrum ($p=0.087$), this finding further support the role of vacA s1 in epithelial damage.

Several studies have demonstrated that gastric infection with *H. pylori* strains containing type s1 *vacA* alleles is associated with a higher risk for development of peptic ulcer disease than is infection with strains containing type s2 *vacA* alleles [103,243,247,248]. This association seems to be less apparent in many Asian countries than in Europe and the Americans [249,250]. Gusmao et al [251] confirmed the association between vacA s1 strains and peptic ulcer in children

We found a significant association between *H. pylori* vacA s1 positive status and the severity of inflammation, as well as depth and activity of inflammation ($p<0.05$). Atherton et al. suggested that s1 genotype is associated with peptic ulcer and more severe gastritis[104]. War_burton et al. reported no relationship between vacA s1 region and histological findings[252]. This finding is controversial, because it is known that strains with s1 genotype produce much greater amounts of toxins.

As regard the vacA s2, significant correlation between vac s2 and the histopathological findings was detected.

Regarding the vacA mid region allele, vacA m2 was the most common (27 out of 50, 54%). These finding are similar to those studies from North Africa including Egypt, Turkey, Iraq, Iran and Saudi Arabia which characterized m2 as the main allele in adults [244,253,254]. Whereas nearly equal distribution of both m1 and m2 alleles has been found in Jordan [255]. Also our study revealed that, vac m2 was present in 46% of symptomatic *H. pylori* infected patients in relation to 16% of the asymptomatic group.

In our study, we found a significant relation between vacA m1 positivity and both severity and depth of inflammation ($p<0.05$). Nogueira C et al, observed strong significant association between vac m1 genotype and the epithelial damage, neutrophilic and lymphocytic infiltrates, atrophic gastritis, and intestinal metaplasia in adults patients from Portugal and Colombia[230]. Atherton and colleagues [104] also presented evidence that m1 strains were associated with greater gastric epithelial damage than m2 strains in North American patients.

Endoscopic features were not different among patients with or without m1 or m2 strains (P>0.05). This is in agreement with Selimoglu, Mukadder A.[a, (238)]

The mosaic combination of s and m allelic types determine the level of cytotoxin produced which has been associated to pathogenicity of the bacterium [(103)]. These combinations in the s and m regions give rise to four possible *H. pylori* genotypes: s1/m1, s1/m2, s2/m1 and s2/m2 with different levels of toxin production[(242)].

In the present study the prevalence of vacA slm combination genotypes was different among *H. pylori* infected cases. The vacA s2/m2 was the predominant genotype (19 out of 35 cases, 54.2%) followed by s1/m1 (12 out of 35, 34.3%). S1/m2 was the most prevalent genotype in Saudi Arabia[(256)], and Turkey [(257)]. In contrast, other predominant vacA genotype was reported in pediatric patients in Brazil, Slovenia, the Midwestern United States (s1/m1)[(239,258,259)]. The discrepancy between different countries might be explained by the fact that the predominant *H. pylori* strain circulating among geographic locations differs with regard to the genomic structure.

In our study, there is a significant relation between symptomatic cases of *H. pylori* and the s2/m2 positivity (p<0.05). There is also a significant relation between s1/m1 positivity and the symptomatic *H. pylori* positive cases (p<0.05).

A study by Singh, et al[(260)] has shown that children with abdominal pain have more frequent association with *H. pylori* strains with s1/m1 allele compared to the children without abdominal pain. Our study reveals the same significant relation. Also, we found a significant relation between hematemsis and s1/m1 positivity.

In our study, we found that 83.3% of infected cases with positive s1/m1 had severe inflammation (p<0.05). There is a significant relation between s1/m1 positivity and the depth of inflammation (p=0.003). These findings support the role of vacA s1/m1 genotype in severe clinical outcomes.

Increased epithelial damage may be explained by a higher level of cytotoxin production by vacA s1/m1 as compared to vacA s2/m2[(103)]. Earlier studies[(261)] also revealed a significant relationship between the level of cytotoxin production and the severity of atrophy, confirming that the cytotoxin is a disease-associated factor. Because the production of cytotoxin primarily depends on the mosaic structure of the vacA gene, especially of the s and m regions[(103)], the association between vacA s1/m1 genotype and the severity of the pathology here, is consistent with these earlier observations.

Liver et al.[(95)] identified the *H. pylori* blood group antigen-binding adhesion gene, babA, involved in the binding activity between bacterial adhesion and human Lewis blood group antigens on gastric epithelial cells.

Of the 95 *H. pylori* infected patients, 44% were positive for babA2. The frequency of babA2 genotype in *H. pylori* strains varied in different countries. The prevalence of the babA2 gene among *H. pylori* infected adults varies from 32 to 72 in western countries and from 39 to 100% in Asia[(262)] in contrast to adults, published data concerning the prevalence and clinical relevance of the babA2 gene in children are scarce and not consistent[(85,257,259)].

In our study, while estimating the relationship between potentially virulent *H. pylori* strains and clinical presentations, babA2 is more common in our symptomatic *H. pylori* infected

(60%) cases than in asymptomatic infected children (12%). It is a statistically significant difference ($p<0.05$). The relations between babA2 positive cases and hematemsis and abdominal pain are significant ($p<0.05$).

In our study, the histopathological picture cannot differentiate between babA2 positive and babA2 negative cases. 50% of the our cases harboring the babA2 positive strains had severe inflammation in comparison to 50% also of the babA2 negative cases had severe inflammation ,also 43% had deep inflammation in gastric samples in comparison to 50% of babA2 negative cases had also deep inflammation ($p>0.05$). Also, the endoscopic picture cannot differentiate between babA2 positive and negative samples, this results agree with studies performed on 47US and 49 Turkish children[257,263]. However, other investigators suggested a significant correlation between the severity of gastric pathology and the presence of babA2 gene in children isolates[219,247,264] suggesting possible geographic differences.

One of the most recently reported virulence gene of *H. pylori* is babA2 and studies on the relationship between this genotype and the clinical disease associated with *H. pylori* in different countries and regions have produced different results, probably because (1) the study populations differ; (2) patients infected with certain genotype strains will develop different clinical disease over time and (3) the pathogenesis of their *H. pylori* associated diseases involves several genes and factors that interact. In addition, interaction between the host and the bacteria has an important role in the pathogenesis of *H. pylori*[265].

Some authors suggested that heterogenecity among *H. pylori* strains in the expression of the babA2 protein might be a factor that contribute to different clinical outcomes among H. pylori-infected humans[266]. Also, Pride et al[267] suggested the diversity within babA2 gene sequence, which could explain the lack of correlation of the babA2 genotype to the severity of the histolopathological alterations within our *H. pylori* positive patients.

In Japan, they observe that both the babA2 positive strains and the babA2 negative strains colonize in the stomach and that there are adherence factors other than the babA2. They investigated the presence of the hpaA gene, one of the bacterial adhesins in babA2 negative strains and they speculated that the babA2 negative strains can colonize in human stomach because of the presence of other bacterial adhesins[268]. This theory may explain the similarity in our histopathological findings between babA2 positive and negative samples

On examining the association of the main virulence genes in each strain, the simultaneous presence of babA2+cagA+S1, (the triple positive combination) was found in 5 of the symptomatic *H. pylori* cases and not found in the asymptomatic *H. pylori* positive children.

In conclusion, *H. pylori* infection presents mostly with gastritis in pediatric population and not related to recurrent abdominal pain, but it is strongly related to hematemsis, and antral nodularity is an important predictor of *H. pylori* infection. Antral predominant gastritis is the main pattern of gastritis in our sample histologically. Among virulence factors, cagA and vacA s1 are correlated with some clinical presentations and histopathological findings. BabA2 is frequently found in the symptomatic *H. pylori* positive cases, although it does not seem to play a role in the pathogenesis of histopathological alterations.

SUMMARY

Helicobacter pylori infection is a common and universally distributed bacterial infection. It is predominately acquired in childhood, and more than three forths of the population in developing countries is infected during childhood. In developed countries, infection in children is less frequent. It is the most frequent cause of chronic gastritis and peptic ulcer, and is directly associated with gastric carcinoma.

Our aim in the present study is to correlate the main bacterial virulence factors babA2, vacA, and cagA with the histopathological parameters of h pylori related gastritis, the endoscopic picture and with the clinical presentations. This will be important for the future policies for the eradication of h pylori in order to prevent severe diseases in children and adults. Our study adds new pieces of information in this respect.

To achieve this goal, the present study was carried out on 95 symptomatic children who referred for endoscopy suffering from hematemsis, abdominal pain and/or vomiting. 50 of those children were diagnosed to have *H. pylori* infection by rapid urease test, histopathology and PCR and 45 children were diagnosed as *H. pylori* negative. A third group of 25 asymptomatic children were diagnosed as *H. pylori* positive using the stool antigen test.

Statistical analysis of data obtained from the present study showed the following results:

1- Hematemsis is the most common clinical manifestation in patients who referred to our pediatric gastroenterology clinic for upper gastrointestinal endoscopy (54.7%) with statistically significant association between h pylori and hematemsis.
2- Antral nodularity is a significant predictor of *H. pylori* infection.
3- The histological picture of symptomatic H. pylori-infected children was characterized by a more severe inflammatory cell infiltrate, highly active inflammation and an increased number of lymphoid follicles compared with those who were *H. pylori* negative.
4- The histological picture of *H. pylori* infected children with RAP and those with hematemsis, characterized by significantly more inflammation compared with those not complaining .
5- The most prevalent virulent gene is vacA (72%) then cagA (52%) then babA2 (44%) among *H. pylori* positive cases.
6- As regard vacA s/m combined genotypes, s2/m2 is the most common, then s1/m1 then s1/m2 and s2/m1 with equal prevalence.
7- Significant relations are found between babA2, cagA, vacA s1, s1/m1 and s2/m2 positivity and presence of symptoms among *H. pylori* infected children.
8- Antral nodularity was more common in cagA-positive and in vacA s1 positive samples.
9- Among virulence factors, cagA and vacA s1 are correlated with some clinical presentations and histopathological findings
10- We could not detect statistical association between the babA2 status and the severity of the endoscopic and histopathological picture.
11- The triple positive (simultaneous presence of vacA s1, cagA, and babA2) was found in 5 of our symptomatic cases and not found in the asymptomatic children.

CONCLUSION

1. The most frequent gastrointestinal complaint in children referred for endoscopy is hematemsis, and *H. pylori* has an important role. However, neither of abdominal pain nor vomiting is associated with h pylori.
2. Nodular gastritis is the most common endoscopic findings of *H. pylori* infection, and most probably associated with cagA and s1 allele positivity.
3. Antral predominant gastritis seems to be the main pattern of gastritis in *H. pylori* positive cases.
4. There is a statistically significant difference between *H. pylori* infected and non infected groups as regard the severity, activity and presence of lymphoid follicles.
5. It seems that hematemsis an abdominal pain are associated with sever inflammation in antral samples.
6. It would appear that there is a high prevalence of babA2, cagA, vacA s1, s1/m1, and s2/m2 among symptomatic *H. pylori* positive patients especially those complaining of abdominal pain and hematemsis.
7. We had confirmed, a significant correlation between the severity of histological changes and the presence of the vacA s1 and cagA in the *H. pylori* genome
8. The present study could not detect any association between babA2 and the severity of histopathological or endoscopic changes.