

RESULTS

Over a period of 12 months, between June 2011 and June 2012, 95 pediatric patients were referred to our pediatric gastroenterology clinic for upper gastrointestinal endoscopy because of hematemesis, abdominal pain and /or vomiting. *H. pylori* have been looked for during endoscopy. 50 symptomatic *H. pylori* positive children and 45 symptomatic *H. pylori* negative children were detected via rapid urease test, histopathology and PCR). Among the studied lab parameters, only Hb was affected in the *H. pylori* positive children (mean \pm SD =10.81 \pm 1.14). These patients compared to 25 asymptomatic *H. pylori* positive children diagnosed by stool antigen. The three groups were age and sex matched as shown in table (2).

Hematemesis 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) as shown in table (3). In symptomatic *H. pylori* positive children with hematemesis, abdominal pain was an associated symptom in 48.7% (19 out of 39) and vomiting was an associated symptom in 69.2% (27 out of 39).

The amount of vomited blood was either moderate (34%) or severe (32%), while mild hematemesis was reported in (34%).

Hematemesis cases (52) were classified as: 39 (75%) had *H. pylori* gastritis, 6 (11.5%) had GERD, 5(9.6%) had varices, a case of vasculitis and a case of esophageal polyp.

As shown in table (3), of the total 50 symptomatic *H. pylori* positive patients, 31 cases (62%) presented with recurrent abdominal pain. Vomiting was an associated symptom in 38.7 % (12 out of 31) patients and hematemesis in 61.3% (19 out of 31) patients. Recurrent abdominal pain was the only complaint in 8 patients (25.8%). While in symptomatic *H. pylori* negative cases, 13.3% (6 out of 45 cases) presented with RAP. Family history of abdominal pain in other sibling was found in 27% and history suggestive of peptic disease in adults of the same family was obtained in 57% of patients in symptomatic *H. pylori* positive cases.

Table (4) shows the characteristics of abdominal pain in the symptomatic children. 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 ($p<0.05$).

Hematemesis is significantly higher in *H. pylori* positive cases compared to *H. pylori* negative cases ($p<0.05$). There is no difference between *H. Pylori*- positive and -negative groups with regard to abdominal pain and vomiting as shown in table (3).

Results

Table (2): Comparison between the studied groups according to demographic data

	H pylori positive Symptomatic (n = 50)		Non helicobacter (n = 45)		H pylori positive non symptomatic (n = 25)		Test of sig.	p
	No.	%	No.	%	No.	%		
Sex								
Male	21	42.0	27	60.0	14	56.0	$\chi^2 = 3.310$	0.191
Female	29	58.0	18	40.0	11	44.0		
Age								
Min. – Max.	1.0 – 13.0		0.01 – 12.0		1.0 – 10.0		$^{KW}\chi^2 = 4.959$	0.084
Mean \pm SD.	3.09 \pm 1.85		3.04 \pm 3.37		3.42 \pm 2.25			
Median	3.0		2.0		3.0			

χ^2 : Chi square test

$^{KW}\chi^2$: Chi square for Kruskal Wallis test

*: Statistically significant at $p \leq 0.05$

Z: Z for Mann Whitney test

Results

Table (3): Comparison between symptomatic *H. pylori* positive and symptomatic *H. pylori* negative according to clinical presentation;

	Symptomatic <i>H. pylori</i> positive (n = 50)		Symptomatic <i>H. pylori</i> negative (n = 45)		Total (n = 95)		χ^2	P
	No.	%	No.	%	No.	%		
Vomiting^s								
Negative	30	75.0	19	70.4	49	73.1	0.176	0.675
Positive	10	25.0	8	29.6	18	26.9		
Abdominal pain[#]								
Negative	19	70.4	39	86.7	58	80.6	2.861	0.091
Positive	8	29.6	6	13.3	14	19.4		
Hematemesis ♦								
Negative	11	22.0	32	71.1	43	45.3	23.057*	<0.001*
Positive	39	78.0	13	28.9	52	54.7		

#: Cases of Vomiting and Hematemesis were excluded from abdominal pain

^s: Cases of Abdominal pain and Hematemesis were excluded from Vomiting

♦: Cases of Hematemesis ± cases of vomiting and abdominal pain

χ^2 : Chi square test

*: Statistically significant at $p \leq 0.05$

Table (4): Characteristics of abdominal pain in Symptomatic *H. pylori* positive and Symptomatic *H. pylori* negative children:

Abdominal pain	Symptomatic <i>H. pylori</i> positive (n = 31)		Symptomatic <i>H. pylori</i> negative (n = 6)		χ^2	P
	No.	%	No.	%		
Abdominal pain associated with meals	9	29.0	5	83.3	6.302*	0.021*
Postprandial pain	15	48.4	3	44.2	0.005	1.000
Nigh time pain associated with nocturnal awakening	16	51.6	0	0.0	5.456*	0.027*
Fasting pain relived by food	17	54.8	0	0.0	6.087*	0.022*

χ^2 : Chi square test

*: Statistically significant at $p \leq 0.05$

I. Gross endoscopic results

Table (5), shows comparison of the result of endoscopic examination, between symptomatic *H. pylori* positive and *H. pylori* negative children.

There is a significant negative association between *H. pylori* infection and esophageal erythema. While, we found a significant association between endoscopic nodular antrum and symptomatic *H. pylori* infection ($p < 0.05$).

Normal antrum is seen in only 7 cases of symptomatic *H. pylori* positive cases (14%), while it seen in 66.7% (30 of 45) of symptomatic *H. pylori* negative cases. It is a statistically significant difference ($p < 0.05$).

The sensitivity, the specificity, the PPV, the NPV and the accuracy of antral nodularity for *H. pylori* infection are 82, 100, 100, 83.33, 90.53% respectively.

Significant relation between *H. pylori* and duodenal erythema is also present.

Table (5): Comparison between symptomatic *H. pylori* positive and symptomatic *H. pylori* negative children according to endoscopic findings

	Symptomatic <i>H. pylori</i> positive (n = 50)		Symptomatic <i>H. pylori</i> negative (n = 45)		χ^2	P
	No.	%	No.	%		
Esophagus						
Normal	24	48.0	4	8.9	17.429*	<0.001*
Erythema	26	52.0	41	91.1		
Fundus						
Normal	26	52.0	21	46.7	0.270	0.604
Erythema	24	48.0	24	53.3		
Antrum/Pylorus						
Normal	7	14.0	30	66.7	27.628*	<0.001*
Erythema	22	44.0	15	33.3	1.133	0.287
Nodularity	41	82.0	0	0.0	64.917*	<0.001*
Duodenum						
Normal	16	32.0	29	64.4	10.00*	0.002*
Erythema	34	68.0	16	35.6		

χ^2 : Chi square test

*: Statistically significant at $p \leq 0.05$

II. Histopathological findings:

The histopathological analysis was performed in all of the 50 symptomatic *h pylori* positive cases and the 45 symptomatic *h pylori* negative children.

Esophagus:

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 ($p>0.05$).

Antrum

Antral predominant gastritis is the main pattern of gastritis in our samples histologically 92% (46 out of 50). While, gastritis in *H. pylori* negative cases was eosinophilic (15 cases), chemical (10 cases), hypersecretory (5 cases), PHG (5 cases), **Meneterier's (one case), Combined (Eos/chemical) (one case).**

Duodenum

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.

Gastric biopsy specimens were observed from the antrum and 5 histopathological parameters were applied on the samples according to modified Sydney classification which are:

- (1) Severity of inflammation
- (2) Depth of inflammation
- (3) Activity of inflammation
- (4) Presence of lymphoid follicles
- (5) Presence of eosinophils.

The comparison of histopathological parameters between symptomatic *H. Pylori*-positive and negative groups are summarized in table (6)

50% of the symptomatic *H. pylori* positive specimens are associated with severe inflammation compared to 15% of the *H. pylori* negative specimens. This is statistically significant difference.

The activity of inflammation is significantly higher in symptomatic *H. pylori* positive group than the symptomatic *H. pylori* negative other.

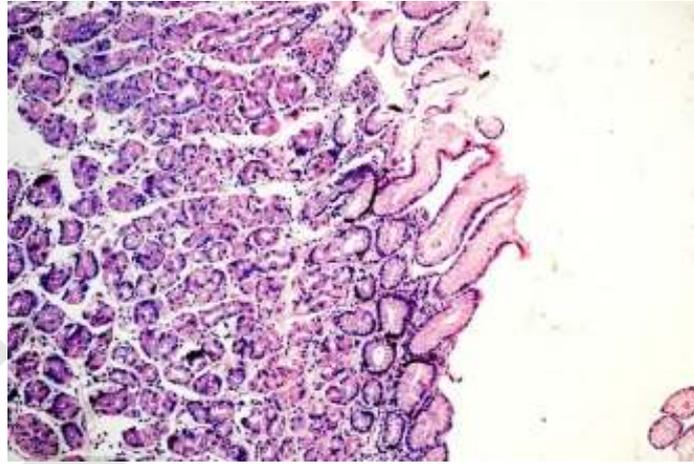
Lymphoid follicles are significantly more prevalent in biopsies from *H. Pylori*-infected children than the non infected children.

Biopsies from *H. pylori* infected subjects revealed a great number of cases with deep inflammation (46%) in relation to non infected children (32.5%), although not statistically significant.

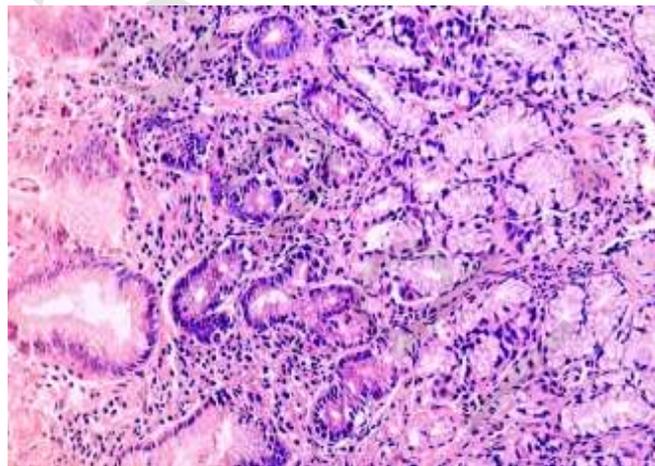
No statistically significant difference between the two groups as regard the eosinophils.

Results

Cases of h pylori realted gastritis showed disorganization of the surface epithelium with a chronic nonspecific infiltrate of the lamina propria by a lymphohistiocytic infiltrate which was superficial or deep (reaching beyond the level of the gastric pits).



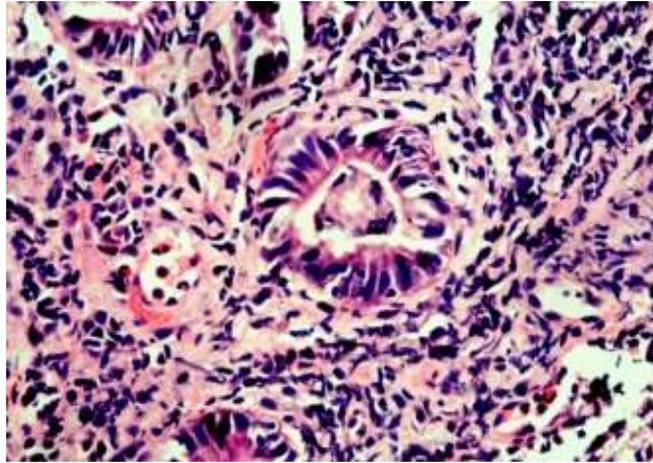
A



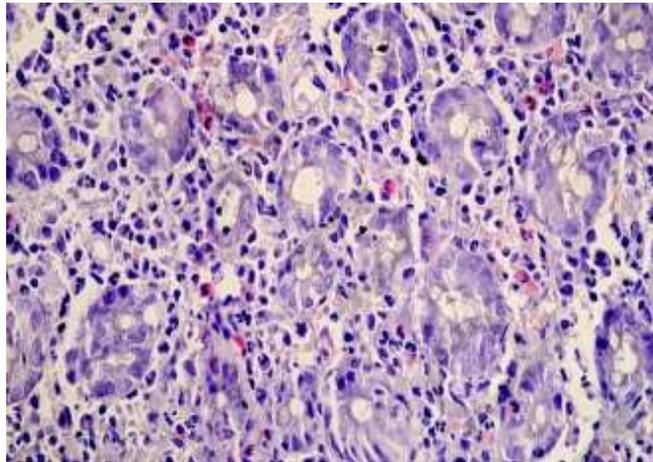
B

Figure (2): The inflammatory infiltrate was seen limited to the upper gastric mucosa in superficial cases (a) and extending beyond the gastric pits (b) in the deep cases. (H&E, x100).

A minor eosinophilic element was noted.

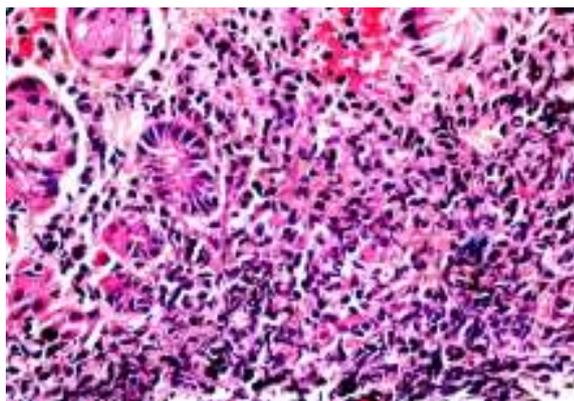


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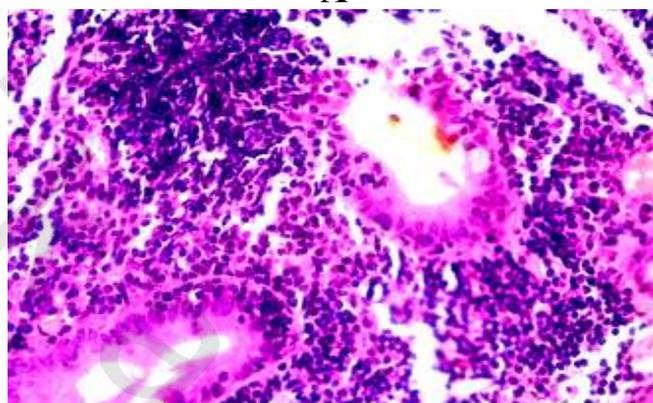


B

Figure (3): Eosinophils are seen (a) marginating in the blood vessels (x400) and (b) in the lamina propria (x200). (H&E).



A



B

Figure (4): Signs of activity were seen in the form of a neutrophilic infiltrate (a) in the lamina propria and (b) infiltrating the glandular epithelium. (H & E x200)

Lymphoid follicles with reactive germinal centers were observed also.

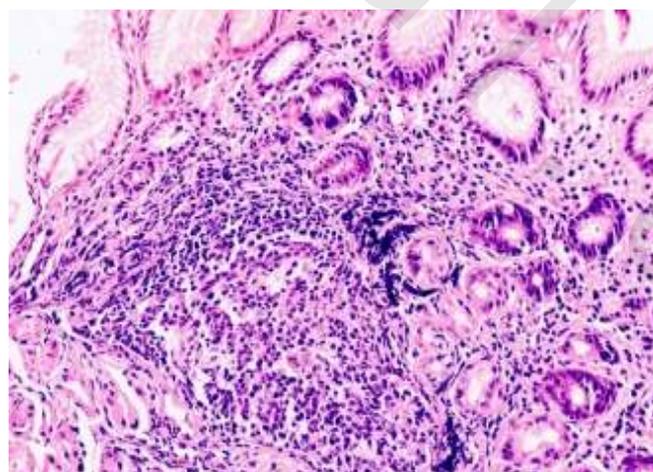


Figure (5): Lymphoid follicles with reactive germinal centers in the mucosa.(H&E, x100).

Results

Table (6) details the frequency of these histopathological findings in the symptomatic *H. pylori* infected and non infected groups.

Table (6): Comparison between symptomatic *H. pylori* positive and symptomatic *H. pylori* negative according to histopathological findings in the antrum

	Symptomatic <i>H. pylori</i> positive (n = 50)		Symptomatic <i>H. pylori</i> negative (n = 45)		χ^2	P
	No.	%	No.	%		
Severity of Infl						
Mild	25	50.0	34	85.0	12.056*	0.001*
Severe	25	50.0	6	15.0		
Depth of infl						
Superficial	27	54.0	27	67.5	1.688	0.194
Deep	23	46.0	13	32.5		
Activity						
No Activity	28	56.0	36	90.0	12.505*	<0.001*
Active	22	44.0	4	10.0		
Lymphoid follicles						
Yes	33	66.0	4	10.0	28.785*	<0.001*
No	17	34.0	36	90.0		
Eosinophils						
Yes	2	100.0	22	55.0	1.575	^{FE} p=0.498
No	0	0.0	18	45.0		

χ^2 : Chi square test

FE: Fisher Exact test

*: Statistically significant at $p \leq 0.05$

III. Relation between the clinical presentations and the pathology among symptomatic *H. pylori* positive children.

III. A- Relation between the clinical presentations and the endoscopic picture among symptomatic *H. pylori* positive children:

H. pylori positive patients with and without vomiting and abdominal pain cannot be differentiated according to endoscopic picture as shown in tables (7,8).

As regard hematemesis, we found a negative association between hematemesis in *H. pylori* positive cases and erythema of the esophagus as shown in table (9).

Table (7): Relation between vomiting and the endoscopic picture among symptomatic *H. pylori* positive children (n=50):

	Symptomatic <i>H. pylori</i> positive				χ^2	P
	Without vomiting (n=30)		With vomiting (n=20)			
	No.	%	No.	%		
Esophagus						
Normal	12	40.0	12	60.0	1.923	0.166
Erythema	18	60.0	8	40.0		
Fundus						
Normal	15	50.0	11	55.0	0.120	0.729
Erythema	15	50.0	9	45.0		
Antrum/Pylorus						
Normal	2	6.7	5	25.0	3.350	0.100
Erythema	14	46.7	8	40.0	0.216	0.642
Nodularity	25	83.3	14	70.0	3.252	0.130
Duodenum						
Normal	12	40.0	4	20.0	2.206	0.137
Erythema	18	60.0	16	80.0		

χ^2 : Chi square test

*: Statistically significant at $p \leq 0.05$

Results

Table (8): Relation between abdominal pain and endoscopic picture among symptomatic *H. pylori* positive children (n=50):

	Symptomatic <i>H. pylori</i> positive				χ^2	P
	With abdominal pain (n=19)		Without abdominal pain (n=31)			
	No.	%	No.	%		
Esophagus						
Normal	7	36.8	17	54.8	1.529	0.216
Erythema	12	63.2	14	45.2		
Fundus						
Normal	8	42.1	18	58.1	1.202	0.273
Erythema	11	57.9	13	41.9		
Antrum/Pylorus						
Normal	3	15.8	4	12.9	0.014	1.000
Erythema	9	47.4	13	41.9	0.030	0.863
Nodularity	13	68.4	26	83.9	1.057	0.412
Duodenum						
Normal	5	26.3	11	35.5	0.455	0.500
Erythema	14	73.7	20	64.5		

χ^2 : Chi square test

*: Statistically significant at $p \leq 0.05$

Results

Table (9): Relation between hematemesis and the endoscopic picture among symptomatic *H. pylori* positive children (n=50):

	Symptomatic <i>H. pylori</i> positive				χ^2	P
	Without hematemesis (n=11)		With hematemesis (n=39)			
	No.	%	No.	%		
Esophagus						
Normal	0	0.0	24	61.5	13.018*	<0.001*
Erythema	11	100.0	15	38.5		
Fundus						
Normal	3	27.3	23	59.0	3.455	0.063
Erythema	8	72.7	16	41.0		
Antrum/Pylorus						
Normal	1	9.1	6	15.4	0.282	^{FE} p=1.000
Erythema	7	63.6	15	38.5	2.207	^{FE} p=0.178
Nodularity	10	90.9	31	79.5	0.758	^{FE} p=0.662
Duodenum						
Normal	3	27.3	13	33.3	0.145	^{FE} p= 1.000
Erythema	8	72.7	26	66.7		

χ^2 : value for Chi square

FE: Fisher Exact test

*: Statistically significant at $p \leq 0.05$

III. B-Relation between the clinical presentations and the histopathological findings among symptomatic *H. pylori* positive children:

There was no significant association between vomiting and the any of the histopathological parameters as shown in table (10). The histopathological picture of *H. pylori* infected children with RAP characterized by more severe inflammation compared with those not complaining of RAP ($p < 0, 05$) as shown in table (11).

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 ($p < 0.05$) as shown in tables (12).

Table (10): Relation between vomiting and the histopathology among symptomatic *H. pylori* positive children (n=50):

	Symptomatic <i>H. pylori</i> positive				χ^2	P
	Without vomiting (n=30)		With vomiting (n=20)			
	No.	%	No.	%		
Severity of infl						
Mild	14	46.7	11	55.0	0.333	0.564
Severe	16	53.3	9	45.0		
Depth of infl						
Superficial	17	56.7	10	50.0	0.215	0.643
Deep	13	43.3	10	50.0		
Activity						
No Activity	17	56.7	11	55.0	0.014	0.907
Active	13	43.3	9	45.0		
Lymphoid follicles						
Yes	19	63.3	14	70.0	0.238	0.626
No	11	36.7	6	30.0		
Eosinophils						
Yes	1	100.0	1	100.0	-	-
No	0	0.0	0	0.0		

χ^2 : Chi square test

*: Statistically significant at $p \leq 0.05$

Results

Table (11): Relation between abdominal pain and the histopathology among symptomatic *H. pylori* positive children (n=50):

	Symptomatic <i>H. pylori</i> positive				χ^2	P
	Without abdominal pain (n=19)		With abdominal pain (n=31)			
	No.	%	No.	%		
Severity of infl						
Mild	13	68.4	12	38.7	4.160*	0.041*
Severe	6	31.6	19	61.3		
Depth of infl						
Superficial	12	63.2	15	48.4	1.035	0.309
Deep	7	36.8	16	51.6		
Activity						
No Activity	11	57.9	17	54.8	0.045	0.833
Active	8	42.1	14	45.2		
Lymphoid follicles						
Yes	11	57.9	22	71.0	0.897	0.344
No	8	42.1	9	29.0		
Eosinophils						
Yes	2	100.0	2	100.0	-	-
No	0	0.0	0	0.0		

χ^2 : Chi square test

*: Statistically significant at $p \leq 0.05$

Results

Table (12): Relation between hematemesis and the histopathology among symptomatic *H. pylori* positive children (n=50):

	Symptomatic <i>H. pylori</i> positive				χ^2	P
	Without hematemesis (n=11)		With hematemesis (n=39)			
	No.	%	No.	%		
Severity of infl						
Mild	9	81.8	16	41.0	5.711*	0.017*
Severe	2	18.2	23	59.0		
Depth of infl						
Superficial	8	72.7	19	48.7	1.991	0.158
Deep	3	27.3	20	51.3		
Activity						
No Activity	7	63.6	21	53.8	0.344	^{FE} p = 0.734
Active	4	36.4	18	46.2		
Lymphoid follicles						
Yes	5	45.5	28	71.8	2.653	^{FE} p=0.151
No	6	54.5	11	28.2		
Eosinophils						
Yes	1	100.0	1	100.0	-	-
No	0	0.0	0	0.0		

χ^2 : value for Chi square

FE: Fisher Exact test

*: Statistically significant at $p \leq 0.05$

IV. Virulence factors of *H. Pylori*:

IV. A- Prevalence of *cagA*, *vacA*, *babA2* in *H. pylori* positive children:

By using multiplex PCR, we examined the prevalence of *cagA*, *vacA* and *babA2* genes to define the different genotypes of *H. Pylori*.

As shown in table (13), the most prevalent virulent gene is *vacA* (72%) then *cagA* (52%) then *babA2* (44%).

Also, the most common *s* allele is *s2* and the most common *m* allele is *m2*.

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.

Table (13): Distribution of the *H. pylori* positive cases according to the studied genes (n = 75)

	No.	%
babA2		
Negative	42	56.0
Positive	33	44.0
CagA		
Negative	36	48.0
Positive	39	52.0
VacA		
Negative	21	28.0
Positive	54	72.0
VacA s		
Negative	30	40.0
Positive	45	60.0
S1		
Negative	59	78.7
Positive	16	21.3
S2		
Negative	46	61.3
Positive	29	38.7
VacA m		
Negative	25	33.3
Positive	50	66.7
M1		
Negative	52	69.3
Positive	23	30.7
M2		
Negative	48	64.0
Positive	27	36.0
VacA alleles		
s1/m1	12	32.4
s1/m2	3	8.1
s2/m1	3	8.1
s2/m2	19	51.4

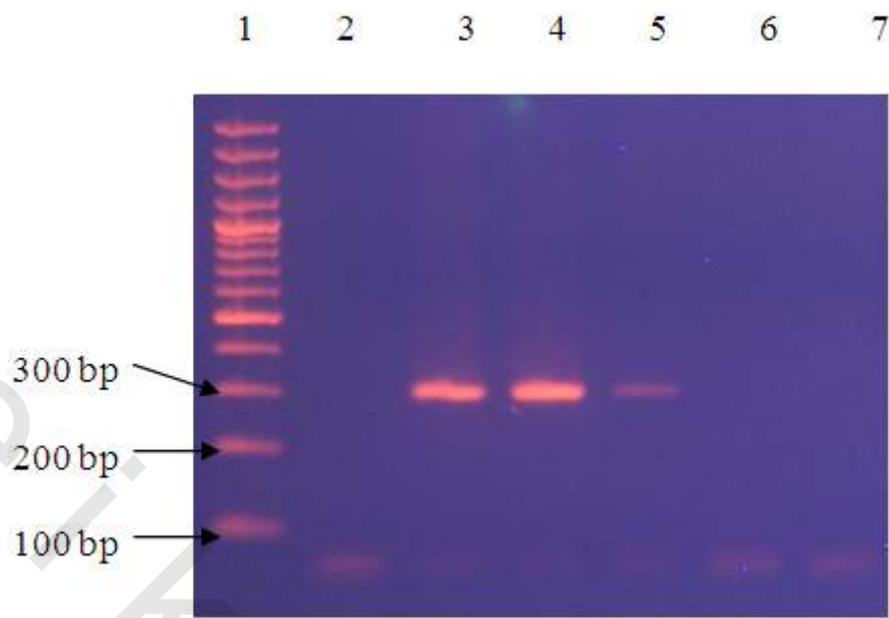


Figure (6): 2% agarose gel electrophoresis showing 296 bp PCR products of the glmM (UreC) gene (lanes 3, 4 and 5). Lane 1 shows 100 bp molecular weight marker (Fermentas).

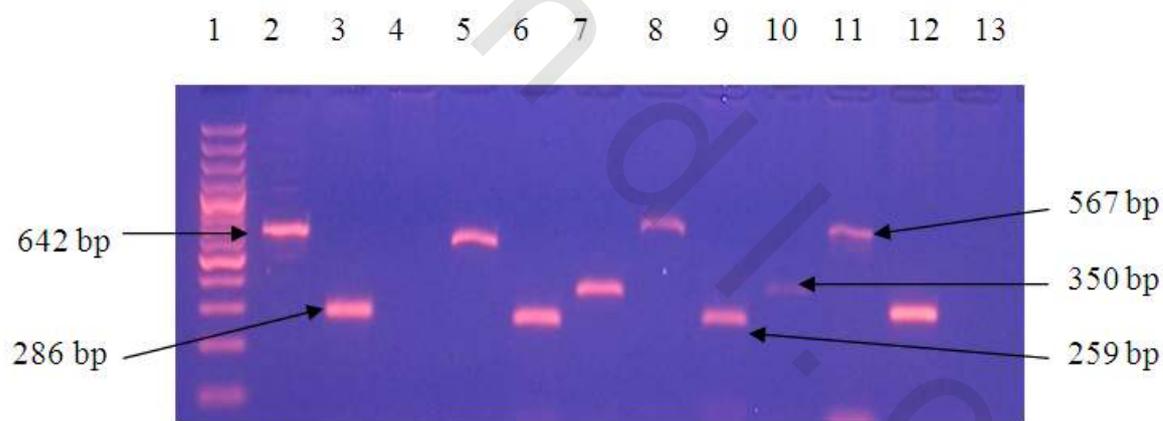


Figure (7): 2% agarose gel electrophoresis showing PCR products of the cagA gene (lanes 7 and 10), vacA s1 (lanes 6, 9 and 12), vacA s2 (lane 3), vacA m1 (lane 5 and 11), vacA m2 alleles (lane 2 and 8) respectively. Lane 1 shows 100 bp molecular weight marker (Fermentas).

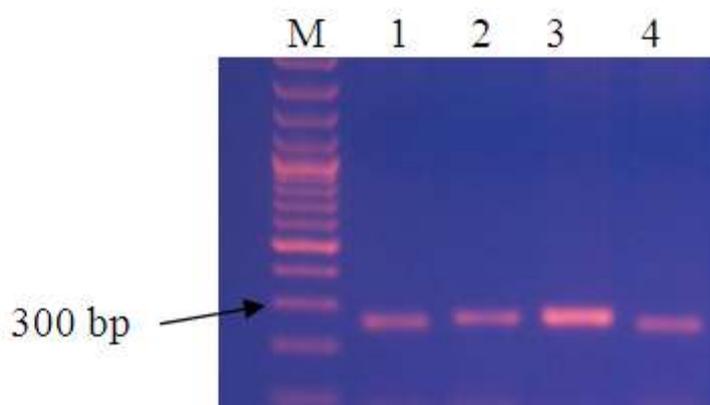


Figure (8): 2% agarose gel electrophoresis showing 271 bp PCR products of the babA2 gene (lanes 1,2,3 and 4). Lane M shows 100 bp molecular weight marker (Fermentas).

IV. B-Virulence factors of *H. pylori* and it's relation to clinical presentations among *H. pylori* positive children:

By using multiplex PCR, we examined the prevalence of *cagA*, *vacA* and *babA2* genes in symptomatic *H. pylori* positive cases and compare the results to the asymptomatic group, to define the different genotypes of *H. pylori* and to relate them with the presence of symptoms in *H. pylori* positive patients, as shown in table (14).

CagA positive strains are present in 70% of the symptomatic cases while it is present in only 16% of the asymptomatic group, the difference is statistically significant.

There is a statistical significant relation between *babA2* positivity and the presence of clinical symptoms. *BabA2* is present in 60% (30 out of 50) cases in symptomatic *H. pylori* positive cases while it is present in only 12% (3 out of 45) cases in asymptomatic children.

Most of the symptomatic cases are *vacA* positive (80%, of the symptomatic group and 56% of the non symptomatic group with a statistically significant difference ($p < 0.05$).

As shown in table (14), the most common *s* allele in the symptomatic group is *s2* 46% (23 out of 50 cases), and the most common *m* allele is *m2* 46 % (23 out of 50).

There is a significant relationship between presence of clinical symptoms and presence of *s1* positive strains. *S1* genotype is detected in 30% of the symptomatic group in relation to 4% of the asymptomatic *H. pylori* positive patients.

Table (14) also shows *vacA* *s/m* combined genotypes in relation to the presence or absence of the symptoms in the two *H. pylori* positive groups. There is a higher prevalence of *vacA s2/m2* positive strains over other *vacA* alleles (38%), this is followed by *s1/m1* then *s2/m1* + *s1/m2* (equal prevalence of 4%). There is a statistically significant relation between presence of symptoms and both *s2/m2* positivity and *s1/m1* positivity.

Hematemesis:

While estimating the relationship between potentially virulent *H. pylori* strains and clinical presentations, significant relations are found between *babA2*, *cagA*, *vacA s*, *vacA m*, *s1/m1* and *s2/m2* positivity and hematemesis, as shown in table (15).

Vomiting:

As shown in table (16), There is a high percentage of *babA2* among vomiting cases (65%) compared to children not complaining of vomiting (36.4%), it is a significant relationship ($p < 0,05$). Neither of the *vacA s*- and *m*- alleles are associated with vomiting; in addition, *cagA* status does not appear to be correlated with vomiting. A lack of correlation with vomiting is also found with all of the *vacA s* and *m* combinations.

Abdominal pain:

Presence of *babA2*, *cagA*, *vacA s1* or *s1/m1* positive strains is significantly associated with abdominal pain, as a complaint in symptomatic *H. pylori* positive children as shown in table (17).

Results

Table (14): Comparison between symptomatic *H. pylori* positive cases and asymptomatic *H. pylori* positive children according to genes (n=75):

	Symptomatic <i>H. pylori</i> positive (n = 50)		Asymptomatic <i>H. pylori</i> positive (n = 25)		χ^2	P
	No.	%	No.	%		
babA2						
Negative	20	40.0	22	88.0	15.584*	<0.001*
Positive	30	60.0	3	12.0		
CagA						
Negative	15	30.0	21	84.0	19.471*	<0.001*
Positive	35	70.0	4	16.0		
VacA						
Negative	10	20.0	11	44.0	4.762*	0.029*
Positive	40	80.0	14	56.0		
VacA s						
Negative	12	24.0	18	72.0	16.000*	<0.001*
Positive	38	76.0	7	28.0		
s1						
Negative	35	70.0	24	96.0	6.713*	0.010*
Positive	15	30.0	1	4.0		
s2						
Negative	27	54.0	19	76.0	3.401	0.065
Positive	23	46.0	6	24.0		
VacA m						
Negative	13	26.0	16	64.0	10.148*	0.001*
Positive	37	74.0	9	36.0		
m1						
Negative	33	66.0	19	76.0	0.784	0.376
Positive	17	34.0	6	24.0		
m2						
Negative	27	54.0	21	84.0	6.510*	0.011*
Positive	23	46.0	4	16.0		
VacA alleles						
s1/m1	12	24.0	0	0.0	7.143*	^{FE} p = 0.006*
s1/m2	2	4.0	1	4.0	0.0	^{FE} p = 1.000
s2/m1	2	4.0	1	4.0	0.0	^{FE} p = 1.000
s2/m2	19	38.0	0	0.0	12.723*	<0.001*

χ^2 : Chi square test

FE: Fisher Exact test

*: Statistically significant at p ≤ 0.05

Results

Table (15): Relation between hematemesis and different genotypes among *H. pylori* positive children (n=75):

	<i>H. pylori</i> positive(n=75)				χ^2	P
	Without hematemesis (n=36)		With hematemesis (n=39)			
	No.	%	No.	%		
babA2						
Negative	28	77.8	14	35.9	12.326*	<0.001*
Positive	8	22.2	25	64.1		
CagA						
Negative	23	63.9	13	33.3	7.002*	0.008*
Positive	13	36.1	26	66.7		
VacA s1						
Negative	32	88.9	27	69.2	4.311*	0.038*
Positive	4	11.1	12	30.8		
VacA s2						
Negative	28	77.8	18	46.2	7.984*	0.005*
Positive	8	22.2	21	53.8		
VacA m1						
Negative	29	80.6	23	59.0	4.101*	0.043*
Positive	7	19.4	16	41.0		
VacA m2						
Negative	29	80.6	19	48.7	8.236*	0.004*
Positive	7	19.4	20	51.3		
VacA alleles						
s1/m1	1	16.7	11	35.5	9.006*	0.003*
s1/m2	2	33.3	1	3.2	0.404	^{FE} p = 0.610
s2/m1	1	16.7	2	6.5	0.269	^{FE} p = 1.000
s2/m2	2	33.3	17	54.8	14.316*	<0.001*

χ^2 : value for Chi square

FE: Fisher Exact test

*: Statistically significant at $p \leq 0.05$

Results

Table (16): Relation between vomiting with different genotypes among *H. pylori* positive children (n=75):

	<i>H. pylori</i> positive				χ^2	P
	Without vomiting (n=55)		With vomiting (n=20)			
	No.	%	No.	%		
babA2						
Negative	35	63.6	7	35.0	4.881*	0.027*
Positive	20	36.4	13	65.0		
CagA						
Negative	28	50.9	8	40.0	0.699	0.403
Positive	27	49.1	12	60.0		
VacA s1						
Negative	45	81.8	14	70.0	1.221	^{FE} p = 0.341
Positive	10	18.2	6	30.0		
VacA s2						
Negative	35	63.6	11	55.0	0.461	0.497
Positive	20	36.4	9	45.0		
VacA m1						
Negative	39	70.9	13	65.0	0.241	0.624
Positive	16	29.1	7	35.0		
VacA m2						
Negative	37	67.3	11	55.0	0.959	0.327
Positive	18	32.7	9	45.0		
VacA alleles						
s1/m1	6	26.1	6	42.9	3.977	^{FE} p=0.072
s1/m2	3	13.0	0	0.0	1.136	^{FE} p=0.560
s2/m1	3	13.0	0	0.0	1.136	^{FE} p=0.560
s2/m2	11	47.8	8	57.1	3.102	0.078

χ^2 : value for Chi square

FE: Fisher Exact test

*: Statistically significant at $p \leq 0.05$

Results

Table (17): Relation between abdominal pains with different genotypes among *H. pylori* positive children (n=75):

	<i>H. pylori</i> positive				χ^2	P
	Without abdominal pain(n=44)		With abdominal pain(n=31)			
	No.	%	No.	%		
babA2						
Negative	30	68.2	12	38.7	6.411*	0.011*
Positive	14	31.8	19	61.3		
CagA						
Negative	26	59.1	10	32.3	5.246*	0.022*
Positive	18	40.9	21	67.7		
VacA s1						
Negative	39	88.6	20	64.5	6.305*	0.012*
Positive	5	11.4	11	35.5		
VacA s2						
Negative	30	68.2	16	51.6	2.105	0.147
Positive	14	31.8	15	48.4		
VacA m1						
Negative	33	75.0	19	61.3	1.608	0.205
Positive	11	25.0	12	38.7		
VacA m2						
Negative	31	70.5	17	54.8	1.925	0.165
Positive	13	29.5	14	45.2		
VacA alleles						
s1/m1	3	21.4	9	39.1	6.667*	0.022*
s1/m2	2	14.3	1	4.3	0.082	^{FE} p=1.000
s2/m1	1	7.1	2	8.7	0.827	^{FE} p=0.566
s2/m2	8	57.1	11	47.8	8.929*	0.003*

χ^2 : value for Chi square

FE: Fisher Exact test

*: Statistically significant at $p \leq 0.05$

IV. C-Endoscopic picture and different genotypes of *H. pylori* among symptomatic *H. pylori* positive children:

As shown in tables (18-25):

Esophagus:

There is a strong association between the presence of *cagA* and the esophageal erythema ($p=0.019$). The same relation is present between the *vacA* s allele and esophageal erythema endoscopically. However the frequency of esophageal erythema is lower in children with *babA2* positive *H. pylori* infection (13 out of 30).

Fundus:

Significant relation is present between s2 and erythema of the fundus.

Antrum:

There is a negative relationship between normal antrum and the *cagA* positivity ($p=0.020$). Also, none of our *vacA* s1 cases are associated with normal antrum.

Antral erythema is strongly associated with *cagA* positivity ($p=0.004$). This relation cannot be found between *vacA* or *babA2* and the antral erythema ($p>0.05$).

Endoscopically, antral nodularity is more common in *cagA* positive patients ($p<0.05$). Also, significant relation is found between antral nodularity and *vacA* s1. No relationships are found between *vacAs2*, *vacA* m or *babA2* and nodularity.

Results

Duodenum

No statistically significant relationships are found between any of the discussed genes and duodenal erythema ($p>0.05$).

Table (18): Relation between CagA status and endoscopic findings among symptomatic *H. pylori* positive children(n=50)

	CagA				χ^2	P
	-ve (n=15)		+ve (n=35)			
	No.	%	No.	%		
Esophagus						
Normal	11	73.3	13	37.1	5.510*	0.019*
Erythema	4	26.7	22	62.9		
Fundus						
Normal	9	60.0	17	48.6	0.549	0.459
Erythema	6	40.0	18	51.4		
Antrum/Pylorus						
Normal	5	33.3	2	5.7	6.652*	^{FE} p=0.020*
Erythema	2	13.3	20	57.1	8.179*	0.004*
Nodularity	8	53.3	33	94.3	11.931*	^{FE} p=0.002*
Duodenum						
Normal	7	46.7	9	25.7	2.118	^{FE} p=0.191
Erythema	8	53.3	26	74.3		

χ^2 : value for Chi square

FE: Fisher Exact test

Results

Table (19): Relation between VacA s1 status and endoscopic findings among symptomatic *H. pylori* positive children(n=50)

	VacA s1				χ^2	P
	-ve (n=35)		+ve (n=15)			
	No.	%	No.	%		
Esophagus						
Normal	20	57.1	4	26.7	3.907*	0.048*
Erythema	15	42.9	11	73.3		
Fundus						
Normal	19	54.3	7	46.7	0.244	0.621
Erythema	16	45.7	8	53.3		
Antrum/Pylorus						
Normal	7	20.0	0	0.0	3.488	^{FE} p=0.087
Erythema	14	40.0	8	53.3	0.758	0.384
Nodularity	26	74.3	15	100.0	4.704*	^{FE} p=0.030*
Duodenum						
Normal	12	34.3	4	26.7	0.280	0.746
Erythema	23	65.7	11	73.3		

χ^2 : value for Chi square

FE: Fisher Exact test

*: Statistically significant at $p \leq 0.05$

Results

Table (20): Relation between vacA s2 status and endoscopic findings among symptomatic *H. pylori* positive children (n=50)

	VacA s2				χ^2	P
	-ve (n=27)		+ve (n=23)			
	No.	%	No.	%		
Esophagus						
Normal	8	29.6	16	69.6	7.936*	0.005*
Erythema	19	70.4	7	30.4		
Fundus						
Normal	10	37.0	16	69.6	5.265*	0.022*
Erythema	17	63.0	7	30.4		
Antrum/Pylorus						
Normal	4	14.8	3	13.0	0.032	^{FE} p=1.000
Erythema	13	48.1	9	39.1	0.410	0.522
Nodularity	22	81.5	19	82.6	0.011	^{FE} p=1.000
Duodenum						
Normal	9	33.3	7	30.4	0.048	0.827
Erythema	18	66.7	16	69.6		

χ^2 : value for Chi square

FE: Fisher Exact test

*: Statistically significant at $p \leq 0.05$

Results

Table (21): Relation between vacA m1 status and endoscopic findings among symptomatic *H. pylori* positive children(n=50)

	VacA m1				χ^2	P
	-ve (n=33)		+ve (n=17)			
	No.	%	No.	%		
Esophagus						
Normal	17	51.5	7	41.2	0.480	0.488
Erythema	16	48.5	10	58.8		
Fundus						
Normal	19	57.6	7	41.2	1.209	0.272
Erythema	14	42.4	10	58.8		
Antrum/Pylorus						
Normal	6	18.2	1	5.9	1.410	^{FE} p= 0.398
Erythema	14	42.4	8	47.1	0.098	0.754
Nodularity	27	81.8	14	82.4	0.002	^{FE} p=1.000
Duodenum						
Normal	11	33.3	5	29.4	0.079	0.778
Erythema	22	66.7	12	70.6		

χ^2 : value for Chi square

FE: Fisher Exact test

*: Statistically significant at $p \leq 0.05$

Results

Table (22): Relation between vacA m2 status and endoscopic findings among symptomatic *H. pylori* positive children (n=50)

	VacA m2				χ^2	P
	-ve (n=27)		+ve (n=23)			
	No.	%	No.	%		
Esophagus						
Normal	11	40.7	13	56.5	1.239	0.266
Erythema	16	59.3	10	43.5		
Fundus						
Normal	11	40.7	15	65.2	2.981	0.084
Erythema	16	59.3	8	34.8		
Antrum/Pylorus						
Normal	4	14.8	3	13.0	0.032	^{FE} p=1.000
Erythema	13	48.1	9	39.1	0.410	0.522
Nodularity	21	77.8	20	87.0	0.709	^{FE} p= 0.479
Duodenum						
Normal	9	33.3	7	30.4	0.048	0.827
Erythema	18	66.7	16	69.6		

χ^2 : value for Chi square

FE: Fisher Exact test

*: Statistically significant at $p \leq 0.05$

Results

Table (23): Relation between s1/m1 status and endoscopic findings among symptomatic *H. pylori* positive children (n=50)

	s1m1				χ^2	P
	-ve (n = 38)		+ve (n = 12)			
	No.	%	No.	%		
Oesphagus						
Normal	20	52.6	4	33.3	1.361	0.243
Erythema	18	47.4	8	66.7		
Fundus						
Normal	21	55.3	5	41.7	0.675	^{FE} p= 0.411
Erythema	17	44.7	7	58.3		
Antrum/Pylorus						
Normal	7	18.4	0	0.0	2.570	^{FE} p=0.174
Erythema	17	44.7	5	41.7	0.035	^{FE} p=1.000
Nodularity	27	71.1	12	100.0	4.453*	^{FE} p=0.046*
Duodenum						
Normal	13	34.2	3	25.0	0.356	^{FE} p=0.728
Erythema	25	65.8	9	75.0		

χ^2 : value for Chi square
FE: Fisher Exact test

Results

Table (24): Relation between VacA alleles and endoscopic findings among symptomatic *H. pylori* positive children (n=50)

	VacA alleles							
	s1/m1 (n=12)		s1/m2 (n=2)		s2/m1 (n=2)		s2/m2 (n=19)	
	No.	%	No.	%	No.	%	No.	%
Esophagus								
Normal	4	33.3	0	0.0	2	100.0	12	63.2
Erythema	8	66.7	2	100.0	0	0.0	7	36.8
Fundus								
Normal	5	41.7	1	50.0	1	50.0	14	73.7
Erythema	7	58.3	1	50.0	1	50.0	5	26.3
Antrum/Pylorus								
Normal	0	0.0	0	0.0	0	0.0	3	15.8
Erythema	5	41.7	2	100.0	2	100.0	5	26.3
Nodularity	12	100.0	2	100.0	1	50.0	16	84.2
Duodenum								
Normal	3	25.0	1	50.0	2	100.0	5	26.3
Erythema	9	75.0	1	50.0	0	0.0	14	73.7

Results

Table (25): Relation between babA2 status and endoscopic findings among symptomatic *H. pylori* positive children (n=50)

	babA2				χ^2	P
	-ve (n = 20)		+ve (n = 30)			
	No.	%	No.	%		
Esophagus						
Normal	7	35.0	17	56.7	2.257	0.133
Erythema	13	65.0	13	43.3		
Fundus						
Normal	10	50.0	16	53.3	0.053	0.817
Erythema	10	50.0	14	46.7		
Antrum/Pylorus						
Normal	3	15.0	4	13.3	0.028	^{FE} p = 1.000
Erythema	9	45.0	13	43.3	0.014	^{FE} p = 1.000
Nodularity	17	85.0	22	73.3	0.952	^{FE} p = 0.489
Duodenum						
Normal	5	25.0	11	36.7	0.751	0.386
Erythema	15	75.0	19	63.3		

χ^2 : Chi square test
FE: Fisher Exact test

IV. D- *H. pylori* genotypes and histopathological findings

Relation between histological parameters determined in gastric biopsy specimens and *H. pylori* genetic status are shown in tables (26- 33).

1- Severity of inflammation:

The severity of inflammation is assessed in gastric samples. 60% of the cagA positive strains are associated with severe inflammation compared to 26.7% of the cagA negative strains. This is statistically significant difference.

There are significant relationships between vacA s1 positivity and vacA m1 positivity and severity of inflammation. No relationships are found between vacAs2 or babA2 and severity of inflammation.

The presence of s1/m1 positive strains are associated with severe inflammation. VacA m2 positive strains are not associated with any of the histopathological parameters.

2- Depth: depth of involvement of the gastric mucosa (above or below the gastric pits)

VacA s1 and vacA m1 positive genotypes are associated with the depth of inflammation ($p<0.05$). No relationships are found between cagA, vacA m2 or babA2 and the depth of inflammation.

There is a significance difference between m1 positive and m1 negative samples as regard the depth of inflammation. Also a significant relation is found between the depth of inflammation and s2 positivity.

There is a significant difference between s1/m1 positive samples and s1/m1 negative as regard the depth of inflammation.

3- Activity: (i.e. presence of neutrophils)

CagA –positive genotypes are strongly associated with higher activity in the antrum ($p<0.05$).

Also there is a significant relationship between vacA s1 positivity and the activity. While, a lack of correlation with the activity is found with vacA s2, vacA m and babA2 in the studied samples.

4- Lymphoid follicles:

There is a strong association between presence of lymphoid follicles in the antrum and individual vacA s1 positive genotypes, compared to the negative genotypes ($p=0.0011$). The same relationship could not be observed between cagA, vacA s2, vacA m or babA2 and the presence of lymphoid follicles.

5- Eosinophils;

There is no relationship between any of the studied genes and the presence of eosinophils ($p>0.05$).

Results

Table (26): Relation between CagA status and histopathological findings among symptomatic *H. pylori* positive children (n=50)

	CagA				χ^2	P
	-ve (n=15)		+ve (n=35)			
	No.	%	No.	%		
Severity of Infl						
Mild	11	73.3	14	40.0	4.667*	0.031*
Severe	4	26.7	21	60.0		
Depth of infl					1.384	0.239
Superficial	10	66.7	17	48.6		
Deep	5	33.3	18	51.4		
Activity					8.179*	0.004*
No Activity	13	86.7	15	42.9		
Active	2	13.3	20	57.1		
Lymphoid follicles					0.004	0.948
Yes	10	66.7	23	65.7		
No	5	45.5	12	34.3		
Eosinophils					-	-
Yes	1	100.0	1	100.0		
No	0	0.0	0	0.0		

χ^2 : Chi square test

*: Statistically significant at $p \leq 0.05$

Results

Table (27): Relation between vacA s1 status and histopathological findings among symptomatic *H. pylori* positive children (n=50)

	VacA s1				χ^2	P
	-ve (n=35)		+ve (n=15)			
	No.	%	No.	%		
Severity of Infl						
Mild	21	60.0	4	26.7	4.667*	0.031*
Severe	14	40.0	11	73.3		
Depth of infl						
Superficial	23	65.7	4	26.7	6.445*	0.011*
Deep	12	34.3	11	73.3		
Activity						
No Activity	23	65.7	5	33.3	4.468*	0.035*
Active	12	34.3	10	66.7		
Lymphoid follicles						
Yes	20	57.1	13	86.7	4.079*	0.043*
No	15	42.9	2	13.3		
Eosinophils						
Yes	1	100.0	1	100.0	-	-
No	0	0.0	0	0.0		

χ^2 : Chi square test

*: Statistically significant at $p \leq 0.05$

Results

Table (28): Relation between vacA s2 and histopathological findings among symptomatic *H. pylori* positive children (n=50)

	VacA s2				χ^2	P
	-ve (n=27)		+ve (n=23)			
	No.	%	No.	%		
Severity of Infl						
Mild	14	51.9	11	47.8	0.081	0.777
Severe	13	48.1	12	52.2		
Depth of infl						
Superficial	11	40.7	16	69.6	4.154*	0.042*
Deep	16	59.3	7	30.4		
Activity						
No Activity	13	48.1	15	65.2	1.469	0.226
Active	14	51.9	8	34.8		
Lymphoid follicles						
Yes	19	70.4	14	60.9	0.500	0.480
No	8	29.6	9	39.1		
Eosinophils						
Yes	1	100.0	1	100.0	-	-
No	0	0.0	0	0.0		

χ^2 : Chi square test

*: Statistically significant at $p \leq 0.05$

Results

Table (29): Relation between VacA m1 and pathological findings among symptomatic *H. pylori* positive children (n=50)

	VacA m1				χ^2	P
	-ve (n=33)		+ve (n=17)			
	No.	%	No.	%		
Severity of Infl						
Mild	21	63.6	4	23.5	7.219*	0.007*
Severe	12	36.4	13	76.5		
Depth of infl						
Superficial	23	69.7	4	23.5	9.628*	0.002*
Deep	10	30.3	13	76.5		
Activity						
No Activity	20	60.6	8	47.1	0.836	0.361
Active	13	39.4	9	52.9		
Lymphoid follicles						
Yes	20	60.6	13	76.5	1.258	0.262
No	13	39.4	4	23.5		
Eosinophils						
Yes	1	100.0	1	100.0	-	-
No	0	0.0	0	0.0		

χ^2 : Chi square test

*: Statistically significant at $p \leq 0.05$

Results

Table (30): Relation between VacA m2 status and pathological findings among symptomatic *H. pylori* positive children (n=50)

	VacA m2				χ^2	P
	-ve (n=27)		+ve (n=23)			
	No.	%	No.	%		
Severity of Infl						
Mild	15	55.6	10	43.5	0.725	0.395
Severe	12	44.4	13	56.5		
Depth of infl						
Superficial	14	51.9	13	56.5	0.109	0.741
Deep	13	48.1	10	43.5		
Activity						
No Activity	14	51.9	14	60.9	0.410	0.522
Active	13	48.1	9	39.1		
Lymphoid follicles						
Yes	18	66.7	15	65.2	0.012	0.914
No	9	33.3	8	34.8		
Eosinophils						
Yes	1	100.0	1	100.0	-	-
No	0	0.0	0	0.0		

χ^2 : Chi square test

Results

Table (31): Relation between s1/m1 status and pathological findings among symptomatic *H. pylori* positive children (n=50)

	s1m1				χ^2	p
	-ve (n = 38)		+ve (n = 12)			
	No.	%	No.	%		
Severity of Infl						
Mild	23	60.5	2	16.7	7.018*	0.008*
Severe	15	39.5	10	83.3		
Depth of infl						
Superficial	25	65.8	2	16.7	8.860*	0.003*
Deep	13	34.2	10	83.3		
Activity						
No Activity	24	63.2	4	33.3	3.292	0.070
Active	14	36.8	8	66.7		
Lymphoid follicles						
Yes	22	57.9	11	91.7	4.635*	FE p= 0.039*
No	16	42.1	1	8.3		
Eosinophils						
Yes	1	100.0	1	100.0	-	-
No	0	0.0	0	0.0		

χ^2 : value for Chi square

FE: Fisher Exact test

*: Statistically significant at $p \leq 0.05$

Table (32): Relation between VacA alleles and histopathological finding among symptomatic *H. pylori* positive children

	VacA alleles							
	s1/m1 (n=12)		s1/m2 (n=2)		s2/m1 (n=2)		s2/m2 (n=19)	
	No.	%	No.	%	No.	%	No.	%
Severity of Infl								
Mild	2	16.7	1	50.0	1	50.0	8	42.1
Severe	10	83.3	1	50.0	1	50.0	11	57.9
Depth of infl								
Superficial	2	16.7	1	50.0	2	100.0	12	63.2
Deep	10	83.3	1	50.0	0	0.0	7	36.8
Activity								
No Activity	4	33.3	0	0.0	2	100.0	12	63.2
Active	8	66.7	2	100.0	0	0.0	7	36.8
Lymphoid follicles								
Yes	11	91.7	2	100.0	1	50.0	12	63.2
No	1	8.3	0	0.0	1	50.0	7	36.8
Eosinophils								
Yes	1	100.0	0	0.0	0	0.0	1	100.0
No	0	0.0	0	0.0	0	0.0	0	0.0

Results

Table (33): Relation between babA2 status and histopathological findings among symptomatic *H. pylori* positive children (n=50)

	BabA2				χ^2	P
	-ve (n = 20)		+ve (n = 30)			
	No.	%	No.	%		
Severity of Infl						
Mild	10	50.0	15	50.0	0.0	1.000
Severe	10	50.0	15	50.0		
Depth of infl						
Superficial	10	50.0	17	56.7	0.215	0.643
Deep	10	50.0	13	43.3		
Activity						
No Activity	9	45.0	19	63.3	1.637	0.201
Active	11	55.0	11	36.7		
Lymphoid follicles						
Yes	13	65.0	20	66.7	0.015	0.903
No	7	35.0	10	33.3		
Eosinophils						
Yes	2	100.0	0	0.0	-	-
No	0	0.0	0	0.0		

χ^2 : Chi square test

Results

Clinical presentations in symptomatic *H. pylori* positive children and triple positive combination:

Table 34 shows that, the triple positive combination (simultaneous presence of babA2+cagA+S1) is present in 5 of the symptomatic cases but not present in the Asymptomatic *H. pylori* positive children.

Table (34): Comparison between the symptomatic *H. pylori* positive cases and the asymptomatic children according to triple positive gene combination

	symptomatic <i>H. pylori</i> positive (n = 50)		Asymptomatic <i>H. pylori</i> positive (n = 25)		Total (n = 75)		χ^2	p
	No.	%	No.	%	No.	%		
babA2 + cagA + S1 positive	5	10.0	0	0.0	5	6.7	2.679	^{FE} p=0.162

FE: Fisher Exact test

*: Statistically significant at $p \leq 0.05$