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.

RECOMMENDATION

1- The critical period of *H. pylori* acquisition is in childhood so, genotyping at childhood is important in future policies for the identification of those at risk of sever disease and will help in planning of eradication programme.

2- 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.

3- Further studies are needed to clarify the exact pathognicity role of babA2 gene also with the use of animal models and with in vitro studies.

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RELATIONSHIP BETWEEN HELICOBACTER PYLORI GENOTYPES, CLINICAL MANIFESTATION AND SEVERITY OF GASTRITIS IN CHILDREN

العلاقة بين موروثات الميكروب الحلزونى وشدة المظاهر السريرية والتهابات المعدة عند الأطفال

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Master of Pediatrics	**الماجستير فى طب الأطفال**

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INTRODUCTION

Helicobacter pylori is a spiral, microaerophilic, gram negative bacterium that permanently colonizes gastric epithelial cells in approximately 25% of the population in developed countries and 70% - 90% in developing countries .[1]

Humans appear to be the only reservoir of H.pylori infection and therefore human contacts remain the major mode for its transmission. Iatrogenic spread through contaminated gastrointestinal equipment has been documented.[2] Water has been shown to be a source for H.pylori infection.[3]

Histological gastritis is essential universal among H.pylori infected individuals .Whereas most infected individuals are asymptomatic, chronic H.pylori infection in susceptible individuals is associated with a variable degree of mucosal damage ranging from mild gastritis and ulcer disease to gastric carcinoma and mucosa–associated lymphoid tissue (MALT) lymphoma.[4] One reason for this phenomenon may be the different pathogenicity of infective H .pylori strains.[5]

The most important virulence determinants of H. pylori are CagA protein and the vaculating cytotoxin A (VacA)[6,7] .Approximately 50% to 60% of H. pylori contain the cagA gene, encoding the CagA protein.The cagA gene is part of cag pathogenicity island (cagPAI),which contains many genes that are related to the virulence and pathogenicity of H. pylori strain. The presence of cagA is a confirmed marker for cag PAI and is associated with more virulent H. pylori strains.[8-10]

5.

The vaculating cytotoxin A gene, which is another important virulence factor of H. pylori, encodes an 87 kD protein that induces vaculation of epithelial cells[11]. The vacA gene is present in all strains of H. pylori and comprises two variable parts. The H. pylori strains have one of two types of vacA signal sequence (s1 and s2)and two types of mid region (m1 and m2).[12,13]

Among the bacterial factors, the ability to adhere to epithelial cells is crucial in the initiation of a gastric inflammatory response.[14-16]. The blood group antigen-binding adhesion BabA has been shown to mediate adherence of H. pylori to human Lewis b (a-1,3/4-difucosylated) blood group antigens on gastric epithelial cells [5]. This attachment resulted in the development of chronic gastritis and gastric atrophy.[16-18]

AIM OF THE WORK

The aim of the work is to correlate the virulence factor, (cagA, VacA and BabA2) with:

1- The histologic parameters of H.pylori related gastritis.

2- The clinical presentations.

7.

PATIENTS

Fifty patients infected with H.pylori (stool Ag positive) referred for endoscopy with upper gastrointestinal symptoms (mostly recurrent abdominal pain, haematemsis…etc.), suggestive of organic disease and severe enough to require endoscopic evaluation, will be included in the study.

Informed consent from the parents will be obtained.

Exclusion criteria were treatment with antisecretory, antimicrobial, or anti-inflammatory medication, for the 3 months preceding the endoscopy.

Twenty five clinically health children (no gastrointestinal symptoms) with H.pylori stool antigen positive will be included as a control group.

METHODS

All patients of this study will be subjected to the following:

1- Through history taking and clinical examination with special stress on age and clinical manifestation, exclusion of patients who received proton pump inhibitor or antibiotic for the last three months.

2- Upper GIT endoscopy (after written consent):

Biopsy specimens will be systemically taken from duodenum, gastric antrum, and body. One of gastric biopsies will be processed for rapid urease test, other biopsy specimen will be processed, paraffin blocked, sectioned into 5μm thick section and submitted for the following:

1- Histopathological assessment according to Sydney classification for gastritis.

2- The Polymerase clain reaction will be used to detect cagA, vacA and $babA_2$ genes of H.pylori using specific primers.

3- In the stool specimens of the control group, polymerase clain reaction will be used to detect cagA, vacA and $babA_2$ genes of H.pylori using specific primers.

9.

RESULTS

The results will be tabulated and analyzed using appropriate statistical methods.

10.

DISCUSSION

Results will be discussed in view of achievement of the aim and compared with other studies published in the literature.

11.

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الملخص العربى

تعتبر الاصابه بالعدوى بالميكروب الحلزوني من العدوى البكتيريه الشائعه عالميا. وقد اصاب اكثر من ثلاثه ارباع السكان في الدول الناميه وتم حيازته في الغالب في مرحله الطفوله. اما في البلدان المتقدمه فالعدوى في الاطفال اقل توترا. انها السبب الاكثر شيوعا لالتهاب المعده المزمن وايضا قرحه المعده وهى مرتبطة مباشرة بسرطان المعدة.

وهدفنا في هذه الرساله هو ربط العوامل الرئيسيه لضراوه البكتيريا وهي الجينات (cagA, vacA, babA) مع كلا من الاعراض المرضيه والمحددات النسيجيه والمرضيه لالتهاب المعده المرتبط بالميكروب الحلزوني وأيضا بالصوره المنظاريه وهذا سوف يكون مهما لوضع سياسات مستقبليه للقضاء على الميكروب الحلزوني من اجل منع الامراض الاكثر شده في كلا من الاطفال والبالغين ولدراستنا اضافات جديده في هذا الصدد.

ولتحقيق هذا الهدف اجريت هذه الدراسه على ٩٥ من الاطفال الذين احيلو لعمل منظار علوي بسبب معاناتهم من آلام البطن والترجيع والقئ الدموي. ٥٠ من هؤلاء الاطفال تم اثبات اصابتهم بالميكروب الحلزوني بواسطه اختبار اليورياز السريع والفحص الدقيق للانسجه (هستوباثولوجي) والفحص الجيني PCR وايضا ٤٥ طفلا تم اثبات خلوهم من العدوى وقد تم تشخيص ٢٥ طفلا لا يشتكون باعراض مرضيه انهم حالات ايجابيه بواسطه اختبار المولد المضاد للميكروب الحلزوني في البراز.

واظهر التحليل الاحصائي للبيانات التي تم الحصول عليها من هذه الدراسه النتائج التاليه:

١- القئ الدموي هو عرض من الاعراض المرضيه الاكثر شيوعا في الاطفال الذين احيلو الى عياده الجهاز الهضمي للاطفال لعمل التنظير العلوي (٥٤.٧%) وتوجد علاقه ذات دلاله بين القئ الدموي والاصابه بالميكروب الحلزوني.
٢- وجود العقيدات المعديه هو مؤشر كبير على الاصابه بالبكتيريا الحلزونيه.
٣- قد تميزت الصوره النسيجيه للاطفال ذوي الاعراض المرضيه والمصابين للميكروب الحلزوني بوجود التهاب شديد واكثر عمقا مع زياده في عدد البصيلات الليمفاويه مقارنه بالحالات السالبه.
٤- الصوره النسيجيه للحالات المصابه بالميكروب الحلزوني والتي تعاني من الام البطن المتكرره وأيضا التي تعاني من القئ الدموي تتميز بالتهاب حاد بشكل ملحوظ مقارنه بالذين لا يشتكون من نفس الشكاوى.
٥- الجينات الاكثر شيوعا في حالات الميكروب الحلزوني الايجلبيه هي vacA (٧٢%) ثم cagA (٥٢%) ثم babA2 (٤٤%).
٦- توجد علاقات هامه بين وجود كلا من الجينات babA2، cagA، vacA s1، s1 / m1 وs2 / m2 ووجود الأعراض المرضية فى الحالات المصابة بالميكروب الحلزونى.
٧- تعتبر العقيدات المعديه اكثر شيوعا في العينات الايجابيه لكلا من cagA و vacA S1.
٨- ترتبط الجينات cagA و vacA s1 ببعض الاعراض المرضيه واالتغيرات النسيجيه
٩- لا توجد علاقه ذات دلاله بين الجين babA2 والتغيرات في الصوره المنظاريه والصوره النسيجيه بالمجهر.
١٠- تم العثور على الثلاثي (cagA, vacA, babA2) في خمسه حالات تشتكي من أعراض الميكروب الحلزوني من عدم وجود هذا الثلاثي في الاطفال بدون أعراض.

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العلاقة بين موروثات الميكروب الحلزونى وشدة المظاهر السريرية والتهابات المعدة عند الأطفال

رسالة مقدمة

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ضمن متطلبات درجة

الماجستير

فى

طب الأطفال

مـــن

أميرة حامد حسب النبى
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[٢٠١٥]

جامعة الإسكندرية
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العلاقة بين موروثات الميكروب الحلزونى وشدة المظاهر السريرية والتهابات المعدة عند الأطفال

رسالة مقدمة من

أميرة حامد حسب النبى

للحصول على درجة

الماجستير

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طب الأطفال

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