Study The Relation Between Persistent Chronic Cough And Helicobacter Pylori Infection in Pediatrics Age Group

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ABSTRACT

Introduction: Helicobacter pylori infection is most commonly a cause of gastritis causing symptoms outside gastro intestinal tract. Cough is one of the most common persistent problems in infant and children especially chronic cough with confusing cause. H.p. gastritis spread to nasopharyngeal cavity in case of gastro-esophageal reflux.

Aims: To study the correlation in-between Helicobacter pylori gastritis and persistent chronic cough in infant and children.

Materials and methods: 2 groups of patients sharing in the study, study group (81) of patients complaining of persistent chronic cough without known cause and control group (41) of patients with persistent chronic cough due to nonspecific laryngeal and pharyngeal infection.

Results: Active infection with Helicobacter pylori was found in 88.8 % (72/81) of children of our study group with persistent chronic cough

But was 26.8 % (11/41) of our controlled group, supported by presence of the antigen of Helicobacter in the children stool. The difference was apparent significantly shown (p, < 00.001). After treatment by using the proper management for H Pylori there was a significant improving of the persistent chronic cough of 92.8% (65/70) of children (p, 00.001).

Conclusions: Persistent chronic cough without recognized cause most commonly due to infection by Helicobacter pylori that leading to laryngeal and pharyngeal inflammation, several manifestations especially persistent chronic cough.

Key Words: Helicobacter Pylori, Chronic Cough, Disease Of Pharynx And Larynx.

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INTRODUCTION

Worrin and Miarshal recorded that the most common etiology of gastrointestinal diseases caused by flagellated spiral Gram negative Helicobacter pylori (HP)[1]. Petirson UL, Stimermann GN, et.al, Frieduman GD, et. al and Hansson S. et. al. They recorded that the most established etiological factor of pediatric acute and chronic gastritis and ulceration of gastric mucosa also the cause of malignant transformation and lymphoma [2,3,4,5]. Helicobacter pylori infection and colonization of mucosa of gastrointestinal tract leads to stimulation of immune and inflammatory systemic response that given life-long immune response suspect to cause diseases and symptoms outside gastrointestinal tract, which involve respiratory system, cardiovascular tract, immune system, hematological and other system affection discussed and recorded by Biek T. et. al, Doure MP, et. al, Jaspirreni A. et. al and Francisch F, et al [6,7,8, 9]. Most infection of Worrin and Miarshal recorded that the most common etiology of gastrointestinal diseases caused by flagellated spiral Gram negative Helicobacter pylori (HP)[1]. Petirson UL, Stimermann GN, et.al, Frieduman GD, et. al and Hansson S. et. al. They recorded that the

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most established etiological factor of pediatric acute and chronic gastritis and ulceration of gastric mucosa also the cause of malignant transformation and lymphoma [2,3,4,5]. Helicobacter pylori infection and colonization of mucosa of gastrointestinal tract leads to stimulation of immune and inflammatory systemic response that given life-long immune response suspect to cause diseases and symptoms outside gastrointestinal tract, which involve respiratory system, cardiovascular tract, immune system, hematological and other system affection discussed and recorded by Biek T. et. al, Doure MP, et. al, Jaspirreni A. et. al and Francisch F, et.al [6,7,8,9]. Most infection of Helicobacter pylori in infancy and children are acquired from infected mother who's minced the food in her mouth before giving her baby causing most common gastritis especially in infancy with its extra gastrointestinal manifestation of persistent chronic cough and respiratory trouble symptoms, the infection leads to inflammation with cytotoxins productions and induction of inflammatory cells for producing cytokines as interleukins 1, 6, 8, 10, 12, 23 causing systemic immune response and inflammation as discussed by Peek RM,et. al [10]. The aim in our study is to document the correlation in-between upper respiratory tract symptoms and H Pylori infections. Upper respiratory infection concludes stomatitis, glossitis, adenoiditis, tonsillitis, sinusitis, rhinitis, pharyngitis, laryngitis and otitis media of infected infants and children [11,12,13]. The upper respiratory tract infection by Helicobacter pylori gastritis and the transmission mode of H Pylori are oral-oral (from infected mother oral to her baby oral), gastric-oral, and fecal-oral [12].

Persistent, chronic cough is defined as a cough in which the patient last for more than two months (8 weeks) in good and well immune system of the patients who have a normal clear radiographic chest, not under medications affecting the inhibitor enzymes of angiotensin converting enzyme and not exposing to irritant substances[12], after exclusion of asthma induced cough, syndrome of postnasal drip causing chronic cough and cough due to Eosinophilic infiltration bronchitis, cough related to and induced by gastro-esophageal reflux.[13] Empirical treatment of the patients with appropriate dose of omeprazole for 15 days was one of best diagnostic and therapeutic trials.

MATERIALS AND METHODS

We enrolled in the study 81 infant and children patients referred to the pediatrics pulmonology unit of Zagazig University hospital suffering from Persistent chronic cough, over a period of more than one-year between December 2015 and April 2017. The inclusion criteria were: (1) normal or near-normal chest radiograph; (2) no exposure to smokers or other irritants (3) Not under treatment with immune suppressive medications (4) not improved after treatment by cough suppression and usual improved after using antihistaminic or inhibitors of proton pump. Age of patients 6 month to 15 years, both sex-matched subjects with no history of persistent chronic cough was included as a control group. They presented to us with benign, chronic laryngeal therapy of bronchitis (5) not asthmatic or Eosinophilic induced bronchitis by test of pulmonary function, histamine challenge and sputum analysis test; and (6) pharyngeal symptoms not improved using usual appropriate treatment for GERD. In our study all the patients underwent full history-taking, symptoms analysis by using questionnaire evaluating for each symptom to mild complaints, moderate complaints, sever complaints and profound complaints. The symptoms related questions including persistent chronic cough, symptoms of upper gastrointestinal tract as (dyspepsia, epigastric heartburn and regurgitation of food) and laryngeal symptoms as (laryngeal spasm, chocking, hoarseness of voice and croup), pharyngeal symptoms (acute, chronic sore throat) stomatitis & glossitis as (halitosis, mouth ulcerations). All patients clinically subjected to full examination starting from general examinations to all systems examination (cardiovascular, respiratory, abdominal and central nervous system examinations. Exclude patients with enlarged thyroid and lymph node glands. Laboratory investigations performed as a routine screening test, assay for immunoglobulin of Helicobacter pylori (IgG) antibody titers with value of 15 IU/ ml is the cutoff point, the result more than it was considered as H pylori positive, to confirm the diagnosis using stool samples for detecting antigen of H pylori, all positive patients treated by triple therapy (amoxicillin, clarithromycin and omeprazole) in appropriate doses.

Ethical considerations

The protocol of our study was done after approval by the ethics committee of the Faculty of Medicine of Zagazig University and health insurance hospitals teams. The consent was obtained from all sharing persons prior to their inclusion.

RESULTS AND ANALYSIS OF COLLECTING DATA

Our research was applied on 122 patients, classified into (2) groups. A study group total (81) patients with persistent, chronic cough, including (51) females and (30) males, with a mean age of 4+4.5 years and a control group total (41) patients with same age and sex, no history of chronic cough, of (27) females and (14) males, with a mean age of 4.8+4.7 yrs. H. pylouri +ve, seropositive rate to H. pylouri was 88.8 % (72/81) in the chronic cough group and 26.8 % (11/41) of controlled group. The difference was shown to be statistically significant (p, < 00.001). Presence of antigen of H. pylouri in stools of children confirm activity of infection in 84% (68/81) of patients in the chronic cough group and in 53.6 % (22/41) of the controlled group; this difference was also found to be significant in statistical analysis (p, 00.001). Thus, at presentation, a totally of 78 children were actively infected with H. p. (i.e. +ve) and 48 patients were not infected with H. p. (i.e. - ve). The mean age was significantly higher in the H pylori infected children (age of 4+4.5 vs. 4.8+4.7 ys; p, 00.001). In the two groups, no significant difference noticed between females and males regarding findings a totally of 54 patients (66.6 %) had one Symptom support positivity of H. pylorii. This was documented in 44 patients 54.3% of H pylori positive patients and in 12 patients 29.2 % of H. pylori -ve children. The prevalence of painful, difficult, disturbed digestion, nausea, vomiting and heartburn was significantly higher in H. pylori +ve children. As for laryngeal & pharyngeal form of laryngitis and pharyngitis, as prevalence of difficult in speaking,

globeus pharyngeus, frequent sensation of a lump in the throat, chronic sore throat and choking was significantely greater in the H. pylori +ve children compared with the H. pylorii -ve ones. The prevalence of UGIT and laryngeal & pharyngeal symptoms among the (122) patients studied is shown in Tabel 1.

Table 2 shown and described laryngoscopic changes as edematous and erythematous hyperemia of the posterior laryngeal wall and Interarytenoid mucosal muscles with phonation changes in all patients with positive H pylori. Eradication of H pylori in 48 out of 72 (66.6%) infected H pylori patients (72/81 of the chronic cough group and 16/41 of the control group) after therapeutic treatment for 6 weeks. All patients were shown improvement and reduced symptoms of dyspepsia and heartburn (epigastric pain) following treatment.

Comparison of H. pylori positive patients' persistent, chronic coughing and other laryngeal and pharyngeal symptoms before and after H. pylorii treatment revealed a significant decrease in the prevalence of the majority of these symptoms, including chronic cough (Tabel 3). Conversely, the prevalence of evaluated symptoms did not significantly change following treatment in the group of patients with unchanged H. pylorii infection status (22 patients).

Table 1. Prevalence of upper gastrointestinal, laryngeal and pharyngeal symptoms

	H pylori positive		**H pylori negative**		
Symptoms	(number 72)	Percent %	(number50)	Percent %	*p*
Upper gastrointestinal					
Dyspepsia	44	61.1%.	12	24.00%	0.005**
Epigastric pain	48	66.60%	12	24.00%	0.005**
Gastroesophageal reflux	22	30.50%	6	12.00%	0.218
Laryngopharengeal					
Dysphonia	38	52.70%	10	20.00%	0.028**
Globus sensation	56	77.70%	10	20.00%	<0.0001**
Frequent throat clearing	62	86.10%	15	30.00%	<0.0001**
Halitosis	18	25.00%	9	18.00%	0.192
Chronic sore throat	38	52.70%	15	30.00%	0.003**
Choking	70	97.20%	7	14.00%	<0.0001**

(122) patients n 72 patients, 59.1%, n50 patients, 40.9%; statistically significant

Table 2. Prevalence of laryngoscopic changes and finding

	H pylori positive		**H pylori negative**		
Symptoms	(number)	Percent%	(number)	Percent %	*p*
Edema & erythema of posterior larynx					
Interarytenoid mucosal heaping	48	66.6%.	16	32.00%	0.112
Contact ulcer	39	54.10%	12	16.60%	0.748
Granuloma	2	2.70%	1	2.00%	0.892
Reinke's oedema	6	8.30%	2	4.00%	0.886
Polyp/nodule	6	8.30%	2	4.00%	0.844
Leukoplakia	12	16.60%	7	14.00%	0.668
	11	15.20%	4	8.00%	0.929

Table 3. Studies performed for HP and pharyngitis, sinusitis, otitis media, laryngitis, glossitis and stomatitis

Author/year	**N of patients**	**Sites**	**Methods**	**Positive results**
Pharyngitis				
44	54	Pharynx tissue	TDI-FP, Giemsa	40% , 10%
46	74	Pharynx tissue	PCR, culture	28% , 06%
Laryngitis				
116	39	Laryngeal biopsy	RUT	17.60%
Sinusitis				
56	19	Sphenoid sinus T.	PCR	21%
51	15	Maxilary sinus T.	PCR	19%
52	16	Ethmoid sinus T.	PCR	34%
Otitis media				
25	12	Middle ear effusion	Culture	1%
60	22	Middle ear effusion	PCR	64%
67	42	Middle ear effusion	PCR	16%
61	42	Middle ear mucosa	PCR	9%
29	22	Middle ear effusion	Culture, PCR	1%
68	34	Middle ear effusion	CLO	65%
62	26	Middle ear mucosa	Culture, PCR	10%
Glossitis and stomatitis				
74				
86	44	DP	CLO, culture	100%
84	24	DP, saliva	IHC	82%
72	76	Saliva	Culture, PCR	10%, 80%
68	62	Oral mucosa	PCR	76%
	38	Tongue	Culture, PCR	78%, 86%

IHC immunohistochemistry, CLO Campylobacter-like organism test, PCR polymerase chain reaction, RUT rapid urease test.

DISCUSSION

Worrin and Miarshal recorded that the most common etiology of gastrointestinal diseases caused by flagellated spiral Gram negative Helicobacter pylori (HP) [1]. Petirson UL, Stimermann GN, et.al, Frieduman GD, et. al and Hansson S. et. al. They recorded that the most established etiological factor of pediatric acute and chronic gastritis and ulceration of gastric mucosa also the cause of malignant transformation and lymphoma [2,3,4,5]. Helicobacter pylori infection and colonization of mucosa of gastrointestinal tract leads to stimulation of immune and inflammatory systemic response that given life-long immune response suspect to cause diseases and symptoms outside gastrointestinal tract, which involve respiratory system, cardiovascular tract, immune system, hematological and other system affection discussed and recorded by Biek T. et. al, Doure MP, et. al, Jaspirreni A. et. al and Francisch F, et.al [6,7,8,9]. Most infection of Helicobacter pylori in infancy and children are acquired from infected mother who's minced the food in her mouth before giving her baby causing most common gastritis especially in infancy with its extra gastrointestinal manifestation of persistent chronic cough and respiratory trouble symptoms, the infection leads to inflammation with cytotoxins productions and induction of inflammatory cells for producing cytokines as interleukins 1, 6, 8, 10, 12, 23 causing systemic immune response and inflammation as discussed by Peek RM,et. al[10]. The aim in our study is to document the correlation in-between upper respiratory tract symptoms and H Pylori infections. Kasepoglu B, et. al, Richards RJ. Et. al, Akerss S, et. al. They revealed that upper respiratory infection concludes stomatitis, glossitis, adenoiditis, tonsillitis, sinusitis, rhinitis, pharyngitis, laryngitis and otitis media of infected infants and children [11,12,13]. The upper respiratory tract infection by Helicobacter pylori gastritis and the transmission mode of H Pylori are oral-oral (from infected mother oral to her baby oral), gastric-oral, and fecal-oral [12].

Our study results recorded (up to 88.8 %) of diseased children with persistent and chronic coughing showed suffering from active infection by H. pylori. Which were high significant as that of infection among the matched age and sex of controls without cough. Piestolesi M. et. al. recorded that Helicobacter pylori infection leads to release of great numbers of pre-inflammatory and vasoactive cytokines (interleukine 8 and TNFa), enzymatically generated oxidation products of arachidonic acid and acute phase protiens. It is increased and it is a sensitive indicator of inflamation of H. pylori or its exotoxins into the upper respiratory tract may induce acute, chronic inflamation of upper respiratory tract and respiratory airway, resulting in a persistent, chronic, dry cough in those patients [14]. This mechanism is supported by Karlberj G. et. al. Study which found a high concentration of interleukine 8 and tumor necrosis factors a, in samples of induced sputum from non-asthmatic patients with chronic, dry cough, including those with idiopathic cough [15]. Other possible explanation by Hirschil AM et. al. Focus on the relation between H. pylori and gastro-esophageal reflux disease, still a poor complexing understood association [16]. Malferthiner P et al. Stated that continuous releasing of inflamatory cells in the proximal stomach could result in H. pylori colonization, which could produce direct or indirect effects on the esophageal mucosal wall, increasing esophageal sensitivity to acid [17]. Frinkel D, et. al. recorded that H. pylori infection may had affection on lower esophageal sphincter motility directly through inflamation at the gastro-esophageal junction. As a result, exposure of the lower esophagus to Studies performed for HP and pharyngitis, sinusitis, otitis media, laryngitisIHC immunohistochemistry, CLO, reflux episodes, could result in chronic cough and chronic throat-infection, that lead to affection of laryngeal mucosal signs and symptmso [18]. Sulivian PA, et. al, Vaeuzi MF, and Abilson TI, et. al. Recorded a higher significant prevalence of a wide range of laryngeal and pharyngeal symptoms in H. pylori +ve diseased children, compared with H. pylori -ve patients. That agrees with our laryngoscopic results, especially edematous and erythematous hyperemia of the posterior laryngeal wall and heaping of Interaraytenoid mucosa, were higher prevalent in the infected group, but that difference not statistically significante. Laryngo-scopic results in H. pylori +ve patients :(1) Erythematous hyperemia of the medial surface of each one of araytenoids; (2) Heaping the mucosa of Interarytenoid; (3) Granulomatous swelling of left vocal process and thickening of both vocal folds; (4) contact ulceration; (5) Reinke's space collecting fluids and edema; (6) thick white patches of tongue and the mouth [19,20,21]. Therefore, Lacsetti M, et. al discussed that lack of response to empirical treatment by omeprazole therapy should not be followed by associated treatment for gastro-esophageal reflux agree with another research about contributing factor and the presence of inflamatory cells in the upper respiratory passage could increase the sensitivity of the afferent fibers, and this might explain the wide range of laryngeal & pharyngeal forms in H. pylori +ve patients [22]. Recently, H. pylori were positively identified in 36.3% of specimens of vocal fold, that document the link between H pylori infection and organic lesions of vocal fold. Persistent, chronic, cough is a common most problem with different etiologies. Our study with different etiological causes of H. pylori infection in the etiology of chronic, persistent cough of an unidentifiable reason agrees with the study of Yanig C. et. al. [23]. H. pylori active infection was statistically more prevalent in patients with chronic cough comparing with controlled group. Chuing KF, et. al. revealed that treatment and eradication of H pylori infection result in improvement and disappear of patient symptoms [24]. There is no definitive mechanism join the relation between persistent, chronic cough and H pylori infection of gastrointestinal tract but management with proton pump inhibitors improves the life of the patients.

CONCLUSION

The results of our study agree with a potential relationship between infection of Helicobacter pylori and different chronic, non-specific laryngeal & pharyngeal symptoms,

mainly persistent, chronic cough. In spite of the definitive mechanism and pathophysiology is unknown. But investigations of H pylori and therapeutic treatment and diagnosis of H pylori and persistent, chronic cough support this relationship.

Conflict of Interest

Conflict of interest declared none.

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