

Helicobacter Pylori infection and Persistent Itching

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Background and study aim: *Helicobacter (H) pylori* is a worldwide prevalent infection with wide range of gastric and extra-gastric diseases. There is evidence in the literature linking *H pylori* to many skin diseases. The current study aimed at determining the frequency of *H pylori* among patients with persistent itching and evaluates impact of *H pylori* treatment on the course of the disease.

Patients and Methods: Two hundred eighty patients with persistent itching were tested for *H pylori* antigen in their stool. Patients with and without *H pylori* antigen positivity were compared. *H pylori* positive cases were treated by 2 weeks regimens.

Results: One hundred thirty patients (46.4%) were positive for *H pylori* stool

antigen. Patients with and without *H pylori* stool antigen positivity were comparable in their demographic and laboratory parameters except for Ig E which was more positive among *H pylori* negative cases. *H pylori* positive cases had 60%, 20%, and 20% rates of complete resolution, partial resolution and non-resolution of itching after *H pylori* treatment respectively.

Conclusion: Among patients with persistent itching recruited in the current study, 46.4% had an evidence of *H pylori* infection. *H pylori* positive cases with persistent itching did not have elevated Ig E levels. Out of 130 *H pylori* positive cases 60% had complete resolution of itching after treatment of *H pylori*.

INTRODUCTION

Helicobacter (H) pylori is the most prevalent infection around the globe with higher prevalence rate in the developing countries. Although this gram negative spiral bacteria inhabits the gastro-duodenal mucosa; it is linked to gastric and many extra-gastric disease states. The spectrum of gastro-duodenal affection mostly passes through asymptomatic infection. Furthermore, with time the infection evolves from acute and chronic gastritis, peptic ulcer to the most serious hazard; the gastric cancer [1,2].

The extra-gastric effects attributed to *H pylori* are matters of discussion in the literature. It had been postulated to have an impact on many metabolic, cardiac, neurological, allergic, ocular, haematological, dermatological, and hepatobiliary diseases. However, many of the attributed effects are no

more than epidemiological associations [3]. Among the confirmed extra-gastric effects attributed to *H pylori* infection are iron deficiency anemia, primary immune thrombocytopenia (ITP), and vitamin B12 deficiency which necessitates a test and treat strategy for *H pylori* infection [1,2].

The association between *H pylori* infection and skin diseases was postulated not only from epidemiological studies, but also from clinical studies [4]. Previous reports documented a possible relation between active *H pylori* infection and allergic and non-allergic skin diseases [4,5]. The aim of the current study is to investigate the frequency of *H pylori* infection among patients with persistent itching and evaluate the impact of *H pylori* treatment on the course of the disease.

PATIENTS AND METHODS

This was a prospective study conducted over 2 years from March 2019 to February 2021 recruiting patients with persistent itching. All patients were evaluated initially in dermatology clinics before being referred for further evaluation in gastroenterology clinics. Patients with persistent itching were examined for *H. pylori* antigen in their stools after the standard precautions. Patients were divided into 2 groups. Groups I; are patients with persistent itching and positive *H. pylori* antigen in stool and Groups II; are patients with persistent itching and have negative results for *H. pylori* antigen in stool. Patients of both groups were compared for their demographics, clinical and laboratory data prospectively.

Definitions:

- *Itching or pruritis*: Defined in this study as persistent sensation of itching in absence of any identifiable local or systemic causes.
- *Response to treatment*: is defined as complete or partial disappearance of the intense desire for itching. In *H. pylori* positive group assessment of the response was done at least 4 weeks after finishing the treatment.
- *Treatment of H. pylori* followed the guidelines and vary from one case to another per the circumstances [1]. For treatment naïve patients the triple therapy (PPI, clarithromycin, and amoxicillin) was used, while for patients with recent exposure to or potential risk of resistance to clarithromycin, levofloxacin based quadruple therapy was used [1,2].

Inclusion criteria:

- Adult patients of 18 years and older
- Patients with persistent itching

Exclusion criteria

- Patients unwilling to participate
- Patients who received treatment for *H. pylori* or PPI within 4 weeks prior to the commencement of the study.
- Patients with known allergic diseases e.g. allergic asthma
- Patients with known skin diseases
- Patients with known allergy to the proposed anti-*H. pylori* treatments

All patients were subjected to:

- Full history taking including any history of allergic diseases
- Thorough clinical examination
- *H. pylori* antigen detection in stool. (On Site *H. pylori* Ag Rapid Test, CTK Biotech, USA). It is a lateral flow chromatographic immunoassay for qualitative assessment of *H. pylori* antigens depending on the use of monoclonal antibodies against *H. pylori* conjugated with colloid gold. Positive cases were marked with two bands of color changes (one test band and one control band).
- Lab work up that included: ALT, AST, CBC, TSH, serum bilirubin, creatinine, serum Ig E, CRP, ESR
- *H. pylori* positive cases were treated by 2 weeks course

Statistical analysis

Primary end point of the current study was determination of *H. pylori* prevalence among patients with persistent itching

Secondary end point of the current study was determination the response to *H. pylori* treatment among positive cases with persistent itching.

Data were analyzed using SPSS version 20. Data were expressed as number and percentage for qualitative variables and mean \pm standard deviation for quantitative ones. P value of < 0.05 indicates significant results. Comparison between the two groups was done using *t*-test and Chi-square test.

RESULTS

Patient demographics

This study included 280 consecutive patients with persistent itching and according to their positivity (n=130) or negativity (n=150) to *H. pylori* stool antigen were classified as group I and II respectively. The prevalence of *H. pylori* among patients with persistent itching is 46.4% (130/280). The age and gender were comparable in both groups (Table 1).

Laboratory data of both groups

When both groups were compared regarding the common causes of persistent itching, it was clear that liver biochemical profile and thyroid function were comparable between the 2 groups (Table 2). The acute phase reactants CRP and ESR and CBC were also comparable between the

2 groups. However, the *H pylori* negative group had higher frequency (73.4%) of IgE positivity in comparison to none (0%) among *H pylori* positive group ($P < 0.001$).

Response to *H Pylori* treatment

In this study all *H pylori* positive cases were treated for 2 weeks duration. Treatment was individualized case by case according to the

situation e.g. previous treatment failure.....etc. The response to treatment was evaluated 4 weeks after completion of the treatment course. Out of the *H pylori* positive patients 60% ($n=78$) had complete resolution of symptoms, while 20% ($n=26$) had partial response in contrast to 20% ($n=26$) who did not improve (Figure 1). When compared to the *H pylori* negative group who showed no response to anti-histamines.

Table (1): Demographic data distribution between studied groups.

	Group I (n=130)	Group II (n=150)	P
Age (years)	47.26±11.74	45.28±10.88	0.095
Sex			0.77
Male	62 47.6%	69 46.0%	
Female	68 52.4%	81 54.0%	

No significant difference or association between groups.

Table (2): Lab characteristics of both groups.

	Group I (n=130)	Group II (n=150)	P
Thyroid function			0.174
Normal	112 86.2%	120 80.0%	
Abnormal	18 13.8%	30 20.0%	
SGOT (IU/L)	29.63±9.36	32.57±10.87	0.211
SGPT (IU/L)	31.58±7.41	33.63±8.88	0.136
Total bilirubin (mg/dl)	1.21±0.22	1.27±0.35	0.0856
CRP			0.058
Negative	130 100.0%	144 96.0%	
Positive	0 0.0%	6 4.0%	
Ig E			0.00**
Negative	130 100.0%	110 73.4%	
Positive	0 0.0%	40 26.6%	
Elevated ESR	0 0.0%	0 0.0%	1.0
Hemoglobin (gm/dl)	12.25±3.08	11.88±2.85	0.35
WBCs x10³	7.56±1.85	6.99±2.12	0.33
PLT x10³	187.63±60.63	179.36±58.36	0.23

** Highly significant

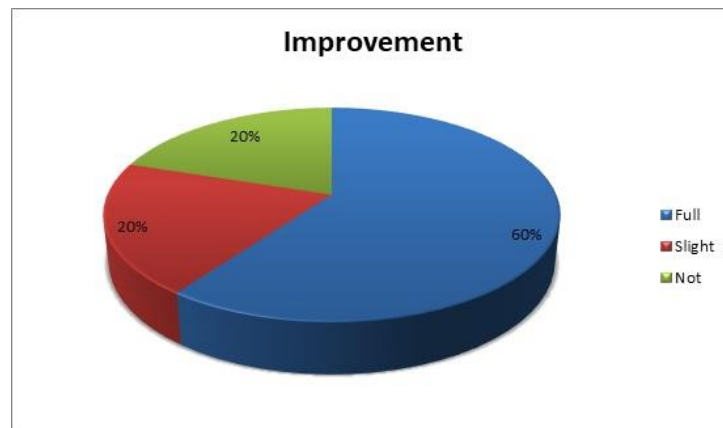


Figure (1): Patterns of response among *H pylori* positive patients.

DISCUSSION

H pylori have been linked to many skin diseases in many epidemiological studies as well as clinical ones. The link of skin diseases mainly pruritic skin diseases among *H pylori* patients have been attributed to many mechanisms. The most widely accepted is autoimmune one. It seems that following the prolonged infection with *H pylori*, an interaction with the host immune system do occur. *H pylori* trigger antigens that cross-react with T cells and provoke autoantibodies resulting in loss of tolerance to self-antigens in the skin [6]. The association of *H pylori* to allergic diseases have been questioned and some reports postulated protective role of *H pylori* against allergy with documentation of an inverse relationship between prevalence of *H pylori* and allergic diseases [7]. The lack of Ig E detection among *H pylori* patients with pruritis in this study may favor this assumption

There is growing practice behavior among dermatologists in our community to investigate cases of persistent itching for *H pylori*. Although this is not supported by any current clinical practice guidelines [1,2], however it may be justified by the growing evidence in the literature linking *H pylori* to a variety of skin disorders [5,8]. The high prevalence of *H pylori* among patients with persistent itching (46.4%) reported in the current study is another support to this trend. In fact, this high prevalence is in agreement with Kandyil et al. [9], who reported *H pylori* prevalence rate of 80% (8/10 patients) among patients with refractory pruritus and also with Saleh et al. [10], who reported a rate of 63.4% (50/63) among patients with rosacea.

In the current study there were no significant differences between both groups as regard the age and sex. This is in agreement with Marae et al., who reported similar results for patients having palm and sole of psoriasis with and without *H pylori* [11].

The common causes of itching usually seen in our community e.g. liver diseases and thyroid dysfunction were ruled out. This favors the hypothesis that *H pylori* is presumably a direct cause of itching and the link is not just an epidemiological association. The lack of Ig E positivity among our *H pylori* positive cohort (0%, $P < 0.001$) favors the possibility that a direct non-allergic mechanism stands behind. Although we did not found studies focusing *H pylori* and skin diseases targeting Ig E measurement, one study among children showed high prevalence of food specific Ig E levels among children with *H pylori* infection [12] probably this finding is not applicable for skin diseases.

The results of the current study are in agreement with the study of Kandyil et al. [9], who reported a possible relationship between refractory pruritus and active *H pylori* infection which was confirmed among 8 out 10 patients focused. The terms of response after *H pylori* treatment reported by Kandyil et al., were 62.5% (5/8) complete relief, 25% (2/8) temporary relief of pruritus, while the remaining 12.5% (1/8) did not respond. These figures were not different from the 60%, 20%, and 20% reported respectively in the current study. The clinical terms of response defined in the current study and in the study of Kandyil et al., are usually the target of practitioners and patients as well rather than bacteriological terms of *H pylori* eradication and this would explain why confirmation of

eradication was not an endpoint of both the current study nor in the study of Kandyil et al.

We believe that both the high frequency of *H pylori* among patients with persistent itching and the high (60%) itching relief rate reported in the current study would alarm both dermatologists and gastroenterologists in our developing countries to consider *H pylori* in the differential diagnosis. However, we believe it is an advice rather than a recommendation based on the available evidence.

The current study had some limitations. First, the lack of *H pylori* detection by more accurate methods of diagnosis e.g. urea breath test (UBT), upper endoscopy and histopathology. Because we performed *H pylori* stool antigen detection under the standard precautions and hence its sensitivity would be as high as UBT, similar to what we reported in earlier studies [13]. Furthermore, in our clinical practice stool antigen is frequently used due to cost and availability issues. Second, is the lack of *H pylori* eradication confirmation after treatment. Previous studies [9-11] did not target eradication as an end point.

In conclusion, among patients with persistent itching focused in the current study, 46.4% had an evidence of *H pylori* infection. *H pylori* positive cases with persistent itching did not have elevated Ig E levels. Out of 130 *H pylori* positive cases 60% had complete resolution of itching after treatment of *H pylori*.

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Conflict of interest: None.

Ethical consideration:

All patients signed an informed consent to participate in the study and to perform the relevant investigations after explanation of all steps. The current study was carried in concordance with sound medical practice and in line the ethics raised in the declaration of Helsinki.

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