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Prevalence of *Helicobacter pylori* infection and its associated diseases in low socio-economic workers in tertiary care hospital of Lahore, Pakistan

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Abstract

Helicobacter pylori is endemic worldwide and causes gastric ulcers, gastroesophageal reflux disease (GERD) and gastric carcinoma. Purpose of the present study was to determine the prevalence of *H. pylori* and its associated diseases among low socio-economic population attending a tertiary care hospital in Lahore, Pakistan. Total 603 patients with gastrointestinal (GI) tract problems were included from March 2015 to December 2016. Strip detection test, urea breath test (UBT), endoscopy and biopsies were performed to confirm the presence of *H. pylori.* Out of 603 patients, 48 patients were positive for *H. pylori* and the prevalence was assessed up to 7.9 %. Patients han females (31.3%). Age and gender betwaged >40 years were more affected than other young age groups. Males (68.8%) were more affected teen the two groups did not show significant association with *H. pylori* infection ($p>0.05$). But they were found to be inversely proportional to each other ($p<0.01$). Gasrtro Esophageal Reflux Disease (GERD) (6.3%, $p>0.05$) was not found to be statistically associated with the presence of *H. pylori* but hiatal hernia was strongly associated ($p<0.05$). In conclusions, the prevalence of *H. pylori* infection in a single tertiary care hospital is 7.9% and is decreasing due to improved overall hygiene and awareness. This also includes some people that show high perseverance on their health problems. Hiatal hernia is strongly associated with *H. pylori* infection ($p<0.01$) indicating hernia as common predisposing factor for this infection more than any other disease. The difference in infections in age and gender ($p<0.01$) shows exposure of the affected group more than the other group.

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Introduction

H. pylori is the cause of gastrointestinal ulcers which mostly affect the stomach. It is prevalent worldwide being more common in developing countries than developed ones. Different factors are known to be the reason for its spread in different populations. Pakistan is one of the developing countries in South Asia with common *H. pylori* infections [1]. According to World Gastroenterology Organization Global Guideline in September 2011, the incidence of *H. pylori* infection in adults and infants of Bangladesh was > 90 % and 58% respectively [2]. In other countries such as Hong Kong, India, Japan, Sri Lanka, Egypt, and Saudi Arabia, the incidence of *H. pylori* was reported as 13 %, 88 %, 70 %, 72 %, 90 %, and 80 %, respectively in adults [3].

The incidence of *H. pylori* infection is higher in developing countries among the people with a low socio-economic status. Additionally, place of birth and ethnicity factors are also included in it. Although, the overall prevalence of the infection is decreasing due to the improvement of living standards, birth cohort effect, genetic effects and moving from rural area to urban areas. However, the rate of post-treatment occurrence is higher in developing countries. The majority of studies used either serologic testing or urea breathing test for diagnosis, histologic testing or polymerase chain reaction [4].

A systematic search in MEDLINE and EMBASE databases for the prevalence of *H. pylori* was conducted which included reports from 1970 to 2016. Reports covering 62 countries were concluded that Africa having the highest pooled prevalence of *H. pylori* infections with 70.1% and Oceana with the lowest prevalence rate of 24.4%. The report also showed 4.4 billion individuals were infected with *H. pylori* worldwide in 2015 [5].

The prevalence of *H. pylori* infection and its associated diseases in Asian countries are not the same. Due to limited data available for different countries, annual frequency rate of gastric cancer per 100,000 in various Asian countries are summarized from the literature review and WHO statistics [6]. The occurrence of *H. pylori* is high in India and Bangladesh but low gastric cancer rates have been reported. On other hand, this ratio is opposite in Japan. Factors that influence the etiology of gastric cancer include *H. pylori* strain as well as host genetic background and gastric acid secretion. Personal hygiene and dietary habits may influence the incidence [7].

It is well known that *H. pylori* can form biofilms and coccoid forms from spiral forms that help it to survive in the harsh conditions of stomach. These microorganisms disintegrate the defensive mucous layer of the stomach and duodenum, which enables corrosive acid to enter into the sensitive coating underneath. Subsequently, both the acid and the microscopic organisms aggravate the covering and cause irritation, or ulcer [8]. These ulcers ultimately may convert into various diseases such as erosions, infiltration by lymphoreticular tissue, fibrosis etc. known to be associated with *H. pylori* infection [9]. *H. pylori* have strongly been associated with multiple clinical disorders such as, peptic ulcer disease, gastric adenocarcinoma and lymphoma and many other diseases of the gastrointestinal tract [10]. GERD, hiatal hernia and Candidiasis are the three associated diseases found in the studied population co-existing with *H. pylori* infection [11]. Other diseases like adenocarcinoma, squamous cell carcinoma, erosions, obstructive mass, malignancy/nh lymphoma, benign mucosa, ulcer, erythematous changes, teliangectasis, oesophageal web, infiltration of lymphoreticular tissue were not found in *H. pylori* infected population. The co-existence of these diseases may be found in other populations with different prevalence rates which are needed to be studied. The aim was to determine the current prevalence of *H. pylori* infection and to indicate the diseases that are associated with *H. pylori* infection in our population.

Materials and methods

Study area and sampling method

The study was conducted at Nawaz Sharif Social Security Teaching Hospital, Lahore, Pakistan. It is a corporate hospital situated on Multan road, Lahore, at Mansoorah for the treatment of Government employees, workers and labor with very low income in Punjab, Lahore, Pakistan. Blood samples were drawn randomly from the patients (n=603) who visited the hospital due to gastrointestinal (GI) problems during March 2015 to December 2016.

No age limits were assigned to include in the study. All cases with old and new *H. pylori* infections were included. Low socio-economic conditions were confirmed by checking low incomes of families, overcrowded residence, poor hygienic facilities, sanitation problems and dietary insufficiencies during taking clinical history. Informed written consent was obtained from all patients during this time period.

Strip Detection

The *H. pylori* antibody rapid test device (Bioplus. Greece) was used for strip test detection. This device is 95.1 % sensitive and has 94.1 % specificity (*Varia & Holton, 1989; Evans et al., 1989*).

Urea Breath Test (UBT)

It is a reliable test for *H. pylori* detection with 90% sensitivity and 95% specificity. The sensitivity of test may vary depending upon the concentration of *H. pylori*. Samples of breathed out breath were gathered, and the isotopic carbon in the breathed-out breath was measured using a Gas Isotope Ratio Mass Spectrometer System (ABCA-NT System, Europa Scientific, Ltd. USA).

Endoscopy and biopsy

The procedure guidelines for endoscopy were followed as described by British Society of Gastroenterology (BSG) and BSG Quality and Safety Indicators for Endoscopy [12, 13]. Proton Pump Inhibitors (PPIs) were stopped at least one week before the endoscopy.

Patients with long-term drugs history known to cause gastritis and lesions indicating malignancy on endoscopy were excluded for biopsy. The patient less than 18 years of age was also excluded for biopsy. Biopsy specimen of 4mm size was taken from either the infected site or normal mucosa of the gastric antrum. One or two biopsies were taken 5 cm proximal to the pylorus, near the incisura angularis in the lesser curvature or in the great curvature opposite to it [14].

Microscopy

Biopsies were collected in normal saline. Methanol was used to fix biopsies followed by Giemsa staining of prepared smears. Biopsy specimen was picked using sterile swab and placed on clean microscopic slide [15].

Data analysis

Data were entered into Microsoft Excel 2007 and then transferred to SPSS version 21 to analyze.

The rankings for the symptoms and findings of endoscopy on upper GI tract for the patients were mild, moderate and severe on the basis of severity of infection as classified by World Health Organization's ICD-10. Simple descriptive statistics such as percentages, frequencies, ratios and proportions were used for the analysis of data in this study. The categorical outcomes and their associations were measured by Chi square test at 5% level of significance and 95% confidence Interval.

Results

Strip and urea breath tests were performed to confirm the presence of *H. pylori* in blood samples of patients. Out of 603 patients, 47 (7.8%) were positive for strip test while as, 45 (7.5%) were positive for UBT. Results of these two tests are compiled in **Table 1**. Mean age of patients in *H. pylori* positive group was 46 ±16 years. Male pateients were found more prone to *H. pylori* than female patients. The overall prevalence of *H. pylori* was 7.9%.

Table 1: Strip detection test and Urea Breath test results for *H. pylori* diagnosis

n=48	Strip Test	Urea Breath Test	Gastritis	Esophagitis	Duodenal ulcers
44	Positive	Positive	43	1	0
3	Positive	Negative	1	2	0
1	Negative	Positive	1	-	-

Data showed an inverse association between age and gender parameters as the relationship between two age groups was (X^2=16.185, $P < 0.01$, CI=95%) as shown in **Table 2** and **Fig. 1**.

Table 2: Age-wise frequencies of *H. pylori* infections in males and females

Age	Esophageal Biopsy	Stomach Biopsy	Duodenal Biopsy	Males n=33	Females n=15	Total	P-value (CI=95%)
18-40	0	18	0	6	12	18	< 0.01
>40	3	27	0	27	3	30	

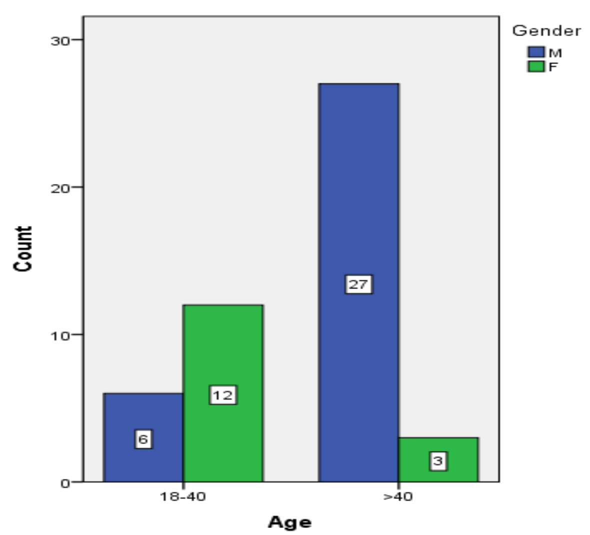

Fig. 1: Age-wise distribution of *H. pylori* infection in different genders (Source: Personal collection)

There was no sufficient association of age and gender with the site of infection ($p>0.05$), which reveals that these two parameter did not have any effect or association with the *H. pylori* infection in any of the three studied sites i.e. esophagus, stomach, and duodenum endoscopically or in biopsies as shown in **Table 3**.

Table 3: Association of endoscopic and biopsy results of the locations of infection with age and gender

Site of infection	Chi-Square value		*P value*	
	Age	**Gender**	**Age**	**Gender**
Esophageal Endoscopy	5.333	1.455	*0.069*	*0.483*
Stomach Endoscopy	6.933	6.109	*0.074*	*0.11*
Duodenal Endoscopy	1.252	1.455	*0.263*	*0.23*
Esophageal Biopsy	1.920	1.455	*0.166*	*0.23*
Stomach Biopsy	0.385	1.34	*0.54*	*0.25*
Duodenal Biopsy	-	-	-	-

GERD and Candidiasis were not found statistically associated with the presence of *H. pylori* 3 (6.3%, $p > 0.05$) but hiatal hernia was strongly associated ($p<0.01$) (**Table 4**). Hiatal hernia, GERD and Candidiasis were the only three associated diseases present with *H. pylori* infection in the studied population. Other diseases which did not co-exist with *H. pylori* infection included adenocarcinoma 9 (1.5%), squamous cell carcinoma 6 (1%) and others which were not significant to mention. Prevalence of other diseases in the population is summarized in **Table 5**.

Table 4: Association of *H. pylori* status with other diseases

Clinical findings	*H. pylori* Status		*P value* (CI=95%)
	Positive	**Negative**	
GERD	3	45	0.08
Hiatal Hernia	9	39	0.001*
Candidiasis	3	45	0.4

***Highly significant association

Table 5: Complete clinical findings prevalent in the study population

Clinical findings	Esophagitis (%)	Gastritis (%)	Duodenal (%)
H. pylori infection	3 (0.5)	48 (7.9)	0
Adenocarcinoma	9 (1.5)	0	0
GERD	6(1)	3 (0.5)	6 (1)
Squamous cell carcinoma	6 (1)	0	0
Erosions	15(2.5)	3 (0.5)	9 (1.5)
Candidiasis	24 (4)	0	0
Fibro collagenous Tissue/Fibrosis	3 (0.5)	3 (0.5)	0
Hiatal Hernia	30 (5)	12(2)	0
Others *	60 (10)	369 (61.2)	120 (20)
NB (No Biopsy)	447 (74.1)	165 (27.3)	468 (77.6)
	Total=603	Total=603	Total=603

*Others = Obstructive mass, Malignancy/NH lymphoma, Benign Mucosa, ulcer, Erythmatous changes, Teliangectasis, Oesophageal web, Infiltration of Lymphoreticular tissue

Discussion

Prevalence of *H. pylori* varies from region to region [5]. In view of territorial pervasiveness estimates, there were around 4.4 billion people with *H. pylori* disease worldwide in 2015 [5]. More than half of the total population was observed to be infected. Among individual nations, the predominance of *H. pylori* infection shifted from as low as 18.9% in Switzerland (95% CI, 13.1_24.7) to 87.7% in Nigeria (95% CI, 83.1_92.2) [16]. There was a great difference in the prevalence of *H. pylori* in developed 40% and in developing countries 80-90% and the list of factors affecting its prevalence is also large.

The overall prevalence varied from as low as 11% to as high as 69% in these countries. This observation was related to rapid changes in socioeconomic status of many subpopulations in these countries and increased use of antimicrobials for infections. Another review in 2014 stated the decrease in *H. pylori* prevalence in European countries from 48% to 16% in subjects born during 1970s to 80s and also declined from 38% to 14% in Cag A positive cases in same age group [17,18].The reduction in *H. pylori* prevalence in our studied population 7.9 % depicts the same reasons. We supposed that the increased antibiotic usage, urbanization, and improved hygiene awareness in the general population and low patient presentation for treatment are the major factors for such a low prevalence rate.

It is obvious from our investigations of prevalence studies that males 33 (68.8%) are more affected by *H. pylori* infection than females 15 (31.3%) [19]. This trend was also observed by Darko et al. (2016)[17] where males were significantly associated with *H. pylori* infection with a summary odds ratio of 1.16 and 95 % confidence interval (CI) and Moayyedi et al. (2002)[20] (29% in males versus 26% in females. The reasons for males being affected more could be working and eating in unhygienic conditions and the use of public toilets with fewer sanitation facilities. On other hand, the increasing trend of infectivity was observed for increasing age in 19 different countries in another study by Bruce and Maaroos (2008) [16] but there was an overall decreasing trend in prevalence in these countries. A study from Sweden indicated a steady increase of prevalence from the age group 20-29 with 10% to 40-50% in age group 70 and above [21]. The age group having more infections with *H. pylori* was >40 years in our study coinciding with the study by Perez-Perez et al. (2004) [21] indicating that there is more exposure to a working person as labor or working men surrounded with low socioeconomic factors. Although the younger age group also shows to be infected the extent of acute infections that presented during the study is thought to be less due to their overall immunity and non-symptomatic state of health.

In a study comprising of birth cohorts in urban China a striking decreasing trend in prevalence of *H. pylori* was found by Yu et al. (2017) [22] which they concluded was due to increase per capita gross domestic product GDP (R2=0.914 and 0.997 and p=0.011 and 0.000, respectively). High prevalence rate was obtained in a 1950-1959 birth cohort followed by a decrease in the rate in following cohorts ($p<0.001$) [22].

The higher rate was observed in older than 40 years age group (57.7% in 40-49 years of age) (38.1% in 30-39 years age people) and was lower in city residents than in non-city residents at all ages [23, 24]. In another study by Robertson and colleagues, overall *H. pylori* sero-prevalence was 32% and ranged from less than 20% in individuals 21-30 years and up to 54% in individuals aged more than 60 years after testing 500 consecutive blood samples from Australia in 2003[25]. These same reasons explain the increased prevalence of *H. pylori* infections in the older age group than the young one in our studied population.

Studies on *H. pylori* epidemiology have plainly exhibited a major etiologic role of this bacteria for various gastroduodenal diseases, including GERD, gastric as well as duodenal ulcer, gastric MALT lymphoma, and distal gastric malignancy [26]. But in an investigation from Spain, the predominance of *H. pylori* in GERD patients was lower than in the overall public [27]. In any case, the annihilation of *H. pylori* among kids and young people was not related with expanded manifestations of GERD in an investigation from Israel [28]. These results-imposed speculations upon whether GERD is caused by *H. Pylori* itself or there are some other factors involved in this disease. In another investigation from the Netherlands, GERD was present significantly more often (33% versus 9.7%, $P < 0.001$) in people with Dutch ethnicity, who had a low *H. pylori* pervasiveness (18.5%), than in people of Turkish descent, who had a substantially higher *H. pylori* prevalence (60.6%) [29]. *H. pylori* strain separated from patients with GERD showed comparative bacterial destructive properties as *H. pylori* strains secluded from duodenal ulcer patients[30]. Hence *H. pylori* and GERD cannot be associated because the association of *Helicobacter pylori* infection and GERD remains controversial with the geographical location being a strong contributor to the heterogeneity of results in different studies. This was also observed in our study by only 3(6.3%) cases of GERD in *H. pylori* infected patients *P*-value 0.08. Overall patients with GERD were 15(2.5%). Presence of *H. pylori* was associated with reduced severity across the spectrum of GERD, especially in Indians.

On other hand, hiatal hernia had a strong association with the *H. pylori* infected patients, *p* value=0.001. It is well known that *H. pylori* is one of the reasons for hernia [31] and high gastric acid secretion is significantly associated with an increased risk of hiatal hernia. This is obvious clearly in our studied population as well.

Candida genus inhabits the oral cavity, pharynx, and intestines of most healthy people in equilibrium with other normal flora. The esophagus, stomach, and small intestine are only a way of passage for them [32]. One study showed coexistence of candidiasis and *H. pylori* in only 11% of the studied population and demonstrated no significant association between the two [32] which coincides with our results. Results of our study did not show any significant association between candidiasis and *H. pylori*. Persistent fungal colonization can lead to pathological changes in high-risk patients. Fungal infection of the gastrointestinal tract is usually endogenous. But exogenous infection is also possible from solid food contaminated with fungi. Recently, a fact that *H. pylori* can facilitate fungal colonization of gastric mucosa has drawn much attention. Much research work is required to be done on this perception.

Conclusion

The prevalence of *H. pylori* infection in a single tertiary care hospital in Lahore is 7.9% and is decreasing due to improved overall hygiene and awareness. This also includes some people that show high perseverance on their health problems. Some people may even take medicine on their own or by visiting local clinics. Hiatal hernia is strongly associated with *H. pylori* infection ($p<0.01$) indicating hernia as common predisposing factor for this infection more than any other disease. The difference in infections in age and gender ($p<0.01$) shows exposure of the affected group more than the other group. There is a great need to increase the circle of our investigation but studying single hospital observations shows us the situation at glance.

Low prevalence rate might be due to the fact that acute infections are less common in most people than chronic asymptomatic infections, so the turnout of such patients was low in our study group.

Conflict of Interest

Authors have no conflict of interest. No financial interest/relationships relating to the topic of this article have been declared.

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