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Original Article

Distribution of *Helicobacter pylori* infection and abnormal body- mass index (BMI) in a developing country

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Abstract

Introduction: *Helicobacter pylori* is prevalent in developing nations. We determined the prevalence of *H. pylori* infection in relation to body-mass index (BMI) of dyspeptic patients and related comorbid conditions.

Methodology: In a cross-sectional study, dyspeptic patients were enrolled and tested for *H. pylori* infection. "Underweight" was defined as BMI lower than 18.4; "Healthy" 18.5 to 23; "Overweight" 23.1-27.9; and "Obese" greater than 28.

Results: Six hundred and ninety-eight patients were included, with a mean age of 44 ± 16 years. Males were 373/698, 53%. *H. pylori* was positive in 399/698, 57%. Underweight were 36 (5%); BMI-healthy 168 (24%); overweight 236 (34%) and obese 258 (37%). *H. pylori* infection was present in 65/273 BMI-healthy patients ; 24% compared to obese 208/273; 76% (P < 0.001). In the *H. pylori*- positive with a "healthy" BMI, dyslipidemia was seen in 6/65; 8% compared to obese 53/208; 25% (P = 0.005); type 2 diabetes in 8/65; 12% with a "healthy" BMI compared to obese 54/208; 26% (P = 0.022) and coronary artery disease in 4/65; 6% of BMI-healthy compared to obese 38/208; 18% patients (P = 0.018). Multivariate analysis showed that age 31-50 years (OR 1.77, 95% CI 1.13-2.77), BMI > 23.1 (OR 2.91, 95% CI infection. 2.01-4.20), and type 2 diabetes (OR 2.41, 95% CI 1.43-4.06) were risk factors for *H. pylori*

Conclusions: *H. pylori* infection was prevalent in the 31-50-year age group. Abnormal BMI was associated with *H. pylor*i infection.

Key words: *Helicobacter pylori*; BMI; overweight; type 2 diabetes.

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Introduction

Helicobacter pylori (*H. pylori*) is a Gram-negative spiral-shaped microaerobic microorganism that is prevalent in developing Asian countries [1]. It is associated with gastritis, peptic ulcer, gastric carcinoma and lymphoma [2–4]. Extragastric manifestations of *H. pylori* infection are cardiovascular, hematological, immunological and dermatological [5–7]. *H. pylori* has a feco-oral route of transmission and is prevalent in people living in crowded conditions and having a poor socioeconomic status [8]. *H. pylori* infection has decreased in the developed world i.e. United States, Western Europe and in some Asian countries such as Japan, etc. *H. pylori* was detected in 58% of children at the age of 15 years in Pakistan [9]. It tends to increase with age and in people with low socioeconomic status [9].

Obesity has increased rapidly worldwide in the past few years, particularly in developing countries. Urbanization, lifestyle changes and an unhealthy energy-dense diet, contribute to obesity in our country, where one-in-four adult is overweight [10]. Obesity is a non-communicable disease that is linked to microbiome in animals and humans. Obesity is associated with impaired immune response [11,12]. Recent studies of *H. pylori* and obesity have revealed that obese individuals have a higher prevalence of *H. pylori* infection [11,12]. A systematic review showed that insulin resistance accompanying obesity was positively related to *H. pylori* infection [13]. In contrast, another study looking at the association between body-mass index (BMI) and *H. pylori* infection, was negative [14]. An inverse correlation between obesity and *H. pylori* has been also described [15]. On the other hand, an increase of weight has been observed following eradicationof *H. pylori* [16]. Therefore, the evidence of the role of *H. pylori* infection in human obesity is inconclusive and controversial [17]. These contradictory reports suggest a need to study further the relationship between obesity and *H. pylori* infection. Obesity is a public health problem in our country. It is also associated with hypertension, dyslipidemia and cardiovascular disease. A higher prevalence is not restricted to urban population [10]. In this study, we

determined the prevalence of *H. pylori* infection in relation to BMI of dyspeptic patients and the association between comorbid conditions such as hypertension, type 2 diabetes, dyslipidemia and coronary artery disease, and *H. pylori* infection.

Methodology

The study was conducted among adults who attended the gastroenterology clinic for dyspeptic symptoms that included abdominal discomfort or pain, bloating and nausea, and underwent gastroscopy from January 2015 to December 2016 at a tertiary care centre. Data were collected on anthropometric measurements, complete blood count, fasting blood hemoglobin A1c, lipid profile i.e. serum cholesterol, triglycerides, high density lipoprotein (HDL), low density lipoprotein (LDL) and very low density lipoprotein (VLDL) cholesterol, and the results of the *H. pylori* test. The study was reviewed and approved by the ethics committee. After enrolment, medicalhistory was taken and physical examination and base-line tests were performed. Height in meters and weight in kilograms were recorded. BMI was calculated as weight in kilograms divided by the square of height in meters. Modified criteria of BMI calculation was used for South Asians [18], as they have different associations between BMI, percentage of body fat and health risks than Europeans [18]. "Underweight" was defined as BMI lower than 18.4; "Healthy" 18.5 to 23; "Overweight" 23.1-27.9; and "Obese" greater than 28. The criterion used for type 2 diabetes was fasting plasma glucose (FPG) level of 7. 0 mmol/L [19]. Blood pressure was recorded using an automated sphygmomanometer. Criterion used for hypertension was value greater than 140/90 mm Hg as defined by the JCN 7 (Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure) [20]. Dyslipidemia was defined according to the National Cholesterol Education Program (NCEP) ATP III Guideline for serum cholesterol > 200mg/dl; triglycerides > 200mg/dl; HDL < than 40mg/dL; LDL > than 160mg/dL and VLDL cholesterol > 30mg/dL [21]. Coronary artery disease included angina (stable and unstable), myocardial infarction, and sudden cardiac death [22]. The inclusion criteria were adults over 18 years of age with dyspepsia for more than six months. Patients who were on antibiotics (in the last 2 months), acid reducing drugs such as histamine-2 receptor blockers and proton pump inhibitors (in the last 2 weeks) were excluded from having C-14 Urea Breath Test for *H. pylori* infection. Pregnant and lactating females, patients with inflammatory bowel disease, celiac disease, and those not willing to participate were excluded. Written informed consent was obtained for gastroscopy. All participants received written and verbal information about the study. Six hundred and ninety-eighty patients with a history of dyspepsia for the previous 6 months underwent either gastroscopy

Table 1. Association of Helicobacter pylori with body-mass index.

		***Helicobacter pylori* infection**		
		Positive n (%) 399 (57)	**Negative n (%) 299(43)**	**P value**
Age (years)	18-30	78(20)	81(27)	
	31-50	158(40)	66(22)	< 0.001
	51-65	125(31)	119(40)	
	>65	38(9)	33(11)	
Gender	Male	209(52)	164(55)	0.518
	Female	190(48)	135(45)	
Body-mass index	Underweight	15(4)	21(7)	
	Normal	65(16)	103(36)	< 0.001
	Overweight	111(28)	125(40)	
	Obese	208(52)	50(17)	
Comorbid factors				
Coronary artery disease	Yes	52(13)	29(10)	0.174
	No	347(87)	270(90)	
Hypertension	Yes	63(16)	26(9)	0.005
	No	336(84)	273(91)	
Type 1 diabetes	Yes	73(18)	27(9)	0.001
	No	326(82)	272(91)	
Dyslipidemia	Yes	73(18)	32(11)	0.005
	No	326(82)	267(89)	

P < 0.05 was significant;

with biopsy and histological examination, or ^{13}C-urea breath test (^{13}C-UBT), or *H. pylori* stool antigen (HpSA) test [23-24]. Patients were diagnosed as *H. pylori* infection-positive if any of these tests was positive. Written informed consent was obtained from all participants.

Statistical analysis

Statistical analysis was carried out with the SPSS version 16.0 software program. Results were expressed as mean ± standard deviation. Univariate analysis was carried out using the chi-square test and a multivariate analysis by regression analysis. P-value of < 0.05 was statistically significant.

Results

There were 373 (53%) male patients and 325 (47%) female.Their age ranged from 18 to 90 years with a mean age of 44 ± 16 years.The age range of males was 18-85 years and of females 18-90 years. *H. pylori* infection was detected in 399 (57%). The mean age and standard deviation (SD) of the two groups of patients were similar. The mean age of the BMI-healthy was 38.4 ± 18 years. There was a significant difference between the mean age of overweight and obese vs underweight (P = 0.005) and vs healthy (P < 0.001), respectively. A total of 41 (6%) were smokers and 100 (14%) consumed alcohol. Co-morbid conditions included coronary artery disease in 89 (13%), hypertension in 89 (13%), type 2 diabetes in 100 (14%) and dyslipidemia in 105 (15%).

H. pylori infection prevalence was high in up to 50 years of age and reduced in the sixth decade (Table 1-2). The prevalence of *H. pylori* infection was 15 (4%) in patients with low BMI.*H. pylori* infection was highly positive in obese 208 (76%) compared to those with normal BMI 65 (24%) (P < 0.001). There was no difference in the prevalence of *H. pylori* infection in BMI-healthy patients 65/168; 37% compared to those who were overweight 111/236; 63% (P = 0.096). However, *H. pylori* positivity was higher in obese patients 208/258; 65% compared to overweight 111/236; 35% (P < 0.001).

H. pylori infection in obese vs BMI-healthy was significantly associated with coronary artery disease in 38/208; 18% patients (P = 0.018) compared to 4/65; 6%, respectively; type 2 diabetes in obese 54/208; 26% (P = 0.022) compared to 8/65; 12% BMI-healthy; and dyslipidemia in obese 53/208; 25% (P = 0.005) compared to 6/65; 8% in BMI-healthy. Multivariate analysis in the 31-50year age group (OR 1.77, 95% CI 1.13-2.77), showed that BMI >23.1 (OR 2.91, 95% CI 2.01-4.20), and type 2 diabetes (OR 2.41, 95% CI 1.43-4.06) were risk factors for *H. pylori* infection (Table 2).

Discussion

The study showed that the prevalence of *H. pylori* infection was lower in patients who were underweight compared to BMI-healthy or with a higher BMI. The number of underweight patients was small. In this study, *H. pylori* infection did not show any gender distribution (Table 1). A previous study demonstrated that males who were *H. pylori* infection-positive had higher LDL cholesterol levels and significantly lower HDL cholesterol levels than the *H. pylori*-negative [25]. Our study did not show similar results. We did not have many patients who were smokers or consumed alcohol to analyze *H. pylori* infection in relation to these social habits. *H. pylori* infection in subjects defined as BMI-healthy, overweight and obese, was 16%, 29%, and 51%, respectively. Our subjects, with a mean age of 44 years, were younger than in a previous study [14]. In this study, overweight and obese patients had a higher rate of *H. pylori* infection compared to the BMI-healthy

Table 2. Multivariate analysis of risk factors predicting H. pylori infection.

	Odds Ratio (95% Confidence Interval)	P value
Age (years)		
18-30	1.0	< 0.001
31-50	1.77 (1.13-2.77)	0.01
51-65	0.66 (0.42-1.03)	0.06
> 65	0.65 (0.34-1.22)	0.18
Body mass index		
< 18.5	1.0	< 0.001
18.5-23	1.07 (0.48-2.37)	0.86
> 23.1	2.91 (2.01-4.20)	< 0.001
Type 2 Diabetes		
No	1.0	
Yes	2.41 (1.43-4.06)	0.001

P value < than 0.05 was significant.

individuals (Table 1). These findings are important, as adverse health outcomes are known to be associated with overweight and obesity.

H. pylori initiates a low-grade inflammation that induces mechanisms leading to expression of virulence peptides that resemble host antigens. The stimulated host immune responses include gastric epithelial cytokine secretion; *H. pylori* increases the levels of tumour necrosis factor-alpha and other cytokines that promote inflammation [26]. Host immunological reaction is unable to clear *H. pylori* infection which persists as a chronic infection. *H. pylori* infection could induce insulin resistance, disturb glucose and lipid homeostasis, and metabolism of adipocytokines [27]. It increases serum levels of triglycerides, cholesterol, LDL cholesterol, apolipoproteins B, and decreases apolipoprotein A and HDL cholesterol levels [28-29]. Undesirable abnormalities induced by *H. pylori* may increase the risk of cardiovascular disease especially in diabetic patients [30]. In a previous study, *H. pylori* infection was demonstrated in 57% of the obese group, which was higher than the 27% in the control group [25]. Another study, however, did not show increased *H. pylori* infection among overweight/obese young individuals as reported previously [31]. These patients might have been exposed to bacteria other than *H.pylori* that may have altered the gastrointestinal microflora constitution that contributed to obesity. There is a constant interplay between diet, gut microbiome and host health status. Gut microbiome and *H. pylori* are reported to be associated with obesity [32,33]. *H. pylori* and gut microbiota have an effect on the host's metabolism. Obesity is associated with an increased susceptibility to infection by different pathogens [34].There is an impaired immune function which increases with the grade of obesity [35]. Various cellular changes involving immunological cells include a low maturation of monocytes into macrophages and reduced bactericidal activity of polymorphonuclear cells in obese subjects [36-37]. Obese individuals also demonstrate a decrease in natural killer cell activity [38]. Type 2 diabetics are prone to chronic infections. An association between *H. pylori* infection and type 2 diabetes ($P = 0.001$) was demonstrated in our study (Table 1).

South Asian people frequently do not appearto be overweight as compared to other ethnic groups. However, they have a tendency for central obesity that leads to storing of fat around their stomach [18]. Central obesity is linked to an inherited gene and higher rate of diabetes and acute coronary syndrome [18]. The prevalence of overweight and obesity has increased in recent years in Pakistan [10].The obesity epidemic is taking place in developing countries and is not necessarily driven by changes of *H. pylori* prevalence [39]. *H. pylori* infection is prevalent in patients with above-normal BMI in the 31-50-year age group. There is a temporal association between *H. pylori* and patients with above-normal BMI. However, chronic *H. pylori* infection effect is not the only explanation for our results.

Conclusion

There was a low *H. pylori* infection in adults with low BMI and ahigher prevalence in obese compared to those with a normal BMI and the overweight. *H. pylori* infection in obese was significantly associated with coronary artery disease, type 2 diabetes and dyslipidemia in our population. A large community-based study is recommended in order to further understand these associations at general population level.

Authors' Contributions

BS and JY analysed the data and drafted the manuscript, ZA critically reviewed the analyses. ZA, RA, SSF and SA reviewed and commented on initial and final drafts of the manuscript, all authors read and approved the final manuscript.All authors have participated in drafting of the manuscript and/or critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript.

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