

## RESEARCH ARTICLE

# Prevalence of *Helicobacter Pylori* Infection in Dyspeptic Patients in Andkhoy Afghanistan

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### Abstract

**Background:** The prevalence of *Helicobacter pylori* (*H. pylori*) infection is reported to be more than 50% worldwide. It has been associated with peptic ulcer disease, gastric carcinoma, and mucosal-associated lymphoid tissue lymphoma. The seroprevalence of *H. pylori* varies greatly among societies and geographical locations. The objective of this study was to determine the seroprevalence and factors associated with *H. pylori* infection among dyspeptic patients in Afghanistan. **Materials and Methods:** This cross-sectional study was designed to determine the seroprevalence of *H. pylori* among dyspeptic patients in an outpatient clinic in Andkhoy, Afghanistan from January 2017 to April 2017. Data were obtained from patients using a questionnaire, including socio-demographic data and history of smoking and dyspeptic symptoms. Serum samples were also collected from the patients and tested for *H. pylori* antibodies using the enzyme-linked immunosorbent assay. **Results:** A total of 152 patients with dyspepsia were included in the analysis; 59 were men (40.0%), and 93 were women (60.0%). The overall seroprevalence of *H. pylori* was 75.6%. The predictor of seroprevalence of *H. pylori* was found to be illiteracy (odds ratio [OR] 4.99, 95% confidence interval [CI] 1.03–24.17), epigastric pain (OR 12.01, 95% CI 3.56– 40.52), and rural population (OR 9.66, 95% CI 3.36– 27.82). There was an inverse association between employed status and seroprevalence of *H. pylori* (OR 0.08, 95% CI 0.01– 0.52). **Conclusions:** The seroprevalence of *H. pylori* was high among patient with dyspepsia in an outpatient clinic in Afghanistan. Illiteracy, unemployment and rural populations, and epigastric pain were significantly associated with *H. pylori* infection.

**Keywords:** *H. pylori*- prevalence- dyspeptic patients- Afghanistan

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### Introduction

*Helicobacter pylori* is a Gram-negative bacteria that colonizes the gastric mucosal layer and is probably the most common infectious disease worldwide (Khedmat et al., 2013; Valliani et al., 2013; Hooi et al., 2017). It has been associated with peptic ulcer disease, gastric carcinoma, and mucosal-associated lymphoid tissue lymphoma (Goto et al., 2013; Jafar et al., 2013; Ashtari et al., 2015). In most cases, *H. pylori* infection is asymptomatic. Of those tested for *H. pylori*, 17% will develop peptic ulcers (Abdallah et al., 2014). The infection occurs during early childhood, and if left untreated, it may persist for a lifetime (Niknam et al., 2014).

There are many differences in the prevalence of *H. pylori* among different societies and geographical

locations (Abebaw et al., 2014). It has infected more than half of the people in the world (Correa and Piazzuelo, 2011; Diaconu et al., 2017). The prevalence of *H. pylori* is higher in developing countries than in developed countries (Torres et al., 2000). The prevalence of *H. pylori* is related to socioeconomic conditions, socio-demographic profiles, hygiene, and life style characteristics of people (Salih, 2009). Among the socio- demographic characteristics age, gender, occupation, and alcohol consumption are associated with the prevalence of *H. pylori* (Mages et al., 2006). *H. pylori* infection is related to deficiencies in sanitary facilities, overcrowded living and insufficient supplies of water (Dube et al., 2009; Zhong et al., 2012). It is believed that this infection is more common among lower social classes and in poor countries (Woodward et al., 2000).

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Several studies have demonstrated that there is a high *H. pylori* infection rate in Middle Eastern countries (Almadi et al., 2007; Malekzadeh et al., 2009; Khedmat et al., 2013). However, there is no study that has been conducted in the adult population of Afghanistan. Therefore, this study was conducted to determine the seroprevalence and factors associated with *H. pylori* infections among a population of adult patients with dyspepsia attending an outpatient clinic in Afghanistan.

### Materials and Methods

A total of 152 patients were present at an outpatient clinic in Andkhoy, north of Afghanistan, from January 2017 to April 2017.

Inclusion criteria were as follows: 1) age of 18 years and older, 2) dyspeptic patients from an outpatient clinic with symptoms such as abdominal pain, abdominal bloating, epigastric pain, nausea, vomiting, heartburn, and early satiety for at least 3 months, 3) persistent or recurrent symptoms occurring at least three times per week for more than 6 months in the year. The key exclusion criteria were as follows: 1) usage of antibiotic treatment 1 month before recruiting, 2) usage of proton pump inhibitors or H2-blockers 2 weeks before recruiting, and 3) incomplete data.

The diagnosis of dyspepsia was based only on physical examination and patient history. For this study, dyspepsia was defined as having one or more of these symptoms for 3 months or more: epigastric pain, abdominal pain, abdominal bloating, nausea, vomiting, early satiety, and heartburn (Miwa et al., 2012). The patients were evaluated during a clinic visit, and the study protocol included an assessment of the data obtained from each patient.

In this study, data from a questionnaire, including socio-demographic data (age, sex, occupation, residence, education, and marital status), history of smoking, physical findings, fasting blood sugar (FBS), and blood pressure were collected from participants. Gastrointestinal symptoms were evaluated from the questionnaires completed by the patients from the questions concerning dyspeptic symptoms. Serum samples were also collected from the patients and tested for *H. pylori* using ELISA to detect *H. pylori* antibodies. The study was approved by the scientific review committee of Balkh Regional Hospital.

#### Statistical analysis

The mean and standard deviation (SD of the variables were presented. Categorical variables were expressed as number and percentage. Continuous and categorical data were compared using the t-test and  $\chi^2$ -test, respectively. Univariate and multivariate logistic regressions were performed to analyze the association between anxiety and risk factors and target organ lesions. Odds ratios (ORs) with 95% confidence intervals (CIs) were used for comparisons. All the prognostic variables with  $p < 0.05$  in the univariate logistic regression analysis were entered into multivariate logistic regression analysis to determine independent predictors. A p-value of  $< 0.05$  was considered statistically significant. All analyses were performed with the SPSS 24.0 software package (SPSS, Armonk, NY:

IBM Corp).

### Results

A total of 152 dyspeptic patients were included in the study. The characteristics of all patients with and without *H. pylori* infection are summarized in Table 1. The mean age of patients was  $50.8 \pm 18.6$  years, 59 were men (40.0%), and 93 were women (60.0%). The mean age of the patients who were *H. pylori*-positive and *H. pylori*-negative was  $51.5 \pm 18.5$  years and  $48.4 \pm 19.2$  years, respectively. There was a statistically significant difference in the seroprevalence of *H. pylori* and education status ( $P=0.019$ ). Unemployment was more common among patients with *H. pylori* infection (22.6% versus 13.5%;  $P = 0.002$ ). Rural residence was associated with *H. pylori* (70.4% versus 35.1%;  $P < 0.001$ ). However, there was no statistically significant association between the prevalence of *H. pylori* infection and other factors, such as gender, marital status, body mass index, and smoking status, systolic blood pressure, diastolic blood pressure, and FBS.

The seroprevalence of *H. pylori* based on the gastrointestinal symptoms is indicated in Table 2.

Table 1. Characteristics of Patients with and without *Helicobacter pylori* Infection

	<i>H. pylori</i> -positive (n = 115)	<i>H. pylori</i> -negative (n = 37)	p value
Age, mean, years	51.5±18.5	48.4±19.2	0.735
Male, number (%)	46 (40.0)	13 (35.1)	0.597
Level of education			0.019
Illiterate	91 (79.1)	20 (54.0)	
Primary/private education	5 (4.3)	3 (8.1)	
Secondary	5 (4.3)	2 (5.4)	
High school or more	14 (12.2)	12 (32.4)	
BMI, mean	23.6±3.6	23.2±4.6	0.735
Systolic blood pressure, mean	138.0±28.2	140.6±23.6	0.093
Diastolic blood pressure, mean	91.4±17.6	94.8±17.6	0.886
Fasting blood glucose, mean	106.1±23.5	104.9±20.5	0.942
Marital Status			0.973
Single	19 (16.5)	6 (16.2)	
Married	88 (76.5)	28 (75.7)	
Others	8 (6.9)	3 (8.1)	
Occupation			0.002
Employed	8 (6.9)	11 (29.7)	
Unemployed	26 (22.6)	5 (13.5)	
Housewives	57 (49.6)	12 (32.4)	
Farmers	24 (20.9)	9 (24.3)	
Rural residence	81 (70.4)	13 (35.1)	<0.001
Smoking status			0.378
Current smoker	45 (39.1)	16 (43.2)	
Past smoker	6 (5.2)	4 (10.8)	
Non smoker	63 (54.8)	17 (45.9)	

BMI, body mass index

Table 2. Relation between *Helicobacter pylori* Infection and Gastrointestinal Symptoms

	<i>H. pylori</i> - positive (115 patients)	<i>H. pylori</i> - negative (37 patients)	p value
Abdominal pain	49 (42.6)	12 (32.4)	0.272
Epigastric pain	102 (88.7)	21 (56.7)	<0.001
Nausea	52 (45.2)	20 (54.0)	0.515
Vomiting	48 (41.7)	16 (43.2)	0.872
Early satiety	47 (40.9)	18 (48.6)	0.405
Heartburn	55 (47.8)	20 (54.0)	0.510
Abdominal bloating	43 (37.4)	10 (27.0)	0.250

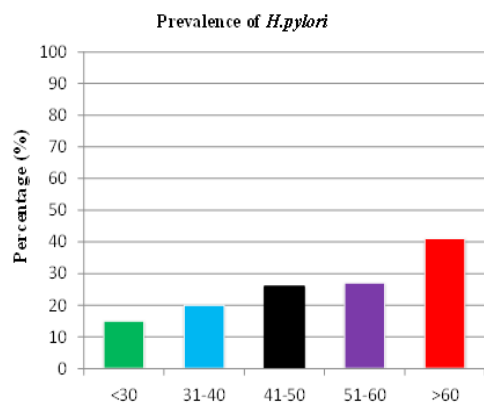


Figure 1. Prevalence of *H.pylori* Infection in Dyspeptic Patients among Different Age Groups

Epigastric pain was more common in patients with *H. pylori* than in those without it (88.7 versus 56.7%, respectively;  $P < 0.001$ ). There was no association between *H. pylori* infection and other gastrointestinal symptoms, such as abdominal pain, nausea, vomiting, early satiety, heartburn, and abdominal bloating. Figure 1 indicates the seroprevalence of *H. pylori* infection in dyspeptic patients among different age groups. The multivariate logistic analysis was used to determine the relationship between *H. pylori* infection and level of education, employment status, epigastric pain, and rural residency. *H. pylori* infection was considered a depended variable. Illiterate patients had 4.99 times higher risk of developing *H. pylori* infection (95% CI 1.03–24.17) compared to those have high school or more education. Patients who had epigastric pain had 12.01 times higher risk of *H. pylori* infection (95% CI 3.56–40.52), and compared to those who are urban residents, rural residents 9.67 times higher chance of *H. pylori* infection (95% CI 3.36–27.82). There was an inverse association between employed status and prevalence of *H. pylori* (OR 0.08, 95% CI 0.01–0.52) (Table 3).

## Discussion

To our knowledge, this study is the first study conducted in the Afghan population to investigate the epidemiology of *H. pylori* among patients with dyspepsia using the serologic method. Therefore, the results of

Table 3. Multivariate Logistic Regression Analysis for Prediction of Prevalence of *Helicobacter pylori*

Variables	Multivariate logistic regression		
	OR	(95% CI)	p value
Illiterate	4.99	(1.03–24.17)	0.046
Employed	0.08	(0.01–0.516)	0.008
Epigastric pain	12.01	(3.56–40.52)	<0.001
Rural residents	9.67	(3.36–27.82)	<0.001

OR, Odds ratio; CI, confidence interval

our findings help us to understand how big a public health problem in *H. pylori* infection is in the Afghani population. Epidemiological studies have frequently relied on serological tests for *H. pylori* infection detection, including retrospective studies to determine the prevalence or incidence of infection (Blaser, 1998).

According to the results of our survey, the seroprevalence of *H. pylori* infection among patients with dyspepsia in the northern part of Afghanistan was 75.6%. This percentage is similar to the reported data from Pakistan in patients with dyspepsia (Naz et al., 2013). By contrast, a previous study from Iran in symptomatic patients with gastrointestinal symptoms found higher results (84.8%) than our findings (Khedmat et al., 2013b). However, in our study, the prevalence of *H. pylori* was higher than that seen in other prevalence results of 65.7%, and 49.7% that were reported among symptomatic patients in different countries (Alazmi et al., 2010; Mathewos et al., 2013). These differences are most likely associated with the testing methods, socio-economic status of the study populations, and geographical variation in the prevalence of infection (Ndip et al., 2004).

In the present investigation, the highest seroprevalence of *H. pylori* was observed in those who were illiterate. This finding is in accordance with the results of other studies (Sýkora et al., 2009; Yücel et al., 2009; Oling et al., 2015) and might be due to higher education levels are more knowledgeable of hygiene. It could be explained by relevant studies that found higher education levels of parents to be as a protective factor against *H. pylori* infection (Santos et al., 2005). Since the education level is increasing in Afghanistan (Review, 2015), it may be concluded that the prevalence of *H. pylori* infection will decrease in the future.

In this study, the patients who were employed had a low *H. pylori* infection prevalence. This result is comparable with the results of other studies (Klein et al., 1991; Santos et al., 2005) and can be justified by the better living conditions among families with a higher income as well as the factors that contribute to the high acquisition of infection, such as inadequate living resources and poor sanitation.

In the current study, *H. pylori* infection was associated with higher rates of epigastric pain. The results of previous studies (Rosenstock et al., 1997; Marie, 2008; Siai et al., 2008) are in agreement with this findings. However, a study which was done in Iran is not comparable with our



result (Niknam et al., 2014). The applicability of non-ulcer dyspepsia subtype definition has been questioned in a previous study (Kay et al., 1994). The present findings can be explained by the point that other studies have failed to establish a link between *H. pylori* infection to specific non-ulcer dyspepsia subtypes (Holtmann et al., 1994; Trespi et al., 1994).

We found that rural residency is associated with *H. pylori* infection. It is in line with other studies that reported *H. pylori* infection was higher among rural residents (Bani-hani et al., 2006; Lim et al., 2013; Tsongo et al., 2015; Nagy et al., 2016) in contrast, another study showed a high rate of *H. pylori* infection among urban residents (Santos et al., 2005). This finding is likely explained by some factors that increase the susceptibility of the rural residents to this infection, such as poor education and lower socioeconomic status in rural areas.

This study has some limitations. The sample consisted of a single-center data source. The single-center nature of this study may affect its generalizability to the entire population of Afghanistan. Furthermore, the patients were selected on a convenience basis, which could lead to a potential source of bias. In addition, the sample size was small for assessing some risk factors. Finally, the cross-sectional nature of the study makes it difficult to find out causality. On the other hand, our data would be beneficial to accumulate additional data regarding this infection because it was the first study on prevalence and risk factors of *H. pylori* infection among adult dyspeptic patients attending an outpatient clinic in Afghanistan.

In summary, this study showed a high prevalence of *H. pylori* infection in the patients with dyspepsia in an outpatient clinic in Afghanistan. The risk factors that have a significant association with the prevalence of *H. pylori* infection in dyspeptic patients are illiteracy, unemployment, epigastric pain, and rural population. Therefore, further study is required to investigate the burden of this infection in the community.

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## References

- Abdallah TM, Mohammed HB, Mohammed MH, et al (2014). Sero-prevalence and factors associated with *Helicobacter pylori* infection in Eastern Sudan. *Asian Pac J Trop Dis*, **4**, 115–19.
- Abeba W, Kibret M, Abera B (2014). Prevalence and risk factors of *H. pylori* from dyspeptic patients in Northwest Ethiopia: A hospital based cross-sectional study. *Asian Pac J Cancer Prev*, **15**, 4459–63.
- Alazmi WM, Siddique I, Alateeqi N, Al-Nakib B (2010). Prevalence of *Helicobacter pylori* infection among new outpatients with dyspepsia in Kuwait. *BMC Gastroenterol*, **10**, 14.
- Almadi MA, Aljebreen AM, Tounesi FA, et al (2007). *Helicobacter pylori* prevalence among medical students in a high endemic area. *Saudi Med J*, **28**, 896–8.
- Ashtari S, Pourhoseingholi MA, Molaei M, et al (2015). The prevalence of *Helicobacter pylori* is decreasing in Iranian patients. *Gastroenterol Hepatol Bed Bench*, **8**, 23–9.
- Bani-hani KE, Shatnawi NJ, El Qaderi S, et al (2006). Prevalence and risk factors of *Helicobacter pylori* infection in healthy schoolchildren. *Chin J Dig Dis*, **7**, 55–60.
- Blaser MJ (1998) Clinical review: *Helicobacter pylori* and gastric diseases. *BMJ*, **316**, 1507–10.
- Correa P, Piazuolo MB (2011). *Helicobacter pylori* infection and gastric adenocarcinoma. *US Gastroenterol Hepatol Rev*, **7**, 59–64.
- Diaconu S, Predescu A, Moldoveanu A, Pop CS, Fierbințeanu-Braticevici C (2017). *Helicobacter pylori* infection: old and new. *J Med Life*, **10**, 112–17
- Dube C, Tanih NF, Clarke AM, et al (2009). *Helicobacter pylori* infection and transmission in Africa: household hygiene and water sources are plausible factors exacerbating spread. *Afr J Biotechnol*, **8**, 6028–35.
- Goto Y, Ari Syam F, Darmindro N, et al (2016). Prevalence and risk factors for *Helicobacter Pylori* infection among healthy inhabitants in Northern Jakarta, Indonesia. *Asian Pac J Cancer Prev*, **17**, 4747–53.
- Holtmann G, Goebell H, Holtmann M, et al (1994). Dyspepsia in healthy blood donors - Pattern of symptoms and association with *Helicobacter pylori*. *Dig Dis Sci*, **39**, 1090–8.
- Hooi JKY, Lai WY, Ng WK, et al (2017). Global prevalence of *Helicobacter pylori* infection: systematic review and meta-analysis. *Gastroenterology*, **153**, 420–9.
- Jafar S, Jalil A, Soheila N, et al (2013). Prevalence of *Helicobacter pylori* infection in children, a population-based cross-sectional study in west iran. *Iran J Pediatr*, **23**, 13–8.
- Kay L, Jørgensen T, Jensen KH (1994). Epidemiology of abdominal symptoms in a random population: Prevalence, incidence, and natural history. *Eur J Epidemiol*, **10**, 559–66.
- Khedmat H, Karbasi-Afshar R, Hossein Khedmat, Agah S, Taheri S (2013). *Helicobacter pylori* infection in the general population: A middle eastern perspective. *Caspian J Intern Med*, **4**, 745–53.
- Klein PD, Graham DY, Gaillour A, et al (1991). Water source as risk factor for *Helicobacter pylori* infection in Peruvian children. gastrointestinal physiology working group. *Lancet* **337**, 1503–6.
- Lim SH, Kwon J-W, Kim N, et al (2013). Prevalence and risk factors of *Helicobacter pylori* infection in Korea: nationwide multicenter study over 13 years. *BMC Gastroenterol*, **13**, 104.
- Malekzadeh R, Derakhshan MH, Malekzadeh Z (2009). Gastric cancer in Iran: epidemiology and risk factors. *Arch Iran Med*, **12**, 576–83.
- Marie MAM (2008). Seroprevalence of *Helicobacter pylori* infection in large series of patients in an Urban area of Saudi Arabia. *Korean J Gastroenterol*, **52**, 226–9.
- Mathewos B, Moges B, Dagne M (2013). Seroprevalence and trend of *Helicobacter pylori* infection in Gondar University Hospital among dyspeptic patients, Gondar, North West Ethiopia. *BMC Res Notes*, **6**, 346.
- Miwa H, Ghoshal UC, Gonlachanvit S, et al (2012). Asian consensus report on functional dyspepsia. *J Neurogastroenterol Motil*, **18**, 150–68.
- Moges F, Kassu A, Mengistu G, et al (2006). Seroprevalence of *Helicobacter pylori* in dyspeptic patients and its relationship with HIV infection, ABO blood groups and life style in a university hospital, Northwest Ethiopia. *World J Gastroenterol*, **12**, 1957–61.
- Nagy P, Johansson S, Molloy-Bland M (2016) Systematic review

- of time trends in the prevalence of *Helicobacter pylori* infection in China and the USA. *Gut Pathog*, **8**, 8.
- Ndip RN, Malange AE, Akoachere JFT, et al (2004). *Helicobacter pylori* antigens in the faeces of asymptomatic children in the Buea and Limbe health districts of Cameroon: A pilot study. *Trop Med Int Health*, **9**, 1036–40.
- Niknam R, Seddigh M, Fattahi MR, et al (2014). Prevalence of *Helicobacter pylori* in patients with dyspepsia. *Jundishapur J Microbiol*, **7**, doi:10.5812/jjm.12676.
- Oling M, Odongo J, Kituuka O, et al (2015). Prevalence of *Helicobacter pylori* in dyspeptic patients at a tertiary hospital in a low resource setting. *BMC Res Notes*, **8**, 256.
- Review N (2015). Afghanistan education for all 2015 national review Afghanistan national education for all (EFA).
- Rosenstock S, Kay L, Rosenstock C, et al (1997). Relation between *Helicobacter pylori* infection and gastrointestinal symptoms and syndromes. *Gut*, **41**, 169–76.
- Salih B a (2009). *Helicobacter pylori* infection in developing countries: the burden for how long?. *Saudi J Gastroenterol*, **15**, 201–7.
- Santos IS, Boccio J, Santos AS, et al (2005). Prevalence of *Helicobacter pylori* infection and associated factors among adults in Southern Brazil: a population-based cross-sectional study. *BMC Public Health*, **5**, 118.
- Siai K, Ghazzi M, Ezzine H, et al (2008). Prevalence and risk factors of *Helicobacter pylori* infection in Tunisian children: 1055 children in Cap-Bon (northeastern Tunisia). *Gastroenterol Clin Biol*, **32**, 881–6.
- Sýkora J, Siala K, Varvařovská J, et al (2009). Epidemiology of *Helicobacter pylori* infection in asymptomatic children: A prospective population-based study from the czech republic. Application of a monoclonal-based antigen-in-stool enzyme immunoassay. *Helicobacter*, **14**, 286–97.
- Torres J, Perez-Perez G, Goodman KJ, et al (2000). A comprehensive review of the natural history of *Helicobacter pylori* infection in children. *Arch Med Res*, **31**, 431–69.
- Trespi E, Broglia F, Villani L, et al (1994). Distinct profiles of gastritis in dyspepsia subgroups - their different clinical-responses to gastritis healing after *Helicobacter-Pylori* eradication. *Scand J Gastroenterol*, **29**, 884–8.
- Tsongo L, Nakavuma J, Mugasa C, et al (2015). *Helicobacter pylori* among patients with symptoms of gastroduodenal ulcer disease in rural Uganda. *Infect Ecol Epidemiol*, **5**, 26785.
- Us D, Haşçelik G (1998) Seroprevalence of *Helicobacter pylori* infection in an asymptomatic Turkish population. *J Infect* **37**, 148–50.
- Valliani A, Khan F, Chagani B, et al (2013). Factors associated with *Helicobacter pylori* infection, results from a developing country - Pakistan. *Asian Pac J Cancer Prev*, **14**, 53-6.
- Woodward M, Morrison C, McColl K (2000). An investigation into factors associated with *Helicobacter pylori* infection. *J Clin Epidemiol*, **53**, 175–81.
- Yücel O, Sayan A, Yildiz M (2009). The factors associated with asymptomatic carriage of *Helicobacter pylori* in children and their mothers living in three socio-economic settings. *Jpn J Infect Dis*, **62**, 120–4.
- Zhong C, Li K-N, Bi J-W, et al (2012). Sodium intake, salt taste and gastric cancer risk according to *Helicobacter pylori* infection, smoking, histological type and tumor site in China. *Asian Pac J Cancer Prev*, **13**, 2481–4.