

## Reviewer's Comments

### Prevalence of *Helicobacter pylori* among Asymptomatic Populations in Sana'a, Yemen

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#### Abstract

**Background:** *Helicobacter pylori* consider the most important cause of chronic gastritis and also the most important etiological factor responsible for the duodenal and gastric ulcer and have an important role in the pathogenesis of gastric cancer.

**Objective:** The aim of the present study to know the prevalence of *H. pylori* among the khat chewing adults in compared to non-khat chewing among asymptomatic populations.

**Methods:** A total of 82 healthy subjects were screened to find out the prevalence of *Helicobacter pylori* using stool antigen card test during the period started in 16 April 2018 and ending in 8 May 2018 in Sana'a, Yemen. Predesigned questionnaire was used to collect information such as age, sex, education status, khat chewing, smoking, tobacco chewing, occupation, and tests results all above data were recorded for each subject. Patients who had taken proton pump inhibitors or antibiotic for a month prior to study were excluded.

**Results:** Out of these 82 asymptomatic individuals, 36 were found positive for *Helicobacter pylori* by the test, giving a prevalence of 43.9 %. A prevalence of 26.9 % (62.9 % of khat chewing) was khat chewing individuals and it had statistically significant difference. A prevalence of 14.6 % was seen among cigarette smoking participants.

**Conclusion:** The present study revealed substantial prevalence of *Helicobacter pylori* in khat chewing healthy subjects. A higher prevalence of *Helicobacter pylori* seen in these subjects may be contributed to khat chewing. Identification of khat chewing populations, who do not show symptoms of *Helicobacter pylori* infection, is essential for controlling the infection and it still remains a challenge for the clinicians.

**Key words:** *H. pylori, Prevalence, Stool Antigen Test, Khat Chewing, Asymptomatic, Risk factors.*

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#### 1. Introduction:

*Helicobacter pylori*, previously known as *Campylobacter pylori*, is a gram-negative, microaerophilic bacterium usually found in the stomach. It was identified in 1982 by Australian scientists Barry Marshall and Robin Warren. Over 80% of individuals infected with the bacterium are asymptomatic, and it may play an important role in the natural stomach ecology <sup>(1)</sup>. More than 50% of the world's populations have *H. pylori* in their upper gastrointestinal tract <sup>(2)</sup>. Infection is more common in developing countries than Western countries <sup>(3)</sup>.

*Helicobacter pylori* consider the most important cause of chronic gastritis and also the most important etiological factor responsible for the duodenal and gastric ulcer and have an important role in the pathogenesis of gastric cancer <sup>(4)</sup>.

In a case control study in Nairobi country the prevalence of *H. Pylori* infection was found to be higher among khat chewers, indicating that Khat chewing could be a predisposing factor to gastrointestinal disorders <sup>(5)</sup>. Also In another study the prevalence of gastrointestinal disorders was found to be higher among khat chewers,

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indicating that khat chewing could be a predisposing factor to gastrointestinal disorders and H. Pylori infection. Community-based awareness creation about the adverse effect of khat use is thus recommended <sup>(6)</sup>.

Raja'a YA et.al revealed in his study that khat chewing is significantly associated with duodenal ulcer due to stress that follows khat chewing. This phenomenon is very common and is induced by the effect of amphetamine like action of cathine present in khat. Another possible factor can be due to *Helicobacter pylori* associated with khat chewing <sup>(7)</sup>.

Khat is an evergreen plant found commonly grown in Yemen, Ethiopia, Kenya, Sudan, Madagascar and South Africa <sup>(8)</sup>. The plant is known by different names in different countries but in most of the literature it is known as Khat <sup>(9)</sup>. People chew the leaves and young bud of khat for social and psychological reasons <sup>(10,11)</sup>. The psycho-stimulant effect of khat is due to the alkaloid chemical ingredient cathinone present in the fresh leaves of the khat plant <sup>(12,13)</sup>. Many people use khat for different purposes: for social recreation, to keep awake while driving long distances <sup>(14,15)</sup>, to reduce physical fatigue and to work hard for a long time <sup>(16)</sup>. It is believed that students in colleges and universities commonly use khat to improve their academic performance but the fact is the opposite. The result of one study showed that the mean cumulative Graded Point Average (GPA) of non-chewers was found to be significantly higher than that of chewers <sup>(17,18)</sup>.

The astringent characteristics of the tannins in khat accounts for periodontal disease, stomatitis, oesophagitis and gastritis <sup>(12)</sup>. Tannins and cathinone contribute to constipation, the most common medical complaint of the khat user. In a randomized controlled trial, Heymann et al. 1995 <sup>(19)</sup> reported a delay in gastric emptying after chewing khat, which was attributed to the sympathomimetic action of the cathinone. Moreover, Gunaid et al. 1999 <sup>(20)</sup> found out that khat prolongs entire gut motility and Makonnen 2000 <sup>(21)</sup> reported that khat produced constipation in mice and an antispasmodic action on guinea-pig isolated ileum. The antispasmodic effect of khat extract was observed to be similar to that of d-amphetamine.

Khat is abundantly available in Yemen and is a highly valued export commodity in the country. The number of khat chewers has significantly increased in this country and khat consumption has become popular in all segments of the Yemeni population <sup>(16,22)</sup>. There were many previous studies reported a positive association between Khat chewing and gastrointestinal disorders such as dental problems, gastritis and constipation <sup>(12,19,20,21)</sup>. According to some researchers, hemorrhoids are also considered to have associations with khat chewing <sup>(21,23)</sup>. In developing countries such as Yemen, there was no study conducted to assess the prevalence and the association between the khat chewing in compared to non-khat chewing in asymptomatic populations. Therefore, it is important to study prevalence of H. pylori infection and the associated risk factors among these subjects.

## 2. Materials and Methods:

A total of 82 healthy subjects were screened to find out the prevalence of *Helicobacter pylori* using Stool Antigen card test during the period started in 16 April 2018 and ending in 8 May 2018 at Sana'a, Yemen. Predesigned questionnaire was used to collect information such as age, sex, education status, khat chewing, smoking, tobacco chewing, occupation, and tests results all above data were recorded for each subject. Individuals who had taken proton pump inhibitors or antibiotic for a month prior to study were excluded.

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Data were analysed by the chi-square test to compare the association between different variables and positive *Helicobacter pylori* rates. A value of  $P < 0.05$  was considered statistically significant. Calculations were done using the software package SPSS 21.0.

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### 3. Results:

A total of 82 study participants were included in the present study. Fifty patients of the study sample were male and 28 of them had positive stool antigen result. In addition, 18 of thirty two females had positive stool antigen result and 14 had negative result. The relationship between stool antigen result and sex was not statistically significant ( $P$ -value = 0.9821). In other hand, only 8 patients had not level of education. However, the relationship between stool antigen result and education status was not observed ( $P$ -value = 0.71).

**Table 1.** Distribution of *H. pylori* according to gender and education status

variable		Stool Antigen Result		Total	P-value	95% Confidence Interval	
		ve-	ve+			Lower	Upper
Gender	M	28	22	50	0.982	0.405	2.421
	F	18	14	32			
	Total	46	36	82			
Education status	No	4	4	8	0.71	0.177	3.281
	Yes	42	32	74			
	Total	46	36	82			

In the current study, there was a statistically significant difference between stool antigen result and Khat chewing subjects ( $P$ -value = 0.003). 47 of the study sample were not khat chewing and 33 of them had negative stool antigen result. However, 22 of 35 study participants, that were khat chewing subjects, had positive stool antigen result (table 2). The same result was observed between stool antigen result and cigarettes smoking subjects ( $P$ -value = 0.002). In this study, 12 patients of 15 smoked patients had positive stool antigen result. In contrast, no relationship was observed between stool antigen result and tobacco chewing ( $P$ -value = 0.119). There were 36 of 79 non-tobacco chewing subjects had positive stool antigen result (table 2).

**Table 2.** Distribution of *H. pylori* according to khat chewing, cigarettes smoking, and tobacco chewing.

variable		Stool Antigen Result		Total	P-value	95% Confidence Interval	
		ve-	ve+			Lower	Upper
Khat Chewing	No	33	14	47	0.003	1.577	10.088
	Yes	13	22	35			
	Total	46	36	82			
Cigarettes Smoking	No	43	24	67	.002	1.839	27.927
	Yes	3	12	15			
	Total	46	36	82			
Tobacco Chewing	No	43	36	79	0.119	0.445	0.666
	Yes	3	0	3			

Relationship between stool antigen result and age groups was not statistically significant. However, 43 of study sample were subjects aged 20-29 years; 16 of them had positive stool antigen result (table 3). The relationship between stool antigen result and occupation was analyzed in the table 3. Result in this table shows that significantly relationship ( $P$ -value =0.03). 13 physicians of 15 had negative stool antigen result. On other hand, 12 housewives of 18 had positive stool antigen Result. However, 5 of 12 students had positive stool antigen result and 7 of them had negative.

**Table 3. Distribution of *H. pylori* according to age group and occupation**

variable		Stool Antigen Results		Total	P-value
		ve-	ve+		
Patient Age	20 - 29	27	16	43	0.163
	30 - 39	16	13	29	
	40 - -49	3	4	7	
	>=50	0	3	3	
	Total	46	36	82	
Occupation	Accountant	1	2	3	0.030
	Businessman	3	3	6	
	Physician	13	2	15	
	Driver	1	0	1	
	Engineer	3	1	4	
	Housewife	6	12	18	
	Nurse	6	1	7	
	Pharmacist	3	1	4	
	Policeman	2	1	3	
	Security	0	3	3	
	Student	7	5	12	
	Teacher	1	3	4	
	Radiology technician	0	2	2	
	Total	46	36	82	

Sixty seven of the study sample were not cigarette smoking and 20 of them had positive stool antigen result. However, 15 of 35 study participants, that were khat chewing subjects, have positive stool antigen result (table 4).

**Table 4. Distribution of cigarettes smoking subjects according to khat chewing**

Variable		Khat chewing		Total	%
		No	Yes		
Cigarettes Smoking	No	47	20	67	81.7 %
	Yes	0	15	15	18.3 %
Total		47	35	82	100 %

#### 4. Discussion:

The number of khat chewers has significantly increased in Yemen and khat consumption has become popular in all segments of the Yemeni populations. According to previous studies, Khat chewing had a positive association with gastrointestinal disorders such as dental problems, gastritis and constipation <sup>(6)</sup>.

Yet, in Yemen, there have been no study reports showing the association between khat chewing and positively *H. pylori* in asymptomatic populations. In the present study, there was a significant association between khat chewing and positively *H.*

pylori test ( $P$ -value = 0.003). The overall prevalence of *H. pylori* infection among participants was 43.9 %, which is comparable with other findings reported in Ethiopia <sup>(24)</sup>. In a study conducted on healthy Omani blood donors, the overall prevalence for *Helicobacter pylori* was 69.5% <sup>(25)</sup>. In a study from India, 254 individuals were screened for *Helicobacter pylori* which were positive in 56.7% asymptomatic individuals <sup>(26)</sup>. The overall prevalence recorded in our study (43.9 %) is less in comparison to the other studies. This can be explained by the fact that prevalence of *H. pylori* varies widely by geographic area, age, race, and ethnicity and socioeconomic status.

Similar results were shown in a study from Kanpur, India, where 44.23% asymptomatic subjects positively *Helicobacter pylori* test <sup>(27)</sup>.

In the current study, 62.9 % of khat chewers had positively *H. pylori* by stool antigen card test. This prevalence was higher than other study (Moharram et al., 2015) which showed that the prevalence of *H. pylori* infection among Kath chewing subjects was 21.4% <sup>(28)</sup>. This agree with (Raja'a et al., 2000) who showed that this effect can be due to *H. pylori* associated with khat chewing, beverages consumed during the session or insecticides and chemicals used for growing the khat plants <sup>(7)</sup>. Life style habits have been recognized as important risk factors for acquisitions of various infections, including *H. pylori* infection. Lots of researchers reported inconsistent results regarding the association of cigarettes smoking and its prevalence to *H. pylori* infection <sup>(24)</sup>.

According to study findings, smoking showed a trend of significant association with *H. pylori* infection. There was correlation between smoking and *H. pylori* positivity. Similar results have been reported in many previous studies (A-Ameri & Alkadasi, 2013) <sup>(29)</sup>. Another major health concern is the concurrent use of tobacco and khat in countries where these substances are used in combination, as tobacco use is a well-known factor for the development of various diseases. It has been reported that up to 61% of khat chewers smoke cigarettes <sup>(30)</sup> and that smokers usually consume more cigarettes during khat chewing sessions <sup>(31)</sup>.

In a recent study, approximately 42.9 % of khat users reported use of tobacco, implying that khat chewing might serve as a “gateway” to tobacco use. A recent systemic review also showed that the prevalence of tobacco use among khat chewers is significant, especially among high school and university students, and health-care workers in certain African countries and the Middle East. It is clear that concomitant khat chewing and tobacco use has several adverse effects. First, a combination of these two deleterious habits could potentiate the detrimental effects of each other in the causation of various systemic and oral health problems, including malignant and premalignant oral lesions. Second, as the co-occurrence of khat chewing and tobacco smoking dependence is increasing remarkably, khat use might interact with tobacco use, thus hampering tobacco-cessation programs <sup>(32)</sup>. Advanced molecular based studies have revealed that pathogenicity of *H. pylori* is predominantly influenced by smoking. Smoking might be a major risk factor entailed in modulating the susceptibility of an individual suffering with ulcers to *H. pylori* infection. Evidently, study on *H. pylori* positive asymptomatic and symptomatic subjects with acid peptic disease showed that the risk of virulent infection was escalated by smoking in both groups of individual <sup>(33)</sup>.

Statistically significant association was observed ( $P$ -value = 0.030) in the prevalence of *H. pylori* infection and type of occupations in this study which is in line with other studies <sup>(34, 35)</sup>. Presumably, the variation in prevalence could be due to the difference in the lifestyles, exposure to potential environmental sources and habits.

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In our study, age wise distribution showed maximum prevalence in the age group of 20-29 years; 30-39 years was (44.4%); 36.1 % respectively, and minimum in the age group of more than 50 years (8.3%). This goes in accordance with a similar Indian study in which the maximum prevalence was in the age group of 30-39 years (50.7%) and minimum in the age group of more than 70 years (20%)<sup>(27)</sup>. In a study from Mumbai, age related prevalence of *Helicobacter pylori* showed similar results as ours with maximum prevalence of 58% in the age group of 30-39 years<sup>(36)</sup>.

Our study revealed that there was not a correlation between sex and *H. pylori* positivity ( $P = 0.982$ , this result is in agreement with study performed by (Abo-Shadi *et al.*, 2013),<sup>(37)</sup> but disagree with other studies (A-Ameri & Alkadasi, 2013)<sup>(29)</sup>.

Among the socio-demographic characteristics of the participants, statistically significant difference was not obtained for educational attainment which is in agreement to studies<sup>(38, 39)</sup> and inconsistent to other studies<sup>(34, 40)</sup>. The absences of association in this study might be due to less number of non-educated subjects that cause difficulty to compute the association.

## 5. Conclusion:

Based on the findings, it was concluded that khat chewing is a common practice among Yemeni adults. The result of this study depicts that *H. pylori* prevalence are significantly associated with khat chewing. Identification of khat chewing populations, who do not show symptoms of *Helicobacter pylori* infection, is essential for controlling the infection and it still remains a challenge for the clinicians

The present study findings call for further research especially in a longitudinal study which is more costly and time-consuming to strengthen our current study findings. Regulatory bodies may need to devise strategies to counter the expansion of Khat chewing and other substance uses which pose continuing public health risks. Community based health education is also needed.

## Conflict of interest

The authors declare that they have no competing interests

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