Prevalence of Helicobacter pylori infection, its correlation with gastroduodenal diseases and the incidence of gastric cancer in Nepal

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ABSTRACT

Background and aims: The *Helicobacter pylori (H. pylori)* prevalence in Asian countries is highly variable, with higher seroprevalence shown in the previous studies of developing Asian countries. We aimed to determine the current *H. pylori* prevalence, correlate with gastroduodenal diseases and study gastric cancer incidence in Nepal.

Methods: Among 3357 patients referred for endoscopy, 2820 eligible patients underwent upper gastrointestinal endoscopy with biopsy; *H. pylori* was considered positive when either of Rapid Urease Test (RUT) or histopathology showed positive result.

Results: The *H. pylori* prevalence was 29.4% in overall distribution, 41.1% in gastritis and or duodenitis, 69.5% in gastric ulcer, 84.7% in duodenal ulcer, 20.8% in gastric polyp and 11.5% in gastric cancer. The *H. pylori* infection was significantly associated with gastritis and or duodenitis [P<0.001; Odds Ratio (OR) 1.53, 95% Confidence Interval (CI) 1.47-1.59], gastric ulcer (P<0.001; OR 18.62, 95% CI 12.40-27.81), duodenal ulcer (P<0.001; OR 48.89, 95% CI 25.23-94.75), gastric polyp (P=0.001; OR 7.66, 95% CI 3.18-18.44) and gastric cancer (P=0.005; OR 3.78, 95% CI 1.82-7.86). The age-standardized (world) annual rate of gastric cancer in Kaski district of Nepal was 3.3 per 100,000.

Conclusions: The *H. pylori* prevalence in Nepal was lower than that shown in the previous studies of developing Asian countries, but was significantly high in gastritis and or duodenitis, and peptic ulcers. Similarly, the gastric cancer incidence was also low in Nepal and was significantly associated with *H. pylori*. Further study is needed to establish the association of *H. pylori* with gastric cancer in Nepal.

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INTRODUCTION

It is estimated that one-half or more of the world's adult population has *Helicobacter pylori* (*H. pylori)* infection.[1] The prevalence of *H. pylori* infection and its related diseases in various Asian countries is highly variable, with higher prevalence shown in developing Asian countries, but there has been only limited information available regarding the actual distribution of *H. pylori*. The *H. pylori* infection has been linked with peptic ulcer disease, non-cardia gastric adenocarcinomas and gastric mucosa associated lymphoid tissue (MALT) lymphomas.[2-6] The World Health Organization and International Agency for Research on Cancer consensus group classified *H. pylori* as a definite carcinogen.[7]

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However, the low rate of gastric cancer incidence was noted with high prevalence of *H. pylori* infection in India, Philippines, or Thailand; on the other hand, the high rate of gastric cancer incidence was observed in Japan and Korea with variable prevalence of *H. pylori*.[8-10] The study suggests that *H. pylori* infection is not the only factor related to gastric cancer risk.[11,12] This Asian enigma could be because of the influence of other variables such as bacterial virulence factors, concomitant environmental factors, host susceptibility and immune response. Nevertheless, the significance of the association of *H. pylori* with gastric cancer cannot be underestimated. The aims of our study were to determine the prevalence of *H. pylori* infection, correlate its association with related gastroduodenal diseases and find out the incidence rate of gastric cancer in Nepal.

METHODS

Among a total of 3357 patients referred for upper gastrointestinal (GI) endoscopy, only 2820 patients were eligible for the study. The exclusion criteria for the study were: 1) patients who had received proton pump inhibitors or histamine 2-receptor antagonists for a minimum of 2 weeks and antibiotics for 4 weeks prior to the enrollment in the study;[13] patients who had Antacid, Bismuth, Non-steroidal anti-inflammatory drugs or had triple therapy of *H. pylori* eradication in the past, 2) patients with a diagnosis of portal hypertensive gastropathy, esophageal varices and hepatic encephalopathy, 3) patients with an abnormal coagulation profile, 4) patients with severe co-morbid conditions such as heart failure, kidney failure, etc. and 5) patients not giving an informed consent for the study.

All eligible 2820 subjects underwent upper GI endoscopy at the tertiary referral hospital of western region of Nepal at Manipal Teaching Hospital and Kaski Sewa Hospital, located at Pokhara city of Kaski district of Nepal during a period of May 2010 to April 2013. Some patients diagnosed of having gastric cancer were received from other local hospitals (Western Regional Hospital and Gandaki Medical College) of Kaski, Nepal. Nepal is a developing country of South Asia with a population of 26,494,504 and Kaski is a district of western region of Nepal with a population of 462,098 with an altitude of 1178 meters (m).[14] The annual incidence rate of gastric cancer was determined per 100,000 world population by enumerating all new gastric cancer patients in Kaski district during the three year period (2010 - 2013); in addition to the crude annual rate of gastric cancer, the age-adjusted (world) incidence rate was also calculated according to the population of Kaski district of Nepal and world in different age groups.[14,15]

The informed consent was taken from all study subjects and the study protocol was approved by the ethics committees of the participating centers.

Biopsies from the antrum, corpus and fundus of the stomach were taken for Rapid Urease Test (RUT) and histopathology. The RUT was done by placing the biopsy specimen into test gel and the color changed into red in 20 min to 24 hours time was regarded as a positive result, after incubating the gastric tissue into the test gel at the room temperature.

In all the patients, three endoscopic biopsies taken from the stomach were sent in 10% formalin or Bouin's fluid for histopathology. The tissue biopsies were routinely processed. At least three sections from each tissue biopsy in each case were studied. Sections were of 3 micron thickness. All the tissue had been studied with 2 stains – Hematoxylin-eosin, and Giemsa. The microscopes used were Carl Ziess Axiostar Plus and Olympus CX21. Biopsies were also taken from other representative sites, when endoscopy showed lesions in the oesophagus or duodenum and sent for histopathological examination. The histopathology was used to confirm esophagitis, gastritis and or duodenitis and different neoplastic conditions found during endoscopy.

The *H. pylori* was considered positive when either of RUT or histopathology (figure 1) showed positive result.

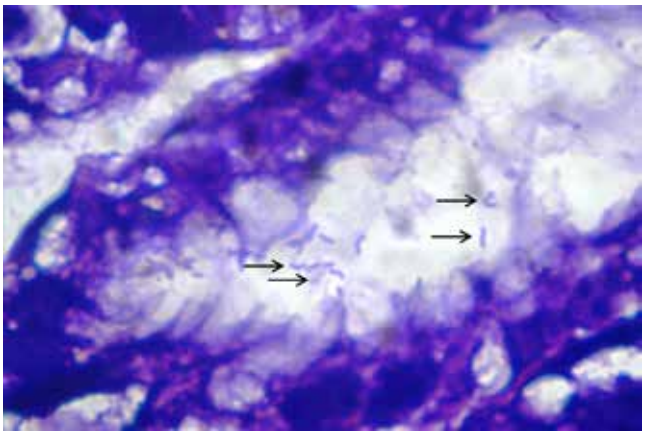

Figure 1: *H pylori* seen in gastric pits (arrows) , Giemsa , 1000x

All data of endoscopy and the *H. pylori* reports were recorded prospectively. The positive and negative results of *H. pylori* were categorized according to the age group, gender and different diagnosis. All variables of the patients were entered each day into a personal computer and data analysis was performed using SPSS 16.0 software (SPSS Inc., Chicago, IL, USA). All data were analyzed statistically by using Chi-square test or Fisher exact test, Odds Ratio (OR) and 95% Confidence Interval (CI), as appropriate. The subjects with normal endoscopic findings were taken as the control group. The P value less than 0.05 was considered to be statistically significant.

RESULTS

Among 2820 eligible patients, males were 54.2% and

females were 45.8% with the mean age of 46.3 years ±17.6 ranging from 8 to 94 years. The distribution of the endoscopic findings was as follows: normal 20.5%, esophagitis 10.2%, gastritis and or duodentis 59.9%, peptic ulcer 5.0% (gastric ulcer 2.9%, duodenal ulcer 2.1%), gastric polyp 0.9%, duodenal polyp 0.2%, esophageal cancer 0.9%, gastric cancer 1.8%, duodenal cancer 0.1%, achalasia cardia 0.1%, hiatus hernia 0.3%, duodenal diverticulum 0.1% and esophageal stricture 0.1%. The distribution of different diagnosis according to the gender, mean age and age groups is shown in tables 1 and 2.

Table 1: Distribution of different diagnosis according to the gender and mean age

Total (N=2820)	Male (n=1529) 54%	Female (n=1291) 45.8%	Mean Age in years (Standard deviation)
Normal (n=578; 20.5%)	278 (48.1%)	300 (51.9%)	38.6 (±15.8)
Esophagitis (n=287; 10.2%)	206 (71.8%)	81 (28.2%)	51.7 (±16.9)
Gastritis and or duodenitis (n=1688; 59.9%)	866 (51.3%)	822 (48.7%)	46.5 (±17)
Gastric ulcer (n=82; 2.9%)	48 (58.5%)	34 (41.5%)	55.1 (±17.6)
Duodenal ulcer (n=59; 2.1%)	44 (74.6%)	15 (25.4%)	46.3 (±18.7)
Gastric polyp (n=24; 0.9%)	12 (50%)	12 (50%)	49.0 (±18.0)
Duodenal polyp (n=5; 0.2%)	4 (80%)	1 (20%)	55.4 (±5.3)
Esophageal cancer (n=25; 0.9%)	15 (60%)	40 (0%)	65.7 (±9.5) [median age: 66]
Gastric cancer (n=52; 1.8%)	42 (80.8%)	10 (19.2%)	66.7 (±12.5) [median age: 68]
Duodenal cancer (n=3; 0.1%)	3 (100%)	0 (0.2%)	45.7 (±23.6) [median age: 44]
Achalasia cardia (n=3 ; 0.1%)	2 (66.7%)	1 (33.3%)	62.0 (±10.4)
Hiatus hernia (n=8; 0.3%)	5 (62.5%)	3 (37.5%)	45.9 (±19.2)
Duodenal diverticulum (n=4; 0.1%)	3 (75%)	1 (25%)	50.5 (±19.3)
Esophageal stricture (n=2; 0.1%)	1 (50%)	1 (50%)	66.5 (±7.8)

Table 2: Distribution of different diagnosis according to the age group

	Age groups						
Total (N=2820)	<20 years (n=99)	20-29 years (n=494)	30-39 years (n=490)	40-49 years (n=522)	50-59 years (n=462)	60-69 years (n=405)	≥70 years (n=348)
Normal (n=578; 20.5%)	37 (37.4%)	174 (35.2%)	119 (24.3%)	97 (18.6%)	69 (14.9)	54 (13.3%)	28 (8%)
Esophagitis (n=287; 10.2%)	10 (10.1%)	25 (5.1%)	25 (5.1%)	64 (12.3%)	56 (12.1%)	66 (16.3%)	41 (11.8%)
Gastritis and or duodenitis (n=1688; 59.9%)	47 (47.5%)	269 (54.5%)	324 (66.1%)	328 (62.8%)	287 (62.1%)	225 (55.6%)	208 (59.8%)
Gastric ulcer (n=82; 2.9%)	2 (2%)	9 (1.8%)	5 (1%)	12 (2.3%)	13 (2.8%)	24 (5.9%)	17 (4.9%)
Duodenal ulcer (n=59; 2.1%)	1 (1%)	14 (2.8%)	7 (1.4%)	10 (1.9%)	13 (2.8%)	5 (1.2%)	9 (2.6%)
Gastric polyp (n=24; 0.9%)	2 (2%)	1 (0,2%)	6 (1.2%)	1 (0.2%)	4 (0.9%)	6 (1.5%)	4 (1.1%)
Duodenal polyp (n=5; 0.2%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	2 (0.4%)	2 (0.5%)	0 (0%)
Esophageal cancer (n=25; 0.9%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	4 (0.9%)	10 (2.5%)	10 (2.9%)
Gastric cancer (n=52; 1.8%)	0 (0%)	0 (0%)	0 (0%)	4 (0.8%)	12 (2.6%)	10 (2.5%)	26 (7.5%)
Duodenal cancer (n=3; 0.1%)	0 (0%)	1 (0.2%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	1 (0.3%)
Achalasia cardia (n=3 ; 0.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	2 (0.5%)	0 (0%)
Hiatus hernia (n=8; 0.3%)	0 (0%)	1 (0.2%)	3 (0,6%)	2 (0.4%)	0 (0%)	0 (0%)	2 (0.6%)
Duodenal diverticulum (n=4; 0.1%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	1 (0.2%)	0 (0%)	1 (0.3%)
Esophageal stricture (n=2; 0.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.3%)

The overall prevalence of *H. pylori* infection was 29.4%; the males had 29.2% and females had 29.6% of *H. pylori*, showing the similar distribution of *H. pylori* among the gender (table 3).

The prevalence of *H. pylori* in ≥20 years age group (20-29 years 24.7%, 30-39 years 29.2%, 40-49 years 32.2%, 50-59 years 34.6%, 60-69 years 27.4% and ≥70 years 31%) was greater than that in <20 years age group (17.2%), which was statistically significant (P=0.001) [table 4].

The *H. pylori* infection was significantly associated with gastritis and or duodenitis [P<0.001; Odds Ratio (OR) 1.53, 95% Confidence Interval (CI) 1.47-1.59], gastric ulcer (P<0.001; OR 18.62, 95% CI 12.40-27.81), duodenal ulcer (P<0.001; OR 48.89, 95% CI 25.23-94.75), gastric polyp (P=0.001; OR 7.66, 95% CI 3.18-18.44) and gastric cancer (P=0.005; OR 3.78, 95% CI 1.82-7.86), but the association of *H. pylori* with esophagitis seems to be inverse (P=0.058; OR 0.35, 95% CI 0.09-1.29). All gastric cancer patients were of non-cardia adenocarcinoma. The gastric polyps were of fundic-gland polyp (12.5%), hyperplastic polyp (50%) and adenomatous polyp (37.5%); among them, 1 patient of hyperplastic polyp and 4 patients of adenomatous polyp had positive *H. pylori*, and pathological feature of gastric mucosa showed that 3 patients of hyperplastic polyp (*H. pylori* positive 1) and 5 patients of adenomatous polyp (*H. pylori* positive 2) had atrophic gastritis with intestinal metaplasia. The distribution of different types of gastric polyps is given in table 6.

Table 3: Distribution of *H. pylori* according to the gender

	H. pylori positive	*H. pylori* negative	P value
Male (n = 1529)	446 (29.2%)	1083 (70.8%)	0.80
Female (n = 1291)	382 (29.6%)	909 (70.4%)	

Table 4: Distribution of *H. pylori* according to the age group

	Age groups							
Total (N=2820)	<20 years (n=99)	20-29 years (n=494)	30-39 years (n=490)	40-49 years (n=522)	50-59 years (n=462)	60-69 years (n=405)	≥70 years (n=348)	P value
H. pylori Positive (n=829; 29.4%)	17 (17.2%)	122 (24.7%)	143 (29.2%)	168 (32.2%)	160 (34.6%)	111 (27.4%)	108 (31%)	0.001
H. pylori Negative (n=1991; 70.6%)	82 (82.8%)	372 (75.3%)	347 (70.8%)	354 (67.8%)	302 (65.4%)	294 (72.6%)	240 (69%)	

The distribution of *H. pylori* infection among different diagnosis was as follows: normal 2.6%, esophagitis 0.7%, gastritis and or duodentis 41.1%, gastric ulcer 69.5%, duodenal ulcer 84.7%, gastric polyp 20.8%, duodenal polyp 0%, esophageal cancer 0%, gastric cancer 11.5%, duodenal cancer 0%, achalasia cardia 0%, hiatus hernia 0%, duodenal diverticulum 0% and esophageal stricture 0% (table 5).

Table 5: Distribution of *H. pylori* according to the different diagnosis

Total (N=2820)	*H. pylori* positive	*H. pylori* negative	P value*	Odds Ratio (**95% CI)
Normal (n=578)	15 (2.6%)	563 (97.4%)		
Esophagitis (n=287)	2 (0.7%)	285 (99.3%)	0.058	0.35 (0.09-1.29)
Gastritis and or duodenitis (n=1688)	693 (41.1%)	995 (58.9%)	<0.001	1.53 (1.47-1.59)
Gastric ulcer (n=82)	57 (69.5%)	25 (30.5%)	<0.001	18.62 (12.40-27.81)
Duodenal ulcer (n=59)	50 (84.7%)	9 (15.3%)	<0.001	48.89 (25.23-94.75)
Gastric polyp (n=24)	5 (20.8%)	19 (79.2%)	0.001	7.66 (3.18-18.44)
Duodenal polyp (n=5)	0 (0%)	5 (100%)	1.0	
Esophageal cancer (n=25)	0 (0%)	25 (100%)	1.0	
Gastric cancer (n=52)	6 (11.5%)	46 (88.5%)	0.005	3.78 (1.82-7.86)
Duodenal cancer (n=3)	0 (0%)	3 (100%)	1.0	
Achalasia cardia (n=3)	0 (0%)	3 (100%)	1.0	
Hiatus hernia (n=8)	0 (0%)	8 (100%)	1.0	
Duodenal diverticulum (n=4)	0 (0%)	4 (100%)	1.0	
Esophageal stricture (n=2)	0 (0%)	2 (100%)	1.0	

^Patients with normal endoscopic findings were taken as the control group
* P value obtained using Chi square test or Fischer exact test as appropriate
**95% Confidence Interval

Table 6: Distribution of different types of gastric polyps

Polyps (N=24)	H. pylori positive	H. pylori negative	Total	P value*
Fundic-gland polyp	0 (0%)	3 (15.8%)	3 (12.5%)	0.083
Hyperplastic polyp:	1 (20%)	11 (57.9%)	12 (50%)	
Atrophic gastritis with intestinal metaplasia (n=3)	1	2		
Adenomatous polyp:	4 (80%)	5 (26.3%)	9 (37.5%)	
Atrophic gastritis with intestinal metaplasia (n=5)	2	3		

* P value obtained using Chi square test or Fischer exact test as appropriate

The crude and age-standardized (world) annual rates of gastric cancer in Kaski district of Nepal were 2.5 and 3.3 per 100,000

world population, respectively during the three year period of 2010-2013.

The age-standardized (world) incidence of gastric cancer per 100,000 during the year 2010-2013, calculated according to the age wise population distribution of Kaski district of Nepal is shown in table 7.

Table 7: Age-standardized (world) incidence of gastric cancer per 100,000 in Nepal during the year 2010-2013.

Age group (Years)	No. of gastric cancers	Population of Kaski district of Nepal according to the age group	Age-standardized (world) incidence rate of gastric cancer in Nepal per 100,000
40-49	4	47523	0.3
50-59	12	34727	0.8
60-69	10	23423	0.6
≥70	26	19512	1.6
Total age-standardized (world) incidence rate of gastric cancer in Nepal per 100,000			3.3

DISCUSSION

More than half of patients referred for endoscopy had gastritis and or duodenitis, although one fifth patients had normal findings and one tenth patients had esophagitis; the prevalence of peptic ulcer disease was 5 %, gastric cancer 1.8% and esophageal cancer 0.9% showing that the gap between peptic ulcer and malignancy was not big.

The median age of presentation of gastric cancer and esophageal cancer was more than 65 years, but that of duodenal cancer was only 44 years, which may not be truly representative of that group of patients, because of the low sample size (three) of duodenal cancer.

The actual *H. pylori* infection rate varies not only between different countries, but also according to the different geographic area of the same country, patient age and socioeconomic status.[16,17]

The *H.pylori* prevalence in developing countries is much higher than the developed countries, which may be due to higher socioeconomic status and improvements in hygiene practices.[17]

Nepal is a small landlocked South Asian developing country with an area of 147,181 square kilometers [14] and has got almost similar socio-cultural background with the other South Asian developing countries like India and Bangladesh. In India, the seroprevalence of *H. pylori* was estimated to be 79% (sample size 238) in 1991 and 67% (sample size 340) in 1994.[18,19] In Bangladesh, the *H. pylori* prevalence was estimated to be 91.7% (sample size 181) in 1997 and 69.7% (sample size 241) in 2003.[20,21] In one study done in Nepal in 1998, the overall seroprevalence of *H. pylori* infection was estimated to be 56.8% (sample size 1142), with lower rate of 41.5% in an isolated rural village.[22]

These studies have given an overall impression of very high prevalence of *H. pylori* in this part of developing world and inadequate sanitation practices, low social class, and crowded or high-density living conditions have been attributed to the higher prevalence of *H. pylori* infection.[23] However, the retrospective study done in Nepal in 2005 showed that the prevalence of *H. pylori* was 33.9% (sample size 224) in dyspeptic patients attending the hospital.[24] The finding was almost similar with slightly decreasing prevalence by 4.4% in another study done in Nepal one year after in 2006 with *H. pylori* prevalence of 29.5% (sample size 203).[25] Our current study done in Nepal with more sample size (2820) also demonstrated the similar result with *H. pylori* prevalence of 29.4%. This indicates that the prevalence of *H. pylori* in developing South Asian countries in the current era might not be very high as was projected from a decade old data. This could be due to the development of the 'westernization' of the life style in those developing countries, which have witnessed increasing prevalence of other diseases of affluent society such as type 2 diabetes.[26] Another potential reason for this decreasing trend of *H. pylori* prevalence could be due to the widespread use of proton pump inhibitors and antibiotics.

One study done in 1998 had used saliva specimen for the diagnosis of *H. pylori* in remote areas of Nepal in two villages Tarap (altitude 3600 m) and Ringmo (altitude 4100 m), and showed low *H. pylori* prevalence of only 11.6% (n=62) in Ringmo village and none in Tarap village (n=38).[27] The study had limitations because of the flaws in the transport of the saliva sample and the sample size was very low. However, the study had emphasized about the need of the study of genetics of bacteria found in remote population because of the exquisite adaptation of *H. pylori* to its host.[28] This may unleash the diverse behavior of *H. pylori* in the population of remote Nepal showing the altered epidemiology *H. pylori* in Nepal.

The study done in China showed that the seroprevalence of *H. pylori* infection was significantly decreased during the 10-year period in Guangzhou, with the overall age-standardized *H. pylori* seroprevalence rate being 62.5% in 1993 and 49.3% in 2003.[29] The decreasing trend of *H. pylori* prevalence was also shown by several other Asian studies.[30-32] The *H. pylori* seroprevalence rate was 74.6% in Vietnam, 58.07% in China, 39.3% in Japan, 59.6% in South Korea, 54.5% in Taiwan, 35.9% in Malaysia, 31% in Singapore and 57% in Thailand.[33-40] On the other hand, the seroprevalence rates in more developed

countries were generally lower with the overall seroprevalence rate of 15.1% in Australia.[41] In the United States, *H. pylori* prevalence varied with different ethnic groups with the prevalence of 60% in Hispanics, 54% in African Americans, and 20% in whites.[42]

One study done in UK showed that the risk of *H. pylori* infection was increased in male gender, living with a partner and poor adult socioeconomic conditions.[43]

However, our study didn't show any significant difference of *H. pylori* prevalence among the gender. This was consistent with the findings of some studies, which did not find gender-related difference in the prevalence of *H. pylori* infection.[44-46]

In our study, the age group <20 years had lower prevalence (17.2%) of *H. pylori* than that of ≥20 years group, which showed the highest prevalence (34.6%) being seen in the age group of 50-59 years followed by higher prevalence (32.2%) in 40-49 years group. This difference in *H. pylori* prevalence among different age group was statistically significant and this again showed the changing epidemiology of *H. pylori* in developing countries, which now seem to be following the pattern of developed countries, showing the rising trend of the prevalence of infection with age during adulthood.[47]

The prevalence of *H. pylori*–related diseases also varies in different geographic regions and patient populations.[8]

Our study showed that *H. pylori* was significantly associated not only with gastritis and or duodenitis and peptic ulcers, but also with the gastric polyp. The patients with combined gastric polyp and *H. pylori* might be high risk factor for gastric cancer. Hence, all the patients with gastric polyp might need to be investigated for *H. pylori* and if both are present, the triple therapy regimen for the eradication of *H. pylori* along with the removal of polyp would be more appropriate to prevent the gastric cancer.

The previous so-called Asian enigma of very high prevalence of *H. pylori* associated with low prevalence of gastric cancer was not obvious in our study, which showed only 29.4% of *H. pylori* prevalence and 1.8% of gastric cancer. The gastric cancer was associated with *H. pylori* positivity in 11.7% which was statistically significant when compared to 2% of *H. pylori* positivity in subjects with normal endoscopic findings taken as the controls, giving an OR of 3.78 (95% CI 1.82-7.86); the median age of gastric cancer patients was 68 years. This was in contrast to the study from Japan where overall OR for gastric cancer was high in younger age with OR of 7.0 for aged 20-29 and 14.5 for aged 40-49; on the other hand, OR was much lower in elderly group, with OR of 3.5 for aged 50-59 and 1.5 for 60-69, which was almost similar to our study.[48] This Japanese study showed that the higher seroprevalence was shown in early cancer than advanced cancer, especially in older subjects, and lower seroprevalence in elderly could be due to seroreversion.[48]

Another study form Japan, in which 123 576 subjects were followed up from 1990 to 2004 with 511 gastric cancer cases, showed adjusted OR for gastric cancer associated with *H. pylori* of 5.1.[49] The age-standardized (world) annual incidence rate of gastric cancer in Kaski district of Nepal was found to be 3.3 per 100,000 population which was consistent with the data from Delhi of India (3.4 per 100,000), but the OR of gastric cancer associated with *H. pylori* in Delhi was only 1.5 than controls.[50] One study done in 2009 showed that the multi-institution hospital-based incidence of gastric cancer in Nepal was found to be 7.5% in male and 4.1% in female among all recorded cancer patients.[51]

The gastric cancer epidemiology has been categorized as high-risk areas (East Asian countries such as China, Japan and Korea), where the age-standardized incidence rate is greater than 20 per 100 000, intermediate risk areas (Malaysia, Singapore and Taiwan) with that of 11–20/100 000 and low-risk areas (Australia, New Zealand, India and Thailand) with that of <10/100 000.[17] According to this categorization, Nepal falls in the low-risk area of gastric cancer incidence.

However, our study was not without limitations. Some of the subjects, who might have consumed the drugs such as proton pump inhibitors or histamine 2-receptor antagonists 2 weeks prior to the test and antibiotics 4 weeks prior to the enrollment in the study, without the knowledge of the investigator, were supposed be excluded from the study, but might have been included because of the sampling error, resulting in the inappropriate *H. pylori* results. Our study did not collect the data on education, monthly income, household size and other variables, and hence, the association of these variables with *H. pylori* could not be assessed. While assessing the incidence of gastric cancers in Kaski district of Nepal, some undiagnosed and unnoticed cases beyond the reach of the investigator, might have been missed and it is difficult to project the incidence of one district to generalize for the country as a whole. Despite these shortcomings, the findings of *H. pylori* prevalence in our study is more robust compared to most other studies of *H. pylori* prevalence based on serology, because our prevalence rates are of active infections and based upon the detection of *H. pylori* on histopathology. The other *H. pylori* prevalence studies done with serology test do not differentiate between active or previous infection. Moreover, the gastric cancer incidence rate and its potential association with *H. pylori* have been determined for the first time in Nepal.

In conclusion, the *H. pylori* prevalence in Nepal was lower than that shown in the previous studies of developing

Asian countries, but was significantly high in gastritis and or duodenitis, and peptic ulcers. Moreover, the gastric cancer incidence was also low in Nepal, but was significantly associated with *H. pylori*. However, further study is needed to establish the potential association of *H. pylori* with gastric cancer in Nepal before recommending *H. pylori* eradication as a means of gastric cancer preventive measure.

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