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## Characteristics of helicobacter pylori infection in a national referral hospital in Bhutan

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### ABSTRACT

**Introduction:** *Helicobacter pylori* (*H. pylori*) is a bacterium causing chronic gastric infection and may cause gastric cancer. It was necessary to see the trend of infection, especially in symptomatic patients. This retrospective descriptive study was aimed to describe the characteristics of *H. pylori* infection in Bhutanese patients referred for an endoscopy to the National Referral Hospital, Thimphu. **Methods:** The sample of the study was randomized 380 medical records of the patients who underwent upper gastrointestinal endoscopy and Rapid Urea Test for symptomatic dyspepsia and peptic ulcer. Data was collected using a survey form designed by the researchers. Data analysis was done using descriptive statistics and either Chi-square or Fisher's exact test. **Results:** The prevalence of *H. pylori* infection was very high (76.6%). The mean age of the infection was 42 with a range from 15 to 84 years. The highest prevalence of infection was observed in the age group 20-29 years (82.7%) and lowest in the oldest age group 70-84 years (66.7%). The analysis showed no significant difference in infection amongst age groups, gender, and endoscopic findings to the positive results at 5% significant level except for monthly prevalence ( $p < 0.001$ ). Gastritis was the commonest endoscopy finding (153/380) and gastro-duodenitis had the highest positivity rate (88.9%). **Conclusions:** The prevalence of infection was relatively high compared with previous studies. Young and middle-aged adults had a high prevalence and this group needs to be given priority for screening and eradication treatment considering limited resources to prevent associated gastric cancer in Bhutan.

**Keywords:** Bhutanese; Endoscopy; H. Pylori prevalence; Rapid urease test.

### INTRODUCTION

*Helicobacter pylori* (*H. pylori*) is a bacterium that is widespread in human population and is responsible for most common chronic symptoms of upper gastrointestinal disorders like gastritis, duodenal ulcer, gastric ulcers and gastric adenocarcinoma<sup>1</sup> and it is an important public health problem in Bhutan. The prevalence of *H. Pylori* infection in Bhutan is the highest among the South Asian countries. The infection was estimated to be approximately 73% in the community-based studies published in 2013<sup>2</sup> and 86% in 2014<sup>3</sup>. The prevalence was around 43-61% in a neighbouring country Nepal<sup>4</sup> and 67% in Bangladesh<sup>5</sup>.

*H. pylori* infection is a serious health concern as its infection results in a higher risk of acquiring gastric cancer<sup>3</sup>. The incidence rate of gastric cancer in Bhutan is twice as high as in the United States. Among all gastro-intestinal related cancers, approximately 46% were gastric cancer in Bhutanese patients<sup>6</sup>. As the infection was found high in all age groups<sup>3</sup> it is expected

that an increasing number of patients would develop chronic gastritis and develop cancer placing higher health burden to hospitals and healthcare cost.

Research studies on *H. pylori* infection in Bhutan and other countries in the South Asia region had just started recently<sup>2-4,7</sup>. More evidence from studies with hospital-based research will be helpful to support the plan for prevention and eradication of the infection especially when there is a lack of information from the recent studies. Also, factors contributing to the high prevalence of *H. pylori* infection were associated with poverty, poor hygiene and sanitation, geographical areas, environment, and educational level<sup>3</sup>. There has been rapid development in Bhutan leading to improvements in the socio-economic conditions of its people<sup>8</sup>. However, the trend of its infection, diagnosis, and treatment remains unclear for the last five years. The Rapid Urea Test (RUT) is highly sensitive (95.6%) and specific to detect active *H. pylori* infection<sup>9</sup>. The facility to diagnose by RUT in gastric biopsy sample is currently available at Jigme Dorji Wangchuck National Referral Hospital (JDWRH) since January 2018 and Central and Eastern Regional Referral Hospitals at Gelephu and Mongar have just started. The hospital-based study was needed as these patients are always symptomatic and seeking health

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care services. The severity of the infection, as well as other co-morbidities, may be different compared with the findings of the community based-survey.

Therefore, this hospital-based study aimed to characterize the trend of *H. pylori* infection in terms of demography, seasonal differences and endoscopy findings in Bhutanese people.

**METHODS**

This is a retrospective descriptive study based on the data of RUT results of all patients who underwent upper gastrointestinal endoscopy (endoscopy) for dyspepsia and peptic ulcer symptoms at JDWRH from 1<sup>st</sup> January 2018 to 31<sup>st</sup> December 2018.

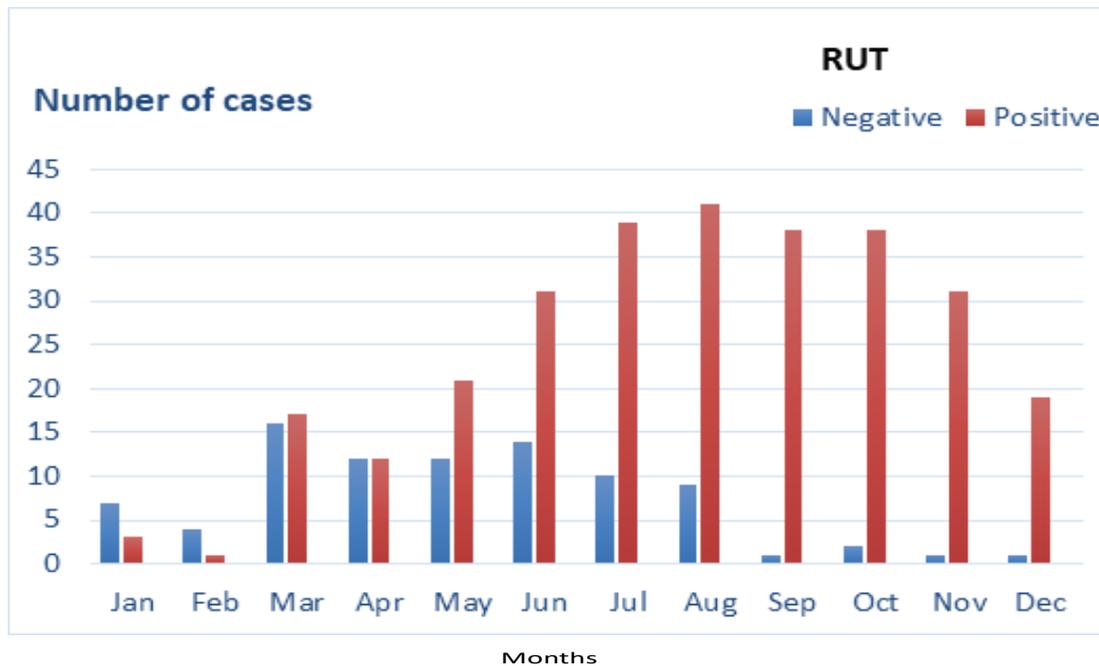
Considering an estimated 3000 individuals who have undergone endoscopy during the study period and expected prevalence of 73%, using Yamane’s Table<sup>10,11</sup> with a precision of determination value (d) at 5%, confidence level 95%, a sample size of 360 was estimated. Upon retrieving the records of endoscopy, only about 1000 individuals had undergone RUT. A systematic random technique was used to sample the records, with a selection of first sample corresponding to random number selected between 1 to 3, and selecting every third individual until 31<sup>st</sup> December 2018.

Inclusion criteria were the records of all patients who underwent endoscopy with the RUT investigation during the study period. Those patients without confirmed test results and unrecorded endoscopy findings were excluded from the study.

**Table 1. Univariate analysis of selected factors associated with positive RUT for *H. pylori* infection (n=380)**

Variables	Total (N)	RUT Test		RUT +ve Prevalence (%)	% within +ve RUT (n=291)	X <sup>2</sup>	Fisher’s exact test	Df	Overall P-value
		+ve count	-ve count						
	380	291	89	<b>76.6</b>					
Age	10-19 yrs	19	15	4	78.9	<b>5.2</b>	3.943	7	0.793
	20-29 yrs	75	62	13	82.7	<b>21.3</b>			
	30-39 yrs	90	66	24	73.3	<b>22.6</b>			
	40-49 yrs	65	52	13	80.0	<b>17.8</b>			
	50-59 yrs	64	47	17	73.4	<b>16.2</b>			
	60-69 yrs	41	30	11	73.2	10.3			
	70-79 yrs	20	15	5	75.0	5.2			
	80-89yrs	6	4	2	66.7	1.4			
Gender	Male	143	107	36	74.8	36.8	0.393	1	0.534
	Female	237	184	53	77.6	<b>63.2</b>			
Months	January	10	3	7	30.0	1.0	68.848	11	0.000*
	February	5	1	4	20.0	0.3			
	March	33	17	16	<b>51.5</b>	5.8			
	April	24	12	12	<b>50.0</b>	4.1			
	May	33	<b>21</b>	12	<b>63.6</b>	7.2			
	June	45	<b>31</b>	14	<b>68.9</b>	10.7			
	July	49	<b>39</b>	10	<b>79.6</b>	<b>13.4</b>			
	August	50	<b>41</b>	9	<b>82.0</b>	<b>14.1</b>			
	September	39	38	1	<b>97.4</b>	<b>13.1</b>			
	October	40	38	2	<b>95.0</b>	<b>13.1</b>			
	November	32	31	1	96.9	10.7			
	December	20	19	1	95.0	6.5			
Endoscopic findings	Normal mucosa	20	16	4	<b>80.0</b>	5.5	6.325	6	0.368
	Gastritis, no atrophy	153	115	38	75.2	<b>39.5</b>			
	Atrophic gastritis	90	69	21	76.7	<b>23.7</b>			
	Gastric erosions	75	58	17	77.3	19.9			
	Duodenal erosions/ulcer	10	7	3	70.0	2.4			
	Gastro-duodenitis	27	24	3	<b>88.9</b>	8.2			
Gastric ulcer	5	2	3	40.0	0.7				

\*p<0.05



**Figure 1. Monthly distribution in the frequency of H. Pylori test (RUT) result**

Following systematic random sampling, a total of 380 samples were selected by the end of December 2018 and were analysed.

The data collection proforma was developed by the researchers and was validated by three professional experts who were general specialist, gastroenterologist, and general surgeon. The reliability of the instrument was field-tested for 20 initial records. The data were analyzed using SPSS software version 25 (IBM Corp. Released 2017). Descriptive analysis was performed and summarized as mean, standard deviation, frequencies, and percentage. Chi-square and Fisher’s exact test were used to evaluate the association between the age group, gender, monthly variation and endoscopic findings with the RUT test results. A statistical association between RUT and demographic and other explanatory variables were assessed at 5% significance level. This study was conducted with the approval of the Research Ethics Board of Health, Ministry of Health, Thimphu, Bhutan vide approval letter number REBH/Approval/2018/104.

**RESULTS**

The results showed that among the 380 records examined, 237 (62.4%) were female and 143 cases (37.6%) were male, and age ranged from 15 to 84 years (mean=42.03, SD=16.3). Of those, 291 patients (76.6%) tested positive to *H. pylori* infection. The infection rate was high in the young adults in the age range of 20-29 years (82.7%) followed by the middle age with 80.0% (age range of 40-49 years). The lowest infection rate was found in the oldest age group range of 80-89 years (66.7%) as depicted in Table 1.

The analysis of age within the RUT positive group found differences in the pattern of distribution. The infection rate was

high in the younger age groups of 20-29 years (62/291, 21.3%) and the age groups 30-39 years (66/291, 22.6%). The infection rates were lower in the older age groups of 40-49 years (52/291), 50-59 years (47/291) and 60-69 years (30/291) 70-79 years (15/291) and 80-89 years (4/291) at 17.8%, 16.2%, 10.3%, 5.2% and 1.4% respectively as shown in Table 1. The youngest age group of 10-19 years also had a lower infection rate (5.2%, 15/291).

The *H. Pylori* infection was found higher among females (184/237, 77.6%) than males (107/143, 74.8%) but not significantly different. Gastritis was the commonest endoscopic findings (153/380) but gastro-duodenitis had the highest rates of infection (88.9%). A high proportion of *H. pylori* infection was also found in the group of individuals having normal mucosa as shown in Table 1.

The results in Table 1 and Figure 1 show that higher frequencies of positive RUT results were found from June to November months (10.7 – 14.1%) and the highest peak was in August (14.1%). The association between the age group, gender, monthly variation and endoscopic findings with the RUT test results showed no significant association of *H. pylori* infection among age groups ( $p=0.793$ ), between gender ( $p=0.534$ ) or categories of endoscopic findings ( $p=0.368$ ), except monthly variation ( $p=0.000$ ).

**DISCUSSION**

The prevalence of *H. pylori* infection in the current study was 76.6% showing an alarming sign for the risk of developing stomach cancer. This prevalence is much higher compared with the findings of previous studies by Vilaichone and team which reported the prevalence of 54.6% using RUT<sup>2</sup>. The difference of

over 20% prevalence from the recent study may be attributed to the variation between community-based study and the hospital-based study as more proportions of symptomatic patients are screened in hospital-based study. With a similar mountainous populace in Nepal, the prevalence of *H. pylori* infection reported was only 61.3%<sup>4</sup>. Together, the present findings confirm the prevalence of *H. pylori* infection using the RUT test in this study is higher than that of the previous studies in Bhutan, Bangladesh, and Nepal<sup>2-5,12</sup>.

It is worth discussing that the different methods of investigating *H. pylori* infection may result in a different range of prevalence rates even when studied in the same setting and group of symptomatic patients seeking treatment. Using a similar setting for investigating *H. pylori* infection, the hospital-based study of Dorji et al<sup>3</sup> reported 86% prevalence rate which had a higher prevalence rate compared to this study. It may be due to the difference in the investigation method used which was based on the serological test. As known, serology shows the lowest specificity and accuracy in comparison with other tests and the antibody titers can remain high for months after the elimination of the infection, attributing to higher prevalence rate in the previous study.

To identify the high-risk group, this study investigated the factors of age, gender, endoscopy findings and periods being tested. The results of these factors related to the prevalence of *H. pylori* infection are discussed further. About 83% (242) positive cases were under 60 years and the high prevalence rates of infection were the groups of early and middle-aged adults. This phenomenon is congruent with previous studies in South Asia and other countries that the prevalence of *H. pylori* infection decreased with increasing age<sup>12</sup> and showed a lower prevalence in the older age group<sup>4,5</sup>. Although this study did not find any significant association between age and *H. pylori* infection ( $p>0.05$ ), it is apparent that the younger age groups consisted of a high-risk group that may develop gastric cancer in later years of their lives. This shows that any program for the elimination of *H. pylori* infection should target even young adult groups of 20-29 years.

The role of gender as a risk factor for *H. pylori* infection is still being debated. Meta-analysis studies recently reported male predominated *H. pylori* infection in adults<sup>13-16</sup>. Again, it is noticeable that the result of this study found a higher prevalence of infection in females (184/291, 63.2%) and a higher infection rate within the female gender (184/237, 77.6%). This study is congruent with the previous study conducted in Bangladesh where higher prevalence was detected in females<sup>5</sup>. In contrary, the previous community-based study of Shiota and his team<sup>12</sup>, showed a high percentage of positive test results in the male Bhutanese group. However, a statistically significant difference in the prevalence of the infection rate between the gender group was not found ( $p>0.05$ ).

All types of endoscopy findings were associated with very high *H. Pylori* infection and prevalence was similar ( $p>0.05$ ). The hospital currently has only a simple white light

endoscope where images cannot be magnified and it is difficult to even for an experienced endoscopist to visualize the gastric findings in detail. With the ongoing training of endoscopists in the hospital, the observational findings in the gastric mucosa are expected to be improved and uniform reporting is expected in future.

Climatic conditions may be related to detecting a high prevalence of *H. pylori* infection in the summer season as shown in Figure 1. *H. pylori* bacteria normally grow within a temperature range of 30°C to 37 °C, with optimum growth at 37 °C and survives in complex foodstuffs such as milk, vegetables, and ready-to-eat foods<sup>1</sup>. The prevalence in this study varied with the months compared to a study in Venezuela<sup>17</sup> which found that the frequency of *H. pylori* infection was significantly high in the rainy season but contradictory to another study in Iran<sup>18</sup> which found the higher frequency in winter months than in spring and hot summer months. Therefore, more studies are needed to see any seasonal variation in detecting *H. pylori* infections.

Other findings found were lack of information on geographic distribution, histopathology sampling and treatment and this could be attributed to the existing documentation practices of the hospital.

## CONCLUSIONS

This study demonstrates again that the prevalence of *H. pylori* infection in Bhutan is very high and increasing, especially in young and middle-aged adults. This indicates that the majority of the Bhutanese population are at high risk of developing gastric cancer later in their life.

## LIMITATIONS AND RECOMMENDATIONS

Since this study was based on retrospective hospital data, the other risk factors for *H.pylori* infection could not be assessed. As an example, the data on geographical location, treatment, treatment outcomes and follow up endoscopy were not accessible due to a lack of information in the record. This can be improved with prospective study designs in the future. The impact of this study on clinical practice is a strong recommendation to provide a non-invasive diagnostic test for younger groups and reevaluation for the eradication of *H. pylori* infection after treatment.

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#### AUTHORS CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

**CLA:** Concept, design, data collection and analysis, manuscript writing and review.

**GPD:** Design, data collection and analysis, manuscript writing and review

**NS:** Design, data collection and analysis, manuscript writing and review

**SD:** Design, data collection and analysis, manuscript writing and review

**KPS:** Design, data collection and analysis, manuscript writing and review

Author agree to be accountable for all respects of the work in ensuring that questions related to the accuracy and integrity of any part of the work are appropriately investigated and resolved.

#### CONFLICT OF INTEREST

None

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