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Original Article

A descriptive cross-sectional study of helicobacter pylori infection in non-ulcer dyspepsia patients in a tertiary care teaching hospital In the Eastern part of Nepal

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Abstract:

Background

In Gastroenterology practice, worldwide, the most common cause of dyspepsia is functional. Functional or non-ulcer dyspepsia is established by gastroduodenoscopy which rules out structural disorders in dyspeptic patients. *Helicobacter pylori*, a gram-negative bacterium in gastric mucosa is associated with non-ulcer dyspepsia, chronic gastritis, gastriculcer and cancer. Worldwide prevalence of *Helicobacter pylori* infection is higher but its association with non-ulcer dyspepsia is less clear.

Material and Methods

The aim of this study was to see the prevalence of *H. pylori* infection in non-ulcer dyspepsia. A cross-sectional study of 340 patients presented at Nobel Teaching Hospital in one year with dyspeptic symptoms underwent clerking, physical examination, gastroduodenoscopy and RUT. Symptomatic patients without any structural lesions were designated as functional dyspepsia. RUT when turned red indicated positive for *H. pylori* infection.

Result

Out of 340 patients, 180 (52.9%) were female and 160(47.1%) were male. Mean age of male and female patients was 35.88 ± 11.8 and 38.11 ± 11.7 respectively. Amongst all participants 150 (44.11%) were housewives and 69(20.3%) were students. Endoscopic findings showed gastritis 205(60.29%) and duodenitis 15(4.42%). RUT was found positive in 62% of gastritis and 86.7% of duodenitis patients (p value = 0.001).

Conclusion

High prevalence of *H pylori* infection in present study may be one of the causative factors in producing symptomatic non-ulcer dyspepsia. Hence, early detection and complete eradication of *H.pylori* infection is mandatory. It will reduce usage of PPIs and also improve quality of life.

Key words: *Non-ulcer dyspepsia, Rapid Urease Test, Helicobacter pylori, Gastroduodenoscopy.*

Introduction:

Dyspepsia is a highly prevalent health issue ranging from 20%-30% worldwide **[1]** and most commonly encountered in developing nations causing a considerable amount of economic loss and morbidity **[2].** Dyspepsia is defined as chronic or recurring painful, difficult or disturbed digestion, which may be associated with symptoms of nausea, vomiting, heartburn, bloating and

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abdominal discomfort **[3].** Dyspepsia can further be elaborated by the following:

(i) Postprandial fullness (Post-prandial distress syndrome),
(ii) Early satiation (meaning inability to finish a normal sized meal) and
(iii) Epigastric pain or burning sensation (Epigastric pain syndrome) **[4].**

The commonest cause of dyspepsia encountered in primary health sector and gastroenterology department worldwide is functional and is also known as non-ulcer dyspepsia. Interestingly Tally NJ et al recorded only one fourth of such dyspeptic cases who had peptic ulcer diseases. In1999, hedescribeddyspepsiaas a group of heterogeneous disorder that was classified into following categories:

(i) Ulcer-like symptoms with upper abdominal pain,
(ii) Dysmotility-like symptoms with epigastric fullness, early satiety and bloating and
(iii) Unspecified dyspeptic patients with symptoms not fitting with either category **[5].**

Functional dyspepsia, according to ROME III criteria, is defined as one or more symptoms of dyspepsia with no evidence of structural diseases in oesophagus, stomach and duodenum that have been excluded by gastroduodenoscopy**[6].** These criteria should be fulfilled for three months with onset of symptoms and at least six months before the diagnosis has been made. The transmission of *H. pylori* occurs from person to person following an oral-oral or fecal-oral route. This microaerophilic, helical bacteria, probably acquired in childhood, is found to be associated with peptic ulcer diseases causing duodenal ulcer in 80-90% and chronic gastritis in 60-75% **[2].**

According to WHO, chronic *H. pylori* infection is also related to gastric carcinogen and may be associated with gastric adenocarcinoma and MALT (Mucosal Associated Lymphoid Tissue) lymphoma. Though the association between prevalence of *H. pylori* infection and peptic ulcer disease like duodenal ulcer and gastritis is well established but regarding the same in the non-ulcer dyspepsia is less clear.

As the prevalence of *H. pylori* infection is very high in developing nations, the present study in Eastern Nepal was designed to see the association between *H.pylori* infection and non-ulcer dyspepsia. The diagnosis of *H. pylori* infection needed invasive gastroduodenoscopy with gastric mucosal biopsy and RUT.

Material and Methods

This study was conducted only after getting Ethical Committee approval from Institutional Review Committee (IRC), Nobel Medical College, Kathmandu University. Hospital Director and Head of Medicine Department of Nobel Teaching Hospital were also informed about this study.

Patients and their care-givers were explained fully about study design, benefit and risks involved in the procedure and a duly signed written consent was taken from each patient.

It was a descriptive cross-sectional study over a period of one year from April 2014 to March 2015. About 340 patients from various parts of Eastern Nepal attended at Nobel Teaching Hospital Medicine department with various dyspeptic symptoms and without any structural lesion as proved by gastroduodenoscopy had participated in this study.

Inclusion criteria

Patients from various parts of Eastern Nepal of both sexes from15 to 60 years of age, presented with dyspeptic symptoms as defined by Rome III criteria, irrespective of having history of anti-*H.pylori* treatment and PPIs (Proton-pump inhibitors) were included.

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Exclusion criteria

Patients below 15 and above 60 years, residing outside of Eastern Nepal, having varices, ulcer, stricture or growth in the esophagus, stomach and duodenum, non-compliant with written consent and patients with abnormal bleeding and clotting time were excluded.

In the present studyat Nobel Medical College Teaching Hospital, Biratnagar, Olympus CV150 for gastroduodenos copy and biopsy and Rapid Urease Test kit (HP), manufactured by Allied Marketing Company, Kolkata were used. We made a Study Format to collect all demographic data for each patient including identity, hospital and study number, habits, profession, symptoms and endoscopic findings. Each patient with non-ulcer dyspepsia was diagnosed clinically as well as endoscopically.For each patient, one punch biopsy sample was put in thefreeze stored RUT kit that was kept at room temperature for 30 minutes before putting the biopsy material and the test results were recorded within 60 minutes. The red or pink colourchange was recorded as positive and any other colour changes that occurred later than 60 minutes were rejected as negative result.

Statistical analysis was done by recording the data in MS Excel 2007 and converted into SPSS 17(Statistical Presentation Systemic Software). The study description was made by expressing the percentage (%), mean, standard deviation (SD) and Pearson Chi-Square Test were calculated according to the data obtained in this study.

Results

Table 1. Mean age and standard deviation of male and female patients:

Number and Sex of patients	Percentage (%)	Mean age ± standard deviation
Male:160	(47.1%)	35.88 ± 11.80
Female:180	(52.9%)	38.11 ± 11.74
Total:340	(50%)	37.06 ± 11.80

NB: *Percentage in parenthesis*

Out of 340 patients, females were 180(52.9%) and 160(47.1%) were male. The mean age and standard deviation of male and female patients were 35.88 ± 11.80 and 38.11 ± 11.74 respectively.

Table 2. RUT positivity, Demographic, Clinical and Occupational characteristics of participants:

Characteristics	Participants (%)	RUT positivity (%)	p value
Sex:-			0.877
Female	180(52.9)	102(56.7)	
Male	160(47.1)	92(57.5)	
Occupation:-			0.007
Housewives	150(44.11)	88(58.7)	
Students	69(20.30)	28(40.6)	
Businessman	52(15.30)	39(75.0)	
Services	23(6.77)	14(60.9)	
Unemployed	23(6.77)	13(56.9)	
Laborers	09(2.64)	05(55.6)	
Others	12(3.53)	05(41.7)	
Retired	02(0.58)	02(100)	
Alcohol consumers:-			0.547
Yes	67(19.70)	41(60.3)	
No	273(80.30)	153(56.3)	
Smoker:-			0.007
Yes	101(29.30)	65(64.4)	
No	239(70.30)	129(54.0)	
Pain abdomen:-			0.439
Dull	165(48.53)	96(58.2)	
Burning	156(45.88)	89(57.1)	
Pricking	14(4.12)	07(50.0)	
Non-specific	05(1.47)	02(40.0)	
Endoscopic findings:-			0.001
Normal study	120(35.29)	54(45.0)	
Gastritis	205(60.29)	127(62.0)	
Duodenitis	15(4.42)	13(86.7)	

NB: *Percentage in parenthesis*

Amongst the total number of 150(44.11%) participants, housewives (20.30%), students (15.3%), businessmen (6.77%) and service-holders were (6.77%)recorded. Alcoholics and non-alcoholics were 19.7%

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and 80.3% respectively.RUT positivity was documented in 56.7% female and 57.5% male patients.RUT was also found to be positive in 62% gastritis and 86.7% duodenitis cases.

Discussion

H.pylori,a ubiquitous bacterium attached to gastric mucosa is found in more than 50% of adult population worldwide **[5].**In developing parts of the world, 80% of the population may be infected by the age of 20,whereasthe prevalence is 20-50% in industrialized countries. The steady increase in the prevalence of *H.pylori* noted with increasing age is due primarily to a cohort effect, reflecting higher transmission during a period in which the earlier cohorts were children**[7].** The varied prevalence of *H.pylori* infection is dependent on age, sex, race, geography, residence in developing country, domestic crowding, unsanitary living condition, unclean food or water and exposure to gastric contents of an infected individual. Two major predisposing factors among them are poor economic condition and less education. The prevalence of *H.pylori* in American blacks and Hispanics is more as compared to whites because of poor socioeconomic status.

The precise pathophysiology of this disorder is not fully understood but is thought due to a complex interaction of increased visceral afferent sensitivity, delayed gastric emptying, or impaired accommodation to food, or psychological stressors. Although benign, these symptoms may be chronic and difficult to treat.

H. pylori is known to cause chronic gastritis,duodenitis and related disorders like ulcer and cancer by inducing inflammatory response by producing ammonia,proteases,phospholipases and increased gastrin level by G cell stimulation**[8].**

Present study showed predominance of female (52.9%) as compared to male (47.1%) participants having functional dyspepsia but RUT positivitywas noted as 56.7% in female and 57.5% in male indicating not much difference in gender. Among the females, delayed gastric emptying time and proximal gastric motor function abnormality were held responsible in gender related differences in the prevalence of functional dyspepsia in one study done by Sarah N Flier et al in Switzerland. Moreover, she also documented gender differences in psychological realm and dyspeptic women experiencing a lesser sense of well being than their male counterparts **[9].**

This study was conducted in the Eastern part of Nepal to see the prevalence of *H.pylori* infection in the non-ulcer dyspepsia patients. The mean age of male and female patients were **35.88** ± 11.80 and **38.11** ± 11.74 respectively [**Table 1**]. In 2015,a similar study done in India by Harsh V Salankar,Sonali B.Rode et alshowed highest prevalence of *H.pylori*infection was more in 31-40 year-age group with a mean age of**38.53**which was very close to our study result**[10]**.The higher rate of infection tends to occur as age advances in those geographical locationswhere lower socioeconomic status and high density of population are prevalent.

Present study in Eastern Nepal revealed the prevalence of *H. pylori* infection was**57.1**% (194/340) in non-ulcer dyspepsia patients who were positive for RUT. More precisely, we found that RUT positive gastritis cases were **62.0%** and duodenitis 86.7% respectively (p = 0.001). Similar study was done in 2006 by Pande PR, Karki BB, Bhattarai MD et al at Shree Birendra Hospital, Nepal **[11]** and revealed 55**%** of prevalence of *H.pylori* infection in erosive antral gastritiswhich reflected almost similar figure with our study.

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H.pylori infection may not cause structural lesion as evidenced by present study where non-ulcer dyspepsia cases who underwent gastroduodenoscopy, had 35.29% normal endoscopic finding.A study done by Tack J et al in 2006 in industrial country like America where as high as 40% non-ulcer dyspeptic patients had no structural lesion and contrarily, their symptoms were produced by gastroesophageal reflux disease [GERD] **[6].**

In 2011, Blaser M et al had reported in Nature that gastric presence of nonpathogenic strain of *H. pylori* might be beneficial in some cases by normalizing stomach acid secretion and even reducing the prevalence of GERD **[12].**

Almost a comparable study carried out in urban area by Shrestha S, Paoudel P, and Pradhan GB et al in 2012 at Nepal Medical College Teaching Hospital at Kathmandu, showed prevalence of *H. pylori* infection in functional dyspepsia was 50.47%.In that study, 47.6% gastritis and 17.87% cases, normal endoscopic findings were recorded. Moreover,average mean age in that study was 20.12 yearsas compared to the same average mean age of 37.06 years in present study [**13].**

It is an established fact that *H. pylori* infection is acquired in childhood and its prevalence increases in developing nations with advancing age which has been documented in those above mentioned studies.

Recently, another cross-sectional hospital based observational study conducted in two different hospitals at Kathmandu, carried out by Thakur SK and Basnet BK in 2012 **[14]** concluded that prevalence of *H.pylori* infection in non-ulcer dyspeptic patients was 42.6% and interestingly that was more than the ulcerated dyspeptic patientsof 22.6% with p = 0.007.Present study showed prevalence of *H.pylori* infection in functional dyspepsia was 57.1%. This wide difference of prevalence of *H.pylori* infection in those above mentioned studies as compared to present study at Nobel Teaching Hospital could be due to variation of average mean age, socioeconomic status and availability of hygienic water.

In present study, 101(29.7%) patients were smokers and 67(19.7%) were alcoholics [**Table 2**].In functional dyspepsia and *H.pylori* infection, there are many risk factors involved such as diet, smoking, spirit, steroid and non-steroidal anti-inflammatory drugs, physical and psychological stress besides age, sex, race, geography and sanitation of water. In our study, among smokers and non-smokers, 64.4% and54.0%were RUT positive respectively. Similarly, in present study, RUT was positive in 60.3%in alcoholics and 56.3% in non-alcoholics. In 2015,ParvezMujawar et al in India have found correlations between smoking and ulcer formation and other risk factors involved in dyspeptic patients and concluded that smoking by itself may not be much of a risk factor unless associated with *H. pylori* infection **[15].**

In present study, there was not much difference of prevalence of *H. pylori*infectionamong smokers and alcoholics as compared to non-smokers and non-alcoholics. Indeed, number of pack-years and quantity or quality of alcohol consumed by each patient was not recorded in this study. Smokers and alcoholics have been found to have ulcers more frequently than teetotalers and smokers. Smoking and spirit appears to decrease healing rates, impair response to therapy, altered gastric emptying and increased risk of *H. pylori* infection as described by SalihBarik et al in Turkish patients in 2007**[16].**

Though gastroduodenoscopy was an invasive procedure but the advantage was that it was easy to perform, comfortable

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and cost-effective as compared to other expensive and time-consuming tests such as **^{14}C** urea breath test, histopathology and culture-sensitivity of *H. pylori* or specialized testing of serum gastrin level and gastric acid analysis. Hence, RUT in dyspeptic patients should be mandatory because *anti-H.pylori* regime will give prompt relief and prevent chronic type B gastritis which may lead to gastric ulcer and cancer.Other advantages of RUT were thatcolour change in RUT kit could be shown to patientsand their care-givers to win their confidence within 60 minutes and it could be performed in all centers with gastroduodenoscopy facility. Moreover, sensitivity and specificity of RUT within 60 minutes were shown to be as high as 89-98% and 89-93% respectively which supplanted other tests for *H.pylori* **[17].**

We encountered few limitations in our study:(i) there was no precise information regarding*anti-H.pylori* medication or PPIs, taken by those patients which might interfere with the RUT results and (ii) we had taken only one biopsy from each patient for RUT for pecuniary reason as compared to multiple biopsies were taken in other study**[14].** Besides those two, non-compliance of many participants in giving written consent for fear of invasive procedure, made the sample size comparatively small in the present study.

Conclusion

Before the discovery of *H. pylori*, the treatment was centered on the dictum by Schwartz of "no acid, no ulcer". Nowadays, although anti-acid treatment is still important but eradication of *H. pylori* is the mainstay of therapy of dyspepsia.

Present study recorded high prevalence of *H.pylori* infection as one of the most important causative factorsin producing symptomatic non-ulcer dyspepsia. Hence, itsearly detection and complete eradicationwill reduce usage of PPIs.Consequently, socioeconomic burden will be relieved and quality of life will be improved. Knowledge of prevalence of *H. pylori* infection in Eastern Nepal in functional dyspepsia would not only accrue cost-effective benefits but also help future researchers to explore means to reduce its prevalence.

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