Section: Medical Gastroenterology

Original Research Article

3 SITE GASTRIC BIOPSIES (INSTEAD OF 5) ARE ADEQUATE FOR HELICOBACTER PYLORI DETECTION IN NON-ULCER DYSPEPSIA

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Abstract

Background: Non-ulcer dyspepsia (NUD) is one of the most common causes of morbidity and economic loss. Helicobacter pylori (Hp) is one of the most common causes of NUD. The aim of the study is to determine the frequency of detection of Hp by 5 vs 3 biopsies in patients with NUD. **Materials and Methods:** Patients presenting with symptoms of dyspepsia but without any endoscopic lesion were taken up for the study. Those with history of any intake of PPI, H2RB, antibiotics, antacids in the last two weeks were also included. Gastric mucosal biopsies were obtained from 5 sites (2-antrum, 2-body, 1-incisura) for HPE and one for Rapid urease test. 5 site vs 3 site biopsies (2-antrum, 1- incisura) and Rapid Urease Test (RUT) were compared. Specimen were examined histologically using the updated Sydney system. **Result:** Gastric biopsies from 100 patients were studied. Histological examination (H & E and Geimsa stain) identified Hp with any of the 5 sites in 86 % and with the 3 biopsy sites in 84 % of patients. RUT was positive in 35 (49.3%) of 71 patients. There was no significant difference between 5 and 3 biopsies studied, while RUT results differed significantly. **Conclusion:** NUD should be evaluated for H.pylori and 3 biopsies in contrast to 5 biopsies can be recommended for H pylori detection by biopsy in NUD.

INTRODUCTION

Dyspepsia is known to result from organic causes, but most patients suffer from non-ulcer or functional dyspepsia.[1] At least 50% of patients who present with dyspepsia, no definite structural or biochemical explanation for symptoms can be identified.[2] H.pylori is one of the most likely causes implicated in the pathogenesis of non-ulcer dyspepsia.[3]

The latest WHO ICD-11β version and the Kyoto Global Consensus of Hp gastritis recommend that the classification of gastritis be based on causative factors, which includes (a) Hp-induced, (b) drug-induced, and (c) autoimmune gastritis. Hp gastritis is a distinct cause of dyspepsia and is therefore an organic disease.[4] Helicobacter pylori infection is prevalent worldwide, occurring in 40% to 50% of the people in developed countries, in 80% to 90% of the people in developing regions.[5]

Histopathological diagnosis of H.pylori infection is considered to be the 'gold standard'.[6,7] Studies on sites for biopsy for the diagnosis of H. pylori infection are conflicting. Genta and Graham,[6] recommend antrum biopsy, while at least one corpus biopsy is recommended by others.[8,9] An optimal biopsy site for the diagnosis of H. pylori has not been currently established.[6]

The present study was carried out to determine the frequency of Hp, optimal sites for biopsy and pattern of gastric mucosal histopathology in non-ulcer dyspepsia patients to better understand and manage non-ulcer dyspepsia.

MATERIALS AND METHODS

This was a single centre, prospective observational study over a period of two years. Informed and written consent was obtained from all the patients. All patients who presented with symptoms of dyspepsia satisfying ROME IV criteria were taken up for the study. A standard clinical proforma was used to collect data from each patient. All patients with normal Upper G.I endoscopy were evaluated by obtaining a sample for RUT followed by five gastric mucosal biopsies according to the Updated Sydney System. Sample for RUT was taken from site B first and then for HPE -- one sample each was obtained from the lesser[A] and the greater [B] curvature of the antrum, both within 2 cm from the pylorus; from the lesser curvature of the corpus about 4 cm

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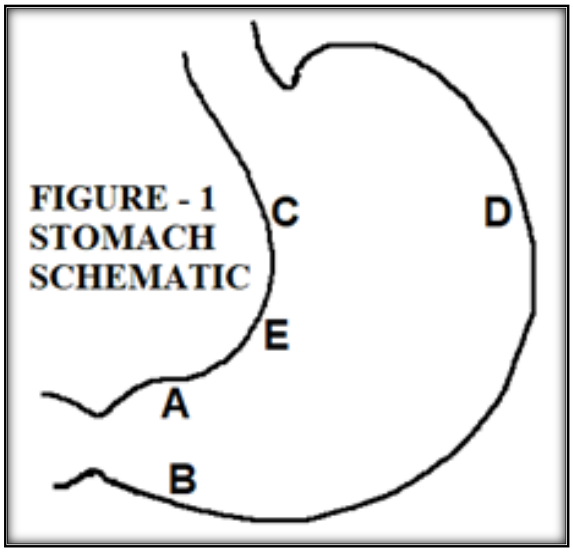
proximal to the angulus[C]; from the middle portion of the greater curvature of the corpus, approximately 8 cm from the cardia[D]; and one from incisura angularis[E] [Figure 1].



Five samples were placed in five different containers with 10% formalin. These specimens were processed and examined histologically by H&E, Giemsa Stains. Samples were reported using the Updated Sydney Classification of Gastritis. The result was considered to be positive if any one of the sites could demonstrate organisms consistent with H.pylori by histology. The yield of all five sites was compared with three sites (two from the antrum and one from incisura - ABE) and RUT.

Inclusion Criteria

Patients were recruited irrespective of any use of proton pump inhibitors, H2 receptor blockers, antacids, antibiotics (including those that act on Hp but not as combination eradication therapy).

Exclusion Criteria

Patients with peptic ulcer disease, absolute/relative contraindication to endoscopy, patients who used non-steroidal anti-inflammatory drugs (NSAIDs) in the last two weeks, chronic use of corticosteroids or immunosuppressants, prior gastric surgery, Hp eradication therapy in the last one month.

Data collected were analysed using a dedicated software IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp. Continuous variables are expressed as mean and categorical variables as percentages. Chi square test was used to test the association between the variables.

RESULTS

A total of 100 patients with dyspepsia who met the inclusion criteria were included in the study. The patients were aged between 16 and 80 years. Mean age of the population studied is 43.2 years. Prevalence of Hp was similar among different age groups (p=0.4). 62 were males and 38 were females. 55 of 62 (88.7%) males and 31 of 38 (81.5%) females were Hp positive. Hp prevalence was not different (p=0.32) between males and females. Of the population studied, 63 were from rural areas and 37 were from urban areas. Of the 63 people from rural areas, 57 (90.47%) were Hp positive and of the 37 people from urban areas, 29 (78.3%) were Hp positive. Region of residence had no significant influence on Hp prevalence (p=0.92). Nutritional status of the people was assessed with body mass index according to Asian grades. There was no statistical significance among different classes of BMI in Hp prevalence (p=0.30). There was no significant difference in Hp detection in people using alcohol (p=0.12) or tobacco (p=0.08). On multivariate analysis male gender was the only predictor for Hp infection (p=0.039).

Of the people studied, 82 had mild chronic inflammation, 13 had moderate chronic inflammation, 3 had mild acute inflammation, 2 had moderate acute inflammation. Hp was positive in 69 of 82 (84.14%) people with mild chronic inflammation and in all the patients with other classes of inflammation [Table 2]. There was no evidence of gastric atrophy or intestinal metaplasia in any of the patients.

Of the people included in the study, 78 people had history of PPI intake at least once in the last two weeks. Hp was positive in 66 of the 78 (84.6%) people. In those who had no history of PPI intake in the prior 2 weeks, Hp was positive in 20 of the 22 (90.9%) people. When only 3 biopsy sites (ABE) were considered 65 of 78 (83.3%) people with history of PPI intake in the prior 2 weeks, were Hp positive. History of PPI intake in the prior 2 weeks did not significantly influence Hp detection either by 5 (p=0.4) or 3 (p=0.7) biopsies [Table 2].

Density of Hp in the 5 biopsies, 3 biopsies (ABE), antrum, incisura and corpus were studied for any influence of PPI intake in the prior 2 weeks. Density of Hp in 5 biopsies (p=0.25), 3 biopsies – ABE(p=0.10), incisura(p=0.16) and corpus(p=0.26) was not influenced by history of PPI intake in the prior 2 weeks. However, people who had no history of PPI intake in the prior 2 weeks had higher density of Hp in the antrum than people with history of PPI intake. Out of 86 people with Hp positive on 5 biopsies, 55 had '+' density (45 with H/o PPI intake in prior 2 weeks), 24 had '++' density (17 with H/o PPI intake in prior 2 weeks), 7 had '+++' density (4 with H/o PPI intake in prior 2 weeks) [Table 3].

Out of the 100 patients studied Hp was positive in 86 patients when the result from all the 5 sites was considered and positive in 84 patients when 3 sites (ABE) were considered. There was no significant difference in Hp detection among 5 and 3 sites (p=0.69). When the result of 5 sites was compared to different combinations of 3 site biopsies in Hp detection, sites ADE result was equal to 5 site biopsies (86%) and other combinations varied from 82% to 85%. There was no significant difference in Hp detection between 5 sites and different combination of 3 site biopsies (p=0.9) [Figure 2]. Hp

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detection in 5 site biopsies (86%) was also compared with different combination of 2 site biopsies. It varied from 73% to 84%. There was no significant difference among 5 site and 2 site biopsies when different combinations were compared together (p=0.6). When 5 site biopsies (86%) were compared to site CD (73%) individually there was a significant difference (p=0.02). When 5 site biopsies (86%) was compared to sites BC (76%, p= 0.07) or any other 2 site biopsies individually, there was no significant difference [Figure 2]. Strength of each site of biopsy was tabulated and compared with result of 5 site together (86%) in Hp detection. Hp was detected maximum in Site A (lesser curvature- antrum) 74% and least in site D (greater curvature-corpus) 56%. There was a significant difference in Hp detection between 5 biopsies and single site biopsy (p=0.00) [Figure 2].

RUT was done in 71 of the 100 patients. RUT was positive in 35 (49.3%) patients. Of the 71 patients both RUT and Biopsy were positive in 34 patients. RUT was false positive in 1 patient and false negative in 35 patients. RUT and biopsies both were negative in 1 patient. RUT results were compared to the results of biopsy from site B, both RUT and site B biopsy were positive in 31 patients, negative in 14 patients. RUT was less effective (sensitivity 49.2%) in detecting Hp compared to all biopsies (p-0.0) or site B biopsy (0.02). PPI use did not influence Hp detection by RUT (p=0.72) [Table 4].

Table 1: Demographic Data

Category		Hp +	Hp -	p value
Age	<20 yrs 21-40 41-60 61-80	2 42 30 12	0 9 5 0	p = 0.4
Gender	Male Female	55 31	7 7	p = 0.32
Region	Rural Urban	57 29	6 8	p = 0.92
BMI	<18.5 18.5-22.9 23-27.9 >28	10 30 38 8	0 6 5 3	p = 0.32
Smoking	Yes No	6 80	3 11	p = 0.08
Alcohol	Yes No	20 66	6 8	p = 0.12

Table 2: Histopathology data

Category		Hp +	Hp -	p value
Inflammation	Mild chronic Moderate chronic Mild acute Moderate acute	69 13 3 2	13 0 0 0	
5 biopsies	PPI + PPI -	66 20	12 2	p = 0.4
3 biopsies	PPI + PPI -	65 19	13 3	p = 0.7

Table 3: Hp Density

Site	Hp Density	PPI +	PPI -	p Value
ALL BIOPSIES (5)	+ ++ +++	45 17 4	10 7 3	p = 0.25
ANTRUM (AB)	+ ++ +++	50 11 0	11 5 2	p = 0.016
INCISURA (E)	+ ++ +++	43 10 2	12 3 3	p = 0.16
BODY (CD)	+ ++ +++	41 11 3	10 7 1	p = 0.26
ABE	+ ++ +++	48 15 2	11 5 3	p = 0.10

Table 4: RUT

Category		RUT +	RUT -	p Value
All biopsies	Positive Negative	34 1	35 1	p = 0.00
Site B	Positive Negative	31 4	22 14	p = 0.02

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PPI	Taken Not taken	27 8	29 7	 p = 0.72

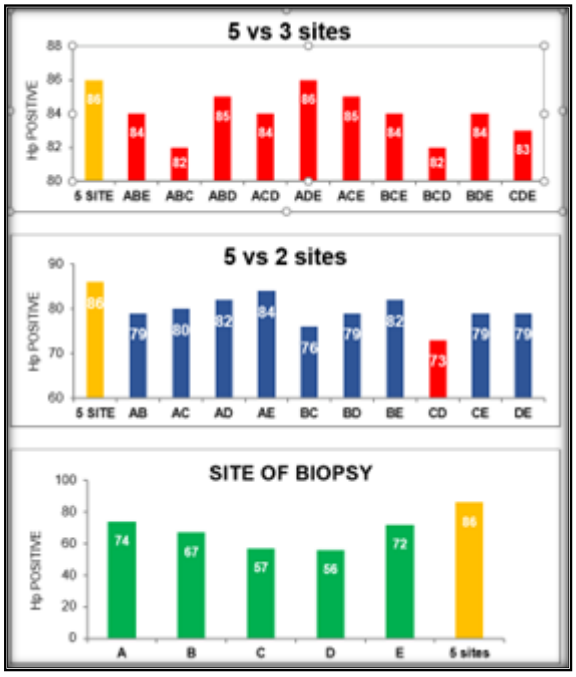

Figure 2: Comparison of biopsy sites

DISCUSSION

This study was done in India, which is geographically a high prevalence (70%) area for H.pylori. The standard indications to test for Hp includes uninvestigated dyspepsia with H.pylori prevalence >20%.[10] AGA guidelines recommend Hp testing with biopsies according to the updated Sydney system.[5] Similar studies were done by Priya Singh et al, Hsi-Chang Lee et al, Li Zhang et al, M.I.Nafeeza et al, to detect Hp in patients with functional dyspepsia.[11–14] Compared to those, this study is unique in including patients irrespective of any use of proton pump inhibitors, H2 receptor blockers, antacids, antibiotics to simulate routine outpatient presentation. There was no correlation of age with Hp positivity in this study and study by Li Zhang et al, which is in contrast to the study done by M.I.Nafeeza et al where Hp was more prevalent in age >50 yrs and study by Priya Singh et al where Hp was less prevalent in older people (age >60yrs).[11,13,14] In this study Hp prevalence was not different between males and females. In a meta-analysis by Catherine de Martel et al, there was a significant male predominance of H. pylori infection consistent across populations from various countries.[15] In this study, there was no difference in Hp prevalence among rural and urban populations. This was in contrast to the study done by Monica Contreras et al of patients from Venezuela which showed higher prevalence in rural areas than urban areas.[16] In studies done by Chengfu Xu et al, Mohamad Suki et al, Basit Siddiqui et al with C13 breath test, Hp prevalence showed a positive correlation to BMI.[17–19] In contrast in this study, Hp prevalence was similar in patients under different BMI categories. Similar to the studies done by Mohie Aldeen Abd Alzaher Khalifa et al (Urea breath test), Mohammad Hussain Hamrah et al (serology), Li Zhang et al there was no difference in Hp prevalence among smokers and non-smokers in our study also.[13,20,21]. In study done by Li Zhang et al there was a positive association of Hp prevalence with alcohol consumption. In our study there was no such association.[13]

In our study, Hp detection rate by histology was not influenced by history of PPI intake in the prior 2 weeks. However, there was significantly less Hp density in antrum in people with history of PPI intake in the prior 2 weeks. Results were similar to the study by Kuipers EJ et al.[22] This study showed that there was no significant difference between the standard 5 biopsies and 3 biopsies (2-antrum and 1-incisura) in detection of Hp. It also showed that any combination of 3 site biopsies did not differ from standard 5 site biopsies in detection of Hp. Different combinations of 2 site biopsies also were not significantly different when studied together, but 2 site combination of the corpus (CD) was inferior to 5 site biopsies when studied individually. Single site biopsy from any of the 5 sites was not efficient in Hp detection compared to the 5 site biopsies. We recommend any combination of 3 site biopsies of the standard 5 site biopsies of the Updated Sydney system for Hp detection in non-ulcer dyspepsia. 3 biopsies are time saving and cost effective compared to 5 biopsies. Results of this study are in concordance with the previous study by Genta et al which recommended combination of biopsies from incisura, prepyloric antrum of greater curvature and corpus of greater curvature for Hp detection.[6] We do not recommend combination of 2 sites or single site biopsy for Hp detection in NUD, as the results of single site biopsies, combination of 2 sites from corpus were inferior to 5 site biopsies. Though other combination of 2 site biopsies did not differ significantly from 5 site biopsies, we do not recommend 2 site biopsies as they are affected by patchy Hp distribution. RUT was less sensitive in Hp detection, so RUT alone is not recommended for Hp detection in NUD.

Limitations

Data regarding regular or intermittent use of PPI's, PPI used, dose of PPI used was not obtained in detail to make any conclusive remarks about the influence of PPI.

CONCLUSION

3 biopsies are as effective as 5 biopsies for Hp detection in people with Non ulcer dyspepsia. 3 biopsies are cost effective and time saving compared to 5 biopsies. However, the same recommendation cannot be made when looking atrophy or intestinal

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metaplasia or for Hp in the presence of any endoscopic lesions. RUT alone is not sensitive enough to rule out Hp infection in NUD.

REFERENCES

1. Mahadeva S, Goh K-L. Epidemiology of functional dyspepsia: a global perspective. World J Gastroenterol. 2006 May 7;12(17):2661–6.
2. Richter JE. Dyspepsia: organic causes and differential characteristics from functional dyspepsia. Scand J Gastroenterol Suppl. 1991;182:11–6.
3. Marshall BJ. The 1995 Albert Lasker Medical Research Award. Helicobacter pylori. The etiologic agent for peptic ulcer. JAMA. 1995 Oct 4;274(13):1064–6.
4. Sugano K, Tack J, Kuipers EJ, Graham DY, El-Omar EM, Miura S, et al. Kyoto global consensus report on Helicobacter pylori gastritis. Gut. 2015 Sep;64(9):1353–67.
5. Yang Y-X, Brill J, Krishnan P, Leontiadis G, American Gastroenterological Association Clinical Practice Guidelines Committee. American Gastroenterological Association Institute Guideline on the Role of Upper Gastrointestinal Biopsy to Evaluate Dyspepsia in the Adult Patient in the Absence of Visible Mucosal Lesions. Gastroenterology. 2015 Oct;149(4):1082–7.
6. Genta RM, Graham DY. Comparison of biopsy sites for the histopathologic diagnosis of Helicobacter pylori: a topographic study of H. pylori density and distribution. Gastrointest Endosc. 1994 Jun;40(3):342–5.
7. Malfertheiner P, Megraud F, O'Morain CA, Atherton J, Axon ATR, Bazzoli F, et al. Management of Helicobacter pylori infection--the Maastricht IV/ Florence Consensus Report. Gut. 2012 May;61(5):646–64.
8. Sipponen P. Gastric cancer: pathogenesis, risks, and prevention. J Gastroenterol. 2002 Jan 1;37(13):39–44.
9. Asghar RJ, Parsonnet J. Helicobacter pylori and risk for gastric adenocarcinoma. Semin Gastrointest Dis. 2001 Jul;12(3):203–8.
10. Sleisenger and Fordtran's Gastrointestinal and Liver Disease-2 Volume Set - 10th Edition
11. Singh P, Goswami KC, Gupta BB. Gastric mucosal biopsies in non ulcer dyspepsia: A histopathologic study. Asian J Med Sci. 2016;7(2):80–4.
12. Lee H-C, Huang T-C, Lin C-L, Chen K-Y, Wang C-K, Wu D-C. Performance of Routine Helicobacter pylori Invasive Tests in Patients with Dyspepsia. Gastroenterol Res Pract. 2013.
13. Zhang L, Eslick GD, Xia HH-X, Wu C, Phung N, Talley NJ. Relationship between alcohol consumption and active Helicobacter pylori infection. Alcohol Alcohol Oxf Oxfs. 2010 Feb;45(1):89–94.
14. Nafeeza MI, Isa MR, Kudva MV, Ishak MS, Mazlam MZ, Haron A, et al. Helicobacter Pylori Related Functional Dyspepsia in a Defined Malaysian Population. Malays J Med Sci MJMS. 2000 Jan ;7(1):22–6.
15. de Martel C, Parsonnet J. Helicobacter pylori infection and gender: a meta-analysis of population-based prevalence surveys. Dig Dis Sci. 2006 Dec;51(12):2292–301.
16. Contreras M, Fernández-Delgado M, Reyes N, García-Amado MA, Rojas H, Michelangeli F. Helicobacter pylori Infection in Rural and Urban Dyspeptic Patients from Venezuela. Am J Trop Med Hyg. 2015 Oct 7;93(4):730–2.
17. Xu C, Yan M, Sun Y, Joo J, Wan X, Yu C, et al. Prevalence of Helicobacter pylori infection and its relation with body mass index in a Chinese population. Helicobacter. 2014 Dec;19(6):437–42.
18. Suki M, Leibovici Weissman Y, Boltin D, Itskoviz D, Tsadok Perets T, Comaneshter D, et al. Helicobacter pylori infection is positively associated with an increased BMI, irrespective of socioeconomic status and other confounders: a cohort study. Eur J Gastroenterol Hepatol. 2018 Feb;30(2):143–8.
19. Siddiqui B, Yakoob J, Abbas Z, Azmat R, Fatima SS, Awan S. Distribution of Helicobacter pylori infection and abnormal body- mass index (BMI) in a developing country. J Infect Dev Ctries. 2018 May 31;12(5):342–6.
20. Khalifa M aldeen, Khudair S, Almaksoud A. Cigarette smoking status and Helicobacter pylori infection in non-ulcer dyspepsia patients. Egypt J Chest Dis Tuberc. 2014 Jul 1;63.
21. Hamrah MH, Hamrah MS, Hassan Hamrah M, Kanda M, Hamrah AE, Dahi AE, et al. Prevalence of Helicobacter Pylori Infection in Dyspeptic Patients in Andkhoy Afghanistan. Asian Pac J Cancer Prev APJCP. 2017 26;18(11):3123–7.
22. Kuipers EJ, Uyterlinde AM, Peña AS, Hazenberg HJ, Bloemena E, Lindeman J, et al. Increase of Helicobacter pylori-associated corpus gastritis during acid suppressive therapy: implications for long-term safety. Am J Gastroenterol. 1995 Sep;90(9):1401–6.

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