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Prevalence of oral *Helicobacter pylori* infection in dyspeptic patients with gastric *Helicobacter pylori* infection

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Abstract
Introduction: *H.pylori (HP) infection is a major cause of gastro-duodenal disease burden worldwide, causing benign as well as malignant lesions. Various methods are available for diagnosis of gastric H. pylori (gHP) infection. Presence of oral HP infection is a well documented phenomenon. Rapid urease test is being used as a quick and reliable test for detection of gHP.*
Aim: *We endeavor to find out whether detection of oral H. pylori (oHP) infection, using a cheap but reliable, non-invasive test like rapid urease slide test (RUT) in patients undergoing upper GI endoscopy (UGIE) for dyspepsia, predict the occurrence of gHP.*
Materials and Method: *We serially evaluated 250 patients undergoing routine upper GI endoscopy (UGIE) for dyspepsia over a period of 1 year, for presence of gastric and oral H. pylori. Patients with red flags and significant co-morbidities were excluded.*
Results: *Overall prevalence for gHP was 78.8% (197 out of 250 patients while the overall prevalence of oHP was 63.6 % (159 out of 250 patients). Patients with duodenitis and duodenal ulcer had the highest occurrence of gastric and oral H.pylori infection. Oral RUT was positive in 72.97% cases of duodenitis and 78.04% cases of duodenal ulcer.*
Conclusion: *Oral swab detection of Helicobacter pylori using RUT is helpful to detect the occurrence of gastric H. pylori in those patients with gastro-duodenal lesions, especially duodenitis and duodenal ulcers. This may, in the long run, be helpful to reduce the disease burden of H. pylori related diseases.*
Keywords: *Helicobacter pylori, dyspepsia, rapid urease test, oral plaque, upper GI endoscopy.*

Introduction

For several decades the dictum of "no acid, no ulcer" (originally – "Ohne saueren Magensaft kein peptisches Geschwür") – acid causes ulcer, coined by Dragutin (Carl) Shwarz[(1)], held sway in medical parlance. It took some extra-ordinary Nobel prize winning "Robert Koch style medical detective work" on part of Marshal [(2)] and Warren to overcome this dogma in 1984[(3)]. Their discovery lead to conclusion that the enigmatic spiral bacterium Helicobacter pylori was responsible for about 90% of duodenal ulcers and 80% of gastric ulcers.

However, cheap, non-invasive method to detect gastric H. pylori (gHP) still eludes us. The rapid urease test (RUT) has high sensitivity and

specificity (> 98%) [4]. We endeavor to evaluate if oral Helicobacter pylori (oHP) detection by a simple and cheap dry rapid urease test (RUT), could predict the presence of gastric H. pylori (gHP), in patients undergoing upper GI endoscopy (UGIE) for dyspeptic symptoms and preclude the need for costly endoscopic gastric biopsy in resource poor settings.

Material and Methods

We serially enrolled all the consecutive patients undergoing upper GI endoscopy for dyspeptic complaints from June 2014 to May 2015 (1 year). Routine outpatients referred for upper GI endoscopy for dyspeptic symptoms like, epigastric pain, bloating, fullness, early satiety, belching or various combinations thereof, of at least 4 weeks duration were included. Informed consent was taken. The study was approved by the institutional ethics committee.

Patient <18 years of age, > 60 years of age, pregnant patients, those with significant co-morbidities (CKD, CLD, CCF, pre-existing malignancies), those with recent (within past 1 month) use of antibiotics, those with concurrent NSAIDs use, those with red flags (dysphagia, weight loss, anemia, GI bleed etc.) were excluded from the study. Indoor admitted patients were also excluded from the study.

Each patient was thoroughly evaluated for symptoms using a questionnaire and underwent a thorough physical examination. Before upper GI endoscopy, supra-gingival dental plaque material was obtained using sterile swab sticks. Two sticks were used and scrapings were made, one each on the upper and lower first molars[5] (Song Q. 2000). Material obtained was smeared on dry rapid urease test (RUT) slide impregnated with a drop of sterile normal saline. Slide was observed for color change, from yellow to pink, for at least half an hour as per the manufacturer's instructions.

Each patient underwent upper GI endoscopy with the throat sprayed with local anesthetic. During UGIE, two biopsies were taken, one from the antrum and another from mid-body along the greater curvature. This biopsies were transferred to a slide well of dry rapid urease test and moistened with a drop of normal saline as described earlier. Oral contamination of the biopsy channel during intubation was prevented by application of a tiny ball of soft wax at the tip of the biopsy channel. This was safely dislodged in stomach during the passage of biopsy forceps. Endoscopic finding were documented, especially with regards to presence or absence of gastritis, duodenitis, gastric and duodenal ulcers. Statistical analysis was done by using descriptive and inferential statistics using chi-square test, sensitivity and specificity and software used in the analysis were SPSS 17.0 version and GraphPad Prism 6.0 version and $p<0.05$ is considered as level of significance.

Results

During the study period, a total of 780 patients underwent diagnostic upper GI endoscopy. 283 patients were excluded from the study as per the above exclusion criteria. A total of 497 patients were eligible for inclusion. However, due to financial constraints only the first consecutive 250 patients were included in the study.

Table-1: Age distribution and H. pylori infection

Age groups	RUT positive for Gastric H. pylori (n=197)	RUT positive for Oral H. pylori (n=159)	χ2-value = 0.02
18-39	118 (59.89%)	97 (61%)	p=0.88,NS
40-59	79 (40.1%)	62 (39%)	

Out of these 250 cases, 148 (59.2%) patients were male and 102 (40.8%) were female. The male to female ratio was 1.45:1. Mean age of the patients was 48.8 ± 7.2 years. Duration of symptoms varied from 6.04 ± 1.42 month (mean ± SD). 149 (59.6%) patients had gastritis, 37 (14.8%) had duodenitis, 23 (9.2 %) had gastric ulcer and 41 (16.4%) had duodenal ulcers. Overall prevalence (Table-1) for gastric H. pylori (gHP) was 78.8% (197 out of 250 patients); prevalence among males and females was 80.18 % and 77.69% respectively. The overall prevalence of oral H. pylori (oHP) was 63.6 % (159 out of 250 patients).

Table-2: Upper GI endoscopy findings and H. pylori infection

Findings	Gastric H. pylori + (n=197)	Oral H. pylori + (n=159)	χ- value
Gastritis (n=149)	114 (57.86%)	86 (63.6%)	0.75, p=0.38, NS
Duodenitis (n=37)	30 (81.08%)	27 (72.97%)	1.80, p=0.17, NS
Gastric ulcer (n=23)	17 (73.91%)	14 (60.86%)	3.85, p=0.049, Sig.
Duodenal ulcer (n=41)	36 (87.8%)	32 (78.04%)	4.26, p=0.039, Sig.

Among those with gastritis (n=149), gHP was positive in 114 (57.86%) patients while oHP was present in 86 (63.6%) cases (p = N.S.). Patients with duodenitis (n=37), had gHP in 30 (81.08%) and oHP in 27 (72.97%) patients (p = N.S.). Gastric ulcer patients (n=23) has gHP positive in 17 (73.91%) cases and oHP present in 14 (60.86%) cases (p = 0.049). Whereas, patients with duodenal ulcer (n=41) had gHP detected in 36 (87.8%) and oHP in 32 (78.04%) cases (p = 0.039) (Table-2).

The overall prevalence of gastric H. pylori in gastritis was 59.6%, 14.8% in duodenitis, 9.2% in gastric ulcer and 16.4% in duodenal ulcer (Table-2).

Table-3: Comparison of gastric versus oral Helicobacter pylori infection

Parameter	RUT positive for oral H. pylori (oHP+)	RUT negative for Oral H. pylori (oHP-)	Total	(p value)
Gastric H. pylori positive RUT (gHP+)	135(84.91%)	62(68.13%)	197(78.80%)	9.74,p=0.0018,S
Gastric H. pylori negative RUT (gHP-)	24(15.06%)	29(31.87%)	53(21.20%)	
Total	159(100%)	91(100%)	250(100%)	

Detection of oral H. pylori (oHP) by RUT had a sensitivity of 84.91% (95% CI=78.36-90.08%), specificity of 31.87% (95% CI=22.49-42.47%), positive predictive value of 68.53% (95% CI=61.55-74.94%), negative predictive value of 54.72% (95% CI=40.45-68.44%) and diagnostic accuracy of 65.6% for presence of gastric H.pylori infection (Table-3).

Table-4: Oral H. pylori infection in gastric H. pylori positive patients*

Positive for gastric H. pylori	Oral H. pylori + (n=135)	Oral H. pylori - (n=62)	χ2 value
Gastritis (n=114)	67 (58.77%)	47 (41.22%)	6.48,p=0.010,S
Duodenitis (n=30)	25 (83.083	5 (16.66%)	87.12,p=0.0001,S
Gastric ulcer (n=17)	11 (64.7%)	6 (35.29%)	18,p=0.0001,S
Duodenal ulcer (n=36)	32 (88.8%)	4 (11.11%)	121.7,p=0.0001,S

*24 patients had positive oHP but were negative for gHP (9.6%) and were excluded from this table for analysis.

Occurrence of oHP (oHP+) was analyzed in all patients with positive gHP (gHP+) test (Table-4). Patients with gastritis and gHP+ had oHP detected in 67 (58.77%) and undetected in 47 (41.22%) cases (p = 0.010). Patients with duodenitis and gHP+ had oHP+ in 25 (83.3%) and oHP- in 05 (16.66%) cases (p = 0.0001). 11 (64.7%) patients had oHP+ and 6 (35.29%) had oHP- in those with gHP+ gastric ulcers. (p = 0.0001). Patients with gHP+ duodenal ulcers showed presence of oHP in 32 (88.8%) and absence in 4 (11.11%) cases (p = 0.0001). 24 patients had positive oHP but were negative for gHP (9.6%).

Patients with duodenitis and duodenal ulcer had the highest occurrence of gastric and oral H.pylori infection. Oral RUT was positive in 72.97% cases of duodenitis and 78.04% cases of duodenal ulcer (p=0.0001).

Discussion

Helicobacter pylori has held generations of researchers in bewilderment. It had been found more than a century ago by Polish clinical researcher, W. Jaworski [6] in gastric mucosa and was neglected thereafter, being labeled as "harmless". Relatively recent landmark discovery by Warren and Marshall [7] lead to linking this bacterium to the occurrence of a wide variety of benign and malignant gastro-duodenal lesions, as well as possible extra-gastric associations. One school of thought considers it to be a "commensal" [8], protecting us against diseases like Barrett's esophagus, GERD and lower esophageal adenocarcinoma. However, the disease

manifestations probably far outweigh the "benefits" of this micro-organism.

The overall prevalence of H. pylori is high in developing countries and low in developed countries. In general, H.pylori seropositivity increases progressively with age. In developing countries H. pylori is markedly more prevalent in younger age group.

In our study the overall presence of gastric H.pylori was 78.8%. Louw et al [9], found the presence of gastric H. pylori to be 63% in 106 South African patients, with a lower prevalence among the whites (40%) than in native population (71%). Khan [10] found a gastric H.pylori prevalence of 67% in 528 consecutive endoscopic biopsies. Prevalence was highest in the 26-33 years age group. They found no significant rise in gastric H.pylori prevalence with increasing age. Another recent sero-prevalance study from India [11] in asymptomatic population, found anti H.P IgG/IgA in age less than 10m years, 10-19 years , 20-29 years and 30 – 39 years and more than 40 years, the highest prevalence was seen in 30 -39 years age group. Serological studies from India [12] found H.pylori prevalence of 22%, 56% and 88% (IgG) in 0-4, 5-9 and 10-19 years age group; remaining constant up to the fifth decade. Significant fall in seropositivity for HP was seen from 5th to 7th decade. In our study young patients (<40 years) had a higher prevalence of gastric H.pylori as well as OHP , 59.89% and 61% versus a lower prevalence in 40 -60 years age group viz-.,40.1% and 39% for gHP and oHP respectively.

De Martel [13], conducted a meta analysis and found that male gender was significantly associated with H.pylori infection (summary OR 1.16) in 18 adult populations, indicating it a global and homogeneous phenomenon. However this preponderance was not evident in children. In our study group the overall gastric H. pylori prevalence was 80.18% among males and 77.09% among females (P= zzz). Khan [10] found the prevalence of gastric H.pylori in biopsy studies of dyspeptic patients to be 69% in males and 63% in females. Perri-F et al [14] found the prevalence of H.pylori in organic dyspepsia as 56.2 % in males and 43.8% in females.

Perri-F et al [14] detected H. pylori infection in 71.8% of patients with organic dyspepsia and 65.0 % patients with functional dyspepsia. It was significantly higher in patients with duodenal ulcers (90.4 %). Karczenwska E et al. [15] studied 329 patients with dyspeptic symptoms. 257 (78.1%) patients had chronic gastritis, 15 (4.5%) patients had gastric ulcer and 57 (17.32%) patients had duodenal ulcer (DU). H. pylori detection by PCR in 30 patients with DU was 95% in antral mucosa and 35% in gingival pocket material, which fell to 23% and 10% after 1 week of triple drug therapy. In our study, 149 (59.6%) patients had gastritis, 37 (14.8%) had duodenitis, 23 (9.2%) had gastric ulcer and 41 (16.4%) had duodenal ulcer. gHP was positive in 78.8% and oHP in 63.6%. We could not study the effect of triple drug regimen on gHP / oHP positivity, but we observed a much higher prevalence of oHP in our study (63.6% vs. 35%).

Liu et al. [16] conducted nested PCR study on dental plaques and RUT plus antral biopsy for detection of oHP and gHP respectively, in 443 dyspeptic patients. oHP was found in 59.4% and gHP in 61.6 %. Similarly, DeSousa et al. [17] studied 97 dyspeptic patients and found gHP in 75.5% and oHP in 99.3% using RUT. In our study detection of oral H. pylori (oHP) by RUT had a sensitivity of 84.91% (95% CI=78.36-90.08%), specificity of 31.87% (95% CI=22.49-42.47%), positive predictive value of 68.53% (95% CI=61.55-74.94%), negative predictive value of 54.72% (95% CI=40.45-68.44%) and diagnostic accuracy of 65.6% for presence of gastric H.pylori infection. oHP infection was significantly associated with gHP in patients with duodenitis and duodenal ulcer.

Song et al. [5] demonstrated a specific distribution pattern for H.pylori in the oral cavity, with a higher prevalence in plaques from molars than from premolars or incisors. They postulated that this may be related to the micro-aerophilic

character of H.pylori, with oxygen exposure gradually decreasing from the incisors to the molars, thus favoring growth of H.pylori in molar region. H.pylori positivity was 82.1% for molars, 64.1% for, premolars and 59.0% for the incisor plaques.

The reasons for reported wide variations in oHP prevalence [18] could be related to differences in baseline population characteristics like, age, socio-economic status, place of residence; state of oral/dental hygiene, social habits (like chewing betel quid, tobacco etc.), site of plaque sampling (incisors versus molars) and in case of RUT, on presence of other urease producing bacteria in oral cavity. Development of H.pylori specific RUT will definitely help solve this conundrum and streamline the diagnosis and treatment.

In resource poor setting evaluation of dyspeptic patients, it is imperative to have a point-of-care test that is cheap, easy, non-invasive, reproducible indicator of gastric H. pylori infection. Radio-isotope test though simple, are expensive. Upper GI endoscopy is minimally invasive and costly due to use of disposables (biopsy forceps are costlier than swabs). POC detection of oral *H. pylori* using rapid urease dry test can be useful in predicting the occurrence of gastric *H. pylori*. It can be easily carried out on out-patient basis by nursing staff or physician assistant.

Limitations of this study include a relatively small sample size (due to financial constraints). This study could not include pediatric population, widely found to have the highest incidence of Helicobacter pylori in other studies.

Histopathology analysis of gastric biopsy specimens could not be done, also due to financial constraints. This study included only the referral patients, hence cannot be considered to be a representative of the general population. Long term follow-up and repeating these tests after triple drug therapy would definitely help in better understanding of this enigmatic infection.

Conclusion

Oral swab detection of Helicobacter pylori using RUT is helpful to detect the occurrence of gastric H. pylori in those patients with duodenitis and duodenal ulcers. This may, in the long run, be helpful to reduce the disease burden of H. pylori related diseases. Further development of highly sensitive probes to detect the presence of H. pylori in oral cavity is highly desirable. Probably a larger, prospective population based study with long term follow-up can clear up the association of oral colonization with H. pylori and the development of gastro-duodenal lesions.

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