



Helicobacter Pylori Infection in Gross and Microscopic type of Gastric Adenocarcinoma; a Comparative Study



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Abstract

Objective: To compare the association of helicobacter Pylori (*H.pylori*) infection in Gross and Microscopic type of gastric adenocarcinoma patients attending a tertiary care hospital in Karachi.

Material & methods: This was a Comparative, cross sectional study carried out at Al-Tibri medical college Karachi in collaboration with Diagnostic and research Lab (DDRL) from Feb 2015 to Sep 2015. This study integrated 92 gastric tissues in which 79 were gastric adenocarcinoma tissue and 13 were control sample taken from sleeve gastrectomy. For gross morphology of gastric carcinoma, the gross types were divided into four types, fungating, Ulcerative, infiltrating and polypoid and it was divided into two groups Nondependent *H.pylori* and dependent *H.pylori* gastric carcinoma. For Microscopic type of gastric carcinoma, the tumor was divided into Diffuse and Intestinal type and it was further divided into two groups: Nondependent *H.Pylori* and dependent *H.pylorigastric* carcinoma. SPSS was used to analyze the data.

Results: Gross morphology and microscopic type of gastric carcinoma showed an insignificant P-value of 0.443 which shows that there was no significant difference found between these two parameters. The relation between the dependent *H.pylori* in gross morphology of gastric carcinoma and nondependent *H.pylori* in microscopic type of gastric carcinoma the P-value was found to be 0.52 shows no significant difference and the relation between dependent and nondependent *H.pylori* in microscopic type of gastric carcinoma the P-value was found to be 0.771 shows no significant difference.

Conclusion: Grossly the ulcerated type and microscopically the intestinal type was significantly present in dependent *H.pylori* gastric carcinoma but there was no association found between gross and microscopic type of dependent *H.pylori* gastric carcinoma.

Keywords : Gastric carcinoma; Helicobacter pylori; Sleeve gastrectomy

Abbreviations: *H pylori*: Helicobacter Pylori; DUHS: Dow University of Health Sciences; DDRL: Dow Diagnostic and Research Lab; SPSS: Statistical Package for Social Sciences

Introduction

Gastric cancer represents a major clinical problem, linked with considerable morbidity and mortality [1]. Gastric cancers are diagnosed every year with 1 Million cases reported and it is the 4th most leading cause of death worldwide. Gastric cancer is the 2nd leading cause of cancer related death and approximately 700,000 of people surrender their life because of carcinoma stomach [2]. Gastric cancer is uncommon before the age of 40, but its frequency gradually increase thereafter and peaks in the seventh decade of life [3]. The distinct geographic disparity,

time trends and the migratory effect on the gastric cancer incidence recommend that environmental or lifestyle factors are major contributors to the etiology of disease [4]. Previous to the discovery of the organism, it was recognized that gastric adenocarcinomas characteristically arose in areas of gastritis. When the association between *H. pylori* and chronic gastritis was established, investigators began to take interest in the contributory role of *H. pylori* in gastric cancer. The first studies to examine the association between *H. pylori* and gastric cancer

were ecological, comparing the regional frequency of *H. pylori* with the occurrence of gastric cancer [5]. *Helicobacter pylori* may generate an atmosphere which is highly positive to produce carcinogenesis and share with other life style and environmental exposures.

There is an evidence that consumption of salty foods and N-nitroso compound and low intake of fresh fruits and vegetable augment the threat of gastric cancer. *Helicobacter pylori* gastritis support the growth of nitrosating bacteria which catalyze the production of carcinogenic N-nitroso compound [6]. An area of the world with a low prevalence of *H. pylori* infection tend to have a comparatively low frequency of gastric cancer, but geographic disparity in gastric cancer rates cannot be explained exclusively by variations in *H. pylori* prevalence. For example, populations in many parts of Africa and India have a high prevalence of *H. pylori* infection but a relatively low incidence of gastric cancer [7]. *H. pylori* colonizes the stomach and elicits a gastric mucosal inflammatory response termed “gastritis” in both humans and experimentally infected animals. Once recognized in the human stomach, *H. pylori* and gastric inflammation can persevere for many decades in the lack of antimicrobial treatment. Longitudinal studies point out that gastritis is one of the first noticeable changes in a stepwise pathway of histologic abnormalities that can eventually terminate in gastric cancer: inflammation, gastric atrophy (loss of specialized cell types such as parietal cells and chief cells), intestinal metaplasia (presence of intestinal-type epithelium in the stomach) and dysplasia [8,9].

Grossly, the carcinoma of stomach has wide distinction: polypoid tumor (type I), Fungating tumor (Type II), Ulcerated tumor (Type III), Deeply invasive tumor (Type IV). Fungating tumor grow mainly into lumen, plane, ulcerated and severely invasive tumor develop largely all the way through the wall of stomach [10]. Microscopically, WHO describe gastric carcinoma into: Adenocarcinoma (Intestinal & Diffuse) Papillary, Tubular adenocarcinoma, Mucinous adenocarcinoma, signet ring cell carcinoma, squamous cell carcinoma [11]. The present study was designed to compare the frequency of *H. pylori* infection in gross and microscopic type of gastric carcinoma in a tertiary care hospital of Karachi.

Material and Methods

This was a comparative cross sectional study with Non-probability convenient sampling technique conducted in Dow Diagnostic and research Lab (DDRL) in association with Al-Tibri medical college Karachi from February to September 2015. A total of 92 gastric tissue samples were examined along with Informed consent and Clinical biodata of patients. The study was approved by the Ethical committee of Dow University of health sciences (DUHS) and Isra University Hyderabad Sindh. Overall 92 gastric adenocarcinoma samples were selected in this study. In the frequency of gross types of gastric carcinoma, we found only 16 large biopsy samples out of 79 samples, the rest of 63 samples were small biopsy samples. Therefore, gross

morphological classification was possible only on these 16 samples. The sample size was calculated using an online tool where power of study was set at 80, confidence level was 95% and margin of error was kept at 5%. Patients who had a history of gastrointestinal symptoms with clinical support of Gastric cancer were selected regardless of age and gender, resection specimen as well as gastric cancer biopsies along with this for control samples, sleeve gastrectomy specimen were selected from the patient who had a history of obesity, regardless of age and gender.

Biopsies of tissue taken from cardiac region and post chemotherapeutic carcinoma were excluded. To compare the gross types of gastric adenocarcinoma with microscopic type of gastric adenocarcinoma, the samples were divided into two groups, (according to Lauren and WHO classification), microscopically the tumors divided into two Intestinal type and diffuse type and macroscopically (Borman classification) dividing it into four Type I polypoidy, type II Fungating, Type III ulcerated, type IV Infiltrating. The samples were further divided into two groups dependent *Helicobacter pylori* gastric adenocarcinoma and non-dependent *Helicobacter pylori* gastric adenocarcinoma. Biopsy samples were examined grossly and microscopically. Biopsy materials were fixed in 10% neutral buffered formalin, embedded in paraffin and 5µm sections were set for biopsy materials and they were cut to perform subsequent staining [12]. H&E, Giemsa Stain (for *H. pylori*) were the staining techniques used for staining the slides for histopathological examinations [13].

Statistical analysis

Data analysis was done using statistical package for social sciences (SPSS) version 20.0. All Categorical Variables were expressed in frequency and percentage and continuous variables were stated as Mean and standard deviation Chi square test was used to assess the association between the variables. P value of ≤ 0.05 was taken as statistically significant.

Results

In the total of 92 gastric tissue samples, of these 79% samples were from gastric carcinoma while total 13% were control samples. In these 79% cases 63.3% were males and 36.7% were females. To compare the relation between gross type of gastric carcinoma and microscopic type of gastric adenocarcinoma we found that intestinal type of gastric carcinoma was present in 11.3% in ulcerated type of gastric carcinoma, 3.8% in Fungating type, 3.8% in Invasive type of gastric carcinoma and no intestinal type was found in Polypoid type of gastric carcinoma. 81.1% Intestinal type and 76.9% diffuse type was present in small biopsy sample. In other type of microscopic gastric carcinoma that is diffuse type we found that 11.5% was found in ulcerated type, 11.5% in fungating type and no tumor type found in invasive and polypoid type. The P-value was found to be 0.443 which shows that there is no significant difference noted between these variables (Table 1). On the other hand if we compare the

frequency of Helicobacter pylori between the gross morphology of gastric carcinoma we found that 12.7% Dependent H.pylori was present in ulcerated type of gastric carcinoma, 7.0% was found in Fungating type of Gastric carcinoma and 2.8% was found in Invasive type of Gastric carcinoma. 77.5% dependent H.pylori gastric carcinoma was present in small biopsy sample. So the P-Value was found to be 0.52 which shows that there is no significant difference between these two variables (Table

2). In microscopic type of Gastric carcinoma, 62.5% intestinal type were found in non-dependent H.pylori gastric carcinoma and 37.5% were found in Diffuse type of gastric carcinoma. 67.6% intestinal type were found in dependent H.pylori gastric carcinoma and 32.4% diffuse type were found in dependent H.pylori gastric carcinoma. The P-Value was found to be 0.771, shows non-significant difference (Table 3).

Table 1: Association of Gross type (Macroscopic) with Microscopic type of Cancer.

Type of Cancer (Microscopic)	Gross Type / Macroscopic				Total	P-value
	Small Biopsy	Ulcerated	Fungating	Invasive		
Intestinal	43	6	2	2	53	0.443
	81.10%	11.30%	3.80%	3.80%	100.00%	
Diffuse	20	3	3	0	26	
	76.90%	11.50%	11.50%	0.00%	100.00%	
Total	63	9	5	2	79	
	79.70%	11.40%	6.30%	2.50%	100.00%	

Table 2: Association of Macroscopic type of cancer with groups.

Group	Gross type/Macroscopic				Total	P-value
	Small biopsy	Ulcerated	Fungating	Invasive		
Non-Dependent	8	0	0	0	8	0.52
	100.00%	0.00%	0.00%	0.00%	100.00%	
Dependent	55	9	5	2	71	
	77.50%	12.70%	7.00%	2.80%	100.00%	
Total	63	9	5	2	79	
	79.70%	11.40%	6.30%	2.50%	100.00%	

Table 3: Association of Microscopic type of cancer with groups.

Group	Type of Cancer (Microscopic)		Total	P-value
	Invasive	Diffuse		
Non-Dependent	5	3	8	0.771
	62.50%	37.50%	100.00%	
Dependent	48	23	71	
	67.60%	32.40%	100.00%	
Total	53	26	79	
	67.10%	32.90%	100.00%	

Discussion

Gastric Cancer is the 4th most frequently diagnosed cancer and it is the second most frequent cause of cancer related death worldwide [2,14]. Gastric carcinogenesis is a multifactorial process in which several factors are involved, some milieu lesions are also present, these lesions provide prospect to decrease the mortality rate of gastric carcinoma by earlier recognition of these lesions [15]. Helicobacter pylori is a gram negative bacterium currently colonize the human stomach and also have been the centre of basic biochemical and clinical

research since its innovation [16]. This study compare the association of H.pylori infection in gross and Microscopic type of Gastric adenocarcinoma and according to our study there is no significant difference noted between the presence of H.pylori infection in gross and microscopic type of gastric adenocarcinoma. In our study, grossly the ulcerated type was present in high frequency. In a previous study of USA report that the most common macroscopic type of gastric carcinoma was fungating tumor 36% and ulcerated was 25%, infiltrating 26% and polypoid was 7% [10]. Our study also reveals the presence of intestinal type of gastric carcinoma is more common as compare to diffuse type. Another study from Karachi Pakistan also report that intestinal type was more common than diffuse [17]. A retrospective study from USA determined the frequency of Helicobacter pylori in Intestinal type gastric carcinoma was 89% as compare to diffuse which was 31.8% [18]. Another study reported the reason for increase in frequency of intestinal type of gastric carcinoma was often associated Intestinal metaplasia and presence of helicobacter pylori infection [19]. In our study, grossly the ulcerated type and microscopically the intestinal type were significantly present in dependent helicobacter pylori gastric carcinoma but there is no association found between gross and microscopic type of gastric carcinoma. Another study

reveals grossly type I lesion (protruding type) and type IIa lesion (superficial elevated) are likely to represent intestinal type whereas diffuse type are likely to be type IIc (superficial depressed) or type III (excavated or Ulcerated) lesions [20]. The reason could be the selected cases diagnosed in advanced stages so grossly the lesion was ulcerated and in our society the increase in the frequency of intestinal type was due to the influence of environmental factors, poor hygiene, overcrowding and low socio economic status can lead to development of H pylori and due to this it can progress to intestinal type of gastric carcinoma.

Conclusion

Grossly the ulcerated type and microscopically the intestinal type was significantly present in dependent H.pylori gastric carcinoma but there was no association found between gross and microscopic type of dependent H.pylorigastric carcinoma.

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