PREVALENCE OF HELICOBACTER PYLORI INFECTION IN GASTRIC CANCER IN PATIENTS ATTENDING A TERTIARY REFERRAL UNIT: A CROSS SECTIONAL STUDY

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ABSTRACT

BACKGROUND

The prevalence of gastric cancer is associated with several factors including geographical location, diet, and genetic background of the host. Helicobacter pylori infection is an important etiological factor for the occurrence of non-cardiac gastric adenocarcinoma in developing and underdeveloped countries with poor hygienic conditions. There are no documented studies on the association of gastric carcinoma with H. pylori from the mid Kerala districts of Palakkad, Thrissur and Malappuram. These districts have got the highest incidence in Kerala for carcinoma stomach and Government Medical College, Thrissur is the primary referral institution for such cases.

METHODS

A prospective cross-sectional study was conducted at General Surgery department of a tertiary care hospital of Kerala. Patients suspected to have carcinoma stomach undergoing endoscopy/open surgery, who have consented to take part in the study were tested for H. pylori infection.

RESULTS

Distribution of gastric adenocarcinoma and the prevalence of H. pylori, we found that H pylori was present in 29 cases of total 66 cases Prevalence of H. pylori is 43.9% among gastric carcinoma patients in this study.

CONCLUSIONS

Even though many advances in the understanding of gastric cancer have been made, the disease is still one of the malignancies with the highest incidence and mortality rates worldwide. It is believed that there is an overall decline in gastric cancers due to reduction and eradication of H. pylori infection with improved sanitation. Once carcinoma is detected, H. pylori is not given much significance. It is important to fully understand the inflammatory response initiated by the infection in order to fully block the cascade of events that lead to gastric cancer.

KEYWORDS

Gastric Cancer, Helicobacter pylori, Adenocarcinoma.

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BACKGROUND

Gastric adenocarcinoma is a major global health threat. Almost 1 million cases of gastric cancer are diagnosed each year, establishing this disease as the fourth most common cancer worldwide.[1]

This is one of the common causes of deaths and the etiological factors include salty food, low fibre diet, smoking, alcohol, previous history of gastric surgery, elderly high BMI people, low socio-economic class etc. More incidence of gastric cancers are seen with HNPCC, pernicious anaemia, FAP, Cowden syndrome, Peutz-Jeghers syndrome and Li-Fraumeni syndrome. Clustering of H. pylori infection is seen with gastric cancers that happens in families.[2,3]

There are two histological types of gastric carcinoma. Diffuse-type and intestinal-type adenocarcinoma, with changes through various histological stages. Intestinal-type adenocarcinoma is an end stage of histological transition from normal mucosa→ chronic superficial gastritis→ atrophic gastritis→ intestinal metaplasia→ dysplasia → adenocarcinoma.[4,5] This is more common in males. Many epidemiological studies showed close relation with H. pylori infection and increased incidence of gastric carcinoma by these histological changes.

H. pylori infection is strictly confined to the gastric mucosa, in the stomach and areas of gastric metaplasia and heterotopia in the duodenum. It promotes gastric carcino-genesis through multiple mechanisms. Bacterial toxins or ammonia released by urease activity and autoimmune

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response to gastric antigens initially causes peptic ulcer and later causes chronic gastric inflammation that can progress to the precancerous changes of atrophic gastritis and intestinal metaplasia. Chronic H pylori infection can also contribute to gastric mucosal instability by reducing gastric acid secretion (hypo-chlorhydria), which can promote the growth of gastric microbiome that processes dietary components into carcinogens.

H. pylori is a Gram negative micro-aerophilic spiral bacterium present in the stomach. It infects approximately 50% of the global population.[6] Crude etiologic-fraction calculations of data from studies suggest that 60 percent of gastric adenocarcinomas are attributable to infection with H. pylori.[7] Most infections are asymptomatic but chronic infection with H pylori is considered to lead to gastric ulcer and carcinoma.[8,9] Ammonia, phospholipase and cytotoxins produced by H. pylori in the stomach lumen results in gastric epithelial damage and abnormal cellular proliferation and increased incidence of malignancy. H. pylori decreases the ascorbic acid secretion, in turn reduces the anticarcinogenic effect by affecting the host's immune response towards the infections.

H. pylori infection leading to gastric carcinoma incidence is depending on the bacterial virulence to predispose the malignancy. In peptic ulcer disease CagA was strongly positive and Cag pathogenicity island (Cag PAI) positivity is mainly responsible for the antral gastritis, atrophic gastritis and gastric cancer.[10] Host signalling pathways are activated by H. pylori peptidoglycans to develop gastric malignancy. Vac A toxin present in H.pylori, suppressing the T cell responses helps to live longer and increases the pathogenicity. The host immune response, polymorphism, the environmental factors play a role in the development of gastric carcinoma.

H pylori can be eradicated with a short course of antibiotic treatment-triple drug regimen of lansoprazole 30 mg + amoxicillin 1000 mg + clarithromycin 500 mg twice daily for 2 weeks. Identifying and eradicating H pylori infection could represent a viable strategy to reduce the enormous disease burden of gastric cancer. For this we need to know the prevalence of H. pylori infection in patients with cancer stomach in our population. This study is envisaged in this regard to identify the association of H Pylori in Gastric adeno carcinoma patients in the Mid Kerala. Study of association of H Pylori and gastric adeno carcinoma is significant in that it gives a possible option of reduction in the incidence through the eradication even though the cause of Gastric cancer is multifactorial. Study conducted in India at Institute of Medical Sciences, Banaras Hindu University, Varanasi, 2002 showed many cases of gastric cancer were found to be positive for H. pylori infections.

There are no documented studies on the association of gastric carcinoma with H. pylori from the mid Kerala districts of Palakkad, Thrissur and Malappuram. These districts has got the highest incidence in Kerala for carcinoma stomach and Government Medical College, Thrissur is the primary referral institution for such cases. In 2015-2016 there were 252 cases of carcinoma stomach operated in 6 different units and 274 cases operated in 2016-2017. This cross-sectional study is envisaged to identify the prevalence of H Pylori infection in Gastric adenocarcinoma in the mid Kerala.

METHODS

A Prospective Cross-Sectional study conducted at General Surgery department of a tertiary care hospital of Kerala. Patients suspected to have carcinoma stomach undergoing endoscopy /open surgery tested for H. pylori infection subject to Surgery, Oncology, Gastroenterology.

Patients who has consented to take part in study, All patients suspected with carcinoma stomach and All patients in the initial stages of carcinoma stomach were taken into the study and patients who underwent Neoadjuvant chemotherapy was excluded from the study.

The study period is for two months. Consecutive sampling until the sample size of 67 is achieved which was calculated using the formula-

$$\frac{4pq}{d^2} = \frac{4*60*40}{12^2} \approx 67$$

Consent was obtained from patients coming to surgery department who are suspected or diagnosed of gastric carcinoma. History of the presenting symptoms is collected from the patient. A general examination is performed. The endoscopic punch biopsy specimen is sent to lab for histopathological and microbiological evaluation. H pylori are detected by rapid urease test in the lab. The endoscopic results including site of the carcinoma and presence of H pylori is collected. After completing survey in the study population, the data would be analysed in MS Excel and results would be expressed in proportions.

RESULTS

During the study period of 2 months conducted at Government medical college Thrissur, there were 212 number of endoscopies performed and 66 cases of carcinoma stomach cases were diagnosed on endoscopy and all were sequentially included in the project.

Age	Frequency	Percentage
1-20	3	4.9
21-40	15	22.8
41-60	31	46.7
61-80	17	25.6

Table 1

Particulars	Age
Mean	50.98
Median	54
Mode	54
Minimum	18
Maximum	80

Table 2

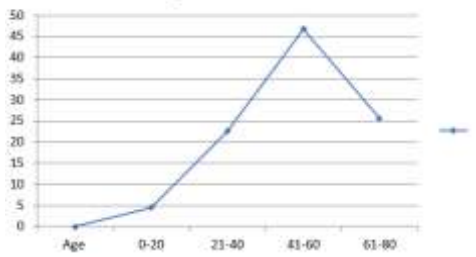

Figure 1. Age Distribution

Maximum gastric carcinoma cases are seen from 41-60 yrs.

The occurrence of gastric carcinoma below 40 years is 27.7% and above 40 is 72.3%. (Figure 1)

The incidence of gastric cancer in the study was more in males with an average of 60.6%. Female population contributed 39.4 percentage (Figure 2).

Gender	Frequency	Percentage
Male	40	60.6
Female	26	39.4
Total	66	100.0

Table 3

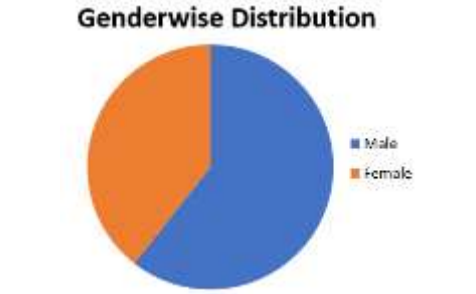

Figure 2. Gender Wise Distribution

Distribution of gastric cancer according to the site of tumours was as follows with distal tumours constituting the majority constituting 69.7% of Gastric adenocarcinoma

Particulars	No.	Percentage
Distal Adeno Carcinoma	46	69.7
Body of Stomach	6	9.1
Proximal Gastric Cancer	9	13.63
Diffuse Gastric Cancer	5	7.57

Table 4

On analysis of H Pylori in these cases done by Histopathology and microbiological assessment we found that H. pylori were present in 29 cases of total 66 cases. Prevalence of H. pylori is 43.9% among gastric carcinoma patients among this cohort. 56.1% there was no identifiable H. pylori in the samples. (Table 4)

H. pylori	Frequency	Percentage
Present	29	43.9
Absent	37	56.1
Total	66	100.0

Table 5

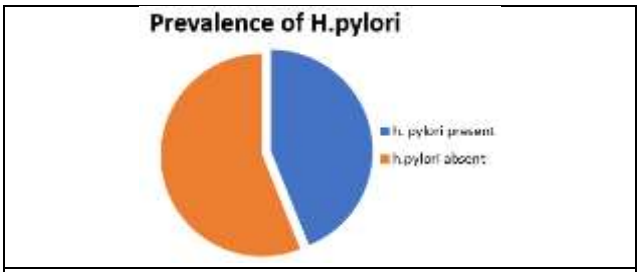

Figure 3. Prevalence of H. pylori

On analysis it was also found that the occurrence of gastric carcinoma below 40 yrs. is 27.7% and above 40 is 72.3% in our population. We analysed whether age co-relates with H pylori colonisation and it was found that the occurrence of H. pylori infection along with gastric carcinoma 7/18(38.8%) below 40 and 22/48(45.8%) above 40 yrs.

The association of H pylori colonisation with relevance to site of tumour was also analysed and it was as follows.

Particulars	No.	H. pylori
Distal Adenocarcinoma	46	21
Body of Stomach	6	2
Proximal Gastric Cancer	9	3
Diffuse Gastric Cancer	5	3

Table 6

More follow up and studies by systematic sampling will provide additional details into this area in our population

DISCUSSION

Reports regarding relationship of H. pylori infection to gastric carcinogenesis are conflicting in various studies. The age pattern of our study correlates most of the studies in this field and the incidence was Maximum gastric carcinoma cases are seen from 41-60 yrs. The occurrence of gastric carcinoma below 40 yrs. is 27.7% and above 40 is 72.3%. The study proves that H. pylori plays an important role in occurrence of gastric cancer. It also seen that although gastric cancer is seen more in males it is more associated with h pylori infection in females. The incidence is increased above 40 yrs. and maximum among 41-60 yrs.

The Gender distribution showed a male preponderance with the incidence of gastric cancer in the study was more in males with an average of 60.6%. Female population contributed 39.4%. This also correlates with western & Indian cancer Registry proportions. The analysis of the site of tumours showed even though there was slight increase in the diffuse and proximal gastric cancers the major bulk of the tumours were constituted by the Distal adenocarcinoma. This is in accordance to the expected distribution and out study also showed a similar distribution with Distal tumours contributing to 46/ 66 cases.

When we analysed the distribution of Gastric adenocarcinoma and the Prevalence of H. pylori the we found that H pylori was present in 29 cases of total 66 cases Prevalence of H. pylori is 43.9% among gastric carcinoma patients among this cohort. 56.1% there was no identifiable H. pylori in the samples.

Similar study conducted by AK Khanna and Friedman GD confirmed increased incidence of gastric adeno carcinoma with previous H. pylori infections.[2,5,6]

Even though the prevalence of H pylori in our population is less than the above studies presence of H pylori in 43.9% among gastric carcinoma patients among this cohort is significant. This suggests the eradication of h pylori in early cases will help to reduce incidence of gastric cancer in our population. More prospective studies are required to analyse the finer details of association of H. pylori in our population with gastric adenocarcinoma. This will also need assessment of other risk factors along with presence of H.pylori.

CONCLUSION

Even though many advances in the understanding of gastric cancer have been made, the disease is still one of the malignancies with the highest incidence and mortality rates worldwide. With improved sanitation, the incidence of H. pylori is very much reduced. The presentation of gastric cancer is usually advanced in Indian scenario due to deficiency in endoscopy services.

Once carcinoma is detected, H. pylori is not given much significance. It is important to fully understand the inflammatory response initiated by the infection in order to fully block the cascade of events that lead to gastric cancer.

To prevent, cure and to provide better treatment for patients diagnosed with the disease, we must carry out more research in different parts of India as we have a very diverse lifestyle when compared to western countries.

We should identify the common issues among diseased individuals who become infected with H. pylori and also among the different strains of the bacteria which are able to colonize and induce inflammation of gastric mucosa.

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