



## GASTRIC CANDIDIASIS IN PATIENTS WITH GASTRIC CARCINOMA

## Pathology

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## ABSTRACT

**Introduction:** Gastric cancer is a heterogeneous disease that demands continued attention and research with regard to prevention, early detection and novel therapeutic options. Candida infection can occur in patients with cancer and cancer related therapy such as chemotherapy, radiotherapy. We have tried to study the endoscopy and histological features of Gastric carcinoma lesions associated with Candidiasis. **Materials and Methods:** Gastric biopsy specimens of 34 gastric carcinoma patients were processed for Histopathological examination (HPE) using Hematoxylin and eosin (H&E) staining and Periodic Acid Schiff (PAS) stain. **Results:** Majority of the gastric carcinoma patients were observed above the age of 61 years, i.e., 24 (70.5%) out of 34 total cases. Most common type was intestinal, 24 (70.5%) out of 34 gastric carcinoma patients followed by diffuse (20.5%) and unclassified (8.8%). Out of 34 gastric carcinoma cases, 6 (17.6%) patients had candidiasis. **Conclusion:** Better way to avoid fungal infections is early recognition; early detection of fungus can help to prevent serious illness. Microbial infection and cancer risk still have to evaluate with evidence based researches.

## KEYWORDS

Candida, Gastric Carcinoma, Histology

## INTRODUCTION

Worldwide, Candida is the most common fungus and also causes most common oral fungal infection in humans. Most of the fungi are commensals and acts as opportunistic infections, can cause infection when the person is immunocompromised or when mucosal barriers ruptured. Fungal infections can range from mild to life threatening infections; some fungal infections cause mild skin rashes, but others can be deadly, like fungal pneumonia [1].

Predisposing factors for Candida infection include an impaired immune system such as malignancy, HIV, patients on corticosteroids, underlying disease states such as diabetes, drugs abuse and prolonged use of antibiotics, decreased digestive secretions, dietary factors, nutrient deficiency, impaired liver function, and altered bowel flora [2]. Candida infection can occur in patients with cancer and cancer related therapy such as chemotherapy, radiotherapy. Patients with blood cancer like leukemia or myeloma are at greater risk for getting a fungal infection than people with other types of cancer [3].

Globally, Gastric carcinoma is often diagnosed at an advanced stage, it is the fourth most common type of cancer and the second leading cause of cancer related death [4]. Lauren classified gastric carcinoma based on histology as intestinal and diffuse subtypes [5]. According to WHO guidelines, gastric carcinoma classified as adenocarcinoma, signet ring – cell carcinoma and undifferentiated carcinoma; however latter is not be widely used. Predisposing factors implicated in the development of gastric carcinoma are nutritional and environmental factors. The ultimate therapy for gastric carcinoma is surgery with chemotherapy or chemoradiation.

Gastric cancer is a heterogeneous disease that demands continued attention and research with regard to prevention, early detection and novel therapeutic options. For gastric carcinoma detection, Endoscopy is the most sensitive and specific diagnostic screening method. Additionally, endoscopic surveillance should be performed one to two times per year in patients who are at higher risk of Gastric Carcinoma [6].

We have tried to study the endoscopy and histological features of Gastric carcinoma lesions associated with Candidiasis.

## MATERIALS AND METHODS

Gastric carcinoma related study which is a prospective, observational conducted for three years in Department of Pathology at Madha Medical College, Chennai. This study was undertaken from November 2015 to October 2018. In this period a total of 34 cases with gastric carcinoma were diagnosed and included. Informed consent has taken from all the patients.

Patient details including age, sex, occupation, locality, symptoms,

food habits, personal history like alcohol, smoking noted. General and systemic examination done to all the patients and findings noted.

All the patients were advised to undergo endoscopy, gastric biopsy and routine investigations. Endoscopy is a diagnostic screening method help[s] to diagnose and staging of gastric carcinoma, studying other pathologies of oesophagus and duodenum associated with gastric carcinoma, to assess type and prognosis of carcinoma and also aids in taking biopsy.

Biopsy specimens were processed for Histopathological examination (HPE) using Hematoxylin and eosin (H&E) staining and Periodic Acid Schiff (PAS) stain. On HPE findings, gastric carcinoma was diagnosed and differentiated as intestinal and diffuse types of gastric carcinoma, based on cytological and architectural heterogeneity. Based on gross appearance by endoscopy of gastric lesions such as exophytic, ulcerated, infiltrative and combined were observed. In Histology specimens, coexisting fungal patterns were also noted.

With the help of endoscopy and histologic findings, results were tabulated. Statistical presentation is in the form of numbers, percentages.

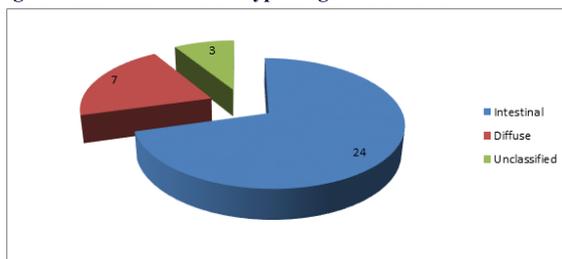
## RESULTS

In a study period of three years, 34 gastric carcinoma cases were observed. Most of gastric carcinoma patients were presented with fever, vomiting, loss of appetite, indigestion. Earliest age of a gastric carcinoma patient observed was 32 years. Majority of the gastric carcinoma patients were observed above the age of 61 years, i.e., 24 (70.5%) out of 34 total cases. Increasing trend noted in the incidence of gastric carcinoma with increase in age (Table 1). Male preponderance noted. 22 (64.7%) out of 34 gastric cancer patients were male and remaining 12 patients (35.2%) were female.

**Table 1: Age and sex distribution of gastric carcinoma patients**

Age in years	Male	%	Female	%	Total	%
30 - 40	2	5.8	0	0	2	5.8
41 – 50	1	2.9	2	5.8	3	8.8
51 – 60	3	8.8	2	5.8	5	14.7
61 – 70	3	8.8	3	8.8	6	17.6
71 – 80	8	23.5	4	11.7	12	35.2
>80	5	14.7	1	2.9	6	17.6
Total	22	64.7	12	35.2	34	100

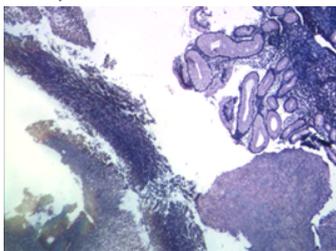
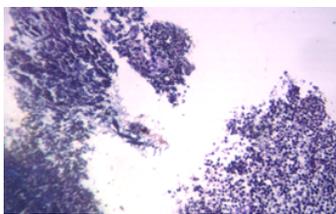
According to Lauren's classification, types of gastric carcinoma incidence assessed. Most common type was intestinal, 24 (70.5%) out of 34 gastric carcinoma patients followed by diffuse (20.5%) and unclassified (8.8%) (Fig 1&2).

**Fig 1: Incidence of Different types of gastric carcinoma**

Out of 34 gastric carcinoma cases, 6 (17.6%) patients had candidiasis. On Histopathological examination, H&E and PAS stains showed fungal filaments of candida such as budding yeast cells and pseudohyphal filaments invading the gastric tumor.

Among 6 patients with gastric carcinoma and existing candidiasis, 5 (83.3%) were detected as intestinal type and one (16.6%) was diffuse tumor. Out of 6 gastric carcinoma patients associated with candidiasis, 4 (66.6%) were males and 2 (33.3%) were females, all the patients were above 50 years age group. Gastric lesions invaded by pseudo hyphal filaments which are strongly suspicious of candidiasis were included. Even cultures suggestive of candida were not considered as an association with gastric carcinoma, as candida has proven as a part of normal flora of GIT.

Out of 6 candida isolates, 2 (33.3%) were identified from nodular lesions with tissue invasion and remaining 4 (66.6%) were detected in Gastric ulcerated lesions of carcinoma patients.

**Fig 2. Microscopic picture showing gastric glands and foci of necrosis (H&E 400X)****Fig 3. Showing foci of necrosis and fungal filaments (H&E 400X)**

## DISCUSSION

Candida is a part of normal flora of the mucous membranes of the respiratory, gastrointestinal and female genital tracts. *C. albicans*, can cause infections ranging from superficial, such as oropharyngeal candidiasis or vulvovaginal candidiasis to systemic, such as fungemia and invasive candidiasis.

Gastric carcinoma is a great negative impact on global health, as an aggressive disease with a poor prognosis plays an important role in public health. Incidence of gastric carcinoma is declining since several decades due to improving food habits like preservation, low salt diet, including fresh fruits and vegetables in diet, eradication of *H.pylori* etc., [7]. Neutropenia increases the risk of infection [8].

In the present study, earliest age of a gastric carcinoma patient observed was 32 years. Majority of the gastric carcinoma patients were observed above the age of 61 years, i.e., 24 (70.5%) out of 34 total cases. Increasing trend noted in the incidence of gastric carcinoma with increase in age. Male preponderance noted. 22 (64.7%) out of 34 gastric cancer patients were male and remaining 12 patients (35.2%) were female.

Janssen CW Jr et al [9] did a study on age and sex distribution of both

intestinal and diffuse types of gastric carcinoma. During this study they noted there is no difference in the rates of diffuse type between the sexes, where as in intestinal type, men was affected with gastric carcinoma more than twice as that of women. They also documented that both types of gastric carcinoma increased with age up to the 70-79 age group, whereas the rates in octogenarians tended to be lower than in septuagenarians.

Cancer research from UK stated that incidence of stomach cancer rise steadily from around the age group of 45-49 years and more steeply from around age 65-69. They have observed highest number of cases in the age group of 85-89 of both sexes [10].

Most common type was intestinal, 24 (70.5%) out of 34 gastric carcinoma patients followed by diffuse (20.5%) and unclassified (8.8%).

Intestinal and diffuse gastric cancer differs in characteristics of pathology, epidemiology and etiology. Intestinal gastric cancers, usually related to *Helicobacter pylori* infection combined with diet and environmental factors. It is usually associated with intestinal metaplasia and exhibit adhesion arranged in tubular and gastric form spreads by lymphatic and vascular invasion [11]. Diffuse tumors often associated with gastritis. These tumor cells lack adhesion and infiltrate the stroma as single cells or small sub groups [12]. Intestinal tumors exhibits longer course, better prognosis and most commonly affects the gastric antrum [13] whereas, diffuse exhibits shorter course, worse prognosis and affects body of the stomach usually [14].

Janssen CW Jr et al [9] reported the incidence of gastric carcinoma as 58% intestinal type, 26% diffuse type and 16% were unclassified.

Out of 6 candida isolates, 2 (33.3%) were identified from nodular lesions with tissue invasion and remaining 4 (66.6%) were detected in Gastric ulcerated lesions of carcinoma patients in this study. Minoli G et al [15] reported out of 149 patients who undergone gastroscopy. 23 patients (15.4%) had candidiasis; among these 42% were in thrush lesions, 31% of candida from nodules with tissue invasion and remaining 27% of candida were related to ulcerated gastric lesions.

As per this study, out of 34 gastric carcinoma cases, 6 (17.6%) patients had candidiasis. Out of 6 gastric carcinoma patients associated with candidiasis, 4 (66.6%) were males and 2 (33.3%) were females, all the patients were above 50 years age group. Katzenstein and Maksem [16] documented 18% candidiasis incidence in gastric ulcers. Scott and Jenkins detected 20% of candida patients were with gastric cancer and 16% of candida patients were with benign gastric ulcer [17].

In contrast to this study, Knoke & Bermlardt [18] and Oehlert and Preuss [19] et al repeated very low incidence of candidiasis in gastric biopsies of 6 (0.23%) out of 2537 patients and 121 (0.59%) out of 20401 patients respectively. This difference in incidence of candidiasis among gastric carcinoma patients may be due to community, food habits and sample size of particular study.

Min Kyu Jung et al [20] did a study on treatment of gastric candidiasis in patients with gastric ulcer disease from 1998 to 2007 period, documented as candida isolated from malignant ulcers were improved with surgical resection and combined chemotherapy and proton pump inhibitors treatment. In their study, benign ulcers were well responded to PPI treatment alone, without antifungal medication. Still the candida and cancer development association is not clearly understood in terms of pathogenic mechanisms and its carcinogenic capability.

## CONCLUSION

Endoscopic surveillance, proper food habits and eradication of *helicobacter pylori* helps to decrease the incidence of Gastric carcinoma. Fungi are difficult to avoid because they are a natural part of environment. Better way to avoid fungal infections is early recognition; early detection of fungus can help to prevent serious illness. Microbial infection and cancer risk still have to evaluate with evidence based researches.

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