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Peritoneal Cytology in the Staging Process of Gastric Carcinoma

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Abstract

Background: Peritoneal carcinomatosis is one of the patterns of recurrence in patients with gastric cancer. The prognosis of patients with advanced gastric cancer invading the gastric serosa because of the high incidence of peritoneal recurrence. Recurrence with this pattern is most likely caused by the presence of free cancer cells in the abdominal cavity exfoliated from the serosal surfaces of the primary gastric tumor. The study aimed to assess peritoneal cytology in the staging process of gastric cancer. **Material & Methods:** This Cross-sectional observational study was carried out in the Department of Surgical Oncology, National Institute of Cancer Research and Hospital, Mohakhali, Dhaka, Bangladesh for twenty-one months, starting from July 2017 to March 2019 following approval of the protocol. 42 study patients were selected based on the inclusion and exclusion criteria. The patients were diagnosed clinically, radiologically, and histopathologically. A structured case record form was used to interview and collect data. The outcome of gastric carcinoma was measured by doing peritoneal cytology. All the data were compiled and sorted properly and analyzed statistically using Statistical Package for Social Science (SPSS-22). The results were expressed as percentages and mean ± SD and presented as tables and charts. **Results:** In the present study, the mean (±SD) age of the subjects was 66.19 (±10.38). The majority (33.3%) were aged 56-65 years. Among the study subjects, 64.3% were males and 35.7% were females. 52.4%, 40.5%, and 7.1%) study subjects had BMI 18.5-24.9 kg/m2, 25-30 kg/m2 and >30 kg/m2. In this study, out of 42 patients, 61.9% were smokers and 83.3% were taking betel leaf in their habit. Here, the majority (69%) of study subjects came from the middle class. In the present study, proximal and distal stomachs were involved in study subjects. The mean ± SD tumor size was 6.20 ± 1.86cm. The majority of study subjects had Type 3 and Type 4 tumors and T4a and N2 stage. In this study, total gastrectomy and lower radical gastrectomy were done in the majority of the patients. The time of index surgery was 1-1.5 hours in the majority of the subjects. In the present study, 64.3% of subjects had cytology positive, 31% had cytology negative and only 4.8% of subjects had suspected cytology. Negative cytology was significantly higher in T1, T2, N0, and N1 stages and positively cytology was significantly higher in T3, T4a, and N2 stages. **Conclusions:** After analyzing the results of the present study, it can be concluded that the majority of subjects had cytology positive, and positive cytology was significantly higher in the T3, T4a, and N2 stages. Negative cytology was significantly higher in T1, T2, N0, and N1 stage.

Keywords:- Gastric carcinoma, Peritoneal cytology, Staging.

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INTRODUCTION

Globally, gastric cancer ranks third in terms of cancer-related deaths. A poor prognosis is associated with an advanced stage of the illness at the time of diagnosis. One of the most frequent locations for metastases in stomach cancer patients is the peritoneum. It is still unclear what causes peritoneal dispersion. Nonetheless, one of the primary contributors to its growth seems to be the existence of peritoneal-free cancer cells. Most patients who receive Intraperitoneal Free Cancer Cells (IPFCCs) do not recover from peritoneal recurrence following surgery. In Japan, peritoneal metastatic gastric cancer patients had a reported 30% five-year survival rate.[1,2,3,4] It was discovered that younger patients had more positive cytology results than older patients. The tumor with positive cytology is substantially bigger than the one with negative cytology.[2,5] The rate of positive cytology has a stronger correlation with the grade of lymphatic invasion. According to several studies, patients with positive cytology results have lower survival curves than all other patients in each stage. These suggest that a positive cytology result is associated with one or more stages worse prognosis. It has been hypothesized that there is a one-stage difference in prognosis between positive and negative cytology findings.[2,6,7,8] Peritoneal metastasis, the most prevalent cause of gastric cancer death, is one of the major patterns of gastric cancer relapse following curative resection. Laparoscopy staging still plays a significant role in the staging of patients with gastric cancer, even with advancements in radiological techniques.[9] However, immunoassay and sophisticated molecular biology techniques used in histopathology are the most researched and controversial enhancement solutions. Despite its extensively documented low sensitivity rate, the traditional Papanicolaou staining cytological technique has been the current standard of care at University Hospital. It has been demonstrated that using an immunoassay approach targeted against the cancer-associated antigen CEA can boost the detection rate over traditional cytology by as much as 14%. Numerous studies have shown that when it comes to detecting IPFCC, reverse transcriptase polymerase chain reaction (RT-PCR) approach is superior to immunoassays and traditional cytology in terms of sensitivity rate. However, this molecular biology method is expensive and time-consuming.[7,8,9] Instead than being treated with the goal of curing, the majority of patients have historically received palliative care. As a result, there is little chance that these patients will survive, and the stomach resection has a major negative impact on their quality of life. Peritoneal washings and the identification of IPFCC, according to a number of researchers from many nations, offer crucial information in the staging process of gastric cancer.[7,9,10,11] Despite the poor prognosis for individuals with positive IPFCC, there are now various promising therapeutic options that have been linked to better survival, thus these people shouldn't be condemned to death. Consequently, it is important to engage these patients in clinical studies and manage them using customised treatment plans. Hopefully, this will result in the creation of a treatment method that is uniformly and widely recognized, as much has been anticipated.[9] the study aims to assess peritoneal cytology in the staging process of gastric cancer. Apart from that, to observe demographic characteristics

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including patient age, sex, BMI, and habitat, To observe clinical characteristics including the location of cancer within the stomach, tumor stage, grade, and nodal involvement, To determine the proportion of positive cytology, to evaluate postoperative complication if any and to observe association of peritoneal cytology with staging were among the specific objectives.

MATERIAL AND METHODS

This Cross-sectional observational study was carried out in the Department of Surgical Oncology, National Institute of Cancer Research and Hospital, Mohakhali, Dhaka, Bangladesh for twenty-one months, starting from July 2017 to March 2019 following approval of the protocol. 42 patients suffering from primary gastric carcinoma admitted to NICRH for operative treatment were the study population. Patients with biopsy-proven primary gastric adenocarcinoma and clinical T2~4a/N0~2/M0 in the preoperative TNM evaluation were included in the inclusion criteria. However, patients with a history of another malignancy, patients with unresectable gastric cancer invading adjacent organs, patients having frank peritoneal metastasis or huge ascites, and patients having a history of NACT for gastric carcinoma were excluded from the study. A purposive non-randomized sampling technique was used. A structured case record form was used to interview and collect data. All the data were compiled and sorted properly and the quantitative data were analyzed statistically by using Statistical Package for Social Science (SPSS-22).

RESULTS

In the present study, the mean (±SD) age of the subjects was 66.19 (±10.38). The majority (33.3%) were in the age group of 56-65 years. 7 (16.7%), 11 (26.2%) and 10 (23.8%) were in the age group of 47-55 years, 66-75 years, and 76-85 years respectively. The youngest and the oldest patients were 47 and 85 years respectively. Among the study subjects, 27 (64.3%) were males and 15 (35.7%) were females. 22 (52.4%), 17 (40.5%) and 3 (7.1%) study subjects had BMI 18.5-24.9 kg/m2, 25-30 kg/m2 and >30 kg/m2. The mean (±SD) BMI was 24.65 (±3.64). In this study, out of 42 patients 26(61.9%) were smokers, 35 (83.3%) were taking betel leaf and only 8 (19%) were alcoholics in their habit. In this study, the majority of study subjects about 69% came from the middle class. only 13 (31%) study subjects came from lower socioeconomic conditions. In the present study, the proximal part of the stomach was involved in 23 (54.8%), and the distal part was involved in 19(45.2%) study subjects.

In, the present study, the Majority 25 (59.5%) of the tumor was 6.1-9.2cm and the mean ± SD tumor size was 6.20 ± 1.86cm. In the present study, the tumor was categorized into Types 0,1,2,3 and 4 according to the Japanese Endoscopic Society (Murakami 1971). 3 (7.1%), 6 (14.3%), 8 (19%), 15 (35.7%), and 10 (23.8%) study subjects had Type 0, Type 1, Type 2, Type 3, and Type 4 tumors respectively.

In the present study, the majority (59.5%) of study subjects were in the T4a stage according to T stage. 2 (4.8%), 5 (11.9%), 10 (23.8%) and were in T1, T2, and T3 stage respectively. According to the N stage, the majority (52.4%) of the subjects were in the N2 stage. 2(4.8%) and

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18(42.9%) were in N0 and N1 stage respectively. In the present study, no (100%) metastasis occurs in all patients. [Table 3]

In this study, upper radical gastrectomy was done in 5 (11.9%) patients, lower radical was done in 18 (42.9%) and total gastrectomy was done in 19 (45.2%) patients. In the present study, the time of index surgery was 1-1.5 hours in 24 (57.1%) subjects and 1.5-2 hours in 18 (42.9%) study subjects.[Table 4]

In the present study, 27 (64.3%) subjects had cytology positive, 13 (31%) had cytology negative and only 2 (4.8%) subjects had suspected cytology. [Table 5]

In this study, only 4 (9.5%) cases developed chest infection, and 6 (14.3%) cases developed wound infection. [Table 6]

Data were expressed as frequency and percentage. A z-proportion test was performed to compare the groups. p-value <0.001 was accepted as the level of significance. In the present study, negative cytology was significantly higher in T1, T2, N0, and N1 stages and positive cytology was significantly higher in T3, T4a, and N2 stages. [Table 7]

Table 1: Distribution of study subjects according to baseline characteristics (n=42)

Baseline characteristics of patients	**Frequency (n=42)**	**Percentage (%)**
The age range of the patients		
47-55	7	16.70
56-65	14	33.30
66-75	11	26.20
76-85	10	23.80
Mean ± SD 66.19 ± 10.38		
Sex of the patients		
Male	27	64.30
Female	15	35.70
BMI (kg/m2) of patients		
18.5-24.9	22	52.40
25-30	17	40.50
>30	3	7.10
Mean ± SD 24.65 ± 3.64		
Personal Habits of Patients		
Smoker	26	61.90
Betel leaf and nut	35	83.30
Alcoholic	8	19.00
Socioeconomic Status of Patients		
Upper Class	0	0.00
Middle Class	29	69.00
Poor Class	13	31.00
Anatomical site of Patients		
Proximal Stomach	23	54.80

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Distal Stomach	19	45.20

Data were expressed as frequency, percentage, and Mean±SD

Table 2: Distribution of study subjects according to tumor size and tumor types (n=42)

Size and type of tumors	**Frequency (n=42)**	**Percentage (%)**
Tumor size (cm)		
2.5-4	10	23.8
4.1-6	7	16.7
6.1-9.2	25	59.5
Mean ± SD 6.20 ± 1.86		
Tumor type		
Type 0	3	7.1
Type 1	6	14.3
Type 2	8	19
Type 3	15	35.7
Type 4	10	23.8

Data were expressed as frequency, percentage, and Mean ± SD.

Table 3: Distribution of study subjects according to T and N staging and metastasis (n=42)

Stages	**Frequency (n=42)**	**Percentage (%)**
Distribution according to T and N staging		
T1	2	4.80
T2	5	11.90
T3	10	23.80
T4a	25	59.50
N0	2	4.80
N1	18	42.90
N2	22	52.40
Distribution according to metastasis		
Variables	Frequency (n=42)	Percentage (%)
Yes	42	100.00
No	0	0.00

Table 4: Distribution of study subjects according to types of surgery and time of index surgery (n=42)

Type of tumors	**Frequency (n=42)**	**Percentage (%)**
Type of surgery		
Upper Radical gastrectomy	5	11.90
Lower Radical gastrectomy	18	42.90
Total gastrectomy	19	45.20
Time of index surgery		
Time (Hr)	Frequency (n=42)	Percentage (%)

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1-1.5	24	57.10
>1.5-2	18	42.90
Total	19	100.0

Table 5: Distribution of study subjects according to peritoneal cytology (n=42)

Type of peritoneal cytology	**Frequency (n=42)**	**Percentage (%)**
Positive cytology	27	64.30
Negative cytology	13	31.00
Suspected cytology	2	4.80

Table 6: Distribution of study subjects according to postoperative complication (n=42)

Postoperative complications	**Frequency (n=42)**	**Percentage (%)**
Chest infection	4	9.50
Wound infection	6	14.30
No complication	32	76.20

Table 7: Association of peritoneal cytology with staging (n=42)

Variables	**Positive cytology**	**Negative cytology**
T staging		
T1	0 (0%)	2 (4.8%)
T2	0 (0%)	5 (11.9%)
T3	5 (11.9%)	3 (7.1%)
T4a	22 (52.4%)	3 (7.1%)
P value<0.001*		
N staging		
N0	0 (0%)	2 (4.8%)
N1	7 (16.7%)	9 (21.4%)
N2	20 (47.6%)	2 (4.8%)
P value<0.001*		

DISCUSSION

In the present study, the mean (±SD) age of the subjects was 66.19 (±10.38). The majority were in the age group of 56-65 years. The youngest and the oldest patients were 47 and 85 years respectively. Among the study subjects, the majority were males and the male-female ratio was 1.8:1. Almost similar to the findings observed by Khan S et al.; Nakagawa et al,[2,5] 22 (52.4%), 17 (40.5%) and 3 (7.1%) study subjects had BMI 18.5-24.9 kg/m2, 25-30 kg/m2 and >30 kg/m2. The mean (±SD) BMI was 24.65 (±3.64). In the current study, smoking 61.90%, taking betel leaf 83.30%, and drinking alcohol 19.00% were found to their habit. This finding was in agreement with the study of Lisiecki et al.[12] In this study, the majority (69%) of study subjects came from the middle class and only 13 (31%) study subjects came from lower socioeconomic condition. In the present study, proximal and distal stomachs were involved in study subjects.

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Apart from that majority of the tumor was 6.1-9.2cm and the mean ± SD tumor size was 6.20 ± 1.86cm. This finding was in agreement with the study of Chuwa et al. and Yamada et al.[13,14] In the current study tumor was categorized as Type 0, Type 1, Type 2, Type 3, and Type 4 according to the Japanese Endoscopic Society (Murakami 1971). The majority of study subjects had Type 3 and Type 4 tumors. Similar findings were observed in a previous study done by Ki et al., Brito et al., Lisiecki et al., and Machairasa et al.[8,12,15,16] It was noticed from the present study that the majority of study subjects were in T4a and N2 stage according to T and N stage. No (100%) metastasis occurred among current study subjects. Similarity was observed in studies of Muntean et al., Lorenzen et al., Lisiecki et al., and Machairasa et al. done previously.[12,16,17,18] However, Ki et al., and Brito et al. found metastasis at various sites.8,15 This may be due to different methodologies. Total gastrectomy and lower radical gastrectomy were done in the majority of the patients. The time of index surgery was 1-1.5 hours in the majority of the subjects. In the present study, 64.3% of subjects had cytology positive, 31% had cytology negative and only 4.8% of subjects had suspected cytology. This finding was in agreement with the studies of Mezhir et al., Ki et al., and Brito et al.[8,15,19] During the operation, strict asepsis was followed in every step and broad-spectrum intravenous antibiotic was given for three days. Initial recovery was uneventful in the cases. However, during the study, few patients developed chest and wound infections. This finding was similar to the study of Ki et al. and Brito et al.8,15 In the present study, negative cytology was significantly higher in T1, T2, N0, and N1 stages and positive cytology was significantly higher in T3, T4a, and N2 stages. Similarity was found in the studies done by Chuwa et al., Yamada et al., Ki et al., Brito et al., and Machairasa et al.[8,13,14,15,16]

Limitations of The Study

The study was conducted in a single hospital with a small sample size and limited resources and facilities. So, the results may not represent the whole community. As the sample was taken purposively, there may be a chance of bias which can influence the results. Besides, the study duration and follow-up period were short in comparison to other studies.

CONCLUSIONS

After analyzing the results of the present study, it can be concluded that the majority of subjects had cytology positive, and positive cytology was significantly higher in the T3, T4a, and N2 stages. Negative cytology was significantly higher in T1, T2, N0, and N1 stages. So it is very important to study of peritoneal cytology before any operation of gastric carcinoma. Which can avoid operation-related morbidity and may change the treatment modality of gastric cancer. Therefore, peritoneal cytology is part of the routine staging workup for patients with gastric cancer.

Ethical approval

The study was approved by the Institutional Ethics Committee.

Recommendation

Similar type of study can be done with larger sample size. Randomized comparative study should be carried out and collecting samples

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from different parts of country is recommended.

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