Clinicopathological Profile of Ca Stomach and Comparison of Preoperative Findings with Peroperative and Histopathological Findings

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ABSTRACT

BACKGROUND
Gastric cancer has been one of the leading causes of cancer-related mortality over the past century. Today it is the 4th most common cancer in the world. Surgery remains the only major curative option. Majority of these cancers are found to be unresectable on laparotomy. It is also frequently seen that patients with a preoperatively resectable cancer as per a staging CT-Scan of the abdomen are found to have unresectable disease on laparotomy. In this study, we are trying to assess the clinico-pathological profile of gastric cancer and tally the preoperative radiological findings with the peroperative and final histopathological findings.

METHODS
It is a short-term prospective, observational study. 50 patients with gastric cancer permitted surgical intervention were prepared, operated, followed-up and preoperative, peroperative and final histopathological findings were tallied.

RESULTS
50 patients with gastric cancer were studied. The maximum age was 76 years and minimum age was 23 years with a mean age of 49.12 years with a standard deviation of 13.9776. Peak incidence was found in the age group of 41-60 years. 54% of the patients were male and 46% were female. The most common symptom was anorexia (94%, z-value 8.8) followed by weight loss (86%, z-value 7.2). The most common sign was anaemia which was present in 80% of the patients (z-value 6.0). 64% of the patients had intestinal type while 36% had diffuse type of gastric cancer. Patients with diffuse type were <50 years of age. Diffuse type was more common in females while intestinal type was more common in males. The accuracy of T, N, M staging on preoperative CT-Scan tallied with peroperative findings is 44%, 38% and 72% respectively. 44% of the patients underwent a palliative surgical procedure, of which 90.9% had poorly-differentiated and 9.1% had moderately-differentiated cancer.

CONCLUSIONS
Preoperative CT-Scan may not be a very accurate staging investigation for gastric cancer. It is poorly-differentiated cancers (both adenocarcinoma and signet-ring cell carcinoma) which have a greater possibility of being inaccurately staged by a preoperative CT-Scan.

KEY WORDS
Gastric Cancer, Clinicopathological Profile, Preoperative Finding, Peroperative Findings
**BACKGROUND**

Gastric cancer is the 4th most common cancer in the world (9% of all cancers) after lung, breast and colorectal cancer. Over all, it is the 2nd most common cause of death but in some Asian countries, it is still the 1st common cause of cancer death.\(^7\)\(^8\)\(^9\) Worldwide the incidence of new cases of gastric cancer in 2002 was 934,000 of which 56% cases were from Asia. Proximal stomach is the commonest site of affection in western countries while distal stomach is more commonly affected in Asian population.\(^5\)\(^7\) The incidence of gastric carcinoma is decreasing in western countries and increasing in the rest of the world.\(^1\) Though there is a decreasing trend over the past few decades, gastric cancer remains a major public health problem in the world.\(^8\)\(^9\) Proximal gastric cancer has a more aggressive clinical course than distal ones & has a poorer prognosis.\(^7\)\(^10\)\(^11\)\(^12\) Over all, the commonest histopathological type is adenocarcinoma & in Asian countries, it is the intestinal type due to intestinal metaplasia.\(^5\) Surgery is the mainstay of treatment.\(^13\)\(^14\) Majority of the patients present with advanced disease & their prognosis is very poor despite availability of modern chemotherapeutic regimen.\(^15\)\(^16\) It is also frequently seen in our hospital that patients with preoperatively resectable gastric cancer as per a staging CT-scan of the abdomen are found to have unresectable disease on laparotomy. Therefore, the need remains to evaluate the efficacy of preoperative staging investigations in accurately staging the disease as determined peroperatively and on final histopathological examination. This study addresses the clinicopathological profile- i.e. clinical presentation, preoperative radiological stage, peroperative findings and the final histopathological staging in patients with gastric carcinoma in a tertiary care hospital in Eastern India.

**METHODS**

After taking approval from the institutional ethics committee, the study was carried out in the Department of General surgery, SSKM Hospital, Kolkata. All patients with clinical suspicion of carcinoma stomach were included. Patients with tumours histologically other than carcinoma stomach and non-compliant patients reluctant to undergo surgery were excluded. A total of 50 patients were considered. Patients with carcinoma stomach meeting the inclusion and exclusion criteria were prepared, followed up, operated and preoperative, peroperative and final histopathological findings were tallied. Preoperatively, selected patients were subjected to a detailed history, clinical examination, investigations (including upper GI endoscopy, routine blood tests, contrast enhanced CT-scan abdomen), correction of anaemia, dyselectrolytaemia, dehydration and other comorbidities. Peroperatively, findings in respect of location of growth, presence of metastasis, ascites, infiltration into adjoining structures, resectability, preoperative staging were assessed. If resectable, the specimen of gastrectomy and lymph nodes was removed. If unresectable, tissue was taken from the mass for histopathological examination. Postoperatively, the specimen was transported to the pathology department in formalin where tissue was taken from the specimen, slides were prepared, stained with haematoxylin and eosin and final histopathological assessment was done.

**Statistical Analysis**

Information was collected according to various pre-defined parameters and was analysed as per standard statistical protocols and tests. For statistical analysis data were entered into a Microsoft excel spreadsheet and then analysed by SPSS 24.0 and GraphPad Prism version 5. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Paired t-tests were a form of blocking and had greater power than unpaired tests. A chi-squared test (χ² test) was any statistical hypothesis test wherein the sampling distribution of the test statistic is a chi-squared distribution when the null hypothesis is true. Without other qualification, ‘chi-squared test’ often is used as short for Pearson’s chi-squared test. Unpaired proportions were compared by Chi-square test or Fischer’s exact test, as appropriate. Z-test (Standard Normal Deviate) was used to test the significant difference of proportions. Explicit expressions that can be used to carry out various t-tests are given below. In each case, the formula for a test statistic that either exactly follows or closely approximates a t-distribution under the null hypothesis is given. Also, the appropriate degrees of freedom are given in each case. Each of these statistics can be used to carry out either a one-tailed test or a two-tailed test. Once a p value is determined, a p-value can be found using a table of values from Student’s t-distribution. If the calculated p-value is below the threshold chosen for statistical significance (usually the 0.10, the 0.05, or 0.01 level), then the null hypothesis is rejected in favour of the alternative hypothesis. p-value ≤ 0.05 was considered for statistically significant.

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**RESULTS**

<table>
<thead>
<tr>
<th>Age (in years)</th>
<th>Lauren’s Types</th>
<th>Diffuse</th>
<th>Intestinal</th>
<th>Total</th>
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<tr>
<td>20-30</td>
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<tr>
<td>31-40</td>
<td>9</td>
<td>18.0%</td>
<td>8</td>
<td>17</td>
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<td>41-50</td>
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<td>18</td>
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<td>51-60</td>
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<td>24.0%</td>
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<tr>
<td>61-70</td>
<td>8</td>
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<td>&gt;70</td>
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<td>Total</td>
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<td>18 (36%)</td>
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<td>Male</td>
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<td>100.0%</td>
<td>18</td>
<td>32</td>
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<td>36.0%</td>
<td>18</td>
<td>36</td>
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<tr>
<td>Ulcerative</td>
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<td>Heteroplastic</td>
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<tr>
<td>Polypoidal</td>
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<tr>
<td>Total</td>
<td>50</td>
<td>100.0%</td>
<td>18</td>
<td>32</td>
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<td>Poorly differentiated</td>
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<td>52.0%</td>
<td>18</td>
<td>44</td>
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<tr>
<td>Total</td>
<td>50</td>
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<td>18</td>
<td>32</td>
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<table>
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<td>Adeno carcinoma</td>
<td>32</td>
<td>64.0%</td>
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<td>32</td>
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<tr>
<td>Signet ring cell carcinoma</td>
<td>18</td>
<td>36.0%</td>
<td>18</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100.0%</td>
<td>18</td>
<td>32</td>
</tr>
</tbody>
</table>

*Table 1. Distribution of Age, Sex, Macroscopic Types, Tumour Grade and Tumour Histopathology in relation to Lauren’s Types*
Pain abdomen
Abdominal tenderness
Amenia
Anemia
Abdominal tensity
Abdominal mass
Ascites
Palpable left supravacuicular lymph nodes

**Table 3. Distribution of Symptoms and Signs**

<table>
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<th>CT-Scan Staging</th>
<th>Peroperative Staging</th>
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<td>T&lt;sub&gt;p&lt;/sub&gt;</td>
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<td>Col %</td>
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**Table 4. Distribution of Palliative Surgeries Performed vs Grade**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Palliative Operation Performed</th>
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<th>Poorly Differentiated</th>
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<td>FJ</td>
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<td>19</td>
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<td>95.0</td>
<td>100.0</td>
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<tr>
<td>Col %</td>
<td>50.0</td>
<td>50.0</td>
<td>90.0</td>
<td></td>
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<tr>
<td>GJ</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Row %</td>
<td>50.0</td>
<td>50.0</td>
<td>91.0</td>
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<td>Col %</td>
<td>50.0</td>
<td>5.0</td>
<td>9.1</td>
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</tbody>
</table>

**Table 5. Distribution of TNM, Staging and Comparison between CT-Scan Staging and Peroperative Staging**

**Table 6. Distribution of Palliative Surgeries Performed**

Carcinoma stomach is the 4<sup>th</sup> most common cancer in the world after lung, breast and colorectal cancer (9% of all cancers according to a study of Clinicopathological Features of Gastric Cancer: A Study based on Cancer Registry Data by Safee A, Moghimi-Dekordi B, Fatemi SR et al in Iran. Now it is the 2<sup>nd</sup> most common cancer causing death worldwide superseded by only lung cancer.<sup>17,18</sup>But in Japan and in Asian countries, it is still the most common cause of death according to a study by Parker SL, Tong T, Bolden S et al [1997] and Curtis RE, Kennedy BJ, Myers MH et al[1985]. The incidence, site, aggression and prognosis of gastric cancer vary considerably in different parts of the world.<sup>19,20</sup> In this study, an attempt was made to study the different clinical features, pathological types, comparison of the peroperative CT-scan staging with the peroperative and final histopathological staging, different surgical treatments received by the patients according to stage.

**Age Incidence**

In this study, total of 50 patients were included. Amongst them, 54% are aged <= 50 years which in some reports is 14.8%<sup>1,2,16,19,20</sup> and 46% are >50 years of age. Mean Age of presentation is 49.12 years. Peak Incidence is found in the Age Group of 41-60 years and least incidence is found in the age group >70 years. This trend corroborates with the global trend that worldwide, gastric cancer is shifting more towards the young as supported by a study by Kim DY, Ryu SY, Kim YJ et al.<sup>21</sup>

**Sex Incidence**

In some published series, male female ratio is 2:1.<sup>1,2,16,19,20,21,22</sup> In this study, 54% of the patients were male and the rest were female and the ratio is 1.17.

**Clinical Presentation**

In a study in Khuzestan, the two most common presentations are weight loss and abdominal pain.<sup>21,22</sup> In a study done by Kabir et al, abdominal pain (100%), vomiting (79%), dysphagia (24%) and weight loss (62%) were predominant symptoms pertaining to gastric carcinoma.<sup>24</sup> Interview of 18,365 patients by the American college of surgeons, common presentations were weight loss (66.6%), abdominal pain (51.6%), nausea/vomiting (34%) and melena (20%). Again Qureshi et al showed common presenting symptoms as weight loss (35%), dyspepsia (76%), anorexia (35%) and vomiting (35%).<sup>25</sup> Saha et al in their study showed that abdominal pain (66.2%) was the commonest symptom...
followed by weight loss (43.3%), indigestion (45.9%), anorexia (39.9%), nausea/vomiting (34.2%), postprandial pain (29%) and melena (9.5%). In this study, the commonest symptom was anorexia (94%) followed by weight loss (86%) with z-scores of 8.8 and 7.2 and were thus, statistically significant. Of the symptoms pertaining to gastric outlet obstruction, vomiting and post-prandial fullness were present in 82% and 84% of the cases with z-scores of 6.4 and 6.8 respectively indicating their significance. The most common sign was anaemia (Present in 80% of the cases) with a z-value of 6.0. Although palpable left supraventricular lymph nodes were present in 18% of the cases, it had a z-value of 6.4 and was thus highly significant.

Site of Lesion
Worldwide, the site of gastric cancer is changing in the western world. Incidence of distal gastric cancer is decreasing, and proximal gastric cancer is increasing (41% and 50% respectively). Recent study from Kerala in India showed that though the predominant site of cancer was the antral mucosa, there was a trend towards proximal shift. Qureshi et al showed that in the Kashmiri population, incidences of cancer in proximal, mid and distal stomach were 42%, 6.2% and 45.7% respectively. Afridi et al reported growth at the cardiac end in 33%, pylorus and antrum in 40%, limitis plastica in 13.3% and only body and body and pylorus in 6.7% of the patients. In this study, the most common site of involvement was the antrum (38%). The body and antrum were involved in 22% of the cases. Diffuse involvement was seen in 36% of the cases with 6% of the cases having spread to and beyond the esophagogastric junction. The antrum, body and cardia were involved in 34% of the cases (30% diffuse and 4% intestinal type).

Macroscopical Types
Macroscopically, gastric cancer has been classified into 4 types - Type I: polypoidal lesion, Type II: Fungating lesion, Type III: Ulcerated lesion and Type IV: infiltrating lesion on the gastric wall or limitis plastica. But, there is considerable overlap between the above different types. Qureshi et al showed 35.5% ulceroproliferative, 26% proliferative, 31% ulcerative and 7.4% infiltrative lesions during endoscopic procedure performed in Kashmiri patients. Another study by Kahir et al showed that ulcerative lesion was 56%, ulceroproliferative lesion 10% and polypoidal lesion 34%. In this study, the most common type was ulceroproliferative (58%) followed by infiltrative (36%). The least common was ulcerative (6%) while the polypoidal type was not found. The infiltrative type was present in all cases of diffuse gastric cancer.

Stage at Presentation
Kim et al reported that 80.3% young patients presented with advanced gastric carcinoma. In a Middle Eastern study, two-thirds of the patients presented with advanced gastric cancer. But in another study, early gastric cancer is more common in young age group than their older counterpart (19.7% vs 13.8%). In this study, 2%, 2%, 48%, 42% 6% of the patients presented with T0, T2, T3, T4a, T4b stage on CT-Scan. 70%, 26%, 4% of the patients had N0, N1, N2 stage on CT-Scan. 94% of the patients had M0 disease while only 6% had M1 disease on CT-Scan. Peroperatively, 4% T2, 8% T3, 46% T4a, 42% T4b were the relative percentages of T-stages found. 24%, 34%, 32%, 10% of the patients had N0, N1, N2, N3 lymph nodal staging respectively. 66% had M0 disease while 34% had metastases and were grouped as M1. In this study, all (100%) of the patients presented with advanced gastric cancer on histopathology. 4% T2, 8% T3, 46% T4a, 42% T4b were the relative percentages of T-stages found. 24%, 34%, 32%, 10% of the patients had N0, N1, N2, N3 lymph nodal staging respectively. 64% had M0 disease while 36% had metastases and were grouped as M1.

Association between Preoperative and Peroperative Staging
The only potential curative therapy is surgical resection. For effective curative treatment, there must be complete resection of all gross disease with no residual microscopic disease. Accurate preoperative staging of gastric cancer is important in planning most effective therapy towards cure or palliation. The depth of intramural tumour invasion and spreading beyond the gastric wall, the involvement of lymph nodes and distant metastases are the most important prognostic factors in gastric cancer. Most patients present with advanced disease at diagnosis, so they could not be considered suitable for resection. In these patients, it is relevant to have a sensitive imaging tool for detection and thus avoid the morbidity of an unnecessary laparotomy. “Imaging techniques” have assumed greater clinical value in the further assessment of an endoscopically or radiologically verified neoplastic lesion of the stomach through the ability to evaluate its extent of invasion, metastatic involvement of lymph nodes and/or distant organs. Because the aim of gastric cancer surgery is to excise the primary lesion adequately, it is very important to know the location of this lesion and the tumour margin before any therapeutic decision can be taken. In this context, the role of CT-Scan in the preoperative staging of gastric cancer has been suggested as an accurate imaging modality for evaluating the extent of primary gastric cancer and nodal involvement of the disease. However, reported results comparing preoperative CT with histopathological findings are variable. Controversy exists as to the value of CT-Scan in the preoperative staging of gastric cancer, because of its limited ability to identify correctly lymph node metastases, invasion of adjacent organs or hepatic and peritoneal metastases. [The surgery clinic Nis Clinical Centre analysed the clinical data of 65 gastric cancer patients and found that in 38% of them, preoperative and intraoperative findings coincided. In 60%, a higher level of gastric cancer was identified while in 2%, it is lower.] Yet, another study reported that the overall accuracy of CT-staging and operability assessment was 72% and 82% respectively. Perigastric fat involvement had a positive predictive value of 91%. The demonstration of local lymph node involvement and/or distant organs. Because the aim of gastric cancer surgery is to excise the primary lesion adequately, it is very important to know the location of this lesion and the tumour margin before any therapeutic decision can be taken. In this context, the role of CT-Scan in the preoperative staging of gastric cancer has been suggested as an accurate imaging modality for evaluating the extent of primary gastric cancer and nodal involvement of the disease.
phase (45 seconds) is accurate for determining the depth of tumor invasion through the wall; the later phase (3 minutes) did not provide additional information. Cancers on the superior or inferior wall of the gastric antrum are difficult to detect and to stage correctly because of poor z-axis resolution and partial-volume averaging effects.\(^{44,45}\) For transverse colon or mesocolon invasion, Andaker et al\(^{46}\) reported a sensitivity of 25% by using incremental CT. By using single-detector row helical CT, Davies et al\(^{47}\) reported improved sensitivity (76%) and specificity (95%). For tumor invasion of the pancreas, the previously reported sensitivity and specificity of CT ranged from 33% to 100% and from 77% to 99%, respectively.\(^{48,49,50}\) The loss of the intervening fat plane does not necessarily imply invasion, and it has been reported that even the presence of an indistinct interface between the two organs is not a reliable sign of invasion, because an inflammatory adhesion can mimic true invasion.\(^ {51}\) Additional scanning in the decubitus position, on the patient's right side, often is used to reduce a false-positive diagnosis of pancreatic invasion by observing a change in the relative location of the gastric tumour and the pancreas. In this study, it was seen that T-stage was lower in 54% and higher in 2% of cases on CT-scan. N-stage was found to be lower in 62% of cases respectively on CT-scan in comparison to the peroperative findings. M-stage was under-staged in 28% of the cases, particularly those having peritoneal deposits. The accuracy of T, N, M staging on CT-scan was 44%, 38% and 72% respectively.

Lauren's Types
The Histological classification of gastric carcinoma is based on Lauren's criteria, which describes that gastric carcinoma is of two major subtypes: INTESTINAL and DIFFUSE. Third type, mixed type (Indeterminate type) is another variant. Relative frequencies are approximately 54% for intestinal type, 32% for diffuse type and 15% for indeterminate type.\(^ {52}\) Regarding histopathological diagnosis, Afridi et al that two-thirds of the patients (66.6%) had diffuse subtype, 20% had intestinal subtype and 13.3% had gastric lymphoma.\(^ {29}\) In this study, 64% of the patients had intestinal type while 36% had diffuse type. The patients with diffuse type were ≤50 years of age and one-third of the patients were ≤30 years of age while the peak incidence of intestinal type was in the age group of 51-60 years (37.5%). The findings were significant with a p-value of <0.0001. The findings are in concordance with the global trend that diffuse type is more common in the younger age group in contrast to intestinal which is more common in older age groups. Diffuse type gastric cancer is more common in young patients, in whom there is a female preponderance,\(^ {53}\) and behaves more aggressively than the intestinal type. The male: female ratio in patients with diffuse type was 1:2 whereas it was 1:9:1 for the intestinal type. Thus, this study has shown that the incidence of diffuse type is more in females while that of intestinal is more in males (p = 0.02787) which again matches with the global trend.

Surgery Done
Optimal surgical therapy offered to a patient with resectable proximal gastric carcinoma is total gastrectomy and to a patient with distal gastric cancer is distal gastrectomy both of which are curative surgery.\(^ {54,55,56,57}\) In case of metastatic cancer, palliative surgery may be done which are palliative gastrojejunostomy\(^ {54,55,56,57}\) or at least feeding jejunostomy. In this study, this protocol is followed. 40% of the patients underwent a palliative feeding jejunostomy, 4% of the patients underwent a palliative gastrojejunostomy. Total gastrectomy was done in 20%, subtotal gastrectomy in 18%, distal gastrectomy in 18% of the patients.

Histopathology
Nakamura et al have shown that poorly-differentiated adenocarcinoma was the commonest histological type in their study which are mostly advanced gastric cancer. But in early gastric cancer, well-differentiated adenocarcinoma was the commonest type (45.5%). In this study, 56% of the patients had poorly differentiated tumours (Including both poorly-differentiated adenocarcinoma and signet ring carcinoma), 30% had moderately-differentiated tumours and 14% had well-differentiated tumours. 64% of the patients had adenocarcinoma and 36% had signet-ring carcinoma. Signet-ring cell carcinoma was found in all the cases of diffuse gastric cancer which is in accordance with global data.

Association between the Tumour Grade and the Operation Performed
Of the 22 patients (44%) who underwent palliative procedures for metastatic disease, 90.9% had poorly-differentiated tumours (including signet-ring cell type) and only 9.1% had moderately-differentiated tumour. Of the 28 patients with poorly-differentiated tumours, 20 (i.e. 71.43%) had metastatic disease and underwent palliative procedures. 2 of the 15 patients (i.e. 13.3%) with moderately-differentiated tumours underwent palliative procedures for metastatic disease.

CONCLUSIONS
Although CT-Scan is a very commonly used preoperative staging investigation for gastric cancer, in our study we found that the accuracy of CT-Scan in T, N, M staging was 44%, 38% and 72% respectively. The disparity between preoperative staging and preoperative findings was more in case of poorly differentiated cancers. Hence, more advanced staging investigations like endoscopic ultrasound are needed for more accurate preoperative staging.

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