ABSTRACT

Objective: To determine the diagnostic accuracy of CT scan in evaluation of Gallbladder Carcinoma (GBC) taking histopathology as gold standard.

Study Design: Cross sectional, Descriptive study. The study was conducted at Department of Radiology, Dow Medical Collage and Civil Hospital, Karachi from 1st January 2014 to 31st December 2014.

Materials and Methods: This study comprises 434 patients of either gender, age between 30 to 70 years, with history of jaundice, pain in right hypochondrium / epigastrium and weight loss with suspicion of carcinoma gall bladder, referred to the Radiology Department of Civil Hospital Karachi over a period of 12 months. Post operated cases without CT scan and patients allergic to the contrast material were excluded from the study. Patients who fulfilled the above mentioned criteria, followed to CT scan with intravenous contrast and findings were documented. Patients were referred for surgery. During surgery sample for histopathology was taken which was used as gold standard. Data were entered and analyzed using computer program SPSS-21. Descriptive statistics were applied to calculate mean and standard deviation for the quantitative variables. The sensitivity, specificity; positive predictive value, negative predictive value, and diagnostic accuracy of CT scan were calculated.

Results: Out of 434 patients there were 183(42%) male and 251(58%) female patients in this study. The overall mean age was 53.37±7.18 years with range 28 (38–66) years. With histopathological findings gallbladder carcinoma (GBC) was found positive in 292 patients and with CT scan findings gallbladder carcinoma (GBC) was found positive in 285 patients. The mean age of patients with positive histopathological findings for gallbladder carcinoma (GBC) was 54.36±6.95 years and the mean age of patients with positive CT scan findings for gallbladder carcinoma was 53.51±7.28 years. 274 patients were true positive and 132 patients were true negative. Sensitivity, specificity, PPV, NPV and accuracy were 94.2%, 92.3%, 96.1%, 88.6%, and 93.5% respectively.

Conclusion: The use of computed tomography can help early diagnosis of GBC. Contrast enhanced MDCT was effective in identifying the criteria for resectability of the tumor and in disease staging. The histopathological diagnosis of the present study correlated well with CT scan in diagnosis of gallbladder malignancy.

Key words: CT scan, diagnostic accuracy, GBC, gallbladder carcinoma, histopathology, MDCT.

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INTRODUCTION

Gallbladder Carcinoma (GBC) is a fatal malignancy although rare. It is the fifth most common gastrointestinal malignancy and the most common biliary tract cancer, surpassing cholangiocarcinoma.1

However, GBC is somewhat uncommon with a low incidence of 1 or 2 cases per 100,000 people.2 A number of demographic variables play a role in GBC. Females have a 40 to 60 % higher incidence of GBC than men.3

The most recognizable cause for development of GBC is chronic cholecystitis. GBC is associated with the nonspecific vague symptoms therefore the early diagnosis is a challenge. Approximately 50% of cases of GBC are found incidentally during laparoscopic cholecystectomy.4 The prognosis of GBC is dismal, with five-year survival rate of 5%.5 It has been reported that early detection of GBC can improve the 5-year survival rate to 75%.
The diagnostic accuracy of CT scan in evaluation of gallbladder carcinoma

The prognosis of GBC is poor due to its late presentation as patients have non-specific abdominal symptoms, direct extension to adjacent vital organs frequently occurs at presentation\(^7\). However, with proper investigations i.e. with imaging, radical surgery can be curative\(^5\). In many patients the disease is revealed during surgery for gallstones, malignancy is detected on histopathological examination of cholecystectomy specimen\(^6\).

Computed tomography (CT) scans helps to differentiate chronic cholecystitis from GBC\(^8\). CT scan obtained in the portal venous phase after iodinated contrast administration is useful to identify concerning features, such as gallbladder wall thickening, mass, biliary obstruction and local invasion into the liver, as well as metastatic disease\(^9\).

Computed tomography (CT) has been reported as a comprehensive tool for imaging and staging of GBC\(^10,11\). The accuracy for cancer staging ranges from 83\% to 93\%\(^12\).

The purpose of this study was to analyze the accuracy of preoperative CT assessment between GBC presenting as an intraluminal mass and an infiltrating tumor taking histopathological findings as gold standard.

**MATERIALS & METHODS**

The patients of either gender with history of jaundice and pain in right hypochondrium / epigastrium with suspicion of GBC referred to Radiology Department of Civil Hospital Karachi from 1\(^{st}\) January 2014 to 31\(^{st}\) December 2014 were included in this study. Other Inclusion Criteria were age 30-70 years, weight loss. Postoperative cases without CT scan examination and patients allergic to contrast material were excluded from the study.

The benefits and risks including radiation hazards and the purpose of this study was explained to each participant and informed consent was obtained from all patients prior to their participation in this study. Patient demographics, clinical history and examination were done and then the patients were subjected to CT scan. Computed tomography was performed on Toshiba Activion 60 slice CT scanner. Scanning protocol included acquisition of axial helical CT sections before and after administration of intravenous contrast extending from the xiphoid process of the sternum to the pubic symphysis at 120kVp & 210 MA. At time of scanning intravenous contrast was administered using power injector at rate of 5 ml per sec followed by acquisition of axial cuts at 4 mm slice thickness in portal-venous phase (60-70 sec's after injection of bolus contrast). The information provided by CT scan was interpreted by consultant radiologist with minimum of five years of experience. Patients were then referred back to surgical units and subjected to surgery. Post-surgery Gallbladder specimens were taken for histopathology in 10\% buffered formalin. Histopathology reports were reviewed by Radiologist and Surgeons. The findings seen on CT scan were documented on a Performa by the researcher. Confounding variables and biasness were controlled by strictly monitoring the inclusion and exclusion criteria. Data were analyzed on statistical package for social sciences (SPSS-21). Descriptive statistics were computed. Frequency and percentage were computed for qualitative variables i.e. gender, CT scan findings and Histopathology findings. Mean ±SD were calculated for quantitative variable i.e. age, the sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of CT.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Informed consent was obtained from all patients for being included in the study.

**RESULTS**

Out of total 434, there were 183(42\%) male and 251 (58\%) female patients in the study. Percentage of patients according to gender distribution is presented in Graph-1. The frequency distribution of gender is also presented in Table-1. The overall mean age was 53.37 ± 7.18 years with range 28(38–66) years.

Table 1: Frequency Distribution of Patients According to Gender (n=434)

<table>
<thead>
<tr>
<th>Frequency (n)</th>
<th>%</th>
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<tbody>
<tr>
<td>Male</td>
<td>183</td>
</tr>
<tr>
<td>Female</td>
<td>251</td>
</tr>
<tr>
<td>Total</td>
<td>434</td>
</tr>
</tbody>
</table>

Among total study subjects, it was observed that with histopathological findings of GBC was found positive in 291(67.1\%) patients and found negative in (32.9\%) 143 patients. Frequency distribution is presented in Table-2. With CT scan findings GBC was found positive in 285 patients and found negative in 149 patients. Frequency distribution is presented in Table 2.

The mean age of patients with positive histopathological findings for GBC was 54.36±6.95 years with range 28(38–66) years and the mean age of patients with positive CT scan findings for GBC was 53.51±7.28 years with range 28(38–66) years.
Sensitivity, specificity, predictive values and diagnostic accuracy of CT scan for the detection of gall bladder carcinoma taking histopathology as gold standard were calculated. The results showed that there were 274 (63.1%) patients true positive, correctly diagnosed and 132 (30.4%) patients were true negative, correctly diagnosed. Sensitivity, specificity, PPV, NPV and accuracy were 94.2%, 92.3%, 96.1%, 88.6%, and 93.5% respectively.

### Table 3: Diagnostic Accuracy of CT Scan Findings to Diagnose Gallbladder Carcinoma with Histopathology as Gold Standard (n=434)

<table>
<thead>
<tr>
<th>CT Scan Findings</th>
<th>Histopathological Findings</th>
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<tbody>
<tr>
<td></td>
<td>Frequency (n)</td>
</tr>
<tr>
<td>Positive</td>
<td>285</td>
</tr>
<tr>
<td>Negative</td>
<td>149</td>
</tr>
<tr>
<td>TOTAL</td>
<td>434</td>
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</table>

The majority of reports suggested that GBC is two to six times more prevalent in women and the incidence peaks in the seventh decade of life.\(^{10-22}\) When stratified by age, the incidence of GBC was 0.3% in those under 50 years of age, 3.8% in those over 50 years old, and 8.8% in those older than 65 years of age.\(^{23}\) In our study, the mean age at diagnosis is 53.37±7.18 and its GBC was prevalent in 183 male and 251 female and so more prevalent in females.

Memon et al in 2005 have shown in their series that the mean age of the patients having gallbladder malignancy was 70.6 years and range from 42 to 85 years.\(^{24}\) In our study the mean age of patients having gallbladder malignancy positive in histopathological findings was 54.36±6.95 years with range from 38 to 66 years and with positive findings in CT scan it was 53.51±7.28, probably the change is due to racial variation and shorter average life span.

In our study, 67.1% patients had positive findings of GBC in histopathology and 65.7% in CT scan findings. In the present study, the mean age of presentation was 53.05±7.5 years for males and 53.60±6.9 years for females, which is almost a two decade less than the reported mean age in western literature. Similar observations have been reported earlier by Kumar et al\(^{25}\) in their experience of 116 cases of carcinoma GB in North India. This variation may represent the regional disease pattern or indicates the changing trend in the disease statistics as a consequence of the improved imaging modalities.

Although CT scan is not routinely used to investigate patients with gallbladder disease symptoms, it is a valuable investigation for suspected cases of GBC. The most common CT finding in GBC is a mass that fills most of an enlarged and deformed gallbladder.\(^{26}\) These masses are typically low in attenuation with variable enhancement.\(^{27}\)

Computed tomography (CT) presentation of GBC is variable. As a symmetric or asymmetric gallbladder wall thickening that may be difficult to distinguish from the scarred gallbladder wall seen in chronic cholecystitis. Gallbladder wall thickening can have an extensive differential diagnosis, including acute and chronic cholecystitis, xanthogranulomatous cholecystitis, and adenomyomatosis as well as diffuse hepatic or systemic diseases such as acute hepatitis, portal hypertension, and congestive heart failure.\(^{28,29}\)

**DISCUSSION**

GBC is an aggressive disease with a poor prognosis in advanced stage. GBC is the fifth most common tumor of the digestive system and the most frequent of those arising in the biliary tree.\(^{10}\) Preoperative diagnosis of GBC is an exception rather than the rule.\(^{13,14}\) GBC is usually diagnosed incidentally following surgery for gall stone disease.\(^{15}\) Most of the patients are asymptomatic and patients suffering from advanced disease have symptoms.\(^{16}\) Those with obstructive jaundice usually present in advanced stages of the disease\(^{17}\) and the five year survival in such cases is less than 5%.\(^{18,19}\)

Table 2: Frequency Distribution of CT Scan Findings and Histopathological Findings for GBC (n=434)

<table>
<thead>
<tr>
<th>CT Scan Findings</th>
<th>Histopathological Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Frequency (n)</td>
</tr>
<tr>
<td>Positive</td>
<td>291</td>
</tr>
<tr>
<td>Negative</td>
<td>11</td>
</tr>
<tr>
<td>TOTAL</td>
<td>291</td>
</tr>
</tbody>
</table>

### Table 3: Diagnostic Accuracy of CT Scan Findings to Diagnose Gallbladder Carcinoma with Histopathology as Gold Standard (n=434)

<table>
<thead>
<tr>
<th>Histopathology Findings</th>
<th>CT Scan Findings</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Positive (n=291)</td>
</tr>
<tr>
<td>Positive (n=285)</td>
<td>274</td>
</tr>
<tr>
<td>Negative (n=149)</td>
<td>17</td>
</tr>
<tr>
<td>TOTAL</td>
<td>291</td>
</tr>
</tbody>
</table>

Graph 1: Percentage of Patients According to Gender (n=434)
The diagnostic accuracy of CT scan in staging of the disease and determining resectability has been reported in various studies. Yoshimitsu et al\textsuperscript{10} reported an accuracy of 83-86\% in diagnosing the local extent of GBC. The accuracy was lowest for thickened gallbladder wall at 54\% and highest for GB mass at 89\%. Kumaran et al\textsuperscript{31}, in their study of 32 patients have reported 93.3\% accuracy in predicting non-resectability using set criteria. Ohtani et al\textsuperscript{12}, found that the sensitivity of CT in detecting the direct spread to the liver of less than 2 cm, more than 2 cm, the extra hepatic bile duct, gastrointestinal tract and pancreas was 65, 100, 50 and 57\% respectively while the positive predictive values (PPV) were 77, 100, 90, 100\% respectively. The PPV was 100\% and 86\% for detection of liver metastasis and involvement of interaortocaval nodes\textsuperscript{19}. They concluded that CT can help in determining resectability and treatment in advanced stages because of high PPV\textsuperscript{19}.

This mismatch between CT and surgical findings limited the sensitivity to 72.7\%, specificity to 100\%, and accuracy to 85\% for determining resectability of GBC\textsuperscript{11}. Kumaran et al\textsuperscript{33}, reported an accuracy of 93.3\% for assessing resectability of GBC.

The sensitivity for diagnosis of intraluminal GBC with and without gallstones was 80\% and 100\% by CT. The sensitivity for diagnosis of infiltrating GBC with and without gallstones was 71.4\% and 75\% by CT, respectively\textsuperscript{27,34}. In our study the sensitivity, specificity, PPV, NPV and accuracy were 94.2\%, 92.3\%, 96.1\%, 88.6\%, and 93.5\% respectively, which was comparable for results found in literature.

**Limitation of the Study:**

The limitation of this study is the small sample size hence more structured studies with larger sample and longer postoperative follow up are required to be carried out, to standardize the treatment of GBC in various stages in a concretized manner.

This study was conducted in the urban area therefore the results might not be generalizable to larger populations this is another limitation.

**CONCLUSION**

The contrast enhanced CT is effective in identifying the criteria for resectability of the tumour and in disease staging. The histopathological diagnosis of the present study correlated well with CT scan diagnosis of gallbladder malignancy.

The use of computed tomography can help early diagnosis of GBC early diagnosis, identification of high-risk cases and providing prophylactic cholecystectomy could offer a potential cure for patients.

In this study a changing epidemiological pattern in the gender distribution as well as a shift of the mean age at diagnosis into the sixth decade of life was observed.

**REFERENCES**


