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A Study of Clinical And Hepatic Parameters in Patients of Carcinoma Gall Bladder

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Abstract

Background: Gallbladder cancer (GBC) is the fifth most common cancer of the gastrointestinal tract (GIT) and one of the most common cancers of the extra hepatic biliary tract with a high rate of mortality [1]. There is no specific clinical presentation of early stage GBC and thus preoperative diagnosis is difficult in many. Chronic inflammation, infection and gallstones are the factors leading to malignant transformation of gallbladder epithelium (GB) [2]. The early diagnosis of GBC is not possible in all and in many the disease is diagnosed at an advanced stage.

Methods: The present study was an observational study done with the aim of studying the clinical and hepatic parameters in patients diagnosed with carcinoma gall bladder. Study was conducted on 72 patients who were diagnosed and staged according to AJCC staging criteria. The clinical profile and liver function tests were noted.

Results: The maximum number of cases (n=24; 33.3%) were in the age range of 41-50 years and in a ratio of M:F- 1:3. About 40.2% of patients presented had increased serum bilirubin levels, more than 50% of patients had deranged liver enzymes (SGOT, SGPT), levels of albumin were below normal in 62.5% cases and 66.6% of had elevated ALP levels. The presence of gall stones on ultrasonography was seen in 79.2% (n=57) of patients.

Conclusion: Liver function derangement is common in patients of carcinoma gall bladder in early as well as late stages and the dysfunction can be due to malignancy or the other diseases affecting liver.

Keywords: GBC; ALP; Gallstones; Liver; Chronic inflammation

Introduction

Gallbladder cancer (GBC) is the fifth most common cancer of the gastrointestinal tract (GIT) and one of the most common cancers of the extra hepatic biliary tract with a high rate of mortality [1]. Data from various studies in India indicates that the disease is very common in Northern India mainly along Gangetic planes. The incidence being 4-5 cases/100,000 population in men and 10.1 per 100,000 in women which is comparable to data from Chile which has highest incidence of GBC in world (7.5/100,000). This distribution suggests high incidence in Northern India [3]. The male to female ratio for GBC is about 1:3 and the disease has the peak incidence rates in the fifth decade of life [4]. Chronic inflammation, infection and gallstones are the factors leading to malignant transformation of gallbladder epithelium (GB) [5]. Majority of the patients are have no symptoms at presentation while a few presents with clinical features that suggest benign disease of GB such as pain in right upper abdomen, occasional episodes of nausea and vomiting [6]. The early diagnosis of GBC is not possible in all and in many the disease is diagnosed at an advanced stage. The derangements in liver function parameter reflects liver injury and along with symptoms and signs of gall stone disease may lead to early suspicion and further evaluation for GBC [7].As already stated GBC is common in Northern India and despite its common prevalence, there is limited data to ascertain a particular parameter as indicator for further evaluation of early GBC.

Material and Methods

The present study was an observational study and was carried over a period of 12 months (January-December 2017). All treatment naïve patients diagnosed with carcinoma gall bladder by imaging and histopathology were included in the study. Chi square test was applied and a P value of <0.05 was considered as significant.

Results

In the present study the age range was 35-81 years with M: F ratio of 1:3. The most common presenting symptom of the cases was pain abdomen (n= 63; 87.5%) followed by loss of appetite (n=35; 48.6%) and jaundice (n=28; 36.1%) other symptoms complained were distension of abdomen, altered sensorium, vomiting, fever and abdominal lump. The most common clinical sign noted was abdominal tenderness(n=49, 68%) followed by right hypochondriac lump (n=33, 45.8%), Icterus(n=28, 38.8%), palpable liver(n=28, 38.8 %), pallor (n=23, 31.9%), ascites clinically (n=17, 23.6%), flapping tremor (n=17, 23.6%), edema (n=17, 23.6%) and other infrequent findings were clubbing and gynaecomastia [8,9]. The total Bilirubin levels were increased in 40.2% of patients, similarly the liver enzymes i.e. ALT, AST and ALP were elevated in 66.6%, 51.3%, 76.3% respectively. The mean values ± standard deviation of total Bilirubin was 5.8 ± 8.8 mg/dl, ALT- 117.7 ± 324.9 IU/L, AST- 129.8 ± 311.6 IU/L, ALP- 310 ± 274.4 IU/L and of albumin was 3.03 ± 0.75 gm/dl and hemoglobin was 11.05 ± 2.2 gm/dl. Gallstones were present in 79.2% of patients.

Presentation of patients was advanced (stage III and IV) in 91.6 % (n=66) and was early (stage I and II) in only 8.4 % (n=6) (Table 1).

	Early stage	Late stage	P value
Demography			
Age (Mean ± SD)	55 ± 10.7	55 ± 11.3	
Gender (M: F)	01:02	01:02.8	
Known gallstone disease n (%)	4(66.6)	27(40.6)	
Alcohol	-	6(9)	0.585
Tobacco	1(16.6)	20(30.3)	
Clinical features			
Pain abdomen	4(66.6)	59(89.3)	0.549
Loss of appetite	3(50)	32(48.4)	
Yellow discoloration of eyes	4(66.6)	24(36.3)	
Distension of abdomen	2(33.3)	15(22.7)	
Vomiting	-	8(12.1)	
Fever	2(33.3)	5(7.5)	
Malena	-	2(3)	
Abdominal tenderness	6(100)	49(74.2)	
RHC lump	2(33.3)	33(50)	
Icterus	4(66.6)	24(36.3)	
Hepatomegaly	1(16.6)	26(39.3)	
Pallor	3(50)	20(30.3)	
Clinically ascites	2(33.3)	14(21.2)	
Edema	2(33.3)	14(21.2)	
Laboratory Parameters			
Haemoglobin			
Normal	3(50)	28(42.2)	0.468
Mild	1(16.6)	24(36.3)	
Moderate	2(33.3)	9(13.6)	
Severe	-	5(7.5)	
Platelet (thrombocytopenia)			
Normal	4(66.6)	60(90.9)	0.121
Mild	2(33.3)	5(7.5)	
Moderate	-	-	
Severe	-	1(1.5)	
ALT			
Normal	2(33.3)	33(50)	0.789
1-3 times UNL	3(50)	21(31.8)	
4-10 times UNL	1(16.6)	10(15.1)	
>10 times UNL	-	2(3)	
AST			
Normal	2(33.3)	21(31.8)	0.477
1-3 times UNL	4(66.6)	27(40.9)	
4-10 times UNL	-	15(22.7)	
>10 times UNL	-	3(4.5)	
ALP			
Normal	2(33.3)	15(22.7)	0.558
Increased	4(66.6)	51(77.2)	
INR			
Normal	4(66.6)	43(65.1)	0.94
Deranged	2(33.3)	23(34.8)	
Albumin			
Normal	2(33.3)	23(34.8)	0.94
Decreased	4(66.6)	43(65.1)	
Total protein			
Normal	3(50)	50(75.7)	0.17
Decreased	3(50)	16(24.2)	
Gallstones			
Males	2(33.3)	11(20.7)	0.481

Table 1: Showing difference in demography, clinical features and laboratory parameters in early (stage I and II) and late stages (stage III and IV) of GBC.

Discussion

Majority of patients with GBC had associated liver dysfunction. Underlying gall stone disease was present in nearly 80% of all cases with GBC. Our findings are concordant with other studies from India and the neighboring Pakistan in terms of demography, clinical features and lab parameters (Table 2).

Characteristics	Central India	Eastern India	North India	Pakistan	Present study
	(n=48)	(n=198)	(n=33)	(n=940)	
Mean Age	55	55	45	46.2	55
M: F	01:04	01:03	01:03	01:03	01:03
Clinical Features (%)					
Pain abdomen	91.6	88.9	87.9	-	87.5
Loss of appetite	60.6	60		-	48.6
Icterus	33.3	32.8	33.3	-	36.1
Distension of abdomen	-	-	-	-	23.6
Altered sensorium	-	-	-	-	13.8
Vomiting	31.2	30.8	30.3	-	11.1
Fever	10.4	11.1	-	-	6.9
Malena	-	-	-	-	2.8
Abdominal tenderness	-	52	-	-	68
RHC lump	79.1	76.3	-	-	45.8
Icterus	37.5	36.4	-	-	38.8
Hepatomegaly	-	-	-	-	38.8
Pallor	-	-	-	-	31.9
Clinically ascites	22.91	22.2	-	-	23.6
Edema	-	-	-	-	23.6
Laboratory parameters					
ALT/ SGPT (IU/ml)	-	-	-	-	51.3
AST/SGOT (IU/ml)	-	-	-	-	66.6
ALP (IU/ml)	938.8	938.6	-	-	215
Albumin (gm/dl)	3.5	3.5	-	-	3.11 (1.28-4.34)
INR	-	-	-	-	1.05
Stages	Stage IV (27)	-	-	-	Stage IV (39)
Gallstones	79.1	80.3	75.7	98.5	79.2

Table 2: Comparison of findings in the present study with other studies from India and Pakistan.

Although ALP levels were high in all studies, we found lower mean ALP levels in comparison to other studies. The lower mean ALP might be due to the lower fraction of patients presenting with obstructive features in our study compared to other studies from India. Zhang et al concluded that ALP was only second to CA-125 as an early marker of GBC however, they could not establish any statistically significant difference in the elevation of ALP according to the stage of GBC [10].

Silk YN et al concluded that laboratory studies were not helpful in identifying patients with early stage GBC. Kanthan R et al concluded that there is no known serological marker for early diagnosis of GBC and that patients presenting with advanced stage disease have significant liver dysfunction; moreover, no parameter assessing liver function is significantly associated with the stage of disease [11,12]. Likewise, Gupta et al from India also observed that biochemical investigations have little or no diagnostic significance in the identification of early stage GBC [13].

Conclusion

These findings conclude that there is no parameter of statistical significance that can aid in detecting the disease at an early stage. Therefore, the emphasis should be on screening those with gall stone disease especially females in the fourth to fifth decade of life. The observation that the majority of patients present in advanced stages of the disease may be due to the lack of awareness among patients and inadequate health facilities. Moreover, since we are still in the curative stage of practice of medicine in India, lack of awareness in the physicians about the risk factors and importance of preventive screening of the population may also be contributory.

A high index of suspicion should be exercised and cases, especially with underlying gall stones and or high ALP levels should be duly evaluated for the development of GBC on a regular basis. The frequency of such evaluation cannot be defined but the frequency can be predicted according the affordability of patients and availability of resources.

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