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TO STUDY THE LEVEL OF CARBOHYDRATE ANTIGEN 19-9 (CA19-9) IN BENIGN AND MALIGNANT GALL BLADDER DISEASE

General Surgery

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ABSTRACT

Background- CA 19-9 although widely used for diagnosis of pancreatic carcinoma and cholangiocarcinoma there is no proper study to associate it with histological grade and TNM staging of pancreatic and cholangiocarcinoma. **Methods-** Hospital based, observational type of study was conducted in the Upgraded Department of General Surgery, Gastro Surgery Department, Gastroenterology Department of SMS Medical College, and Jaipur. **Results-** Mean CA19-9 level in malignant group was 544.15±721.44 U/ml and in benign group was 38.77±79.90 U/ml.There were significant difference in mean level of CA19-9 in case and control groups (p value <0.05). There were significant difference in CA19-9 levels between GBC cases in moderately and poorly differentiated Adenocarcinoma patients. There were significant difference in CA19-9 levels between GBC cases in stage III and stage IV. **Conclusion-** CA19-9 are valuable tool to add in the preoperative diagnosis of the gall bladder carcinoma.

KEYWORDS

CA19-9 , Gallbladder cancer (GBC), Malignant.

INTRODUCTION

Gallbladder cancer (GBC) is one of the most common and aggressive malignant neoplasms of the biliary system, accounting for 3% of all tumors.

CA 19-9 although widely used for diagnosis of pancreatic carcinoma and cholangiocarcinoma there is no proper study to associate it with histological grade and TNM staging of pancreatic and cholangiocarcinoma. As a result this study was undertaken to determine the aforementioned association of CA 19-9.

CA 19-9 is underestimated in its use after curative surgery or chemotherapy of pancreatic carcinoma and cholangiocarcinoma. In this study we wanted to establish if CA 19-9 level both pre and post operatively was associated with survival rate in patients. The CA19-9 antigen is defined by an igg1 mouse monoclonal antibody raised against the human colonic carcinoma cell line SW 1116 by Koprowski and colleagues in 1979. [1]Although the CA19-9 antibody was generated against a colorectal cancer cell line, it is found more frequently in the sera of patients with pancreatic carcinoma [2]

CA19-9 is currently the single most useful blood test in differentiating pancreatic cancer from chronic or recurring pancreatitis with a sensitivity ranging from 70–90% and specificity from 68–91% [3-6] It has been shown that elevated serum concentrations of CA19-9 decrease after curative surgery and conversely that recurrent disease is often associated with an increase in the circulating level of this serum marker, which is a prerequisite for the use in follow-up of pancreatic carcinoma and cholangiocarcinoma.[3]

Due to limited study in India we conducted a study to detected serum levels of Carbohydrate antigen 19-9 (CA19-9) in 40 patients with GBC, 40 patients with benign gallbladder diseases.

MATERIAL AND METHODS

- **Study Design:** Hospital based observational type of study.
- **Study Area:** Proposed study was conducted in the Upgraded Department of General Surgery, Gastro Surgery Department, Gastroenterology Department of SMS Medical College, and Jaipur.
- **Study Period:** Study was conducted from approval of ethics committee till sample size achieved. [May, 2017 – Dec, 2018]
- **Sample Size:** 40 eligible malignant cases would be included in study on first come first basis and benign gall bladder disease comes reported just after each malignant case would be included for benign group.

INCLUSION CRITERIA

- Patient admitted in SMS Hospital
- Cases:- Histologically diagnosed patient with Gall bladder carcinoma who had given written informed consent for study
- **Controls: -** Patients with benign Gall bladder disease who diagnosed by radiological and biochemical investigation.

EXCLUSION CRITERIA

- Who have history of any other cancer
- Patients with Tuberculosis, retroviral diseases and hepatitis.
- Patient with Diabetes, Hypertension
- Subjects who are not willing for study
- Age below 14 years

Statistical analysis

Statistical analysis was performed with the SPSS, version 21 for Windows statistical software package (SPSS inc., Chicago, IL, USA). The Categorical data was presented as numbers (percent) and were compared among groups using Chi square test. The quantitative data was presented as mean and standard deviation and were compared by student's t-test. Probability was considered to be significant if less than 0.05.

For significance cut off values are as follows →
P > 0.05 = not significant
P < 0.05 = significant

OBSERVATIONS AND RESULTS

Table No. 1. Age Incidence of Gall Bladder cancer

Age Group	No. of GB Patients	Percentage %
<40	7	17.5
41-50	6	15.0
51-60	10	25.0
61-70	14	35.0
>70	3	7.5
Total	40	100.00

Table 1 shows- Incidence of gall bladder cancer in > 50 years of age is 67.5%. Gall bladder cancer is mainly a disease of older age group. Incidence below 50 years age is only 32.5%.

Table No. 2. Distribution of GBC according to Gender

Gender	No. of GB Patients	Percentage
Male	16	40.00
Female	24	60.00
Total	40	100.00

Table 2 shows 60% cases were female. Carcinoma gall bladder is mainly a disease of female in our study.

Table No. 3.Comparison of mean levels of tumor markers in case and control group

	N	CA19-9 (U/ml)	
		Mean	SD
Malignant group	40	544.15	721.44
Benign group	40	38.77	79.90
P value		0.001	

Mean CA19-9 level in malignant group was 544.15±721.44 U/ml and in benign group was 38.77±79.90 U/ml.There were significant difference in mean level of CA19-9 in case and control groups (p value <0.05).

Table No. 4.Correlation between CA19-9 markers and tumor size

Tumor size (cm)	N	CA19-9	
		Mean	SD
<5	19	444.97	709.62
>5	21	633.89	737.52
P value		p<0.001	

There were significant difference in serum CA19-9 between GBC cases at different tumor size. Mean level of CA19-9 were higher when tumor size is >5cm.

Table No. 5. Correlation between CA19-9 and degree of differentiation

	n	CA19-9	
		Mean	SD
Well Dif. Adenocarcinoma (1)	6	479.67	767.47
Mod. Dif. Adenocarcinoma (2)	16	450.81	748.34
Poorly Dif. Adenocarcinoma (3)	18	648.62	710.95
p value		0.02 (S)	

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There were significant difference in CA19-9 levels between GBC cases in moderately and poorly differentiated Adenocarcinoma patients.

Table No. 6 Correlation between CA19-9 and tumor stages

	n	CA19-9	
		Mean	SD
Stage 1	3	56.06	67.43
Stage 2	4	212.5	219.15
Stage 3	6	622.83	736.37
Stage 4	27	658.03	785.37
		0.0059	

There were significant difference in CA19-9 levels between GBC cases in stage III and stage IV.

Table No. 7. Correlation between CA19-9 and Lymph Node Metastasis

Lymph Node Status	n	CA19-9	
		Mean	SD
Yes	19	573.84	718.89
No	21	517.28	740.41
		0.808	

There were insignificant difference in Serum CA19-9 levels in patients with Lymph node metastasis and patients without Lymph node metastasis.

Table No. 8.Positive Rate of different tumor marker

	Malignant (40)		Group B (40)	
	No.	%	No.	%
CA19-9	26	65	8	20

Positive rate of CA19-9 was 65% in cases and 20% in control group.

Table No. 9. Evaluation of Sensitivity of CA19-9 in 40 gallbladder cancer cases

	n	Sensitivity
CA19-9 Pc	26	65

Sensitivity of CA19-9 Pc were 65.00%,

DISCUSSION

This study entitled "AN OBSERVATIONAL STUDY OF LEVEL OF **CA19-9** IN BENIGN VERSUS MALIGNANT GALL BLADDER DISEASE" was conducted in the Department of General surgery, SMS Medical College, Jaipur during year 2017-2018. The incidence of GBC had increased in recent years worldwide. In this study we analyzed the correlation between tumor markers and different clinicopathological features of GBC and compare of mean level of these markers in GBC cases and benign gall bladder disease.

In our study there were significant difference in mean level of **CA19-9** in case and control groups (P Value < 0.05). These results are comparable to study, Chaube A, et al. [7] and Yun-Feng Wang, et al. [8] which showed there were significant association between CA125, CA19-9 and Carcinoma gallbladder. And conclude that they have a diagnostic potential for GBC.

GBC is one of the aggressive malignant neoplasm of the biliary system. Early stage GBC lacks typical clinical manifestation, so most patients are at the advanced stage at the time of diagnosis. It is therefore important to diagnose GBC earlier.

Currently, the diagnosis of GBC mainly depends on non-invasive auxiliary imaging and invasive examination such as laparoscopy and biopsy. However, there is no ideal single tumor marker for the diagnosis and prognosis of GBC. [9-11] when these markers are used individually for the diagnosis of GBC, inconsistent results have been obtained. [12-15].

In this study positive rate of CA19-9 are 65 % in cases and 20% in control groups. We conclude that tumor markers were significantly higher in cases than controls.

CONCLUSION

CA19-9 are valuable tool to add in the preoperative diagnosis of the gall bladder carcinoma. Till now there is no definitive tool to confirm gall bladder carcinoma preoperatively. So in that scenario raised marker level along with CECT abdomen finding gives high index of suspicion of gall bladder carcinoma and it helps surgeon to preplan the type of surgery (open/ laparoscopic) and radical/non radical surgery and frozen section of specimen can be planned accordingly. This helps in referring the patient to higher centers if such technical facilities are not available. This prevent the patient to unnecessary undergo two surgery and there by decrease the morbidity of the patient and cost of the treatment.

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