MALIGNANT OBSTRUCTIVE JAUNDICE: A STUDY OF INVESTIGATIVE PARAMETERS AND ITS OUTCOME

Tilakdas S. Shetty[1], Smruti R. Ghetla[2], Salman Tehran Shaikh[3], Vineet Pilania[4], Anindya Gupta[5], Rohit Mundada[6]

[1]*Associate Professor, Department of General Surgery, Topiwala National Medical College, Mumbai.*
[2]*Associate Professor, Department of General Surgery, Topiwala National Medical College, Mumbai.*
[3]*Senior Resident, Department of General Surgery, Topiwala National Medical College, Mumbai.*
[4]*Senior Resident, Department of General Surgery, Topiwala National Medical College, Mumbai.*
[5]*Senior Resident, Department of General Surgery, Topiwala National Medical College, Mumbai.*
[6]*Junior Resident, Department of General Surgery, Topiwala National Medical College, Mumbai.*

ABSTRACT

BACKGROUND
Obstructive jaundice is a surgical condition that occurs when there is an obstruction to the passage of conjugated bilirubin from the liver cells to the intestine. This study has studied five clinical and nine laboratory parameters in patients presenting with malignant obstructive jaundice along with their radiological findings. By studying these parameters, the prognosis of patients with malignant obstructive jaundice and the best possible intervention could be predicted.

AIM
To study the various aetiopathological aspects associated with obstructive jaundice and investigative parameters of these patients thereby evaluating the prognosis.

MATERIALS AND METHODS
This observational study has been conducted in a tertiary institute by collecting data of 50 cases of malignant obstructive jaundice admitted to the surgical wards of BYL Nair Hospital from August 2011 to August 2014 with followup of 3 months to obtain mortality data. Male and female patients above 18 years and below 80 years of age with histologically proven malignant obstructive jaundice were included as part of this study. Data of retrospective cases were obtained from Medical Record section without disclosing the address or identification of the patient.

RESULTS
In this study, a total of 50 cases of histologically proven malignant obstructive jaundice were evaluated. 50 patients were studied out of which 33 were male and 17 were female. Majority of the patients were in the age group of 61-70 years i.e. 21 of them. 11 patients were between 41-50 years of age, 10 were less than 40 years of age and 8 were between 51-60 years. The most common presentation of the patients was with yellowish discolouration of sclera and urine (YDS/YDU) seen in 44 patients followed by pruritus seen in 38 patients. Dilated Common Bile Duct with/without pancreatic duct dilatation was the most common finding on sonography followed by a mass seen in the head of the pancreas. Moderately differentiated adenocarcinoma was the most common finding on histopathology followed by well-differentiated adenocarcinoma.

KEYWORDS
Adenocarcinoma, Jaundice, Mortality, Obstructive Jaundice.

INTRODUCTION: Obstructive jaundice is a surgical condition that occurs when there is an obstruction to the passage of conjugated bilirubin from the liver cells to the intestine. It may be caused by a heterogeneous group of diseases that include both Benign and Malignant conditions. Malignant obstructive jaundice is a clinical picture in which jaundice develops as a result of mechanical obstruction of bile ducts from primary pancreaticobiliary malignancies or metastatic deposits.

This study has studied five clinical and nine laboratory parameters in patients presenting with malignant obstructive jaundice along with their radiological findings. By studying these parameters, the prognosis of patients with malignant obstructive jaundice and the best possible intervention could be predicted. As patients with malignant obstructive jaundice have high morbidity and mortality, early diagnosis of the cause of obstruction is imperative as curative resection is only possible at an early stage.

The management of obstructive jaundice with malignant aetiology is challenging. This is attributable primarily to late presentation of the cases. Therefore, understanding the factors responsible for increased morbidity and mortality guides in appropriate management and eventually improved survival.

MATERIALS AND METHODS: This observational study has been conducted in a tertiary institute by collecting data of 50 cases of malignant obstructive jaundice admitted to the surgical wards of BYL Nair Hospital from August 2011 to August 2014 with followup of 3 months to obtain mortality data. Male and female patients above 18 years and below 80 years of age with histologically proven malignant obstructive jaundice were included as part of this study. Data of retrospective cases were obtained from Medical Record section without disclosing the address or identification of the patient.

All patients recruited into this study after obtaining an informed written consent were subjected to detailed history, clinical examination, laboratory investigations and radiological imaging. The patients were assessed at the time of admission and at the end of 3 months followup with regards to the survival outcome & the prognostic findings along with the outcome were recorded in a structured questionnaire.

Final diagnosis was made by:
   a) Correlating history of the patient with findings on clinical examination (i.e. presence of icterus, pruritus, clay colour stools, etc).
   b) Haematological investigations including Liver Function Tests, Tumour markers viz. CEA & CA19-9 & Radiological investigations viz. USG, CT abdomen.
   c) Histological tissue diagnosis including frozen sections obtained at the time of surgical exploration, histology of resected specimens.
   d) Findings at intervention such as ERCP or surgery.

Patients were then categorised as having Malignant Obstructive Jaundice according to the underlying aetiology. The Clinical & Laboratory parameters were evaluated and noted in the structured questionnaire after the diagnosis was confirmed by the above modalities.

Each case was assessed with respect to age/sex; clinical presentation; radiological investigations; surgical procedure (techniques) if indicated; intra-operative findings; clinical, Biochemical and haematological parameters at the time of admission; mortality at the end of follow up of 3 months.

All the collected data was entered in Microsoft Excel sheet. It was then transferred to SPSS version 17 software for statistical analysis. Quantitative data was presented as mean and standard deviation. Qualitative data was presented as frequency and percentage.

ROC curves were made to compare the efficacy of laboratory parameters like haemoglobin, serum bilirubin etc. as a screening test.

Binary logistic regression analysis was done on the outcome as dependent variables and on symptoms like YDS/YDU, Pruritus, etc. as predictor variables.

P value of <0.05 was considered as significant.

Final data from all cases was statistically studied to reach a conclusion. Analysis has been descriptive with followup of 3 months.

RESULTS: In this study, a total of 50 cases of histologically proven malignant obstructive jaundice were evaluated.

50 patients were studied out of which 33 were male and 17 were female as depicted in Table No. 1.

Gender	Frequency	Percent %
Female	17	34.0%
Male	33	66.0%
Total	**50**	**100.0%**
Table 1: Distribution of the Study Group as per Gender		

Majority of the patients were in the age group of 61-70 years i.e. 21 of them. 11 patients were between 41-50 years of age, 10 were less than 40 years of age and 8 were between 51-60 years of age as illustrated in Table No. 2. This concurs with the fact that malignant obstructive jaundice is a disease that is seen in old age.

Age Group (years)	Frequency	Percent %
< 40	10	20.0%
41-50	11	22.0%
51-60	8	16.0%
61-70	21	42.0%
Total	50	100.0%
Table 2: Distribution of the Study Group as per Age		

The most common presentation of the patients was with yellowish discolouration of sclera and urine (YDS/YDU) seen in 44 patients followed by pruritus seen in 38 patients. Clay coloured stools was a positive complaint in 23 of the cases as depicted in Table No. 3.

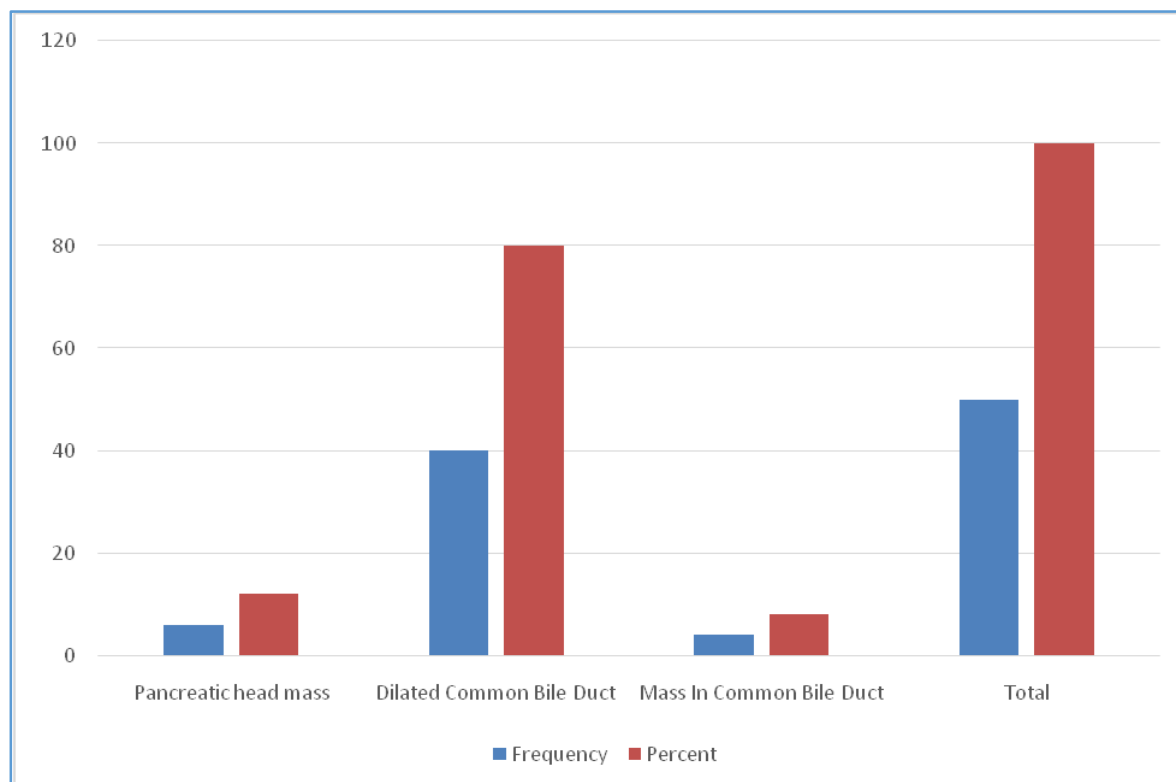| Symptoms	Frequency	Percent %
YDS/YDU	44	88.0%
Clay coloured Stools	23	46.0%
Pruritus	38	76.0%
Palpable Lump (GB)	26	52.0%
Abdominal Pain	28	56.0%
Table 3: Distribution of the Symptoms/Signs		

Distribution of laboratory parameters are depicted in Table No. 4.

Investigation		Frequency	Percent %
Hb.	< 10	17	34.0%
	≥ 10	33	66.0%
WBC	Normal	27	54.0%
	Raised	23	46.0%
Sr. Bilirubin	< 5	9	18.0%
	5 to 10	7	14.0%
	11 to 15	9	18.0%
	15 t 20	10	20.0%
	> 20	15	30.0%
SGOT/SGPT	Normal	15	30.0%
	Raised	35	70.0%
Alkaline Phosphatase	Normal	22	44.0%
	Raised	28	56.0%
Albumin	< 2.5	13	26.0%
	≥ 2.5	37	74.0%
INR	≤ 1.2	32	64.0%
	> 1.2	18	36.0%
Sr. Creatinine	≤ 1.2	45	90.0%
	> 1.2	5	10.0%
CEA	Normal	26	52.0%
	Raised	24	48.0%
CA 19-9	Normal	15	30.0%
	Raised	35	70.0%
Table 4: Distribution of Laboratory Parameters			

Dilated Common Bile Duct with/without pancreatic duct dilatation was the most common finding on sonography followed by a mass seen in the head of the pancreas as depicted in Graph No. 1.
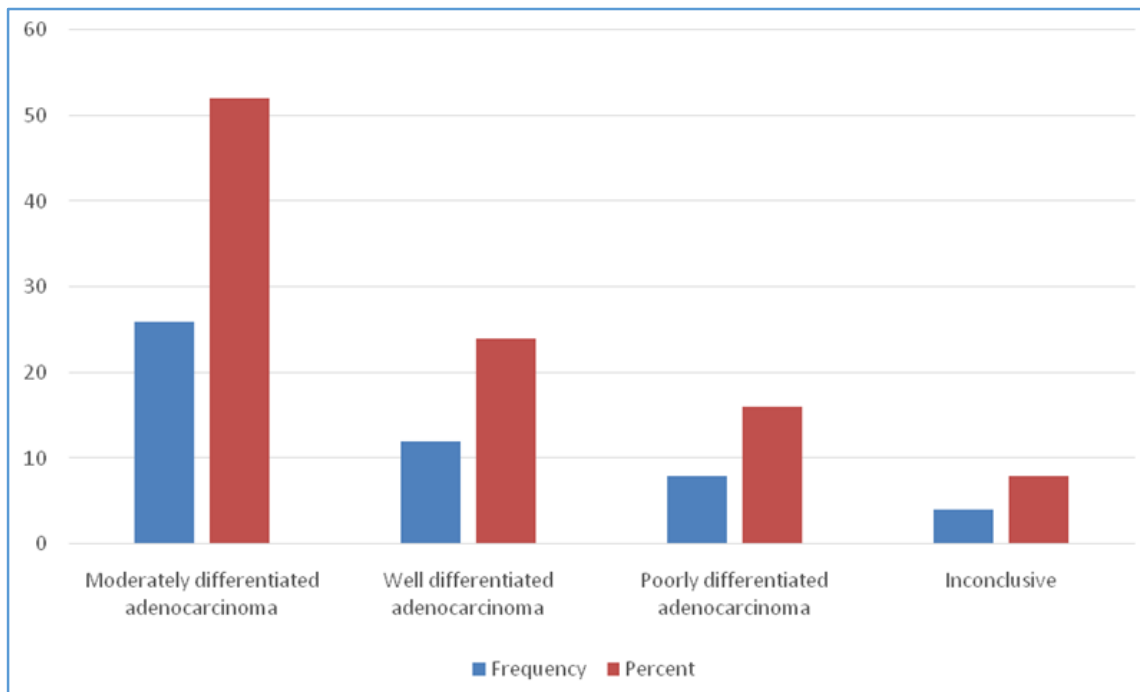

Graph 1: Distribution of USG Findings

| USG	Frequency	Percent %
Pancreatic head mass	6	12
Dilated Common Bile Duct	40	80
Mass In Common Bile Duct	4	8
Total	**50**	**100**
Table 5: Distribution Of USG Findings		

Moderately differentiated adenocarcinoma was the most common finding on histopathology (26 out of 50 patients) followed by well-differentiated adenocarcinoma (12 out of 50 patients) as describe in Graph No. 2.


Graph 2: Distribution of Histopathology Findings

Amongst the 50 patients assessed, 21 underwent Palliative stenting, 19 underwent definitive surgery i.e. Whipple's Procedure & 10 underwent Palliative surgery i.e. Triple Bypass as described in Graph No. 3.
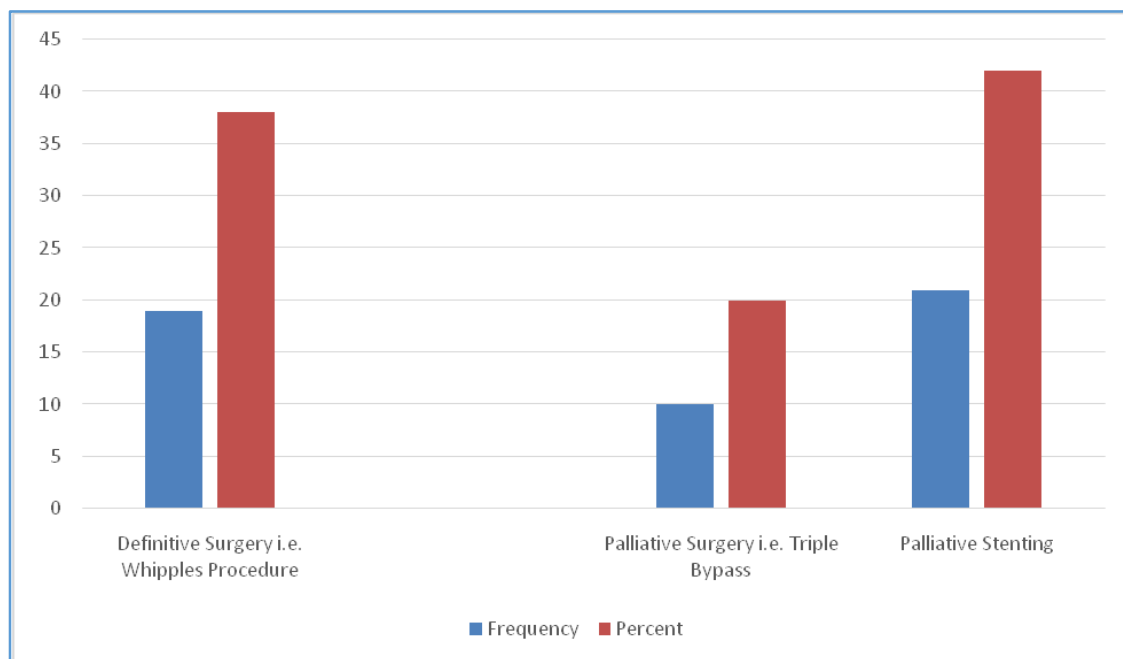

Graph 3: Distribution of the Intervention Done

4 out of the 19 patients who underwent Whipple's Procedure expired at the end of 3 months follow-up. 5 out of the 10 patients who underwent Triple Bypass and 11 out of the 21 patients who underwent stenting expired at the end of 3 months follow-up as depicted in Graph No. 4.
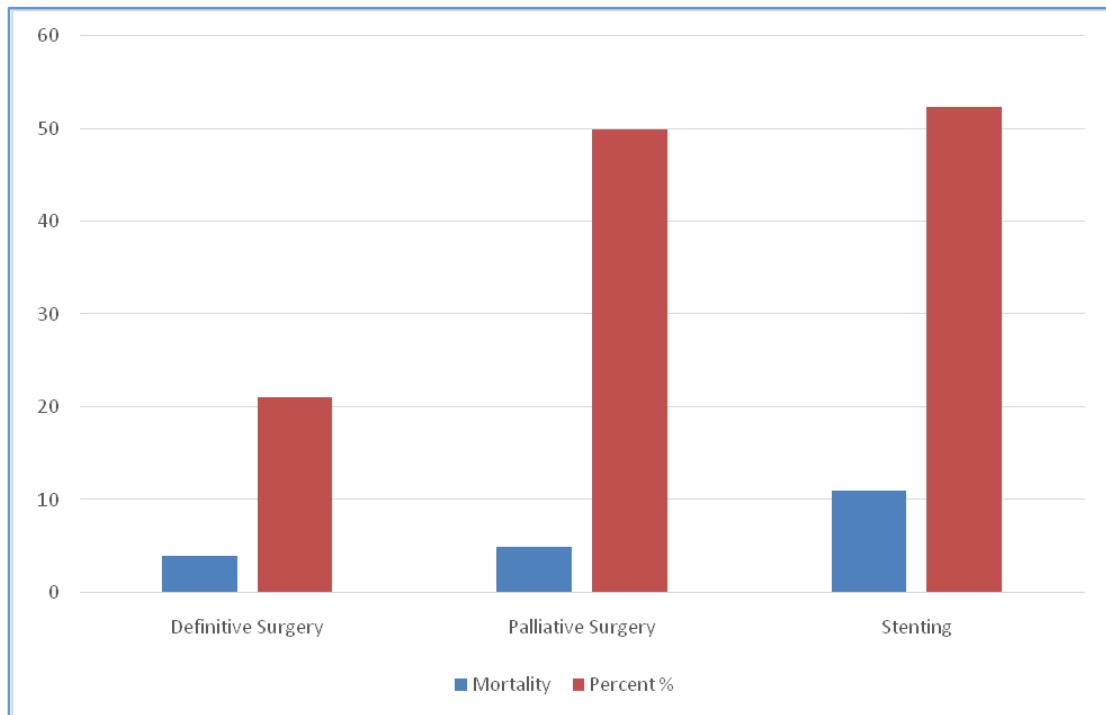

Graph 4: Distribution of Mortality

Receiver Operating Characteristic Curve for laboratory parameters –
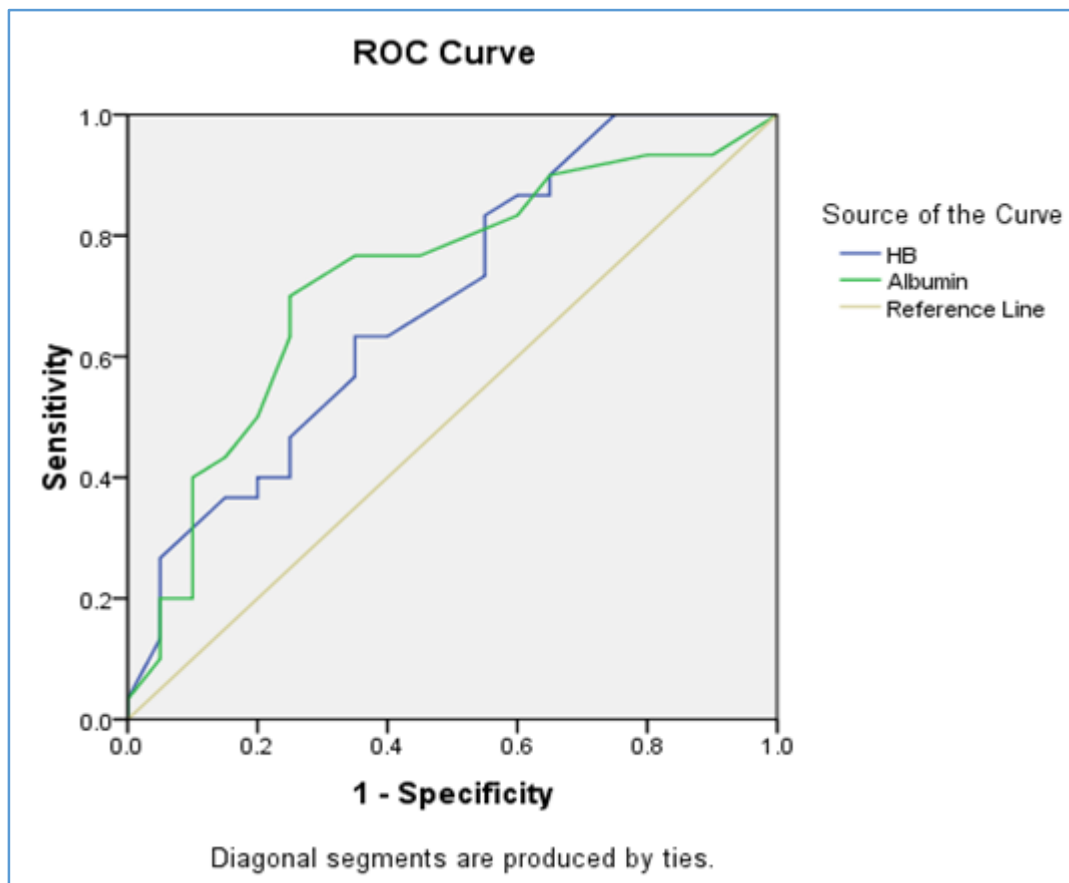
Area Under the Curve for Outcome (Dead/Alive)				
Test Result Variable(s)	Area	Std. Error	p- value	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Hb	0.691	0.077	0.023	0.54	0.842
Albumin	0.727	0.075	0.007	0.58	0.873

Area under curve for Sr. Albumin is 0.727 and that for Haemoglobin is 0.691. Thus, Sr. Albumin < 2.5 is a better predictor for mortality in these patients than Hb< 10.
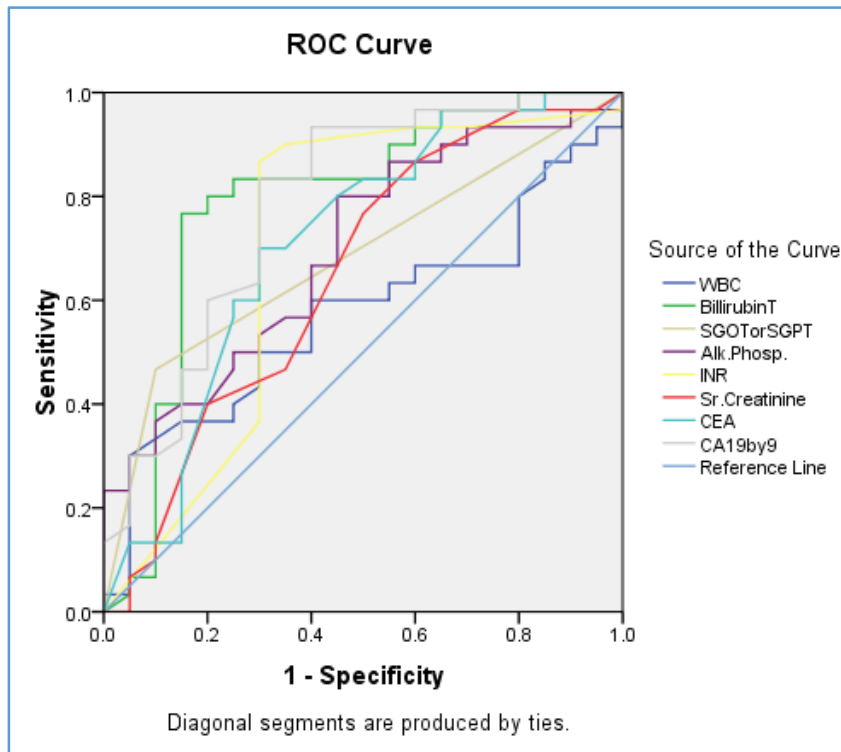
ROC Curve

Diagonal segments are produced by ties.

Area Under the Curve for Outcome (Dead/Alive)				
Test Result Variable(s)	Area	Std. Error	p- value	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Alkaline Phosphatase	0.697	0.075	0.019	0.55	0.844
CEA	0.711	0.079	0.012	0.556	0.866
CA19-9	0.787	0.069	0.001	0.651	0.922
Sr. Bilirubin	0.789	0.073	0.001	0.646	0.932
Sr. Creatinine	0.648	0.083	0.08	0.485	0.81
INR	0.707	0.086	0.014	0.538	0.876
WBC	0.573	0.081	0.384	0.414	0.733
SGOT/SGPT	0.683	0.075	0.029	0.535	0.831

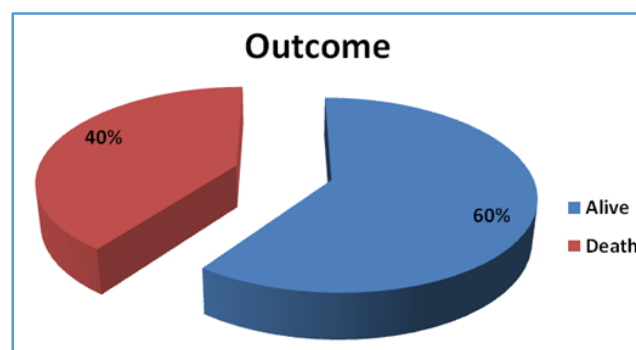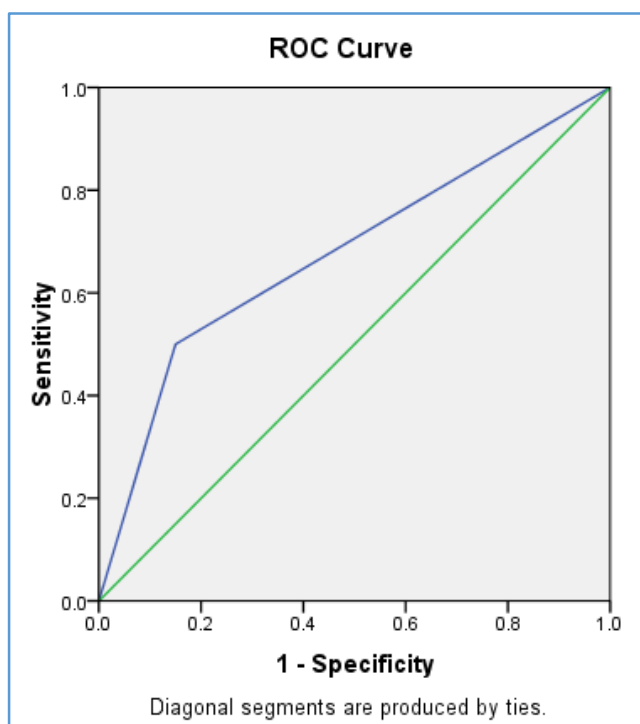| Indicator	Optimum Cut-off (>)	Sensitivity	Specificity
Alkaline Phosphate	280	80.0%	50.0%
CEA	3.7	86.7%	40.0%
CA 19-9	1800	93.5%	60.0%
Bilirubin	20	83.3%	55.0%
Sr. Creatinine	1.2	86.7%	40.0%
INR	1.2	86.7%	70.0%
WBC	11,000	60.0%	60.0%
SGOT/SGPT	70	70.0%	60.0%

Sr. Bilirubin value has a significant 'p' value with the maximum area under curve. For an optimum cut-off value of 20, the sensitivity is 83.3% and specificity is 55%. Thus, Sr. Bilirubin >20 mg/dL is a strong predictor for mortality in these patients.

CA 19-9 level above the optimum cut-off value of 1800 has a sensitivity of 93.5% and specificity of 60% making elevated CA 19-9 level a strong predictor of mortality.

INR>1.2 which is the optimum cut-off value in this study has a sensitivity of 86.7% and specificity of 70% making INR a strong predictor of mortality.

Regression Analysis (Outcome as Dependent Variable)								
Predictor Variables	**B**	**S.E.**	**Wald**	**Df**	**p- value**	**Exp(B)**	**95.0% C. I. for EXP(B)**	
							Lower	**Upper**
YDS/YDU	-2.428	1.35	3.235	1	0.072	0.088	0.006	1.243
Clay-coloured stools	-0.732	0.77	0.905	1	0.341	0.481	0.106	2.174
Pruritus	0.625	0.797	0.615	1	0.433	1.869	0.392	8.911
Palpable lump	1.567	0.779	4.046	1	0.044	4.794	1.041	22.075
Pain abdomen	-0.678	0.653	1.077	1	0.299	0.508	0.141	1.827

From the above analysis of qualitative data, we infer that palpable gallbladder is the most accurate predictor of mortality in these patients with a 'p' value of < 0.05 and with an odds ratio of 4.8.

Graph 5: Distribution of the Final Outcome

Area Under the Curve for Outcome (Dead/Alive)				
Test Result Variable(s): Combined Test (all Parameters)				
Area	**Std. Error**	**p-value**	**Asymptotic 95% Confidence Interval**	
			Lower Bound	**Upper Bound**
0.675	0.077	0.038	0.525	0.825

On analysing the combined quantitative test result variables of all the parameters for its efficacy in predicting the outcome, we see an area under curve of 0.675 with a 'p' value of 0.038 which is statistically significant.

Amongst the 50 patients studied, 30 patients were alive and 20 patients expired at the end of 3 months of follow-up as depicted in Graph No. 5.

DISCUSSION: A total of 50 cases of malignant obstructive jaundice in a tertiary setup were studied for this dissertation. Amongst them, 21 patients underwent Palliative stenting, 19 underwent definitive surgery i.e. Whipple's Procedure & 10 underwent Palliative surgery i.e. Triple Bypass.

Out of the 50 patients, male patients were 33 in number and female 17 in number. Maximum number of patients were in the age group of 61 to 70 years. Most common clinical presentation in patients with malignant obstructive jaundice was painless progressive jaundice evident by yellowish discoloration of urine and sclera seen in 88%. Gallbladder was palpable 84% of the patients. Pruritus was seen in 76% of the patients. Similar clinical patterns were reported by studies published from Pakistan, Ethiopia and other part of the world.[1,2,3,4]

The Gallbladder was palpable in 84% of patients with malignant obstructive jaundice. Serum values of Alkaline Phosphatase and Bilirubin was found to be on the higher side. Similar findings were observed in a study conducted by Cheema et al.[5]

Preoperative routine blood investigations like CBC, LFT, RFT, and radiological investigations, viz. ultrasonography, CT scan for staging were done in all the patients.

Final diagnosis was based upon the histopathological findings. Amongst all the cases, periampullary adenocarcinoma was found to be the most frequent diagnosis in this study. In a study conducted by Khurram et al., cancer of head of pancreas was found to be the most common cause of malignant obstructive jaundice.[6]

Moderately differentiated adenocarcinoma was the most common histological variety of carcinoma followed by well-differentiated adenocarcinoma. The percentage of mortality in the operated cases was found to be 31.03% and amongst the stented cases was found to be 52.38%. Sr. Bilirubin > 20 mg/dL, CA 19-9> 37, CEA> 2.5 and albumin < 2.5 were found to be strong predictors for mortality in malignant obstructive jaundice.

Iranian and Greek study found similar results in the factors predicting mortality in cases of malignant obstructive jaundice.[7,8]

In a study conducted by Shirahatti et al, they analysed 50 patients who underwent palliative bypass surgery for incurable malignant obstructive jaundice.[9] They found that patients having Hb<10 g/dL, serum bilirubin>20 mg/dL, serum albumin <2.5 g/dL and prothrombin index <60% exhibited a higher percentage of mortality and concluded that non-surgical methods may be more suitable in such patients.

LIMITATIONS OF THIS STUDY: Preoperative morbidities like Hypertension, Diabetes were not taken into account on evaluating the final outcome.

a) Operative & Postoperative complications were not studied in this dissertation.

b) Patients who were Immunocompromised with diseases like HIV, lymphoma were not studied exclusively in this dissertation.

Patients with Malignant obstructive jaundice usually present late and this is the primary attributable factor in the high incidence of mortality in these patients.

Studying the above-mentioned clinical and laboratory parameters in cases with malignant obstructive jaundice could help in predicting the prognosis and appropriate management viz. surgical or non-surgical in these patients.

CONCLUSION: Obstructive jaundice is a surgical problem often encountered in our clinical setting and poses diagnostic and therapeutic challenges. Malignant causes being more prevalent in males and in elder age group. Most of patients with malignant obstructive jaundice present late with advanced disease. USG, ERCP and CT scan are important diagnostic modalities for evaluation of patient with obstructive jaundice with ERCP having the additional advantage of being therapeutic as well. Palliative surgery is the only treatment modality for these patients. The result of this study suggests that early diagnosis and treatment plays a vital role in the prognosis of patients with obstructive jaundice.

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