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STUDY FOR EVALUATION OF CLINICAL, BIOCHEMICAL, TUMOR MARKERS AND RADIOLOGICAL PARAMETERS IN PATIENTS OF OBSTRUCTIVE JAUNDICE AT IGIMS, PATNA, BIHAR

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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.

Aims and Objectives : Study and co relate clinical, biochemical, radiological parameters in obstructive jaundice.

Material and methods: Present Study was conducted in IGIMS, Patna, Bihar. All adult patients who was diagnosed as case of obstructive jaundice based on clinical, radiological and pathological criteria. Study divided in two duration due to COVID-19 first May 2019 to February 2020 and second April 2021 to January 2022 (20 months). Purposive sampling, 50 in each group, Total 100.

RESULT: Benign Obstructive Jaundice, 6(12.0%) patients had fever, in malignant obstructive jaundice, 2(4.0%) patients had fever. Association of Fever vs Final diagnosis was not statistically significant (p=0.1403). In benign obstructive jaundice, 4(8.0%) patients had pruritis. In malignant obstructive jaundice, 37(74.0%) patients had pruritis. Association of pruritis vs final diagnosis was statistically significant (p<0.0001).

Conclusion: AST and ALP were higher in malignant obstructive jaundice compared to benign obstructive jaundice which were statistically significant. Mean GGT was higher in malignant obstructive jaundice compared to benign obstructive jaundice which was statistically significant. It was found that mean CA 19.9 was higher in malignant obstructive jaundice compared to benign obstructive jaundice which was statistically significant.

KEYWORDS : Clinical, Biochemical, Tumor Markers, Radiological parameters And Obstructive Jaundice

INTRODUCTION

In this study they will correlate clinical, biochemical, tumor markers and radiological parameters in patients of obstructive jaundice.

Clinical parameters pertaining to history such as age, residence of patient; history of weight loss will be recorded. Biliary disorders are prevalent in females of north India, genetic river belt and Pakistan[1].

Weight loss is defined as more than 4.5 kg or more than 5% of body weight reduction in last 6-12 months. BMI will be calculated by weight (in kilograms) over height squared (in meters). In examination findings palpable gall bladder, ascites and pedal edema will be considered. Gall bladder when distended it can be felt as a tense globular swelling projecting downwards and forwards below the liver just lateral to the outer border of the right rectus muscle (below the tip of the 9th rib). It moves freely with respiration and its upper limit is continuous with the liver. Which can be moved slightly from side to side.[2] Ascites is abnormal accumulation of fluid in abdominal cavity assessed by shifting dullness and fluid thrill. Pedal edema being accumulation of excess fluid in extra cellular space around ankle and feet causing swelling of these areas. In biochemical and tumor markers-Liver Function Tests, Renal Function Tests and Levels of CA 19.9 will be measured according to standard hospital protocol and recorded. The levels of tumor makers CA19.9 and CEA will be biochemically assessed.

The differentiation of benign from malignant strictures in the proximal bile duct is difficult[3]. Benign biliary tumours and strictures such as an inflammatory stricture secondary to choledocholithiasis, Mirizzi syndrome, extrahepatic localized form of primary sclerosing cholangitis (PSC) and idiopathic benign focal stricture are the possible differential diagnoses of a bile duct carcinoma [4]. The clinical findings and laboratory values including tumour marker levels are not specific enough to determine the precise cause of a biliary stricture of the proximal bile duct. The accuracy of alkaline phosphatase isoenzyme in differentiating benign from malignant extrahepatic biliary obstruction has been reported to be up to 80% 7. CA19-9 has been used to differentiate between cholangiocarcinoma and other benign causes of obstruction, but it has a variable sensitivity and specificity [5].

AIMS AND OBJECTIVES

1. To study and co relate clinical, biochemical, radiological parameters in obstructive jaundice.
2. To evaluate the role of these parameters in differentiating between benign and malignant jaundice as a differentiating marker.
3. To determine the cut off levels of CA 19.9 to differentiate between benign and malignant causes of obstructive jaundice.

MATERIAL AND METHODS

Present Study was conducted in Indira Gandhi Institute of Medical Sciences (IGIMS), Patna, Bihar. All adult patients who was diagnosed as case of obstructive jaundice based on clinical, radiological and pathological criteria. Study divided in two duration due to COVID-19 first May 2019 to February 2020 and second April 2021 to January 2022 (20 months). Purposive sampling, 50 in each group,100.

INCLUSION CRITERIA:

- All Patients presenting with obstructive jaundice.

EXCLUSION CRITERIA

- Patients less than 18 years of age
- Patients with other co-existing malignancy
- Patients in whom diagnosis could not be made

SAMPLE SIZE: Purposive sampling, 50 in each group, Total 100

METHODOLOGY:

Routine hematological and biochemical investigations including liver function tests, renal function test, US scan, CT, MRI was performed as indicated. The level of CA19.9 was biochemically assessed and analyzed. The value above 37 IU/ml of CA.19.9 was considered positive.

Obstructive jaundice is defined as the serum Total Bilirubin (TBIL)>1.2 mg% which is above the upper threshold of normal range and any imaging modality showing signs of obstruction of biliary tract. All the cases were evaluated as per the standard protocol and diagnosis was reached. The diagnosis of malignant etiology for obstructive jaundice was pathologically confirmed, by surgical resection or biopsy/FNAC.

RESULT

Our study showed that in BENIGN OBSTRUCTIVE JAUNDICE, 25(50.0%) patients were Female and 25(50.0%) patients were male. In MALIGNANT OBSTRUCTIVE JAUNDICE, 26(52.0%) patients were Female and 24(48.0%) patients were male.. In BENIGN OBSTRUCTIVE JAUNDICE, 19(38.0%) patients had H/O SMOKING/ ALCOHOL. In MALIGNANT OBSTRUCTIVE JAUNDICE, 14(28.0%) patients had H/O SMOKING/ ALCOHOL.

Association of H/O SMOKING/ ALCOHOL vs FINAL DIAGNOSIS was not statistically significant (p=0.2876). In BENIGN OBSTRUCTIVE JAUNDICE, 50(100.0%) patients had H/O JAUNDICE. In MALIGNANT OBSTRUCTIVE JAUNDICE, 50(100.0%) patients had H/O JAUNDICE.

We found that in BENIGN OBSTRUCTIVE JAUNDICE, 6(12.0%) patients had FEVER. In MALIGNANT OBSTRUCTIVE JAUNDICE, 2(4.0%) patients had FEVER. Association of FEVER vs FINAL DIAGNOSIS was not statistically significant (p=0.1403). In BENIGN OBSTRUCTIVE JAUNDICE, 4(8.0%) patients had PRURITIS. In MALIGNANT OBSTRUCTIVE JAUNDICE, 37(74.0%) patients had PRURITIS. Association of PRURITIS vs FINAL DIAGNOSIS was statistically significant (p<0.0001). In BENIGN OBSTRUCTIVE JAUNDICE, 8(16.0%) patients had LOSS OF WEIGH/APPETITE. In MALIGNANT OBSTRUCTIVE JAUNDICE, 35(70.0%) patients had LOSS OF WEIGH/APPETITE.

Association of LOSS OF WEIGH/APPETITE vs FINAL DIAGNOSIS was statistically significant (p<0.0001). In BENIGN OBSTRUCTIVE JAUNDICE, 9(18.0%) patients had URINE DISCOLOURATION. In MALIGNANT OBSTRUCTIVE JAUNDICE, 27(54.0%) patients had URINE DISCOLOURATION.

Association of URINE DISCOLOURATION vs FINAL DIAGNOSIS was statistically significant (p<0.0001).

Our study showed that in BENIGN OBSTRUCTIVE JAUNDICE, 1(2.0%) patients had CLAY COLOURED STOOLS. In MALIGNANT OBSTRUCTIVE JAUNDICE, 24(48.0%) patients had CLAY COLOURED STOOLS. Association of CLAY COLOURED STOOLS vs FINAL DIAGNOSIS was statistically significant (p<0.0001). In BENIGN OBSTRUCTIVE JAUNDICE, 5(10.0%) patients had DM,9(18.0%) patients had HTN and13(26.0%) patients had HTN & DM. In MALIGNANT OBSTRUCTIVE JAUNDICE, 4(8.0%) patients had DM and1(2.0%) patients had HTN. Association of DM/HTN vs FINAL DIAGNOSIS was statistically significant (p<0.0001). Association of H/O ABD SURGERY vs FINAL DIAGNOSIS was not statistically significant (p=0.3723).

We found in BENIGN OBSTRUCTIVE JAUNDICE, 6(12.0%) patients had PALLOR. In MALIGNANT OBSTRUCTIVE JAUNDICE, 14(28.0%) patients had PALLOR. Association of PALLOR vs FINAL DIAGNOSIS was statistically significant (p=0.0455). In BENIGN OBSTRUCTIVE JAUNDICE, 50(100.0%) patients had ICTERUS. In MALIGNANT OBSTRUCTIVE JAUNDICE, 50(100.0%) patients had ICTERUS. In BENIGN OBSTRUCTIVE JAUNDICE, 2(4.0%) patients had SCLN. In MALIGNANT OBSTRUCTIVE JAUNDICE, 8(16.0%) patients had SCLN. Association of SCLN vs FINAL DIAGNOSIS was not statistically significant (p=0.0871). In BENIGN OBSTRUCTIVE JAUNDICE, 1(2.0%) patients had ASCITIS. In MALIGNANT OBSTRUCTIVE JAUNDICE, 5(10.0%) patients had ASCITIS.

Association of ASCITIS vs FINAL DIAGNOSIS was not statistically significant (p=0.0921). In MALIGNANT OBSTRUCTIVE JAUNDICE, 4(8.0%) patients had ASCITIS. Association of ASCITIS vs FINAL DIAGNOSIS was statistically significant (p=0.0412). In BENIGN OBSTRUCTIVE JAUNDICE, 11(22.0%) patients had GB PALPABLE. In MALIGNANT OBSTRUCTIVE JAUNDICE, 38(76.0%) patients had GB PALPABLE. Association of GB PALPABLE vs FINAL DIAGNOSIS was statistically significant (p<0.0001).

Table : Difference of mean TLC, LT (LAKH), Polymor HS, T BIL and AST : Final Diagnosis

		No.	Mean	SD	Min.	Max.	Median	p-value
TLC	Benign Obstructive Jaundice	50	10882.6	3495.1680	6300.0000	19800.0000	11000.0000	0.3518
	Malignant Obstructive Jaundice	50	9900.8	6546.6012	1300.0000	44000.0000	8650.0000	
PLT (LAKH)	Benign Obstructive Jaundice	50	2.2440	0.5500	1.5000	3.1000	2.1000	0.7677
	Malignant Obstructive Jaundice	50	2.2020	0.8382	0.3500	3.7000	2.2000	
Polymor HS	Benign Obstructive Jaundice	50	74.68	10.9478	58.0000	93.0000	72.0000	0.9147
	Malignant Obstructive Jaundice	50	74.4880	6.3166	63.0000	93.0000	75.5000	
T BIL	Benign Obstructive Jaundice	50	8.0840	3.1653	2.5000	13.8000	6.8000	<0.0001
	Malignant Obstructive Jaundice	50	12.0460	3.8512	7.9000	23.3000	10.9500	
AST	Benign Obstructive Jaundice	50	86.3200	31.4555	32.0000	150.0000	92.0000	0.0033
	Malignant Obstructive Jaundice	50	147.8000	140.8054	46.0000	940.0000	106.0000	

DISCUSSION

Farrukh SZ et al[6] (2016) found that out of total 200 patients, mean age was 41.22±12.46 years with 107 (53.5%) females. Ability of ultrasound in correctly diagnosing obstructive reason for stone CBD was found to be 72.5%, dilated CBD without reason 41.7%, proximal obstruction, 63.15%, distal CBD obstruction 60%, and sludge 66.7%.

Overall ability of ultrasound in correctly diagnosing the cause of obstruction was 64.17%. Ultrasound is recommended as the initial examination, which provides a guide to choose patients for either a more advanced non-invasive imaging like MRCP or to an invasive procedure like ERCP.

Verma S et al[7] (2010) found that abdominal pain and clay coloured stools were more frequent in patients with malignant disease.

Carcinoma (Ca) of the head of pancreas was commonest aetiology 37/110 (33.63%) followed by Choledocholithiasis 32/110 (29%), Ca gall bladder 20/110 (18.18%), periampullary carcinoma 6/110 (5.45%), cholangiocarcinoma 4/110 (3.64%), CBD stricture 3/110 (2.73%), acute pancreatitis 3/110 (2.73%) and choledochal cyst 3/110 (2.73%). and HCC(1.8%).

Shetty TS et al[8] (2016) found that data of retrospective cases were obtained from Medical Record section without disclosing the address or identification of the patient. 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 pain abdomen was present in 73.33% patients, dyspepsia in 60%. Itching and clay coloured in 53% of patients. Melena in 10% patients with 36 times increased risk for malignancy. Palpable gallbladder was also statistically significant for malignant aetiology.

Liu W et al[9] (2018) found that the other 166 cases were BOJ, including cholelithiasis, primary sclerosing cholangitis (PSC), IgG4 related sclerosing cholangitis (IRSD), inflammatory stricture of bile duct, and adenoma. The data of the increase-folds of serum CA19-9, TBIL and the ratio of increase-folds of CA19-9 to increase-folds of TBIL was collected and analyzed.

We found that in BENIGN OBSTRUCTIVE JAUNDICE, the mean TLC (mean± s.d.) of patients was 10882.6000± 3495.1680. In MALIGNANT OBSTRUCTIVE JAUNDICE, the mean TLC (mean±s.d.) of patients was 9900.8000± 6546.6012. Difference of mean TLC with both FINAL DIAGNOSIS was not statistically significant (p=0.3518). In BENIGN OBSTRUCTIVE JAUNDICE, the mean PLT (LAKH) (mean± s.d.) of patients was 2.2440± .5500. In MALIGNANT OBSTRUCTIVE JAUNDICE, the mean PLT (LAKH) (mean± s.d.) of patients was 2.2020± .8382. Difference of mean PLT (LAKH) with both FINAL DIAGNOSIS was not statistically significant (p=0.7677).

Hayat JO et al 10 (2005) showed that group 1 (n = 69) had malignant strictures, group 2 (n = 97) had common bile duct stone(s), and group 3 (n = 41) appeared to have recently passed a stone. LFTs in groups 2 and 3 were also analysed at maximal liver enzyme derangement, maximum hyperbilirubinaemia and during acute pain episodes.Group 1 had higher median bilirubin, AST and ALP levels than groups 2 or 3 (p <0.001). In group 1, median rise in ALP exceeded that in AST (4.3 x normal upper limit (NUL) vs. 2.6 x NUL, p < 0.01), but in groups 2 and 3, AST and ALP were similarly elevated (both approximately 2 x NUL). Hospitalization shows in cases group acute pancreatitis in12.8%, jaundice in 30%, and fever in 30% and pain in the right hypochondrium in 95%. By comparing them, was observed that fever and jaundice were the signs and symptoms with statistical significance. Kasapidis P et al [11](2008) found that the cut-off values that provided the best trade-off between sensitivity and specificity were: 8.65 mg/ dL for total bilirubin, 276 U/L for serum alkaline phosphatase and 306 IU/ml for CA19-9. A patient most probably (96%) suffers from cancer, if he has high incriminating values in all these three parameters. A simple, reproducible, easy-to-obtain predictive model with laboratory tests, successfully differentiates choledocholithiasis from malignant biliopancreatic diseases and could be useful for a more cost-effective investigation and treatment of patients with such pathology.

Marrelli D et al [12] (2009) found that the diagnostic accuracy of this tumor marker was evaluated in the present longitudinal study. In 128 patients admitted for obstructive jaundice (87 with pancreato-biliary malignancy and 41 benign disease) serum CA19-9 was measured.

Statistical analysis of marker levels obtained before and after endoscopic biliary drainage was performed in 60 patients. Elevated CA19-9 levels (>37 U/mL) were found in 61% of benign cases and 86% of malignancies.

Kim MS et al [13] (2017) found that 114 patients with serial follow-up data for CA 19-9 level were included in this study (80 patients with malignancy and 34 patients with benign diseases). The compared the levels of CA 19-9 levels and the biochemical value before and after biliary drainage.The rate of CA 19-9 elevation (>37 U/mL) was significantly different between the benign group and the malignant group (59% vs. 90%, p=0.001). Despite the Peterli R et al [14] (1999) found that after treatment the CA19-9 returned to a normal level. One year postoperatively neither abdominal ultrasound nor CT-scan showed any sign of intraabdominal malignancy. Reviewing the literature, they conclude that even very high levels of CA19-9 in cases with obstructive jaundice can be caused by benign diseases.

Wang X et al [15](2017) found that tumor markers showed that CA19-9 level was more than 1,000.0 U/mL (normal range: 0–37 U/mL), CA-50 level was 466.34 IU/mL (normal range: 0–25 IU/mL), and CA24-2 level was more than 200 IU/mL (normal range: 0–20 IU/mL).

Abdominal CT scan and magnetic resonance cholangio pancreatography(MRCP) demonstrated multiple stones located in the lower segment of common bile duct, lower bile duct obstruction, and gallbladder stones.

CONCLUSION

We found that pruritis was more common in malignant obstructive jaundice compared to benign obstructive jaundice which was statistically significant.

It was found that loss of weigh/appetite, urine discolouration and clay coloured stools was significantly higher in malignant obstructive jaundice compared to benign obstructive jaundice.

Pallor, liver cell failure signs and gb palpable were more common in malignant obstructive jaundice compared to benign obstructive jaundice which was statistically significant. We found that T BIL and D BIL were higher in malignant obstructive jaundice compared to benign obstructive jaundice which was statistically significant.

AST and ALP were higher in malignant obstructive jaundice compared to benign obstructive jaundice which were statistically significant.

Mean GGT was higher in malignant obstructive jaundice compared to benign obstructive jaundice which was statistically significant.

It was found that mean CA 19.9 was higher in malignant obstructive jaundice compared to benign obstructive jaundice which was statistically significant.

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