

## Predictors of Outcome among patients with Obstructive jaundice at Bugando Medical Centre in north-western Tanzania

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**Abstract:** Despite recent advances both in preoperative diagnosis and postoperative care, obstructive jaundice still contributes significantly to high morbidity and mortality. A prospective study was undertaken to identify predictors of outcome among patients with obstructive jaundice at Bugando Medical Centre in north-western Tanzania. A total of 138 patients were studied. The male to female ratio was 1:1.6. The median age of patients was 58 years. Patients with malignant obstructive jaundice were older than those of benign type ( $P < 0.001$ ). Ca head of pancreas (65.1%) was the commonest malignant cause of jaundice where as choledocholithiasis (51.9%) was the commonest benign cause. Twelve (9.7%) patients were HIV positive with a median CD 4+ count of 342 cells/ $\mu$ l. A total of 130 (94.2%) patients underwent surgical treatment and the remaining 8 (5.8%) patients were unfit for surgery. The complication rate was 30.4% mainly due to surgical site infections and it was significantly influenced by malignant causes, WBC count  $> 10 \times 10^9/l$  and HIV infection with low CD4 ( $\leq 200$  cells/ $\mu$ l) ( $p < 0.0001$ ). The median hospital stay and mortality rate were 18 days and 20.3%, respectively. A low haematocrit and presence of postoperative complications were the main predictors of the hospital stay ( $P < 0.001$ ), whereas age  $> 60$  years, prolonged duration of jaundice, malignant causes, high bilirubin levels, HIV infection with low CD4+ count ( $\leq 200$  cells/ $\mu$ l) and presence of postoperative complications significantly predicted mortality ( $P < 0.001$ ). In conclusion, our study highlighted the important factors that predict the outcome of patients presenting with obstructive jaundice at BMC; therefore attention should be focused to these factors so as to improve the outcome of these patients.

**Keywords:** Obstructive jaundice, predictors, outcome, Tanzania

### Introduction

Obstructive jaundice is a common surgical problem that occurs when there is an obstruction to the passage of conjugated bilirubin from liver cells to intestine (Mohamed & Syed, 2007). It is among the most challenging conditions managed by general surgeons and contributes significantly to high morbidity and mortality despite recent advances both in preoperative diagnosis and postoperative care (Ahmad *et al.*, 2001). The challenge is even more conspicuous in developing countries where delayed presentation of the disease coupled with lack of modern diagnostic (e.g. Computed Tomography (CT) scan, Percutaneous Transhepatic Cholangiopancreatography (PTC), Endoscopic retrograde Cholangiopancreatography (ERCP) and Magnetic Resonance Cholangiopancreatography (MRCP) and therapeutic facilities (e.g. T-tubes) are among the hallmarks of the disease (Bekele & Yifru, 2000).

Surgery in jaundiced patients is associated with a higher risk of postoperative complications compared with surgery in non jaundiced patients (Hussain & Fatima, 2000; Uslu *et al.*, 2007). These

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complications primarily consist of septic complications (cholangitis, abscesses, and leakage), haemorrhage, impaired wound healing and renal disorders (Uslu *et al.*, 2007).

The outcome of treatment of obstructive jaundice may be poor especially in developing countries where advanced diagnostic imaging and therapeutic facilities are not readily available in most centres (Moghimi *et al.*, 2008). The mortality and morbidity of biliary obstruction are dependent on the cause of the obstruction, and the assessment of any factors which influence the morbidity and mortality in patients with obstructive jaundice in each society is necessary (Moghimi *et al.*, 2008; Pitiakoudis *et al.*, 2004). Understanding factors responsible for increased morbidity and mortality in these patients will better guide appropriate management and lead to improved survival (Buckwate, 1965).

There is paucity of published data regarding factors responsible for increased morbidity and mortality in patients with obstructive jaundice in our environment. This study was conducted to determine the predictors of outcome among patients presenting with obstructive jaundice at Bugando Medical Centre in north-western Tanzania. The findings of this study will better guide appropriate management and lead to improved survival of patients.

## **Methods and Patients**

### **Study design and setting**

This was a prospective study of patients with a clinical diagnosis of obstructive jaundice admitted to the surgical wards of Bugando Medical Centre (BMC) between July 2006 and April 2012. Bugando Medical Centre is a consultant and teaching hospital for the Catholic University of Health and Allied Sciences- Bugando and has a bed capacity of 1000. It is situated in Mwanza City, in north-western Tanzania. It is a referral centre for tertiary specialist care for six regions, namely Mwanza, Mara, Kagera, Shinyanga and Kigoma. It serves catchments population of approximately 13 million people.

### **Study subjects**

During this study, all patients who were admitted to the surgical wards of BMC with a clinical diagnosis of obstructive jaundice were consecutively recruited into the study. Patients with medical jaundice were excluded from the study. All the patients were subjected to detailed history, clinical examination, laboratory investigations which included the liver function tests to see the bilirubin level and the level of serum alkaline phosphatase and alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Other laboratory investigations included HIV testing (using Tanzania HIV Rapid Test Algorithm and CD 4+ count (using FACS or FACSCALIBUR from BD Biosciences USA), white blood cells (WBC) count, Packed red blood cell (RBC) volume, Prothrombin Time, serum creatinine and albumin. Abdominal Ultrasound was the only diagnostic imaging done in all patients to look for the abnormality of intra and extra-hepatic biliary channels, the common bile duct and presence of causative factors like gall stones, tumours, lymph nodes, worms or any abdominal mass.

Advanced diagnostic imaging such as CT scan abdomen, ERCP, PTC and MRCP were not done in any of our patients as these facilities are not available at the centre. The patients were assessed preoperatively, intraoperatively and postoperatively, and the findings were recorded in a pre-tested structured questionnaire.

Details that were recorded included patients' biodata, duration of jaundice, cause of obstructive jaundice, laboratory findings, ultra-sonographic findings, treatment modalities, intraoperative findings, post-operative complications, length of hospital stay and mortality. Preoperative preparations included maintaining good hydration and administration of antibiotics, intravenous dextrose (10%) solution and Vitamin K injections. In anaemic patients blood transfusion was also carried out. During surgery intravenous mannitol was used in all the patients. The nature of

surgical procedure carried out depended upon the cause and the findings at the time of surgery. Patients were followed up till discharge or death.

### Data analysis

Data analysis was done using SPSS computer software version 17.0 (SPSS Inc., Chicago, IL, USA) and STATA version 12.0. Results were reported as percentages for categorical variables. The variables were compared using the Chi-square test or Fisher's exact test if required for categorical variables. Predictors exhibiting a statistically significant relationship with outcome variables in the univariate analysis (p-value less than 0.05) were taken for a multivariate logistic regression analysis to investigate their independence. Odds ratios (OR) and 95% confidence intervals (CI) for OR were calculated. A p-value of less than 0.05 was considered statistically significant.

### Ethical consideration

Ethical approval to conduct the study was obtained from the CUHAS-Bugando/BMC Joint Institutional Ethical Review Committee before the commencement of the study. Informed written consent for the study and HIV testing was sought from each patient before being enrolled into the study.

### Results

Between July 2006 and April 2012, a total of 138 patients with a diagnosis of obstructive jaundice were enrolled in the study. Of these, fifty-four (39.1%) were males and the remaining 84 (60.9%) were females. The male to female ratio was 1: 1.6. The age ranged from 14 to 84 years with a median age of 58 years. The median age of patients with benign causes was 40 years (range 16-52 years), while that of malignant causes was 62 years (range 47-84 years). The difference in age distribution of the benign and malignant disease was statistically significant ( $P < 0.001$ ). The male to female ratio for benign obstructive jaundice was 1:2.4, while it was 1:1.6 for the malignant obstructive jaundice. This difference was statistically significant ( $P < 0.001$ ). Of the 138 patients, 52 (37.7%) had a benign and 86 (62.3%) a malignant cause of obstructive jaundice. Choledocholithiasis was the commonest cause among the benign group in 27 (51.9%) patients, whereas the commonest tumour among the malignant group was carcinoma of the head of pancreas in 56 (65.1%) patients (Table 1).

**Table 1: Causes of obstructive jaundice (N= 138)**

Cause	Response	Frequency	Percentage
<b>Benign cause</b>		<b>52</b>	<b>37.7</b>
	Choledocholithiasis	27	51.9
	Biliary stricture	14	26.9
	Chronic pancreatitis	4	7.6
	Amoebic hepatic abscess	1	1.9
	Cause not identified	6	11.5
<b>Malignant cause</b>		<b>86</b>	<b>62.3</b>
	Ca head pancreas	56	65.1
	Cholangiocarcinoma	10	11.6
	Peri-ampulary Ca	9	10.5
	Ca gallbladder	7	8.1
	Metastatic malignant lymph nodes in the portal hepatitis	4	4.7

The duration of illness ranged from 5 to 46 days with a median of 18 days. The majority of patients, 102 (73.9%) reported to our centre more than 14 days after the onset of illness.

Liver function tests were done in all cases and they show raised levels of Bilirubin and Alkaline Phosphatase in both benign and malignant groups. The differences in serum Bilirubin and Alkaline Phosphatase levels in these two groups were not statistically significant ( $P > 0.001$ ). Serum ALT levels were elevated in 99 (71.7%) of cases. The preoperative median serum bilirubin in patients was 19.6 mg/dl and fell to 2.4 mg/dl two weeks post surgery.

HIV status was known in 124 (89.9%) patients. Of these, 12 (9.7%) patients were HIV positive. Of the HIV positive patients, five (41.7%) patients were known cases on anti-retroviral therapy (ARV) and the remaining 7 (58.3%) patients were newly diagnosed patients. HIV status was not known in 14 (10.1%) patients. CD 4+ count among HIV positive patients was available in only 9 patients and ranged from 48 cells/ $\mu$ l to 820 cells/ $\mu$ l (median of 342 cells/ $\mu$ l). A total of four (44.4%) HIV positive patients had CD4+ count below 200 cells/ $\mu$ l and the remaining 5(55.6%) patients had CD4+ count of  $\geq$ 200 cells/ $\mu$ l.

Abdominal ultrasound was the only diagnostic imaging done in all patients and showed positive findings in 112 (81.2%) patients. A total of 130 (94.2%) patients underwent surgical treatment and the remaining 8 (5.8%) patients were unfit for surgery and were treated conservatively. Of the patients who were unfit for surgery, two patients had benign jaundice due to chronic pancreatitis and choledocholithiasis in a sickler patient with severe anaemia. The remaining six patients had advanced malignant jaundice. None of the patients had non-surgical procedures such as stricture dilatation and stent placement. Laparoscopic surgery was not done as this facility is not available at our centre. The type of surgical procedures performed is shown in Table 2.

**Table 2: Type of surgical procedure performed (N = 130)**

Type of surgical procedure	Number of patients	Percentage
Cholecystojejunostomy	83	63.8
Choledocholithotomy $\pm$ Cholecystectomy	18	13.8
Choledochoduodenostomy	10	7.7
Exploratory laparotomy/inoperable	8	6.2
Tumour resection	6	4.6
Hepaticojejunostomy	4	3.1
Drainage of abscess	1	0.8

Major surgeries like pancreatoduodenectomy, hepatectomy and Whipple's procedure were not performed as majority of patients requiring these procedures presented late with advanced disease and the only treatment option was palliative surgery. Forty-two (30.4%) patients had 52 post-complications. Surgical site infection was the most common post-operative complication accounting for 65.4% of cases (Table 3), and it was significantly influenced by malignant causes [OR=2.76, 95%CI (2.02-9.62),  $p= 0.003$ ], WBC count  $> 10 \times 10^9/l$  [OR = 1.54, 95% CI (1.11-3.87),  $p= 0.023$ ] and HIV infection with low CD4 ( $\leq 200$  cells/ $\mu$ l) [OR= 2.99, 95%CI (1.12-8.54),  $p= 0.001$ ].

**Table 3: Postoperative complications (N= 52)**

Postoperative complications	Number of patients	Percentage
Surgical site infections	34	65.4
Coagulopathy	4	7.7
Renal failure	4	7.7
Wound dehiscence	3	5.8
Abdominal abscess/Peritonitis	2	3.8
Hepatic coma	2	3.8

Pneumonia	1	1.9
Leakage of bile	1	1.9
Paralytic ileus	1	1.9
<b>Total</b>	<b>52</b>	<b>100</b>

The overall length of hospital stay (LOS) ranged from 4 days to 67 days (median 18 days). The LOS for non-survivors ranged from 1 day to 18 days (median 6 days). According to multivariate logistic regression analysis, low haematocrit [OR = 2.99, 95% CI (1.12- 8.33), p = 0.001] and presence of postoperative sepsis [OR = 2.51, 95% CI (2.12- 6.87), p = 0.002] were the main predictors of the hospital stay.

In this study, 28 patients died giving a mortality rate of 20.3%. The causes of death were postoperative sepsis in 11 (39.3%) patients, advanced malignant in 5 (17.9%) patients, renal failure in 2 (7.1%) patients, disseminated intravascular coagulopathy in 2 (7.1%) patients, associated HIV infection in 2 (7.1%) patients, hepatic coma and cardiac arrest in 1 (3.6%) patient each respectively. The cause of death was not established in 5 (17.9%) patients. According to multivariate logistic regression analysis, age > 60 years (OR = 2.64, 95% CI (2.32- 5.87), p = 0.001), prolonged duration of jaundice [OR = 0.45, 95% CI (0.22-0.97), p = 0.13], malignant causes [OR = 2.76, 95% CI (2.02- 9.62), p = 0.003], high bilirubin levels [OR = 1.33, 95% CI (1.10-5.34), p = 0.023], HIV infection with low CD4+ count ( $\leq 200$  cells/ $\mu$ l) [OR = 1.73, 95% CI (1.22- 5.90), p = 0.000] and presence of postoperative complications [OR = 4.22, 95% CI (3.71- 8.45), p = 0.004] significantly predicted mortality

## Discussion

Obstructive jaundice continues to be associated with significant morbidity and mortality despite recent advances both in preoperative diagnosis and postoperative care (Ahmad *et al.*, 2001). In this review, patients with malignant obstructive jaundice were found to be older than those of benign type. Similar age distribution was also reported previously by Chalya *et al.* (2011) at the same centre. Other studies done elsewhere also reported similar observation (Nakayama *et al.*, 1978; Moghimi *et al.*, 2008; Khurram *et al.*, 2008; Syed *et al.*, 2010). As reported by other authors (Moghimi *et al.*, 2008; Chalya *et al.*, 2011), age > 60 years significantly predicted mortality. High mortality rate among patients in this age group may be attributed to their poor surgical risks.

In agreement with other studies (Sharma & Ahuja, 1999; Mohamed & Syed., 2007, Syed *et al.*, 2010), both the benign and malignant obstructive jaundice in this study were found to be more common in females than in males. Female preponderance in both the benign and malignant obstructive jaundice has been ascribed to high prevalence of gall stones in them which is reported to be a risk factor for many benign and malignant conditions causing biliary obstruction (Ullah *et al.*, 2000; Channa *et al.*, 2004; Zarin *et al.*, 2005).

The majority of patients in this study had malignant obstructive jaundice which is in agreement with other studies (Nakayama *et al.*, 1978; Moghimi *et al.*, 2008; Khurram *et al.*, 2008; Syed *et al.*, 2010; Chalya *et al.*, 2011), but in contrast to Bekele & Yifru (2000) in Ethiopia who reported benign obstructive jaundice (choledocholithiasis) as the most common cause of obstructive jaundice. These observations reflect differences in etiological spectrum from one geographical area to another. In the present study, the malignant cause of obstructive jaundice was found to be significantly associated with high postoperative complication and mortality rates reported in another study in Tanzania (Chalya *et al.*, 2011). High postoperative complication and mortality figures in the present study may be attributed to by the fact that patients with malignant obstructive jaundice were older with poor surgical risks than those of benign type.

In this study, more than 70% of patients reported to BMC more than two weeks after the onset of illness. Similar observation has been reported in a recent study by Chalya *et al* (2011). The duration of illness has been reported to be an important predictor of outcome in patients with obstructive jaundice (Han *et al.*, 2003). In this study, prolonged duration of illness significantly predicted mortality. The result of the present study suggested that early diagnosis and treatment plays an important role in the prognosis of patients with obstructive jaundice.

The prevalence of HIV infection among patients with obstructive jaundice in the present study was 9.7% which is higher than 6.5% (Urassa *et al.*, 2007) in the general population in Mwanza region. However, the overall HIV seroprevalence in this study may actually be an underestimate and the magnitude of the problem may not be apparent because HIV status was known in only 89.9% of patients and also many patients were excluded from the study due to failure to meet the inclusion criteria. We could not establish the reason for the high HIV seroprevalence among these patients although it is possible that these patients have an increased risk of exposure to HIV infection. This calls for a need to research on this observation. HIV infection was found to be associated with poor postoperative outcome in these patients. This observation calls for routine HIV screening in patients presenting with obstructive jaundice.

In this study, white cell count had a significant correlation with postoperative complication both in univariate analysis and multivariate analysis. This is in keeping with other studies (Aly & Johnson, 2001; Han *et al.*, 2003). An increasing white cell count usually suggests a patient with a biliary infection (Aly & Johnson, 2001). There is a significant correlation between an increased white cell count and postoperative complications such as acute renal failure, wound infection and pulmonary infection (Han *et al.*, 2003). These complications will result in an increasing mortality.

Patients with obstructive jaundice have increased levels of serum bilirubin and most of the complications in the preoperative and postoperative period in obstructive jaundice have been attributed to hyperbilirubinemia (Wang *et al.*, 2008). In the present study, hyperbilirubinemia was found to be associated with poor postoperative outcome in these patients. Similar finding was also reported by Chalya *et al* (2011). It has been postulated that definitive surgery to relieve obstructive jaundice plays a greater role in reversing the pathophysiological disturbances associated with obstructive jaundice and thus reduce postoperative morbidity and mortality (Kaushik, 2001; Wang *et al.*, 2008; Afify *et al.*, 2010).

In our study, the majority of patients with malignant obstructive jaundice underwent palliative surgery mainly by bypass surgery, whereas the majority of patients with benign obstructive jaundice underwent curative surgery. Similar treatment pattern was also reported by Mohammed *et al* (2007). High incidence of palliative surgery in patients with malignant obstructive jaundice is due to delayed presentation for treatment as a result the majority of patients with malignant conditions report to hospital very late when the disease is in advanced stage, and the only option is palliative surgery.

In our study, complication rate was recorded in 30.4% of cases. Of this, surgical site infection was the most common postoperative complications. Postoperative wound infections in biliary surgery have been reported in literature to be due to contamination of the wound during the surgical procedure (Lee & Chung, 1997; Rakesh *et al.*, 2003; Gurusamy & Samraj, 2007). Our complication rate in this study was higher than that of 22.4% reported previously by Chalya *et al* (2010). High incidence of surgical site infection in our study may be due to contamination of the wound during the surgical procedure. In the present study, complication rate was significantly high in patients with malignant causes, WBC count  $> 10 \times 10^9/l$  and HIV infection with  $CD4 \leq 200$  cells/ $\mu l$ .

The figure for the overall duration of hospital stay in our study was higher than that reported in other studies (Hussain & Fatima, 2000; Uslu *et al.*, 2007; Moghimi *et al.*, 2008). The predictors of the length of hospital stay in this study were low haematocrit and presence of postoperative

complication. These findings are in keeping with other studies (Uslu *et al.*, 2007; Moghimi *et al.*, 2008; Chalya *et al.*, 2011).

Several factors including elder age group, duration of jaundice, malignant causes, high levels of bilirubin and presence postoperative complications (e.g. sepsis, coagulopathy, hepatic coma and renal failure) have been reported in literature to be associated with high mortality rate in these patients (Hussain & Fatima, 2000; Pitiakoudis *et al.*, 2004; Uslu *et al.*, 2007; Moghimi *et al.*, 2008; Chalya *et al.*, 2011). Our mortality rate of 20.3% was higher than reported by others (Moghimi *et al.*; 2008; Chalya *et al.*, 2011). The predictors of mortality in our study were age > 60 years, prolonged duration of jaundice, malignant causes, hyperbilirubinemia and presence postoperative complications mainly sepsis. Similar predictors of mortality was also reported a year earlier by Chalya *et al.* (2011) at the same centre, reflecting no great improvement in outcome of these patients.

The high morbidity and mortality rates in this study are attributed to delayed presentation of disease and lack of modern diagnostic and therapeutic facilities seen in developed world. Findings from this study is a typical example of diagnostic and therapeutic challenges seen in most developing countries where delayed presentation of the disease coupled with lack of modern diagnostic and therapeutic facilities are among the hallmarks of the disease (Bekele & Yifru, 2000).

In conclusion, our study highlighted the important factors that predict the outcome of patients presenting with obstructive jaundice at Bugando Medical Centre. It is important therefore, that attention should be focused to these factors so as to improve the outcome of these patients.

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