

*Research Article***The Management of High Bile Duct Pathologies in the Era of Liver Transplantation.**

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Abstract

Background and Aim of the study: High bile duct pathology may be due to high bile duct injuries, strictures and/or cholangiocarcinoma. This study aimed to: investigate the frequency and types of high bile duct pathologies in a specialized Hepato-biliary unit; their clinical and laboratory presentations; the types of intervention done for repair and finally the outcome of the adopted management. **Methods:** This observational retrospective and prospective study was conducted on patients with high bile duct pathologies through the period from June 2016 to December 2017. Our inclusion criteria were: post Cholecystectomy (open and laparoscopic) high bile duct injuries, post- traumatic high bile duct injuries, post-transplant high bile duct strictures and hilar cholangiocarcinoma. Pre-intervention recorded data for the patients were recorded **Results:** forty patients with high bile duct pathologies were recruited in this study. They included 34 (85%) patients with high bile duct injuries and 6 (15%) patients with cholangiocarcinoma. The group of patients with high bile duct injuries comprised 26 (65%) patients with post cholecystectomy injuries and 8 (20%) patients with post liver transplant injuries.. Bile leakage was observed in 35% and biliary strictures were detected in 65% of patients. Bile duct repair was done in 40% of our studied patients while hepaticojejunostomy and segment 4 resection was done in 25%. Isolated hepaticojejunostomy was also done in 25% of patients. Laparoscopic repair and segment 3 resection with hepaticojejunostomy were done in 5% of patients for each. Types I and II of Clavien-Dindo classification for the outcome of repair were the most common forms which indicates a favorable outcome. **Conclusion:** Our results indicated that the majority of patients were managed by Bile duct repair followed by hepaticojejunostomy and segment 4 resection with hepaticojejunostomy which had excellent results with a very low mortality level not related to the surgical technique and minor grades of complication according to the Clavien-Dindo classification.

Keywords: bile duct, hepaticojejunostomy, Hepato-biliary

Introduction

High bile duct pathologies are conditions that affect the biliary system close to the hilum, one of the most demanding challenges for patient and surgeon alike. Three pathologies or lesions affecting the bile duct at a high level are encountered, and these are post cholecystectomy bile duct injury, post-transplant bile duct stricture and cholangiocarcinoma: The experience gained from liver transplantation have enabled surgeons to become more aware and innovative in managing high bile duct problems (Ball et al., 2010). This study aimed to assess management of high bile

duct pathologies namely bile duct injuries and malignancy in a specialized hepatobiliary center which relied upon the advanced experience gained from liver transplantation.

Patients and Methods

This retrospective and prospective observational study was conducted on patients with high bile duct pathologies. The patients were recruited from Minia University Hospital, hepatobiliary unit, and Maadi Military Hospital, the hepatobiliary and liver transplants unit through the period from December 2016 to December 2017.

Our inclusion criteria were: 1- Post Cholecystectomy (open and laparoscopic) High Bile duct Injuries 2- Post-transplant high bile duct strictures. 3- Hilar cholangiocarcinoma

The exclusion criteria included: 1- Low bile duct injuries. 2- Cirrhotic decompensated patients 3- Cases with severe morbidity leading to inoperability 4- Cases managed by ERCP

Methods

All recruited patients signed informed written consent and were aware about the procedure that will be resorted to in the management that will be offered to him according the ethical committee guidelines of a highly specialized hepatobiliary center. The following data were obtained from the data registry of those patients recruited retrospectively and were done for the patients who were recruited Prospectively.

I- Complete history taking, demographic and clinical assessments.

II- Laboratory investigations.

III- Radiological evaluation.

IV- PRE-Operative assessment.

Results

Our data indicated that our recruited patients with high bile duct pathologies through the study period were of a total of 40 patients that were distributed as follows **figure 1: Group I:** 34 patients (85%) with post traumatic high bile duct injuries.

These were re-classified into: 1- Post cholecystectomy high bile duct injuries which constituted 26 patients (65%) where 12 patients (30%) were post open cholecystectomy and 14 patients (36%) were post lap. cholecystectomy. 2- Post liver transplant bile strictures which included 8 patients (20%).

Group II: 6 patients (15%) with Cholangiocarcinoma.

Our study patients had a mean (+SD) age of 44.2+ 12.42 and 65% of them were females. The BMI ranged from an average of 18 in cases with Cholangiocarcinoma to an average of 40 in cases with post cholecystectomy high bile duct injuries.

Twenty six patients (65%) of patients presented with bile duct strictures and

markedly elevated bilirubin and serum alkaline phosphatase, while 14 patients (35%) presented with bile leakage. Regarding the pre-operative imaging data, MRCP was done in 20 patients (50%), while ERCP was done in the order of 20 patients (50%) and in those groups PTC was done in 5 patients.

The laboratory data indicated that the direct bilirubin, alkaline phosphatase, INR, serum creatinine and TLC were 10.5+ 9.6 mg/dl, 1247.4+1170.4u/dl, 1.4+ 0.29, 1.45 + 0.56 mg/dl and 13800 + 4936.5 cu mm, respectively.

Twelve patients (30%) had CRP level <99 mg/ml while 28 patients (70%) had CRP > 99 mg/ml reflecting activated systemic inflammatory state.

Regarding the **Strasberg's classifications** (Strasberg et al., 2005) of the high bile duct pathologies our results indicated that:

A- In group I: 35% of patients had type E4 bile duct injury (14 patients), 20% were type E3 (8 patients), another 20% were type D (8 patients) and only 10% had type E2 Injuries (4 patients).

B- In Group II: In patients with Cholangiocarcinoma, 5% of patients presented with type I, another 5% presented with type IIIA and the remaining 5 % presented with type IIIB with an average of 2 patients for each.

The operative repair data in this study indicated that the methods adopted for repair in our patients were as follows, (table 1):

1-) Bile duct repair was done in 16 patients (40%) 2-) Hepaticojejunostomy was done in 10 patients (25%) 3-) Segment IV +/- V resection + Hepaticojejunostomy was applied to 10 patients (25%) 4-) laparoscopic repair was done in 2 patients (5.0%) 5-) Segment 3 resection and Hepaticojejunostomy was done in 2 patients (5.0%) Half of our patients (50%) required no blood transfusion and only 40% had only one unit of packed RBCs transfusion while 10 % had either two Packed RBCs units or one packed RBCs and one unit fresh plasma transfusion.

The outcome of management: Regarding the outcome of management of high bile pathologies in our high specialized hepatobiliary centers, the study data showed that two out of the 40 recruited patients, died post-operatively; one of them developed

sepsis and multi-organ failure and the other patient died due to pulmonary embolism? The complications observed in the remaining patients were categorized according to Clavien-Dindo classification (Dindo et al., 2005)

Tables and figures

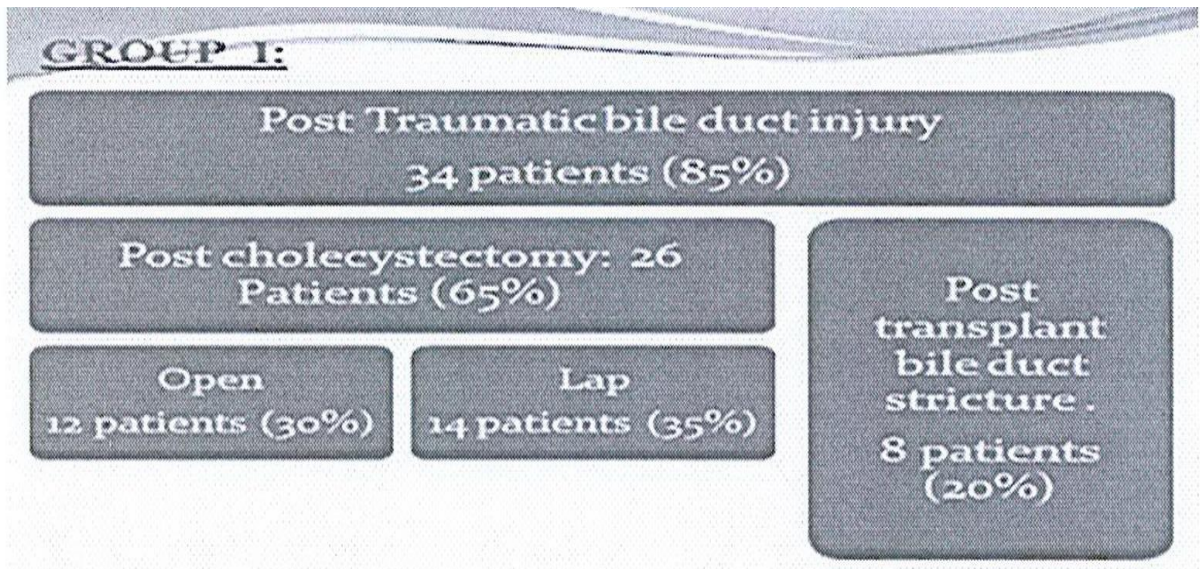


Figure 1: flowchart indicating percentages of patients with bile duct injuries.

Procedure of repair			
Procedure of repair	Procedure	Number	Percent age %
	1-)Hepaticojejunostomy	10	25.0%
	2-) Segment 4 resection + Hepaticojejunostomy	10	25.0%
	3-)Bile duct repair	16	40 %
	4-)laparoscopic repair	2	5.0%
	5-)Segment 3 resection and Hepaticojejunostomy	2	5.0%

Table 1: Procedures of repair of high bile duct pathologies in our series.

Discussion

Our results have indicated that our patients' age was in the range from 24 to 64 years with a mean of 44.2 ± 12.42 , which is similar to the results of other studies where the average age of their patients was 46 years (Singh & Brunt, 2018). However, the age for patients with cholangiocarcinoma was significantly higher with a mean of 55 years which is inconsistent with Tocchi et al., whose patients presenting with cholangiocarcinoma had a mean age was 56 years (Tocchi et al., 2001)

It was of note that the BMI in our patients ranged from a low level (18 kg/m^2) in patients with cholangiocarcinoma to a high level (40 kg/m^2) in patients undergoing cholecystectomy, which may reflect the cholangiocarcinoma associated cachexia which stands against the obesity associated bile duct injury. Gupta et al., 2018, suggested that patients undergoing laparoscopic cholecystectomy with a high BMI $>30 \text{ kg/m}^2$ has a higher rate of conversion to open cholecystectomy to avoid Bile Duct Injury.

Twenty six (65%) of our patients presented with cholestasis with markedly elevated bilirubin which had a mean of $12.2 \pm 10.7 \text{ mg/dl}$ and markedly raised Alkaline phosphatase with a mean of $1247.4 \pm 1170.4 \text{ u/dl}$ which were more obvious in patients with Cholangiocarcinoma, post-transplant bile duct stricture and post cholecystectomy stricture. Furthermore, 14 patients (35%) presented with bile leakage either through the drain or through the wound and biloma if the drain was not present. (Buanes and Mjaland 1996), stated in their studies that bile leak contributed significantly to serious complications where 37 major problems were observed in 25 of their the patients with a percentage of 44%. Similar findings were recently reported by (Parmar et al, 2017)

The baseline characteristics of our patients with bile leakage indicated that 57% of our patients presenting with bile leakage had no drain and only 43% presented with a drain. This may indicate that absence of a drain may be associated with more risk of

exposing the patient to frequent complications' such as biloma, lobulated collection causing sepsis. In our series, U/S guided drainage was done in 36% of patients preoperatively while open drainage was done in 21% of patients where the patients were in severe sepsis and U/S guided drainage failed to drain the biloma and the leak appropriately; so open drainage was mandatory. This rate is less than the percentage reported in other studies where ultrasound-guided drainage of intra-abdominal collections was done in 14 patients (52%), (Kaman, Behera, Singh, & Katariya, 2004).

The baseline characteristics in our data showed that our patients had leukocytosis with a mean of $13,800 \text{ mm}^3$ for TLC and raised serum creatinine (mean of 1.45 mg/dl). This was associated with elevated CRP > 99 in 70% of our patients and elevated INR level with mean of 1.4. These data may reflect the systemic inflammatory state associated with the high bile duct injury. This finding corresponds with the data reported by other studies which mentioned that the clinical signs and symptoms ranging from fever, leukocytosis, abdominal pain, jaundice, and tenderness in the right upper abdominal quadrant, cyanosis secondary to septic shock were associated findings due to bile duct injuries (Baidon & Varon, 2015).

The classification of post traumatic bile duct injury in our series according to the Strasberg classification indicated that 14 patients (35%) had Type E4 bile duct injury, 8 patients (20%) had type E3, 8 patients (20%) had Type D bile duct injury and 4 patients (10%) had Type E2. The data reported by other investigators reported similar results to ours where thirty-one patients (77.5%) had type E1 (circumferential injury to the common duct $>2 \text{ cm}$ from the bifurcation) or E2 (circumferential injury to the common duct $<2 \text{ cm}$ from the bifurcation) bile duct injuries. Type A injury was found in three patients, type C and D injury each in one patient, and type E3 and E4 injury each in two patients. (Frilling et al., 2004)

On the other hand, our patients with cholangiocarcinoma presented with type I in 2 patients (33 %), 2 patients presented with type IIIA (33%) and Two patients presented with type III B (33%), these data may disagree with reports of others which showed that a very low number of patients presented with type I lesions, 19% of patients had type III A lesions, while 22% of patients presented with type III B, 42% had type IV lesions and a very low 17% had type I lesions (Miyazaki et al., 2010).

The procedures for operative repair adopted in our centers showed that the most frequent procedures were the hepaticojejunostomy and segment IV+/- V resection with hepaticojejunostomy which were done in half of our patients; 25% for each procedure respectively. Partial resection of segment IV was performed to obtain non-inflamed, non-scarred, non-ischemic biliary ducts with the purpose of reaching the confluence and achieving a high-quality bilioenteric anastomosis. These data agree with Mercado, M.A., et al, 1999, who stated that partial liver resection of segments IV and V allows adequate exposure of the bile duct at its bifurcation with an anterior approach of the ducts (therefore not jeopardizing the circulation), allowing a high quality anastomosis and better long term outcome. (Mercado et al., 1999). These remarks were recently recommended by (Mercado M. A. et al, 2017)

Bile duct repair was done in 40% of our patients where the repair was done with prolene suture 4-0 over a stent or a t-tube if needed. These procedures were done in patients with side wall injury or with injuries detected intraoperatively. Two of our patients had laparoscopic bile duct injury and repair was done laparoscopically in the same session. This is opposite to what Flum et al, 2003, recommended about bile duct injuries stating that in the presence of a specialized hepatobiliary surgeon, it is recommended to turn the lap surgery into open surgery and start the repair (Flum et al., 2003). Another two patients had segment III resection and hepatico-

jejunostomy for managing cholangiocarcinoma as a palliative procedure to alleviate the obstruction.

It's of note that 85% of our patients had a stent inserted intraoperatively while the other 15 % didn't need a stent inserted. The 6 F stent was inserted in 18 patients (45%), epidural stent in 11 patients (28%), while the t-tube was inserted in 5 patients (12%).

Two of our patients who underwent operative repair needed re-exploration due to high biliary leakage, this may be attributed to the low albumin levels pre-operatively which may be related to the sepsis and malnutrition that resulted in poor healing function and biliary fistula. Regarding the outcome of the repair procedures in our patients, it's of interest that 43% of our patients had no significant morbidity with a smooth post-operative course. However, the remaining group of our patients had varying degrees of morbidity according to the Clavien-Dindo Classification

Conclusion

Our study indicated that high bile duct pathology in our series occurred in 65 % in patients with bile duct injury and 25 % of patients with post-transplant bile duct stricture while 15% was due to cholangiocarcinoma. Furthermore, our results indicated that the majority of patients were managed by hepaticojejunostomy and segment 4 resection & hepaticojejunostomy procedures of repair with excellent results with a very low mortality level not related to the surgical technique and minor grades of complication according to the Clavien-Dindo classification.

Recommendations:

Our study confirmed the concept of referring and reserving cases with high bile duct pathologies to specialized hepatobiliary centers to be managed in order to obtain the perfect outcome because the best chance is always there.

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