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Prognostic factors determining the surgical interference of biliary atresia in Egyptian infants: single-center experience

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Abstract

Background Biliary atresia is associated with considerable morbidity, and it is the most frequent indication for pediatric liver transplantation. Hepatic portoentostomy (HPE), Kasai procedure, is used commonly as the first line of treatment but its long-term efficacy still remains controversial. In this study we decided to illustrate most of the perioperative clinical, biomarkers, histopathological, and surgical parameters that may determine the outcome in operated infants with biliary atresia within 5 years at our center at national liver institute (NLI). We analyzed the perioperative risks for surgical failure in 100 infants with BA, diagnosed and treated from June 2012 to June 2017. Infant included in the study categorized into two groups according to the surgical outcome, failed and successful group. The successful surgical outcome of biliary atresia was determined by the clearance of jaundice within 6 months where total serum bilirubin ≤ 2 mg/dL. Both groups were compared according to perioperative clinical, laboratory, ultrasonographic, endoscopic detection of bile, histopathological characteristics, excised biliary remnant duct size, and type of surgical interference.

Results After surgical interference, infants with successful outcome were 33% and those with failed outcome were 67%. Younger age, lower preoperative serum GGT, delayed onset of jaundice after the first 2 weeks of life, and lower levels of post-operative 1-month serum total and direct bilirubin, were significantly associated with successful outcome ($P = 0.001$, 0.041, 0.025, and 0.001 respectively). Also gall bladder contractility, endoscopic duodenal bile test, degree of hepatic fibrosis, bile duct size, surgical type of BA, and type of surgical interference were significant risk factors affecting the surgical outcome of BA ($P = 0.003$, 0.037, 0.005, 0.024, 0.001, and 0.002 respectively).

Conclusions Younger age and lower preoperative GGT and post-operative 1-month serum total and direct bilirubin level are good predictors for the surgical outcome of BA infants with better performance of age and post-operative 1-month serum total and direct bilirubin level. This may determine infants with the high-priority for transplant referral postoperatively.

Keywords Biliary atresia, Hepatoportoenterostomy outcome predictors

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Background

Biliary atresia (BA) is a progressive, fibroobliterative cholangiopathy of neonates which can affect intra-hepatic and extra-hepatic bile ducts to varying degrees. It causes severe neonatal cholestasis, and if neglected without treatment, a rapid progressive biliary cirrhosis is eventually developed causing death in the first years of life [1, 2]. However, the etiopathogenesis of BA is not fully understood, infectious, immune, genetic, and morphogenic origins have been proposed. This makes prevention and therapies strategies designed to stop progression of the fibro-inflammatory process of the bile ducts are impossible [3]. Kasai et al., classified the infants with BA according to the level of bile duct atresia into three main types; type I BA, the level of atresia is at the level of the common bile duct; type II BA, the level of atresia is at the level of the common hepatic duct; type III BA, the level of atresia is at the porta-hepatis [4]. However, there are several tools that help in diagnosis of cases of BA, liver biopsy and the intra-operative cholangiogram (IOC) considered as gold standard for the diagnosis and have a diagnostic accuracy of 100% [6]. The first line of treatment of BA is surgical which should be performed to achieve the bile drainage through the bile ducts following surgical removal of extrahepatic biliary remnants [4]. Some modifications to the traditional Kasai operation was done via a deep and long incision in the porta hepatis in the fibrous remnant by a scalpel making two well defined anterior and posterior edges for a better hepatoportoenterostomy anastomosis [6]. If surgery fails, or biliary cirrhosis developed, liver transplantation as second line treatment is then necessary, for which BA represents the most frequent indication in the pediatric age group [4, 7]. There are many studies attribute the short-term surgical outcome of the Kasai operation. Some are unalterable prognostic factors, such as the surgical type of BA, degree of cirrhosis or fibrosis at presentation; absence of/or paucity of microscopic bile ductules at the level of section and some are subject to change such as early diagnosis, surgical experience, prevention, and immediate treatment of postoperative cholangitis [3].

Methods

Study population

This retrospective study conducted on infants with BA who underwent surgical interference at the Department of Hepato-pancreato Biliary Surgery, NLI, Menoufia University, within the period from January 2012 to January 2017, with exclusion of infants who had medical records were not fulfilled. All cases were managed preoperatively and postoperatively at the department of Pediatric Hepatology, Gastroenterology and Nutrition, NLI, Menoufia University, Egypt. One hundred infants with continuous follow up and fulfilled medical records involved in this study. The surgical outcome of biliary atresia was determined by the clearance of jaundice within 6 months where total serum bilirubin ≤ 2 mg/dL [8]. The studied cases were divided according to the outcome into two groups, successful group ($n=33$) and failed group ($n=67$).

Etiological diagnosis

All recruited cases underwent full history taking, thorough clinical examination, and routine investigations. Patients who were allocated as having BA, were candidates for an abdominal exploration for visualization of biliary system. Absent gallbladder, fibrotic gallbladder, and/or atretic extrahepatic biliary tree is diagnostic for BA, meanwhile if the gallbladder is present and patent, child underwent IOC. The surgical type of BA was also identified as described in Superina et al. [9]. Routine preoperative investigations included serum bilirubin (total and direct), albumin, total serum proteins, aspartate transaminase (AST), alanine transaminase (ALT), gammaglutamyl transferase (GGT), alkaline phosphatase (ALP), prothrombin time (PT), complete blood count, abdominal ultrasonography with stress on the absence, size, and assessment of GB contractility and doppler US, endoscopic detection of bile by upper GI endoscopy and needle liver biopsy.

Intraoperative liver biopsy and surgical interference

Routine wedge liver biopsies and excised biliary remnants were fixed in formalin and embedded in paraffin. Five-micrometer thick sections were cut, mounted on glass slide, and stained with hematoxylin and eosin (Figs. 1, 2, 3, 4) to evaluate pathological changes and the diameter of duct in the biliary remnants, and Mason-Trichrome stain (Fig. 5) to assess collagen fibers and fibrosis, and Perls' Prussian blue stain to reveal iron deposits. Grade of portal fibrosis was assessed using semi-quantitative histopathological scores as described in Russo et al. [10]. For statistical purpose, we added grades together to be absent or fibrous expansion of some portal areas (mild fibrosis), fibrous expansion of most portal areas (moderate fibrosis), and focal portal-to-portal bridging, marked bridging and cirrhosis considered as (severe fibrosis). The operation is done under general anesthesia, where the infant is put in the supine decubitus and a 5-cm transverse or oblique incision is made about one to two fingers below the right costal margin. The abdomen is explored then IOC is performed where the gallbladder is cannulated with a 24-G intravenous cannula and a burse string is made around it to prevent contrast (Ultravist) leakage (Ultravist; Bayer Health Care Pharmaceuticals

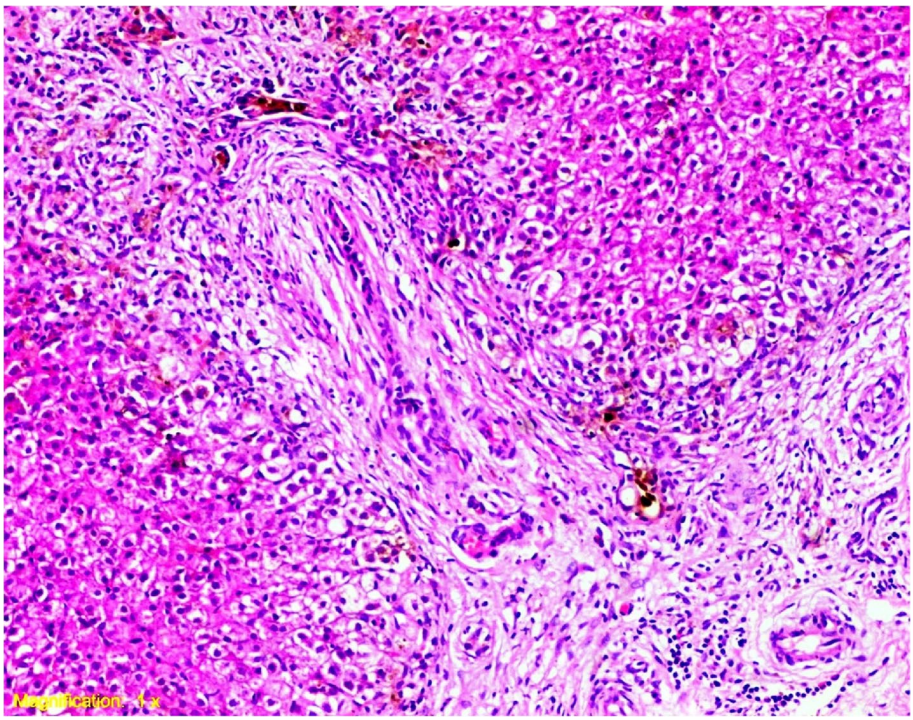

Fig. 1 A case of biliary atresia with failed surgery, portal tract showed edema and moderate fibrosis with bile ductular proliferation with intraluminal bile plugs. (H&E × 100)

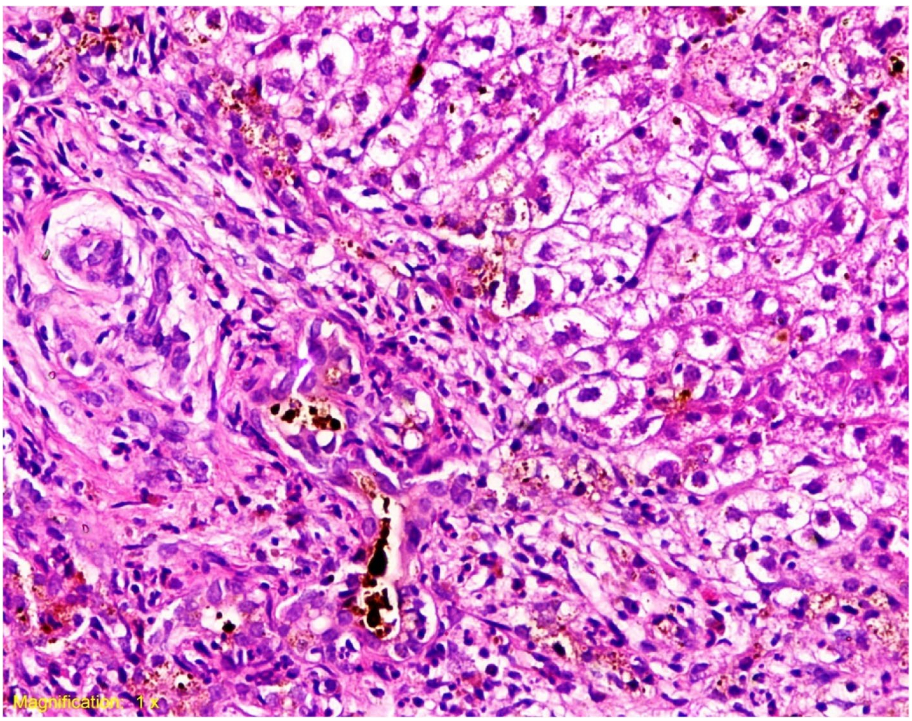

Fig. 2 A case of biliary atresia, portal tract showed bile duct and ductular proliferation with luminal bile plugs. Parenchyma showed cholestatic roasts with intracellular and intracanalicular bile pigments (H&E × 200)

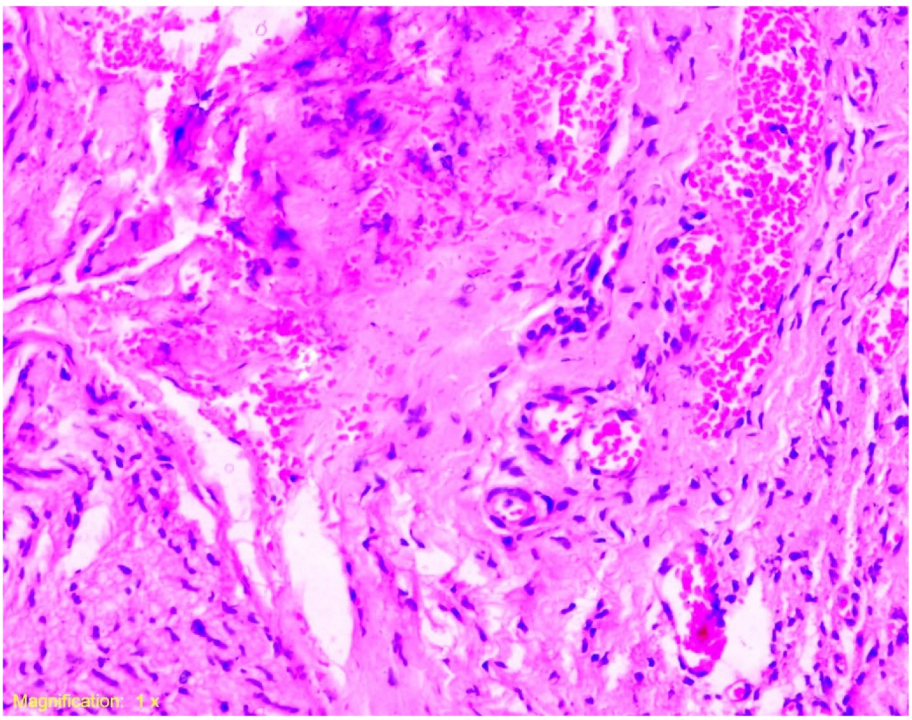

Fig. 3 Picture of Biliary atresia infant with failed surgery showed porta hepatis with bile duct remnant less than 150 µm (H&E × 200)

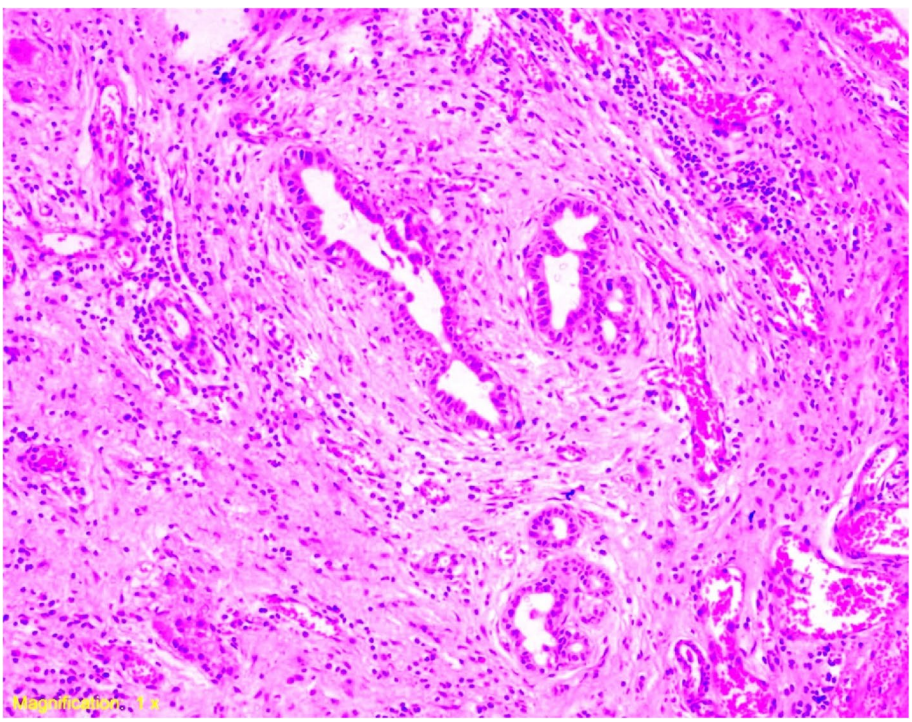

Fig. 4 Porta hepatis in biliary atresia infant with successful surgery with bile duct remnant more than 150 µm (H&E × 100)

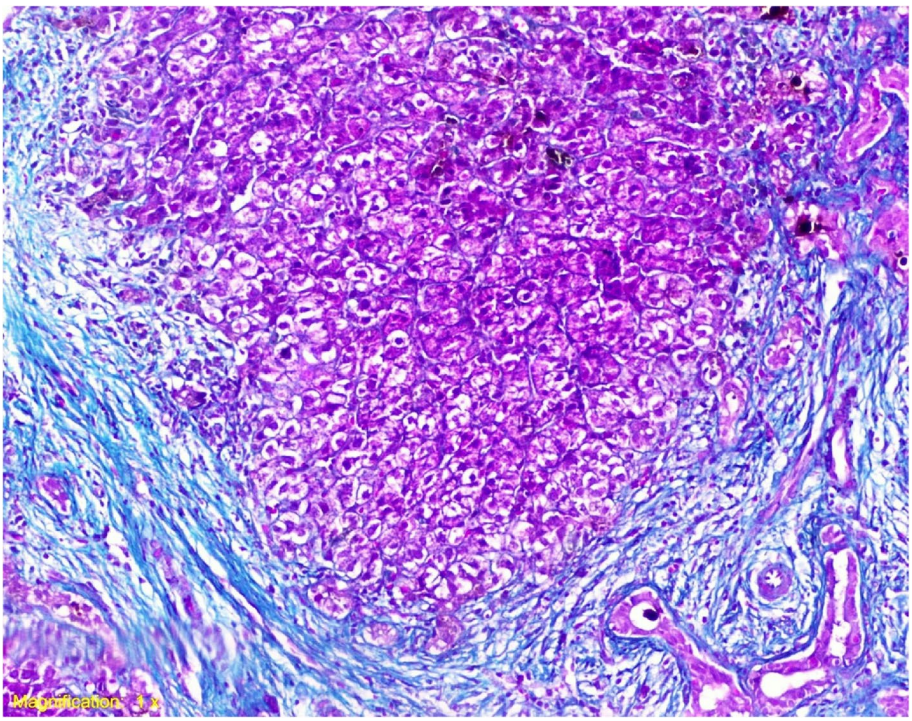

Fig. 5 Masson trichrome stain picture of biliary atresia infant with failed surgery showed severe fibrous expansion with incomplete cirrhotic nodule formation (Masson Trichrome × 100)

Inc., Berlin, Germany). The contrast is injected under guidance of C-arm fluoroscopy (Philips BV 25 gold C-Arm; Philips Medical Systems, Eindhoven, The Netherlands). According to the type of BA the infants underwent three types of surgical interferences. All BA type III cases, cystic biliary atresia, and one case of BA type I underwent hepatoportoenterostomy (Kasai's operation) (Fig. 6), while BA type II cases underwent cholecystoportoenterostomy (Liley's operation) (Fig. 7) and 5 cases of BA type I underwent hepatico-jejunostomy [6]. Intra-operative parameters which analyzed were surgical type of BA by IOC, type of surgery, grade of portal fibrosis, and bile duct diameter of the excised biliary remnant.

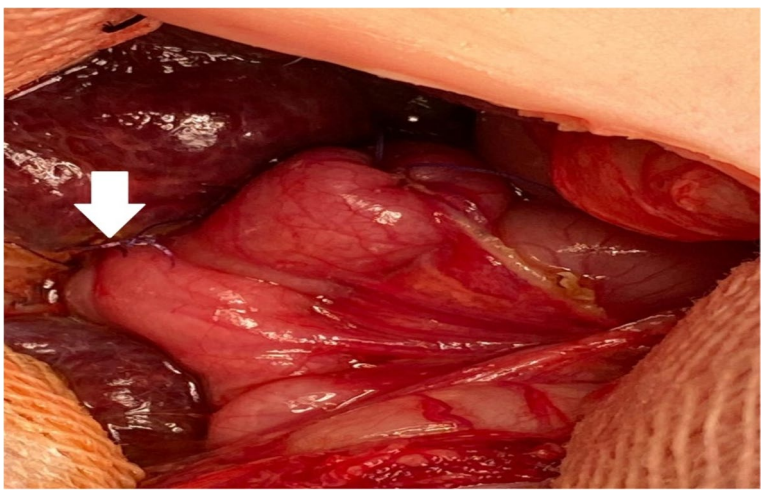

Fig. 6 White arrow directed to hepatoporto-enterostomy anastomosis (Kasai's operation)

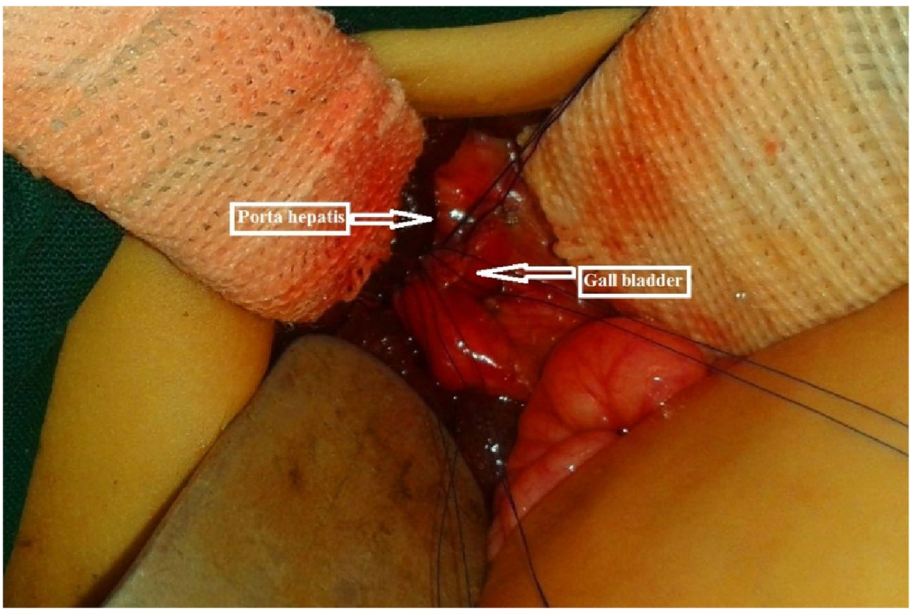

Fig. 7 Cholecysto-portostomy anastomosis (Liley's operation) (Anastomosis between porta hepatis and patent gall bladder)

Postoperative follow-up

Post-operative follow-up parameters were immediate post-operative complications during hospital stay such as complications of portal hypertension (ascites or upper GI bleeding), hepatic encephalopathy, liver failure, and burst abdomen). Also, 1-month post-operative laboratory results and recurrent attacks of cholangitis were analyzed.

Statistical analysis

Descriptive data were expressed as (mean ± SD) and range; or frequency and percent. For quantitative data, significance between the two studied groups was tested by Student's *t* test or Mann–Whitney *U* test and significance between more than two groups was tested by Kruskal–Wallis test. For qualitative and categorical data, significance was tested by chi-square test or Fisher's exact test. Correlation was tested by Spearman's test or Spearman's correlation. The diagnostic performance of statistical significant parameters was assessed by calculating the area under the receiver-operating characteristic (ROC) curve. The cut-off value for optimal clinical performance was determined from the ROC curves. The diagnostic performance was measured as sensitivity and specificity and expressed as percentages. Significance was set to $P < 0.05$. Statistical analysis was performed using statistical package for social science (SPSS) software version 21 (IBM Corp. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.).

Results

Study populations' characteristics

This study included 100 BA infants (50 males and 50 females), who underwent surgical interference with a mean age at surgery (78.03 ± 15.72), and range (31–141 days), at the department of HPB. According to surgical outcome, successful operation achieved in 33 infants (33%), named as successful group, while 67 infants (67%) had failed operation. Comparing the preoperative baseline characteristics between both, age at time of surgery and serum GGT were significantly higher in failed operation compared to the successful operation ($P = 0.001$, 0.041, and 0.025 respectively), and also the onset of jaundice within the first 2 weeks of life, was significantly delayed in the successful operation ($P = 0.025$), while no statistical significance was found between both groups regarding other baseline demographic, clinical, and laboratory parameters (Table 1).

Ultrasonographic and endoscopic findings

Both studied groups were comparable regarding the ultrasonographic findings except gall bladder contractility was statistically significant factor affecting the outcome of BA after surgery ($P = 0.003$). Atretic GB was found in 39 (58.2%) infants in the failed group while 9 (27.3%) in the successful group with ($P = 0.003$). Hepatic subcapsular flow and TC-sign was reported in 29, 29% respectively of all the study population. Endoscopic duodenal bile test had statistically significant difference ($P = 0.037$), where all cases of failed surgery had now

Table 1 Preoperative demographic, clinical, laboratory and endoscopic characteristics according to the outcome

Characteristics	Successful (*n* = 33)	Failed (*n* = 67)	*P* value
Age at surgery (ds)	68.8 ± 14.8	80.9 ± 184.7	0.001*
Male *n* (%)	17(51.5%)	33(49.3%)	0.832
Weight	4.7 ± 0.51	4.6 ± 0.73	0.413
Height	58.4 ± 3.7	57.2 ± 3.1	0.119
Clay stool *n* (%)	33 (100)	67 (100)	1.0
Onset of jaundice			
< 14 days old	15 (45.5%)	46 (68.7%)	0.025*
≥ 14 days old	18 (54.5%)	21 (31.3%)	
TB (mg/dl)	10.9 ± 3.5	11.4 ± 3.34	0.600
DB (mg/dl)	7.6 ± 2.6	8.08 ± 2.8	0.610
ALT (U/L)	134.9 ± 74.9	140.6 ± 84	0.852
AST (U/L)	204.6 ± 114	216.9 ± 106	0.369
Albumin (g/dl)	3.4 ± 0.64	3.5 ± 0.51	0.547
Total protein (g/dl)	5.2 ± 0.98	4.8 ± 0.67	0.124
ALKp (U/L)	480.4 ± 200	622.9 ± 508	0.889
GGT (U/L)	965.1 ± 666.8	898.7 ± 507	0.041*
PT (s)	11.9 ± 1.09	12.1 ± 1.08	0.839
INR	1.03 ± 0.09	1.05 ± 0.10	0.536
Hb (gm/dl)	9.6 ± 1.26	9.7 ± 1.1	0.991
WBC ($\times 10^3$/mcl)	12.5 ± 4.2	13 ± 4.4	0.495
Platelets ($\times 10^3$/mcl)	465.7 ± 165.7	457.2 ± 191	0.553

TB total bilirubin, *DB* direct bilirubin, *ALT* alanine transaminase, *AST* aspartate transaminase, *ALKp* alkaline phosphatase, *GGT* gamma glutamyl-transpeptidase, *PT* prothrombin time, *INR* international normalization ratio, *Hb* hemoglobin, *WBC* white blood cells

* Statistical significant *P* value

Table 2 Ultrasonographic characteristics and endoscopic findings according to the outcome

Characteristics	Successful (*N* = 33)	Failed (*N* = 67)	*P* value
US hepatomegaly	24(72.7%)	50(74.6%)	0.839
US splenomegaly	17(51.5%)	32(47.8%)	0.712
Subcapsular flow	7(21.2%)	22(32.9%)	0.263
HA diameter (mean ± SD)	1.95 ± 0.53	1.9 ± 0.40	0.896
PV diameter (mean ± SD)	4.6 ± 0.93	4.7 ± 0.71	0.421
Ascites	0(0.0%)	2(3.0%)	0.316
TC sign	12(36.4%)	17(25.4%)	0.295
GB contractility			0.003*
Contractile	6 (18.2%)	13(19.4%)	
Non-contractile	18 (54.5%)	15(22.4%)	
Atretic	9(27.3%)	39(58.2%)	
Tubal duct aspirate			
No bile	30(90.9%)	67(100%)	0.037*
Tinge of bile	3(9.1%)	0(0.0%)	

BA biliary atresia, *TC-sign* triangular cord sign, *GB* gallbladder

* Statistical significant *P* value

bile, comparing both the outcome groups, all infant with failed outcome 67 (100%) had no endoscopic duodenal bile at the time of test (Table 2).

Intraoperative histopathological and surgical findings

Both successful and failed groups were comparable regarding the histopathological findings in liver biopsy at the time of presentation, except the grade of hepatic fibrosis is statistically significant factor affecting the surgical outcome of BA ($P = 0.005$). Five (5%) infants had mild fibrosis, all of them had successful outcome, 61 (61%) had severe hepatic fibrosis, most of them (64.2%) had failed outcome (Table 4). Bile duct size at the excised biliary remnant during the operation was statistically significant factor affecting the surgical outcome of BA ($P = 0.024$). Bile duct size remnant was found < 150 μm in 55 of all infants. Most of infants with bile duct size remnant < 150 um had failed outcome (46 out of 67) ($P = 0.024$), (Table 4). Regarding surgical type of BA, 73% of infants were BA type 3, with 56 out of them (83.6%) had significantly failed outcome and all cases of type I BA are successful cases ($P = 0.001$) (Table 3). 79% of infants underwent Kasai portoenterostomy, 16% underwent Cholecystoportostomy, while 5% underwent Hepaticojejunostomy. The outcome among the types of surgical interference were comparable except Hepaticojejunostomy operation, all cases were successful ($P = 0.002$) (Table 3).

Post-operative lab, complications, and recurrent cholangitis

One-month postoperative laboratory tests were comparable, except for serum TB and DB were significantly lower in the successful group (4.7 ± 2.8, 3.2 ± 2.3) vs (8.4 ± 2.5, 6.1 ± 2) respectively in the failed group ($P = 0.001$) (Table 5).

Table 3 Comparing surgical type of BA and type of operation according to the outcome

Characteristics	Successful (*N* = 33)	Failed (*N* = 67)	*P* value
Surgical type of BA			
Type 1	6 (18.2%)	0(0.0%)	0.001*
Type 2	7(21.2%)	9(13.4%)	
Type 3	17(51.5%)	56 (83.6%)	
Cystic BA	3(9.1%)	2(3.0%)	
Type of operation			0.002*
Hepatico-jejunostomy	5(15.2%)	0(0.0%)	
Cholecysto-portostomy	7(21.2%)	9(13.4%)	
Kassai porto-enterostomy	21(63.6%)	58(86.6%)	

Sixty-three infants not recorded immediate post-operative complications, 24 had complications of portal hypertension (ascites and upper GI bleeding), 1 had liver failure, 1 had encephalopathy, and 1 had burst abdomen; while 57 infants had recurrent cholangitis, with no statistical significance difference between the two outcome groups (Table 5).

Clinical performance of age, preoperative GGT, and postoperative serum bilirubin level in predicting surgical success

Age of 61 days or less was predictive of successful outcome with 95% specificity and (79%) sensitivity with 95% confidence interval (95% CI 0.857–0.977), AUROC was 0.917 (Fig. 8). Also, preoperative serum GGT at a cut-off level of 491 U/L or less was predictive of successful outcome with 57% sensitivity and 60% specificity (95% CI 0.512–0.741), AUROC was 0.626 (Fig. 9). In addition, 1-month post-operative serum total and direct bilirubin level had a better performance than preoperative serum GGT in predicting surgical success at a cut-off value of ≤ 7.2 mg/dL, ≤ 5.01 mg/dL with 80%, 76% sensitivity and 70%, 64% specificity, (95% CI 0.747–0.917 and (95% CI:0.699–0.896), AUROC were 0.832 and 0.79 respectively (Figs. 10 and 11).

Multivariate analysis

In this study, variables with significance were age at time of operation, preoperative GGT level, gall bladder contractility, degree of liver fibrosis, diameter of excised remnant bile duct, type of biliary atresia, and 1-month postoperative serum bilirubin level. Age at time of surgery and the type of operation are the most effective factors for the outcome of BA after surgery.

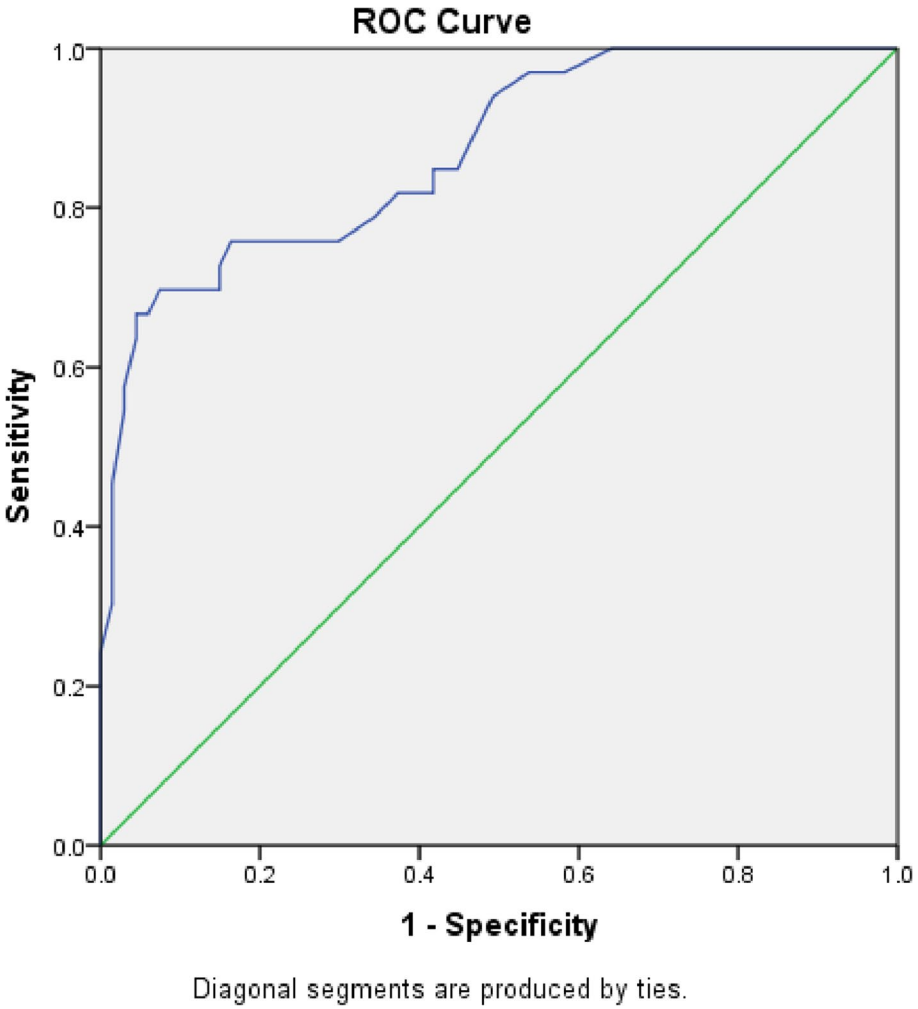

Fig. 8 Receiver operating characteristic curve (ROC curve) of age at surgery by days for predicating success of treatment of biliary atresia. It shows that age at a cut-off value of ≤ 61 days has 79% sensitivity, 95% specificity, 89% PPV 90% NPV, and 90% accuracy

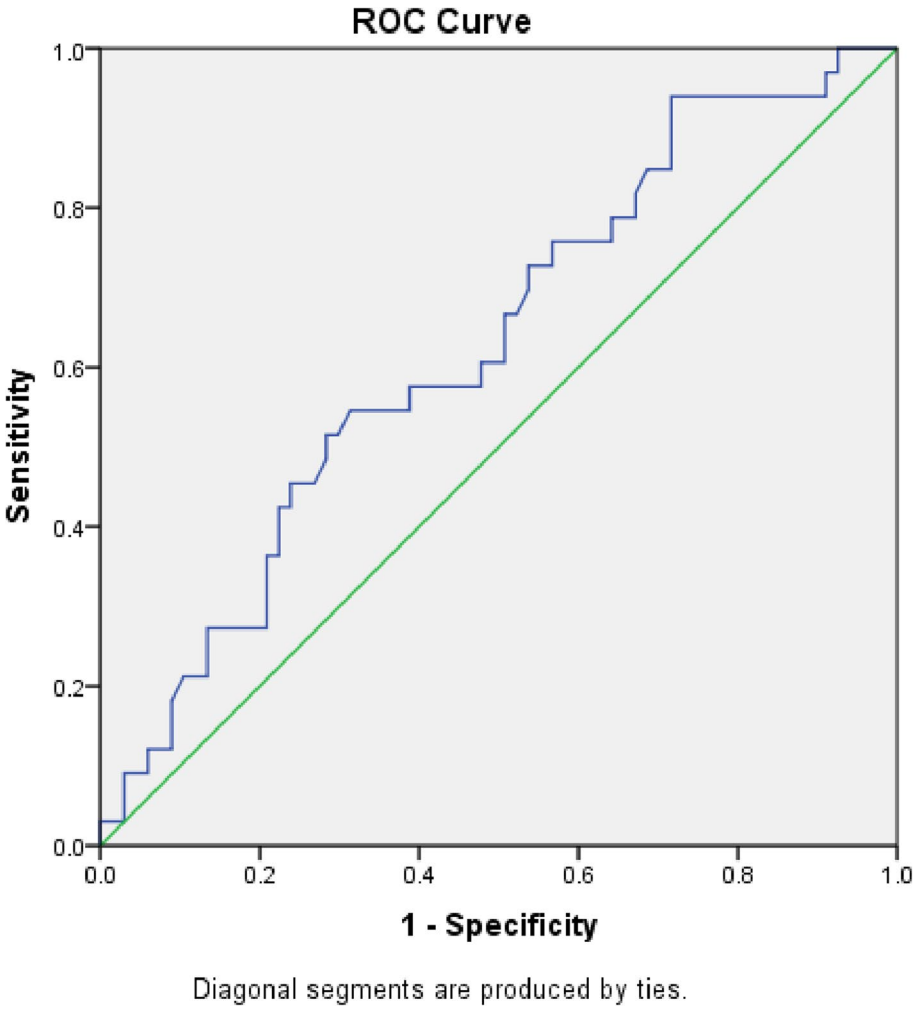

Fig. 9 Receiver operating characteristic curve (ROC curve) of the pre-operative GGT level by UL for predicating success of treatment of biliary atresia. It shows that GGT at a cut-off value of ≤ 491 UL has 57% sensitivity, 60% specificity, 41% PPV 54% NPV, and 59% accuracy

Discussion

Biliary atresia is a progressive fibro-obliterative disease of the intra- and extrahepatic bile ducts in infancy [11]. It is the most frequent indication for pediatric liver transplantation [12, 13]. Marked improvement and prolongation of native liver survival was reported in those children achieved surgical successful outcome within 3 months [14, 15]. There are many factors, which will influence surgical outcome. Some are unalterable (e.g., degree of cirrhosis or fibrosis at presentation; absence/or paucity of microscopic bile ductules at the level of section) and some factors are subject to change (e.g., age, surgical experience, untreated cholangitis). There is no doubt that the fibrotic element of the liver pathology is progressive, but beyond what age an attempt to do HPE is pointless is not known [3]. In this study, we decided to illustrate most of the perioperative parameters that may affect the surgical outcome of biliary atresia. In this study, infants with surgical success were 33 out of 100 (33%), while the other 67 (67%) infants had surgical failure. Our results were agreed with Sangkhathat et al. [16] and Wildhaber et al. [17] who reported a success rate of 33.4, and 36% respectively. On the other hand, success rates in some other studies ranged from 43 to 50% [18].

Analysis of preoperative demographic, clinical and laboratory and characteristics, revealed statistical significant difference between both outcome groups regarding onset of jaundice, age at surgery, and preoperative serum GGT ($P=0.025$, 0.001, and 0.041 respectively), other variables were insignificant (Table 1). Onset of jaundice within first 2 weeks of life is a statistically significant bad prognostic factor for surgical success ($P=0.025$). We were in agreement with Zhou K et al., who recommended the neonatal screening in order to improve outcome of BA patients to reduce the need for early LTs in these children [19].

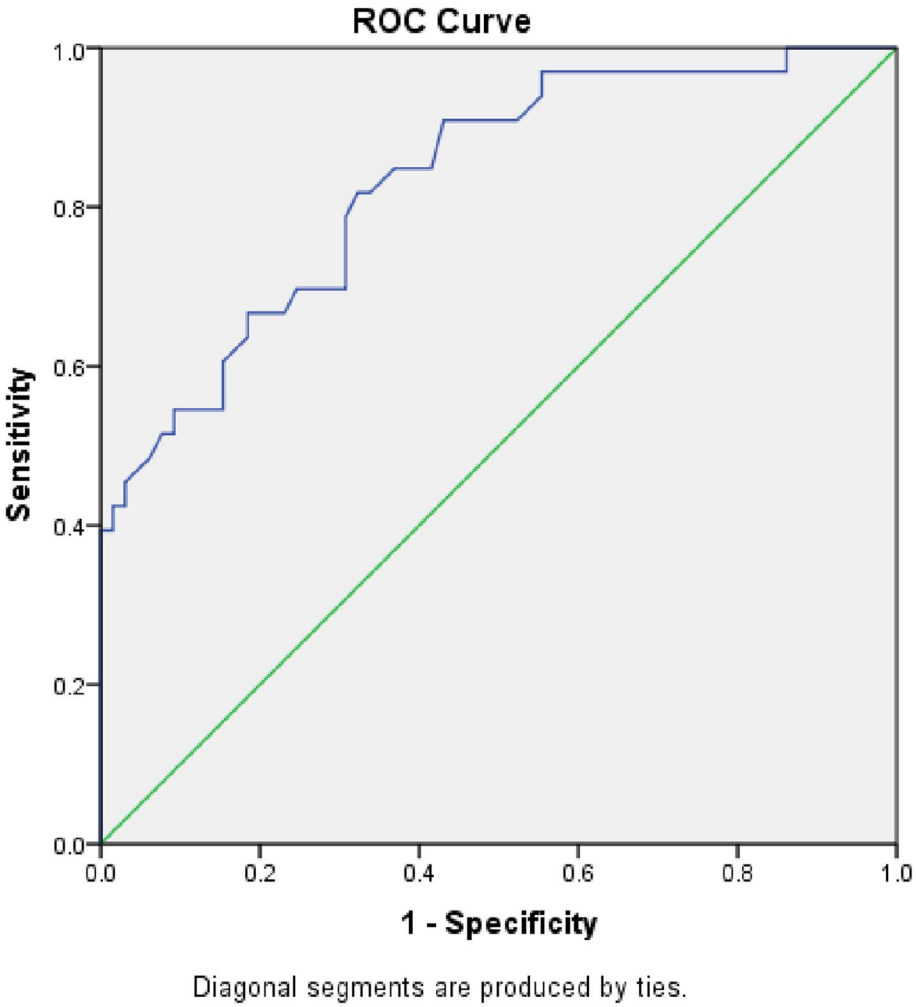

Fig. 10 Receiver operating characteristic curve (ROC curve) of the 1 month post-operative total bilirubin level by mg/dL for predicating success of treatment of biliary atresia. It shows that 1 month post-operative total bilirubin level at a cut-off value of ≤ 7.2 mg/dL has 80% sensitivity, 70% specificity, 57% PPV 87% NPV, and 65% accuracy

The younger age at surgery was significantly good prognostic factor for surgical success where infants aged 61 days or less is a predictive of success with 95% specificity and 79% sensitivity, 89% PPV 90% NPV and 90% accuracy (Fig. 8). Our finding agreed with several studies indicating that age at surgery is a major determinant of short- and long-term surgical outcome, with is a clear evidence that a better outcome obtained when it is performed earlier especially before the first 90 days of life [20]. In hand with our results, Sastiono et al. [21] reported 33.3% success rate in patients operated before 90 days old, and Schoen et al. [22] reported 83% success rate in those who were operated below 75 days old. However, Davenport et al. [23] reported that increasing the age at surgery did not affect adversely the outcome. However, GGT in human exists in hepatobiliary system, spleen, kidney, seminal vesicles and brain, epithelial biliary, and hepatocytes cells constitute the major sources of it. Clinically, higher GGT levels are observed with biliary obstruction than intrahepatic cholestasis [24]. Among the preoperative liver function tests, GGT was the only significant test in this study. Higher levels of GGT were significantly associated with poor surgical outcome. Cut-off value of ≤ 491 U/L can predict operative success with 57% sensitivity, 60% specificity (Fig. 9). Other liver function tests, serum levels of TB, DB, AST, ALT, and ALKp were being lower in the successful group than in the failed group, without statistically significant difference between both groups. Gupta et al., [25] concluded that the liver function tests were found to have a better correlation with the surgical outcome, and higher degrees of cholestasis showed definite correlation with poor surgical outcome, while Sanghai

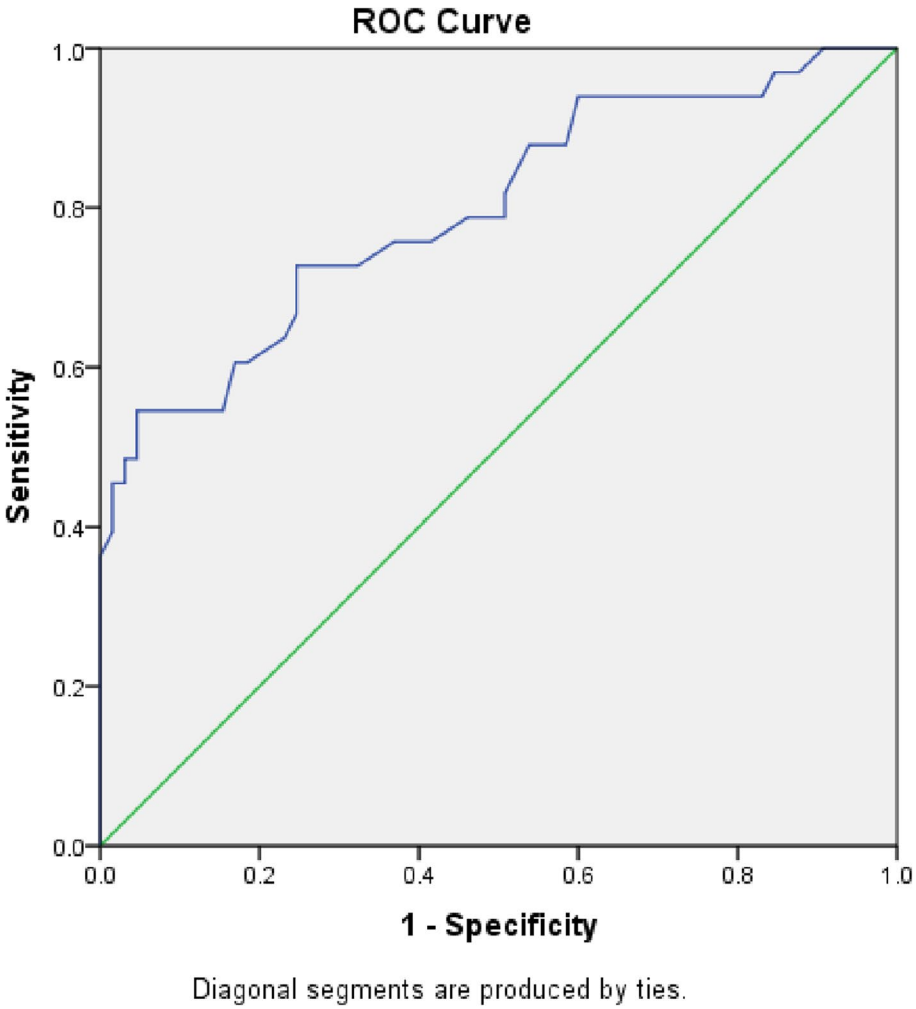

Fig. 11 Receiver operating characteristic curve (ROC curve) of the 1 month post-operative direct bilirubin level by mg/dL for predicating success of treatment of biliary atresia. It shows that 1 month post-operative direct bilirubin level at a cut-off value of ≤ 5.01 mg/dL has 76% sensitivity, 64% specificity, 51% PPV 84% NPV, and 67% accuracy

et al. [26] reported that none of these tests affected the clinical outcome.

Regarding preoperative ultrasonographic characteristics, gall bladder contractility was the only significant prognostic factor in the current study ($P=0.003$ and 0.037 respectively) (Table 2), where gall bladder atresia significantly associated with the failure outcome. It was found in 48 cases; 39 (58.2%) of cases in the failure group and 9 (27.3%) of cases in the successful group. We agreed with Li et al., who reported significant effect of gall bladder size and appearance on the outcome of biliary atresia after surgery.

Preoperative endoscopic data revealed statistical significant difference between both outcome groups regarding endoscopic duodenal bile test ($P=0.037$), (Table 2). Out of the 100 BA infants included in the study, 3 cases had tinge of duodenal bile at the time of examination using the upper gastrointestinal endoscopy, who had successful outcome. Our previous center study [27] revealed that the duodenal tubal duct aspirate test can be used as a diagnostic instrument for BA with 100% sensitivity, 100% specificity, PPV of 100%, and NPV of 100%, and urgent indication of intraoperative cholangiography in cases of duodenal tube test results negative for bile.

In the current study, intraoperative prognostic factors included histopathology of the intraoperative wedge biopsy and excised biliary remnant (Table 4), surgical type of BA, type of operation and Table 3 were analyzed. Liver fibrosis was assessed by Russo score [10] but for statistical analysis we grouped the patient under 3 grades where absent or fibrous expansion of some portal areas named (mild fibrosis), fibrous expansion of most portal areas named (moderate fibrosis), and focal portal-to-portal bridging, marked bridging and cirrhosis considered as

Table 4 Histopathological characteristics according to the outcome

Characteristics	Successful (*N* = 33)	Failed (*N* = 67)	*P* value
Grades of hepatic fibrosis			
Mild	5 (15.2%)	0 (0.0%)	0.005*
Moderate	10 (30.3%)	24 (35.8%)	
Severe	18 (54.5%)	43 (64.2%)	
Ductal proliferation	33(100%)	66(98.5%)	0.481
Bile plugs	32(97%)	66(98.5%)	0.606
Multi-nucleated giant hepatocytes	14(42.4%)	26(38.8%)	0.728
Portal cellular infiltrate	27(81.8%)	61(91.0%)	0.203
Remnant bile duct diameter			
< 150 µm	9 (27.3%)	46(68.6%)	0.024*
≥ 150 µm	24(72.7%)	21(31.4%)	
Surgical type of BA			
Type 1	6 (18.2%)	0(0.0%)	0.001*
Type 2	7(21.2%)	9(13.4%)	
Type 3	17(51.5%)	56 (83.6%)	
Cystic BA	3(9.1%)	2(3.0%)	
Type of operation			
Hepatico-jejunostomy	5(15.2%)	0(0.0%)	0.002*
Cholecysto-portostomy	7(21.2%)	9(13.4%)	
Kassai porto-enterostomy	21(63.6%)	58(86.6%)	

* Statistical significant *P* value

(severe fibrosis). We found that severe grade of hepatic fibrosis was a significant prognostic parameter in predicting the operation failure ($P=0.005$). Salzedas-Netto et al. [28] reported that the rate of fibrosis grade IV is higher in patients with no drainage and all patients with fibrosis grade IV had no biliary drainage after Kasai operation. Gupta et al. [25] detected that the fibrosis in the preoperative liver biopsies was not statistically significant among the outcomes of the studied patients, while Sookpotarom et al. [18] and by Sanghai et al. [26] concluded that the liver histology did not influence the early outcome, this presumably due to the briefness of the follow-up period. Diameter of remnant bile duct < 150 µm significantly associated with the failure outcome. It was found in 48 cases; 39 (58.2%) of cases in the failure group and 9 (27.3%) of cases in the successful group ($P=0.024$). We were in agreement with Chandra and Altman [32] who reported that the presence of bile ducts with a diameter of 150 µm or more correlated with adequate bile flow after surgical intervention and therefore predicts a better outcome. Kahn found absence of bile ducts in fibrous remnants has been reported in the fetal type of BA and is considered a poor prognostic sign in terms of postoperative bile drainage [33].

Table 5 Postoperative characteristics according to the outcome

Characteristics	Successful (*N* = 33)	Failed (*N* = 67)	*P* value
Postoperative 1 month			
Serum TB	4.7 ± 2.8	8.4 ± 2.5	0.001*
Serum DB	3.2 ± 2.3	6.1 ± 2	
Recurrent cholangitis	21 (64%)	36 (54%)	0.282
Immediate post-operative complication			
Absent	27 (81.8%)	46 (68.7%)	0.610
PHT signs	6 (18.2%)	18 (26.9%)	
Liver failure	0 (0.0%)	1 (1.5%)	
Encephalopathy	0 (0.0%)	1 (1.5%)	
Burst abdomen	0 (0.0%)	1 (1.5%)	

* Statistical significant *P* value

Three surgical types of biliary atresia, have been identified and classified by the level of extrahepatic bile ducts. Type 1: atresia within the common bile duct and the gallbladder containing bile; this type is sometimes associated with cystic change in some part of the extrahepatic biliary tree; type 2: atresia limited to the common bile duct and hepatic duct with no bile in the gallbladder but two bile-containing lumens in the proximal remnant; type 3: atresia of the whole biliary tree with upper level of obstruction at the porta hepatis, with no visible bile-containing proximal lumen [1]. Cystic biliary atresia (CBA) is

an uncommon but significant variant of biliary atresia and defined as cystic change in an otherwise obliterated biliary tract [29]. It accounts for approximately 5–10% of biliary atresia cases [30]. In the current study, 73% of BA infants included in the study were BA type 3. Many studies revealed that BA type 3 are usually associated with the worst surgical outcome [13]. These data were in hand with our results, where 56 out of 73 infants (76.7%) with BA type 3 had significantly failed outcome 6 months postoperatively than other types; and all infant with type 1 had successful outcome ($P=0.001$). However, the small number of cases with BA type 1 (6%), BA type 2 (16%), and cystic BA (5%), limits the power of statistical analysis of surgical outcome regarding the surgical type of BA (Table 3).

All infants with BA type 3, cystic biliary atresia and one case of BA type 1 underwent hepatoportoenterostomy (Kasai's operation) (Fig. 6), while all infants with BA type 2 underwent cholecystoportoeterostomy (Liley's operation) (Fig. 7), and 5 cases of BA type 1 underwent hepatico-jejunostomy. There was statistically significance in affecting the outcome ($P=0.002$) regarding type of surgery where all cases underwent Hepatico-jejunostomy had successful outcome. Our results in agreement with Japanese association of pediatric surgeons' classification of biliary atresia [31].

In this study, there is a statistical significance for the bilirubin level at 1 month after surgery affecting the outcome ($P<0.05$) (Table 5). It is comparable to that of Sangkhathat et al., who reported that bilirubin level at 1-month after surgery can be used as predictors of jaundice clearance and as a marker for cholangitis.

According to our multivariate analysis in this study, age at surgery and the type of operation done according to type of BA was of the most effective independent predicting factors of the outcome after surgery.

The limitation of the study is its retrospective nature and the small number of patients with BA type I and type II who did not undergo Kasai portoenterostomy. This may not give accurate idea about the prognostic efficacy of surgical technique on the outcome in our cases.

Conclusions

Younger age and lower preoperative GGT and post-operative 1-month serum total and direct bilirubin level are good predictors for the surgical outcome of BA infants with better performance (i.e., better sensitivity, specificity, PPV, NPV and accuracy) of age and post-operative 1-month serum total and direct bilirubin level. This may determine infants with the high-priority for transplant referral postoperatively.

Abbreviations

BA	Biliary atresia
IOC	Intraoperative cholangiogram
HPB	Hepato-pancreato biliary
HPE	Hepatoportoenterostomy
NLI	National Liver Institute

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Authors' contributions

All authors were involved in the study concept and design. SA, GA, MB, MT, OH, and ES were involved in patients' recruitment, clinical management, and follow-up of the patients. MB, MT, OH, and ES shared in performed surgical interventions. MS blindly reviewed the intraoperative histological findings and designed the histopathological figures. SA, GA, MS, MB, MT, OH, and ES were involved in data collection. MT was involved in statistical analysis, interpretation, and designed the figures. All the authors reviewed the manuscript for the final approval of the version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Declarations

Ethics approval and consent to participate

Informed and written consent was obtained from all parents of infants included in the study. The research protocol of this study was approved and reviewed by the Research Ethics Committee of the NLI, Menoufia University, Egypt, and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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