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Research Article

Mortality of Biliary Atresia in Children Not Undergoing Liver Transplantation in Egypt (Single Institutional Study)

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Abstract

Introduction: Biliary atresia (BA) is a progressive obliterative disorder of intra and extra-hepatic bile ducts leading to hepatic fibrosis and frequently end-stage liver disease.

Aim: The aim of this study is to assess course, prognosis, and causes of death of BA patients who had not undergone Liver transplantation (LTx) and to identify risk factors for pre-transplant mortality in order to assess whether improvement in the prognosis of BA is possible or not.

Patients and methods: This study included 106 patients with BA recruited from Pediatric Hepatology Department, National Liver Institute, Menoufiya University-Egypt, over a period of 5 years divided into two main groups as Post Kasai which subdivided into successful and failed outcome in addition to the neglected BA and neglected BA. Follow up data were collected recording prognosis, complications, survival and cause of death.

Results: Ascending cholangitis (AC) was significantly higher in dead group than living group and 4 year cumulative survival rates were 17.8%, 75% and 0% in post-KPE group, successful and failed outcome respectively, where sepsis was the most common cause of death in 46%.

Conclusion: We concluded that ascending cholangitis was a risk factor for failure of KPE and death. Both failed KPE and neglected BA patients reached nearly the same degree of hepatic dysfunction, Sepsis was the most common cause of death in BA patients and the cumulative survival rate at 4 years was 80%. When KPE was successful, cumulative survival rate at 4 years was 80%.

Keywords: *Biliary atresia; Ascending cholangitis; Survival; Successful and failed outcome and liver transplantation*

Introduction

Biliary atresia (BA) is a progressive obliterative disorder of intra and extra-hepatic bile ducts leading to hepatic fibrosis and frequently end-stage liver disease. If untreated, this disease is uniformly fatal [1].

The Kasai portoenterostomy (KPE) has improved the outcome of BA patients, particularly if performed on children aged younger than 90 days [2]. However, 67% of these patients who had KPE developed chronic liver disease (CLD) and almost all required liver transplantation (LTx) before reaching adulthood. The general approach is that the Kasai procedure is a bridge to LTx [3]. BA is the most common indication for pediatric LTx, representing at least 50% of all pediatric LTx cases [4].

The outcome following the Kasai operation can be assessed in two ways:

1. Clearance of jaundice.
2. Proportions of native liver survival [5].

Long term (10 years or greater) survival have been reported in the range of 27%-53%. Although in another study, only about 15% had true long term survival without jaundice, normal liver biochemistry and no signs of liver disease or portal hypertension (PHT). However, even in this apparently "cured" group, liver histology still remains abnormal [6].

Aim of the Study

The aim of this study is to assess course, prognosis, and causes of death of BA patients who had not undergone LTx and to identify risk factors for pre-transplant mortality in order to assess whether improvement in the prognosis of BA is possible or not.

Patients and Methods

This study included 106 patients with BA recruited from Pediatric Hepatology Department, National Liver Institute, Menoufiya University - Egypt, over a period of 5 years from 2009 to 2013, divided into two main groups:

Group I (Post-KPE group): Consisting of 86 patients (43 male (50%) and 43 female (50%)). Post-KPE patients were sub classified according to post-KPE outcome at 6 months from the operation into two subgroups as successful and failed outcome.

Group Ia (Successful outcome): When total serum bilirubin was ≤ 2 mg/dl at 6 months post-KPE. They were 15 patients (7 male and 8 female).

Group Ib (Failed outcome): When total serum bilirubin was > 2 mg/dl at 6 months post-KPE. They were 45 patients (19 male and 26 female).

There were 17 patients died before 6 months post KPE and 9 patients were lost during the follow up after KPE, they were excluded from the comparison between the successful vs. failed and living vs. dead as they are not fulfilled the criteria for definition of successful or failed Kasai which is determined by the serum bilirubin level at 6 months).

The total number of patients enrolled at the start of the study were 106 out of which, 9 were lost to follow-up. The remaining 97 patients were followed out of which 50 died while 47 survived.

Living group: They were 47 patients (14 successful outcomes, 12 failed outcomes, 17 neglected BA and 4 less than 6 month post-KPE).

Dead group: They were 50 patients (1 successful outcome, 33 failed outcome, 3 neglected BA and 13 less than 6 month post-KPE).

Group II (Neglected BA): This group included 20 patients (14 male (70%) and 6 female 30%) who hadn't undergone Kasai operation as they were diagnosed so late.

The diagnosis BA (for all patients) depended mainly on the positive histopathological findings of liver biopsy and confirmed by intraoperative cholangiogram for patients who undergone Kasai operation.

All patients were subjected to the followings careful history, thorough clinical examination findings, and investigations (liver function tests, full blood count (FBC), prothrombin time (PT) TORCH screen, abdominal ultrasound (U/S) and liver biopsy). Also, associated congenital anomalies were recorded. Follow up data were collected included the follow up prognosis, complications, survival duration and cause of death.

Preoperative and postoperative laboratory data were recorded in group I.
Severity of liver disease at time of last follow up was assessed by the Pediatric End-stage Liver Disease (PELD) score. It is calculated according to the following formula:

PELD 0.436 × age (< 1 year)

PELD Score = 0.480 x Loge (bilirubin mg/dL) + 1.857 x Loge (INR) - 0.687 x Loge (albumin g/dL) + 0.436 if the patient is less than 1 year old (scores for patients listed for liver transplantation before the patient's first birthday continue to include the value assigned for age (< 1 Year) until the patient reached the age of 24 months) + 0.667 if the patient has growth failure (<-2 Standard deviation)

Multiply the score by 10 and round to the nearest whole number. Laboratory values less than 1.0 are set to 1.0 for the purposes of the PELD score calculation.

Statistical Methods: Data were analyzed using the SPSS (Statistical Package for Social Science) program version 21.0, SPSS Inc., Chicago, Illinois, USA.

Results

Total numbers of our cases are 106 patients. Post Kasai patients are 86 (81.1%), neglected BA is 20 (18.9%), their outcome as follow: living patients are 47 (44.3%), while 50 patients (47.2%) were died and 9 patients (8.5%) were lost during their follow up.

The mean age at diagnosis was (56.02 ± 22.60) days while the age at Kasai HPE was 64.40 ± 12.02 in successful post Kasai, while 70.98 ± 17.85 in failed outcome of Kasai.

At presentation, of all total patients (106) 100% had jaundice and 102 (96.2%) had clay stool.

Associated congenital anomalies were found in 12 patients (11.3%) of those patients two had two congenital anomalies. Among these anomalies biliary atresia splenic malformation (BASM) was the most common found in 5 patients (4.7%).

Among these anomalies polysplenia in 4 patients (3.8%), Asplenia in 1 patient, duodenal atresia in 1 patient. TR in 3 patient (2.8%), Situs inversus total is in 1 patient , dextrocardia in 1 patient, VSD in 1 patient, ASD in 1 patient, TGA, 1patient.

Regarding the abdominal U/S findings of the all 106 BA patients, the mean liver span was 7.88±1.22 Cm, hepatomegaly in 69.8%. Splenic length 6.41 ± 1.45 Cm splenomegaly 27.4%. Gall bladder (G.B) was non-contractile in 70 (66%), G.B not visualized 27 (25.5%), atretic GB in2 (1.9%), and contractile G.B 7 (6.6%). Duodenal tubal aspirate was done in 54 patients and all showed no bile.

Histopathological findings of the all 106 BA patients: bile plugs in 103 patients (97.2%), bile duct proliferation in 105 patient (99.1%), Giant cell transformation in 21 (19.8%), there is no fibrosis 31 (29.2%) but fibrosis was mild in 16 (15.1%), moderate 45 (42.5%), severe in 2 (1.9%), and cirrhosis in 12 (11.3%)

The complications of the 97 patients who completed their follow up as recorded in our study as follow; ascites in 54 patients (55.7%), spontaneous bacterial peritonitis in 12 (12.4%), GI bleeding in 23 patients (23.7%), ascending cholangitis in 52 patients (53.6%).

	BA Patients	
	N = 106	
	No.	%
Classification		
Post-KPE	86	(81.1%)
Neglected BA	20	(18.9%)
Outcome		
Living	47	(44.3%)
Dead	50	(47.2%)
Lost during follow up	9	(8.5%)

Table 1: *Outcome of the BA Patients.*

Age Groups	Successful Outcome N = 15	Failed Outcome N = 45	*P*-value
	Mean ± SD	Mean ± SD	
Age at KPE (Days)	12.02 ± 64.40	17.85 ± 70.98	0.226

Table 2: *Comparison between age at KPE in successful and failed outcome groups.*

Time LFTs	At Diagnosis N = 15	Pre KPE N = 15	One Month post KPE N = 15	Six Months post KPE N = 15	Last Lab N = 15
	SD ± Mean	SD ± Mean	SD ± Mean	SD ± Mean	SD ± Mean
BILI.T (mg/dl)	6.22 ± 11.99	4.71 ± 11.03	3.36 ± 5.53	0.45 ± 1.08	041 ± 0.85
BILI.D (mg/dl)	9.52 ± 10.16	3.94 ± 8.12	2.49 ± 3.79	0.46 ± 0.51	0.28 ± 0.35
ALT (U/L)	78.36 ± 118.97	63.49 ± 132.20	58.56 ± 85.60	79.85 ± 86.85	128.73 ± 99.85
AST (U/L)	134.37 ± 194.82	90.53 ± 210.73	74.32 ± 134.33	48.98 ± 97.46	223.30 ± 136.69
GGT (U/L)	682.78 ± 864.53	850.13 ± 1234.67	616.63 ± 882.57	244.12 ± 553.36	320.36 ± 538.50
ALP (U/L)	176.69 ± 442.60	191.62 ± 450.00	302.05 ± 467.57	143.84 ± 319.78	165.82 ± 328.88
Albumin (g/dl)	0.29 ± 3.37	0.36 ± 3.24	0.69 ± 3.30	0.46 ± 3.18	7.05 ± 3.68
PT (sec.)	0.26 ± 12.60	0.44 ± 12.72	1.04 ± 12.78	0.33 ± 12.77	0.26 ± 12.73
INR	0.75 ± 1.05	0.07 ± 1.05	0.07 ± 1.05	0.00 ± 1.10	0.09 ± 1.09

Table 3: *Course of laboratory parameters in successful outcome group.*

Time LFTs	At Diagnosis N = 45	Pre KPE N = 45	One Month post KPE N = 45	Six Months post KPE N = 45	At last follow up N = 45
	SD ± Mean	SD ± Mean	SD ± Mean	SD ± Mean	SD ± Mean
BILI.T (mg/dl)	2.85 ± 11.02	3.21 ± 12.00	3.69 ± 8.87	5.55 ± 11.37	6.09 ± 14.19
BILI.D (mg/dl)	1.93 ± 7.48	2.51 ± 8.36	2.45 ± 6.18	4.09 ± 8.30	4.76 ± 10.78
ALT (U/L)	113.63 ± 135.62	66.83 ± 121.02	103.64 ± 127.98	78.05 ± 81.49	57.13 ± 73.90
AST (U/L)	126.39 ± 180.80	98.25 ± 193.76	82.05 ± 162.51	83.49 ± 120.91	86.04 ± 126.24
GGT (U/L)	526.86 ± 785.67	646.84 ± 868.58	630.94 ± 1023.31	550.39 ± 771.97	437.84 ± 462.06
ALP (U/L)	256.21 ± 458.24	303.18 ± 522.78	295.26 ± 480.91	387.52 ± 588.84	212.89 ± 453.24
Albumin (g/dl)	0.48 ± 3.38	0.43 ± 3.29	1.49 ± 3.32	0.64 ± 2.88	0.69 ± 2.60
PT (sec.)	1.19 ± 12.99	0.68 ± 12.86	1.77 ± 12.79	1.75 ± 14.07	7.51 ± 16.35
INR	0.13 ± 1.07	0.11 ± 1.08	0.11 ± 1.06	0.23 ± 1.29	0.31 ± 1.31

Table 4: *Course of laboratory parameters in failed outcome group.*

Groups LFTs	Successful Outcome N = 15	Failed Outcome N = 45	*P* - Value
	SD ± Mean	SD ± Mean	
BILI.T (mg/dl)	3.36 ± 5.53	3.69 ± 8.87	0.01
BILI.D (mg/dl)	2.49 ± 3.79	2.45 ± 6.18	0.005
ALT (U/L)	58.56 ± 85.60	103.64 ± 127.98	0.189
AST (U/L)	74.32 ± 134.33	82.05 ± 162.51	0.213
GGT (U/L)	616.63 ± 882.57	630.94 ± 1023.31	0.318
ALP (U/L)	302.05 ± 467.57	295.26 ± 480.91	0.887
Albumin (g/dl)	0.69 ± 3.30	1.49 ± 3.32	0.423
PT (sec.)	1.04 ± 12.78	1.77 ± 12.79	0.480
INR	0.07 ± 1.05	0.11 ± 1.06	0.854

Table 5: *Comparison between one month post-KPE laboratory parameters in successful and failed outcome groups.*

Groups LFTs	Successful Outcome N = 15	Failed Outcome N = 45	*P* - Value
	SD ± Mean	SD ± Mean	
BILI.D (mg/dl)	0.46 ± 0.51	4.09 ± 8.30	0.0001 >
ALT (U/L)	79.85 ± 86.85	78.05 ± 81.49	0.547
AST (U/L)	48.98 ± 97.46	83.49 ± 120.91	0.347
GGT (U/L)	244.12 ± 553.36	550.39 ± 771.97	0.308
ALP (U/L)	143.84 ± 319.78	387.52 ± 588.84	0.033
Albumin (g/dl)	0.46 ± 3.18	0.64 ± 2.88	0.167
PT (sec.)	0.33 ± 12.77	1.75 ± 14.07	0.002
INR	0.00 ± 1.10	0.23 ± 1.29	0.370

Table 6: *Comparison between six months post-KPE laboratory parameters in successful and failed outcome groups.*

Parameter	AUROC	Cutoff	P- value	Sensitivity%	Specificity%	PPV%	NPV%	Accuracy%
BILI.T (mg/dl)	0.724	6.2	0.01	60%	82.2%	52.9%	86%	80%
BILI.D (mg/dl)	0.746	4.6	0.005	66.7%	75.6%	47.6%	87.2%	73.3%

Table 7: *Clinical performance of one month postoperative BILI.T&D in predicting successful outcome.*

Groups Survival	Successful outcome N = 15	Failed outcome N = 45	*P*1-value	Neglected BA N = 20	-*P*2 Value	-*P*3 Value
	Mean	Mean		Mean		
Means for Survival Time (Month)	80.44	18.95	0.0001 >	17.96	0.0001 >	0.47

Table 8: *Comparison of survival time among BA groups.*

P1-value: successful outcome vs. failed outcome, P2-value: successful outcome vs. neglected BA, P3-value: failed outcome vs. neglected BA.

Groups Survival	Successful outcome N = 15	Failed outcome N = 45	*P* value
	Mean	Mean	
Survival Time post KPE (Months)	41.25	16.41	0.0001 >

Table 9: *Comparison between survival time post-KPE in successful and failed outcome groups.*

Cumulative Survival (Months)	Successful Outcome %	Failed Outcome %	Neglected BA %
6 Months	100%	100%	95%
12 Months	100%	79.2%	88.2%
18 Months	100%	72%	66.2%
24 Months	80%	50.4%	-
36 Months	80%	27.7%	-
48 Months	80%	10.5%	-

Table 10: *Cumulative survival rates in BA groups.*

Cumulative Survival post-KPE (Months)	Successful Outcome %	Failed Outcome %
6 Months	100%	100%
12 Months	100%	43%
18 Months	100%	24.5%
24 Months	75%	16.4%
36 Months	75%	10.9%
48 Months	75%	-

Table 11: *Cumulative survival rate post-KPE in successful and failed outcome groups.*

Cumulative Survival rate post-KPE (Months)	Post-KPE %
6 Months	79.6%
12 Months	43.7%
18 Months	30.6%
24 Months	21.4%
36 Months	17.8%
48 Months	17.8%

Table 12: *Cumulative survival rate in post-KPE group.*

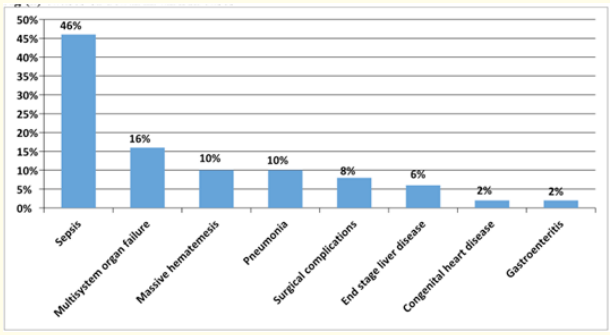

Figure 1: *causes of death in all BA cases.*

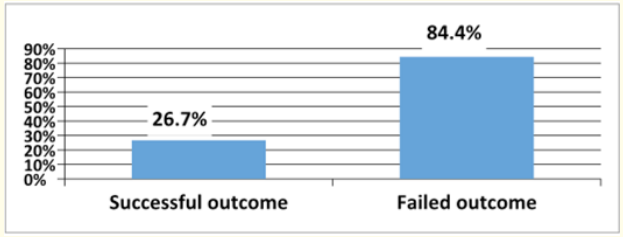

Figure 2: *Ascending cholangitis in successful and failed outcome groups.*

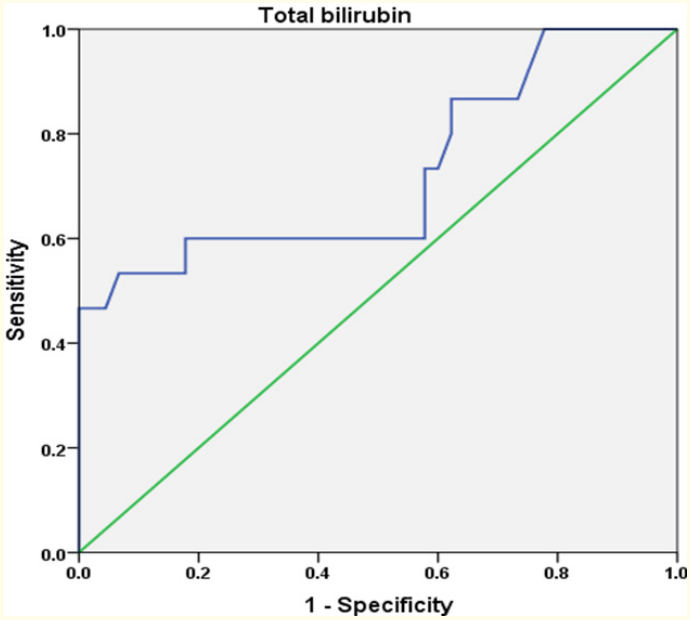

Figure 3: *ROC curve for BILI.T performance in prediction of successful outcome.*

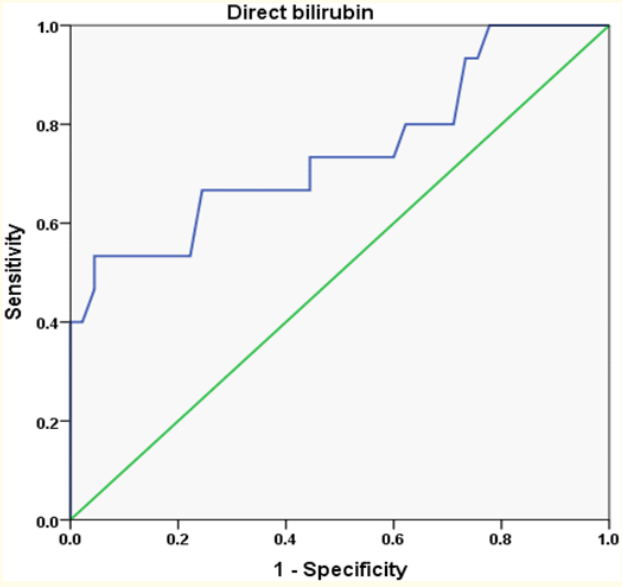

Figure 4: *ROC curve for BILI.D performance in prediction of successful outcome.*

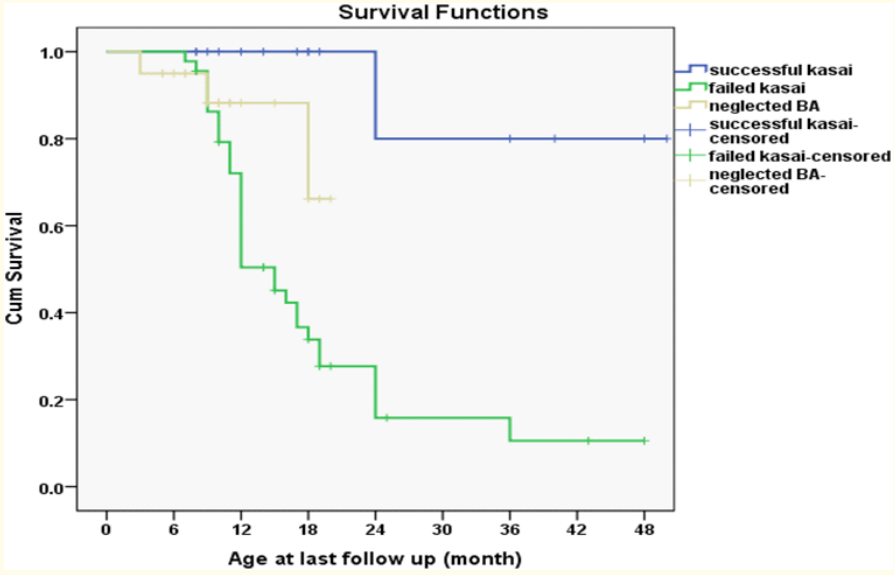

Figure 5: *Kaplan-Meier curve shows cumulative survival rates in successful, failed outcome and neglected BA groups.*

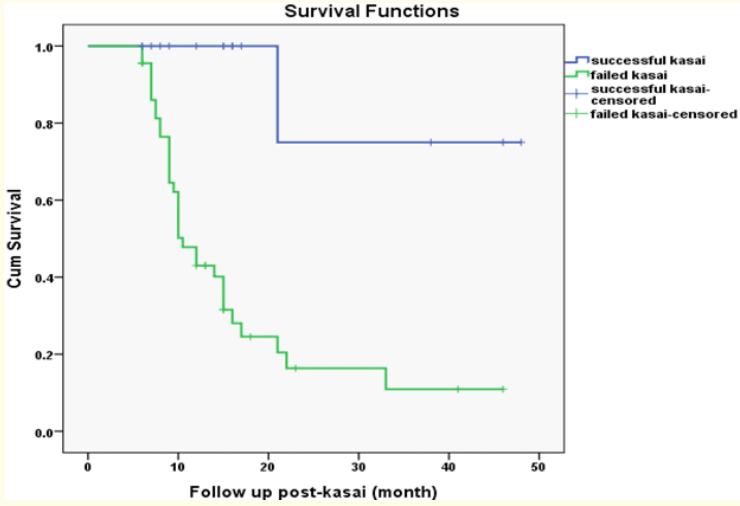

Figure 6: *Kaplan-Meier curve shows cumulative survival rate post-KPE in successful and failed outcome groups.*

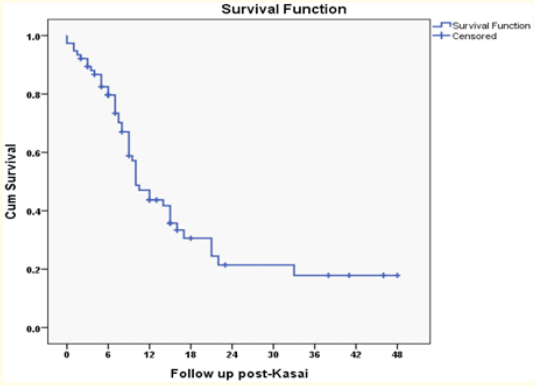

Figure 7: *Kaplan-Meier curve shows cumulative survival rate in post-KPE patients.*

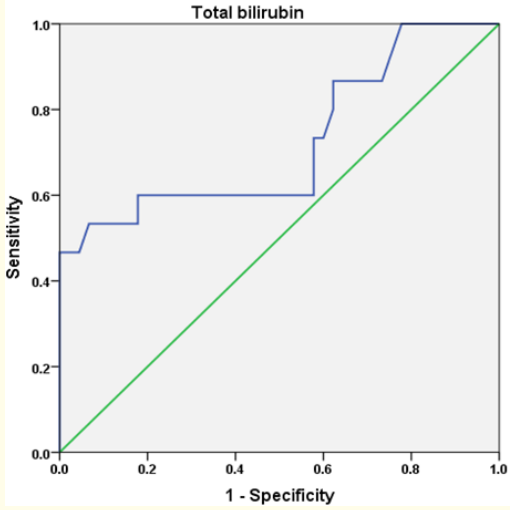

Figure 8: *ROC curve for BILI.T performance in prediction of successful outcome.*

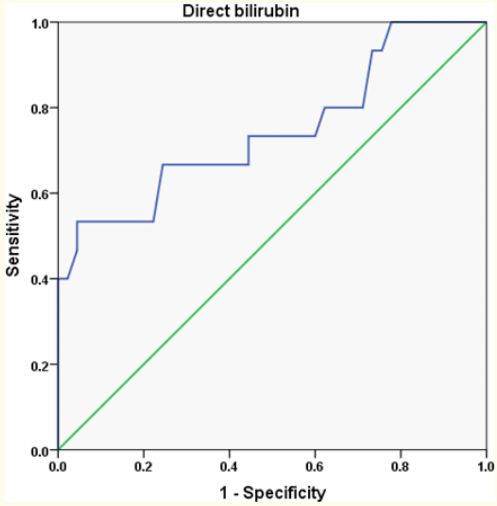

Figure 9: *ROC curve for BILI.D performance in prediction of successful outcome.*

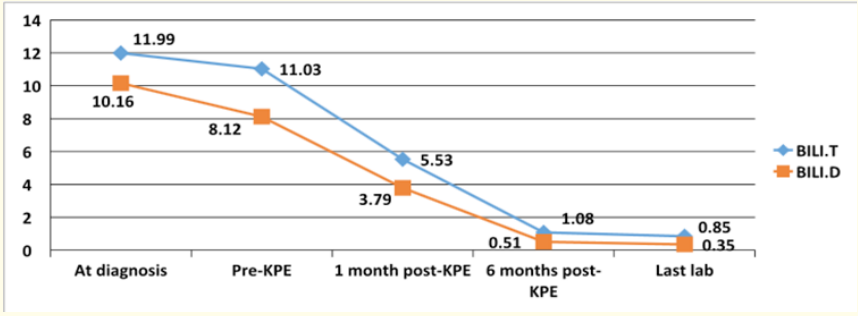

Figure 10: *Curve shows course of BILI.T&D in successful outcome group.*

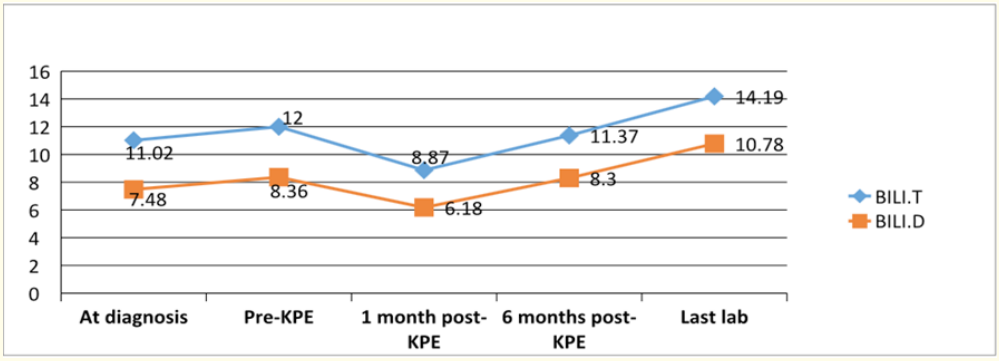

Figure 11: *Curve shows course of BILI.T& D in failed outcome group.*

Discussion

Biliary atresia is one of the main causes of NC and the most common indication for LTx in pediatric patients. Since Kasai introduced KPE, it remains the primary procedure for BA. However, rate of survival with the native liver is relatively low and the majority of patients require LTx [7].

Several prognostic factors have been suggested to predict the prognosis of BA patients. The existence of splenic malformation syndrome, degree of liver fibrosis at operation, experience of the hospital, age at operation and occurrence of postoperative cholangitis have all been reported to be related to operative results [8].

The primary objective of the current work was to evaluate the outcome of BA patients (Single Institutional study). This study included 106 cases, 86 post-KPE and 20 neglected BA attending the Pediatric Hepatology Department, National Liver Institute, Menoufiya University, Egypt.

The mean age at diagnosis was (56.02 ± 22.60) days. In accordance to these results, Shneider., *et al*. [8] in their study about outcome of BA, reported that mean age at diagnosis was (53 ± 29) days.

Jaundice was the presenting symptom in all patients (100%), 96.2% had clay stool and 69.8% had hepatomegaly. In accordance to these results, Okoro., *et al*. [9] in their study about pattern and survival of BA patients, reported that all patients had jaundice and hepatomegaly where 91.7% passed clay colored stool.

Associated congenital anomalies seen in 11.3% of patients such as situs anomalies, congenital heart disease and biliary atresia splenic malformations (BASM 4.7%). In hand with these results Grieve., *et al*. [10] reported that 18.1% of BA patients had associated anomalies.

This study showed that 32.8% of BA patients had antibodies to CMV of IgM type. Consistent with this result, Fischler., *et al*. [11] reported that 38% of BA patients had antibodies to CMV of IgM type.

Ultrasonography of the liver is performed after fasting (with an IV dextrose infusion when needed after observation of blood glucose). BA is suspected when the gallbladder is shrunk despite fasting, when the liver hilum appears hyper echogenic ("triangular cord sign" TC sign) or when there is a cyst at the liver hilum. There should be no evidence of bile duct dilatation. Syndromic BA infants may show other features such as multiple spleens, pre duodenal portal vein, absence of retro hepatic vena cava or abdominal situs inversus, our Ultrasonography results showed that the majority of BA patients (93.4%) had an abnormal GB view in the form of a non-contractile (66%), not visualized GB (25.5%) or atretic GB (1.9%), while 6.6% of BA group had contractile GB. This was in agreement with the finding of Cauduro [12] in his study about diagnostic methods of BA, who reported that the contractility of GB in BA cases could be observed in 19% to 22%.

Liver biopsy had important role in diagnosis where ductular proliferation and bile plugs were the most prominent features found in 99.1% and 97.2% of BA patients respectively. In accordance to these results, the same author Yasser K Rashed., *et al*. [13] in their study about the accuracy of histopathological features for diagnosing BA, reported that ductular proliferation, bile plugs and intracellular bile pigments emerged as the best indicators of BA while multinucleate giant cells transformation and portal cellular infiltration were seen more common in neonatal hepatitis (NH).

One month postoperative Total and Direct bilirubin were significantly lower in successful outcome group (5.53 ± 3.36) and (3.79 ± 2.49) respectively, than that in failed outcome group (8.87 ± 3.69), (6.18 ± 2.54) respectively ($P = 0.01$) and ($P = 0.005$) respectively. In accordance to these results, Goda., *et al*. [14] in their study about predictors of outcome in patients with BA after KPE, reported that Total and Direct bilirubin were significantly different between 2 groups at one month postoperative.

One month postoperative Total bilirubin of less than 6.2 mg/dl had 60% sensitivity and 82.2% specificity and one month BILI.D of less than 4.6 mg/dl had 66.7% sensitivity and 75.6% specificity in predicting successful outcome at 6 month post-KPE. In hand with our results, Lang., *et al*. [15] in their study about which factors predict the success of Kasai operation, reported that the fifth week post-Kasai Total bilirubin was 6.3 mg/dl in failed group. Also Rodeck B., *et al*. [16] who documented that serum bilirubin concentration concentrations above 57 µmol/l at six weeks after the operation should be carefully and frequently monitored with regard to a transplantation requirement in order to optimize pre-transplant management.

This study showed that there was no significant statistical difference between successful and failed outcome groups regarding ALT and AST at one month postoperative ($P > 0.05$).

There was no significant difference between successful and failed outcome groups regarding GGT at one month postoperative ($P > 0.05$).

At six months post-KPE, we reported that BILI.T/D, ALP and PT were significantly lower in successful group than in failed group ($P < 0.0001$, $P < 0.0001$, $P = 0.033$ and $P = 0.002$) respectively, where BILI.T/D in successful outcome group were (1.08 ± 0.45) and (0.51 ± 0.46) respectively. In hand with these results, Leonhardt., *et al*. [17] in their study about predictive parameters in children with BA, reported that normal levels of bilirubin at 6 months post-KPE were associated with 5 year survival with native liver.

Cholangitis is a common complication in BA after Kasai's operation and most episodes develop in the first two years of life. We found that the survival rate was reduced significantly for patients who suffered repeated episodes of cholangitis. In our study, 67.5% of post-KPE patients had cholangitis, in successful outcome group 26.7% had cholangitis and in failed outcome group 84.4% with significant difference ($P = 0.0001$). In accordance to our results, Chittmittrapap., *et al*. [18] reported that the presence of cholangitis was also significantly related to a poor outcome. Also, Grizelj., *et al*. [19] in their study about BA, reported that 42.8% of post-Kasi HPE patients experienced at least one episode of cholangitis.

Ascending cholangitis (AC) was significantly higher in dead group than living group ($P < 0.0001$). This is in agreement with Hung., *et al*. [20] in their study about long-term prognosis of patients with BA, who reported that survival rate was reduced significantly in the first two years post-KPE for patients who suffered repeated episodes of AC.

We reported that disturbed architecture was higher in neglected BA group than successful and failed outcome groups ($P = 0.015$ & $P = 0.003$) respectively. There was no significant statistical difference between neglected BA group and failed outcome group as regarding the occurrence ascites, SBP and GIT bleeding ($P > 0.05$).

ALT and AST were statistically significantly higher in neglected BA group than in failed outcome group ($P = 0.005$ & $P < 0.0001$) respectively. While there was no significant statistical difference between neglected BA group and failed outcome group as regard BILI.T/D, ALP, GGT, albumin, PT and INR ($P > 0.05$). There was no significant statistical difference between neglected BA group and failed outcome group as regard survival time and PELD score at last follow up ($P > 0.05$).

We reported that portal tract edema and infiltrating cells were significantly higher in living group than dead group with ($P = 0.011$ & $P = 0.009$) respectively, while there was no significant statistical difference between two groups regarding bile plugs, ductular proliferation, grade of fibrosis, giant cell transformation and lobular architecture ($P > 0.05$). In hand with these results, Davenport., *et al*. [21] in their study about outcome of older infant with BA, reported that there was no significant difference between two groups regarding parenchymal cholestasis, fibrosis and giant cell transformation.

Cumulative survival rates in neglected BA group were 95%, 88.2% and 66.2% at 6, 12 and 18 months respectively with the mean survival time was 17.9 months.

In our study, mean survival time was 44.8 and 18.9 months in successful and failed outcome groups respectively, with significant difference ($P < 0.0001$). In our study, cumulative survival rates in all post-KPE, successful outcome and failed outcome groups were 79.6%, 100%, 100%, respectively at 6 months post-KPE. While the 2 years cumulative survival rates in post-KPE group, successful and failed outcome groups were 21.4%, 80% and 50.4% respectively. In accordance to these results, Wildhaber., *et al.* [22] reported that 2 years survival rate was 60% in successful outcome group but it was 4.8% in failed outcome group. While, Serinet., *et al*. [23] reported that 2 years survival in post-KPE group was 57.1%.

In our study, 4 year cumulative survival rates were 17.8 %, 75% and 0% in post-KPE group, successful and failed outcome respectively. While Wildhaber, *et al*. [22] reported that 4 years survival in patients who underwent the Kasai operation was 37.4%. Also de Vries., *et al*. [24] reported that 4 year transplant-free survival in all post-KPE patients was 46%.

We reported that the cause of death was sepsis in 46% where it was the most common cause of death, multisystem organ failure in 16%, massive hematemesis in 10%, pneumonia in 10%, end stage liver disease in 6%, surgical complications in 8%, gastroenteritis in 2% and congenital heart disease in 2%.

Consistent with these results, de Vries., *et al*. [24] in their study about mortality of BA, reported that sepsis was the most common cause of death in 30% of cases, Congenital anomalies were the cause of death in 14% of cases as pulmonary dysplasia, cardiomyopathy. GIT bleeding was the cause of death in 9% of cases. Absence of parental consent for LTx was the cause in 9% of cases. Complications of KPE were the cause of death in 7% of cases. Miscellaneous causes were in 16% of cases as lethal hemorrhage in a hepatoblastoma.

Finally we concluded that Pre-operative BILI.T/D had no effect on the outcome of KPE. BILI. T/D at one month postoperative can predict outcome of KPE. Ascending cholangitis was a risk factor for failure of KPE and death. Higher stage of fibrosis in pre-operative liver biopsy was a risk factor for failure of KPE. Complications of PTH were much lower when KPE was successful. Both failed KPE and neglected BA patients reached nearly the same degree of hepatic dysfunction as there was no significant difference between PELD scores in both groups at last follow up. When KPE was successful, cumulative survival rate at 4 years was 80%.

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