An investigation into the outcomes of biliary atresia in Sulaimani, Iraq

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Abstract

Background and objective: Biliary atresia (BA) is a rare childhood disease that is associated with renal failure, cirrhosis, and death. This disease is typically treated through Kasai portoenterostomy which can be associated with some preoperative and postoperative complications. In this regard, the present study was aimed at investigating the relationship between early diagnosis of biliary atresia and its outcomes and complications following Kasai portoenterostomy.

Methods: In a retrospective study, 20 infants with biliary atresia who were treated through Kasai portoenterostomy or who did not receive treatment, were investigated. Required data were collected from their files and analyzed using Pearson Chi-square test through SPSS 20.0.

Results: The results of the present study indicated liver biopsy was an accurate method to diagnose biliary atresia. Stool color was found to be an important clinical indicator on presentation of BA. It was also seen that both groups of infants who received Kasai treatment did not develop cholangitis. Also, liver cirrhosis and portal hypertension were complications that were seen in both groups of patients who received and did not receive Kasai treatment. There was a significant relationship between early diagnosis of BA and survival more than 6 months. However, there was no significant relationship between receiving Kasai treatment and mortality rate.

Conclusion: Infants with biliary atresia survive more in cases of early diagnosis and referral for surgery; therefore, pediatric centers are highly recommended to perform evaluations for BA once they notice neonatal jaundice lasting more than 2 weeks. Effective postoperative care is also recommended for favorable outcomes of Kasai portoenterostomy.

Key words: biliary atresia, Kasai portoenterostomy, renal failure, retrospective study, the Kurdistan Region of Iraq

Introduction

Biliary atresia (BA) is a rare pediatric cholangio-destructive disease that has adverse effects on both the extra- and intra-hepatic biliary tract, and if it is not treated in a timely manner, renal failure, cirrhosis, and death can be among its outcomes [1, 2]. The prevalence of this disease has been reported to vary from 1 out of 8,000 to 1 out of 18,000 live births [3]. BA is usually non-syndromic and has an isolated anomaly [4]; however, it is sometimes associated with various congenital anomalies such as absence of cardiac defects, retro-hepatic inferior vena cava, preduodenal portal vein, situs inversus, asplenia, or polysplenia [5, 6]. Development of BA has been related to different factors; however, recent studies have reported that it is likely to be related to gene mutations [7]. During the first weeks of life, children with BA do not have any clinical signs, but 2-6 weeks after birth, they become increasingly jaundiced [8]. Other clinical signs of BA can include liver growth in size and firmness, anemia, malnutrition diarrhea, prolonged bleeding from the umbilical stump, and splenomegaly [9]. Numerous methods have been proposed and tried for the diagnosis of BA in neonates; however, very few of them have acceptable accuracy. Liver biopsy has been reported as the most helpful examination for BA with a diagnostic accuracy of >90%. It should also be noted that liver biopsy is most accurate if it is performed after 6 weeks of age because most features of BA may be absent before this age, and in that case, an intra-operative cholangiogram may be required [10].

Kasai portoenterostomy, also called hepatoportoenterostomy, was proposed by Morio Kasai in 1959 as an operative treatment for biliary obstruction in infants with non-correctable atresia [11]. In order to stimulate bile flow, reduce hepatic inflammation, prevent postoperative cholangitis, and decrease progressive fibrosis associated with BA, adjuvant medical therapy is commonly conducted after Kasai portoenterostomy [12]. Liver transplantation is used as a treatment method for those cases where the liver is severely impaired due to delayed diagnosis [13].

Although Kasai portoenterostomy is reported to be the most preferred treatment for BA, it has been associated with some preoperative complications such as ventilator associated pneumonia, electrolyte imbalance, DIC, hemorrhage, and sepsis [14] and postoperative complications including portal hypertension, liver failure, upper gastrointestinal bleed, and cholangitis [15].

The present study was carried out in the Pediatrics Teaching Hospital, Shar Hospital, and Shorsh Hospital in Sulaimani, the Kurdistan Region of Iraq, to examine the relationship between early diagnosis of biliary atresia and its outcomes and complications following Kasai portoenterostomy.

Patients and methods

The present investigation was a retrospective study that was carried out on 20 infants with biliary atresia hospitalized in the Pediatrics Teaching Hospital of Sulaimani, the Kurdistan Region of Iraq. Data collection was carried out from September 1, 2012 to September 1, 2016.

Convenience sampling was utilized to select the study sample. Both groups of infants who had received Kasai portoenterostomy (Kasai group) and those who had received no treatment (no-treatment group) were included in the study. After the selection of the infants, their demographic and pediatric characteristics including age, sex, place of residence, weight at the time of diagnosis, associated congenital abnormalities, age at the time of evaluation, color of stool, and color of urine were obtained from their files; as well as data on their liver enzymes at diagnosis time, ultrasonographic findings, and liver biopsy findings. In addition, data on complications and outcomes of BA were obtained from the patients who had undergone Kasai portoenterostomy and from those who had not. All required data of the surviving infants were obtained from the GIT department in the Pediatrics Teaching Hospital and Pediatric Surgical Department in Shar Hospital of Sulaimani, the Kurdistan Region of Iraq. Moreover, data of the infants who had died were obtained from the Histopathological Department of Shorsh Hospital, Sulaimani.

The collected data were analyzed using Pearson Chi-square test through Statistics Package for Social Science (SPSS) version 21. The results are expressed in form of numbers and percentages. The level of statistical significance was set at $p<0.05$.

The study was approved by the Ethics and Scientific Committee of College of Medicine, University of Sulaimani. Moreover, the infants' parents were contacted to obtain their verbal consent for participation in the study.

Results

The results of the present study revealed that of the 20 infants with BA, 14 were female (70%) and 6 were male (30%). They also showed that the infants' age during liver biopsy was less than 1 month (1 infant), 1-2 months (6 infants), and more than 2 months (13 infants). Moreover, it was seen that 14 infants weighed more than 3.5 kg and 6 less than 3.5 kg (See Table 1).

Regarding the patients' clinical characteristics, the results indicated that 3 infants had clinical presentation before 6 weeks of age (15%) and 17 after 6 weeks of life (85%). It was also observed that the stool color was pale in 18 infants (90%) and normal in 2 patients (10%). Moreover, the urine color was dark in 11 infants (55%) and normal in 9 patients (9%) (See Table 2).

Table 1: The infants' demographic characteristics

Variable		N.	%
Sex	Male	6	30.0
	Female	14	70.0
	Total	20	100.0
Age on liver biopsy	< 1 month	1	5.0
	1-2 months	6	30.0
	> 2 months	13	65.0
	Total	20	100.0
Weight	> 3.5 kg	14	70.0
	< 3.5 kg	6	30.0
	Total	20	100.0

Table 2: The infants' clinical features

Variable		N.	%
Clinical presentation	< 6 weeks	3	15.0
	> 6 weeks	17	85.0
	Total	20	100.0
Stool color	Pale	18	90.0
	Normal	2	10.0
	Total	20	100.0
Urine color	Dark	11	55.0
	Normal	9	45.0
	Total	20	100.0

Table 3: The infants' laboratory findings

Variable		N.	%
Elevation degree of liver enzymes	> 2 fold	16	80.0
	< 2 fold	4	20.0
	Total	20	100.0
Ultrasound findings	Triangular cord	7	35.0
	Gallbladder < 1.5cm	13	65.0
	Total	20	100.0
Lee Score liver biopsy finding	> 7	14	70.0
	Unknown	6	30.0
	Total	20	100.0

With regard to the laboratory findings of the patients, the results demonstrated that liver enzymes increased 2 fold in 16 infants (80%) and less than 2 fold in 4 cases (20%). The ultrasound findings revealed that 7 infants had triangular cords (35%) and 13 had gallbladder of shorter than 1.5 cm (65%). In addition, liver biopsy findings showed that Lee Index score was more than 7 in 14 infants (70%) and unknown in 6 patients (30%) (See Table 3).

According to the results, of the 8 infants who had received Kasai portoenterostomy, 7 had cholangitis as a postoperative complication. On the other hand, none of the infants who did not receive Kasai portoenterostomy developed postoperative cholangitis. In this regard, the two groups were significantly different (p=0.000). The two groups were not significantly different in terms of developing liver cirrhosis; 6 infants in the Kasai group and 11 in the no-treatment group had it (p=0.306). Also, the two groups were not significantly different in terms of portal hypertension; 4 patients in the Kasai group and 9 in the no-treatment group had it (p=0.251). The results also indicated that the two groups were not different in the two groups regarding failure to thrive; 5 patients in each group failed to thrive (p=0.361). Moreover, 7 infants in the Kasai group and 12 in the no-treatment group died, but this difference was not significant (p=0.209) (See Table 4).

The results also indicated that in the group with Kasai treatment, 4 infants survived 4-6 months and 6 more than 6 months, and in the group without Kasai treatment, 11 patients survived 4-6 months and 1 more than 6 months. The two groups were significantly different in this regard

Table 4: BA outcomes and complications in the two groups

Variable		Procedure		Total	P-value
		With Kasai	Without Kasai		
Cholangitis	Yes	7	0	7	0.000
	No	1	12	13	
	Total	8	12	20	
Liver cirrhosis	Yes	6	11	17	0.306
	No	2	1	3	
	Total	8	12	20	
Portal hypertension	Yes	4	9	13	0.251
	No	4	3	7	
	Total	8	12	20	
Failure to thrive	Yes	5	5	10	0.361
	No	3	7	10	
	Total	8	12	20	
Death	Yes	7	12	19	0.209
	No	1	0	1	
	Total	8	12	20	

Table 5: Survival duration in the two groups

Variable		Survival duration		Total	P-value
		4-6 months	> 6 months		
Kasai procedure	Yes	4	4	8	0.035
	No	11	1	12	
	Total	15	5	20	

Table 6: Association between survival duration and late/early diagnosis

Variable		Survival duration		Total	P-value
		4-6 months	> 6 months		
Age at diagnosis	1-2 months	0	3	3	0.028
	> 2 months	4	1	5	
	Total	4	4	8	

Table 7: Association between survival duration and weight during Kasai treatment

Variable		Survival duration		Total	P-value
		4-6 months	> 6 months		
Weight during Kasai procedure	> 3.5 kg	3	0	3	0.408
	< 3.5 kg	4	1	5	
	Total	7	1	8	

($p<0.05$), and the infants who received Kasai treatment survived longer (See Table 5).

According to the results regarding the association between early/late diagnosis of BA and the patients' survival duration, all of the patients who were diagnosed during 1-2 months of age survived beyond 6 months, while only 1 of the 4 infants who were diagnosed after 2 months of age survived more than 6 months. This difference was significant ($p<0.05$) (See Table 6).

Furthermore, regarding the association between the infants' weight during Kasai treatment and their mortality, the results revealed that none of the 3 patients who weighed over 3.5 kg died, while 1 of the 4 weighing less than 3.5 kg died; however, this difference was not significant ($p>0.05$) (See Table 7).

Discussion

As revealed by the results of the present study, of the 20 infants, 14 were female (70%) and 6 were male (30%). Similarly, other studies have also reported that the number of females with biliary atresia was more than males [16, 17]. It was observed that evaluation and follow-up were initiated after 6 weeks of age for most of the infants. In their study, Shneider et al. (2006) reported that initial evaluation happened at the mean age of 54 days [16]. Narsimhan (2001) also stated that 60% of patients with BA referred for surgery after 90 days of age [18].

Stool color was an important tool for clinical identification and presentation of BA. This tool revealed BA in 18 patients (90%). Stool color was also introduced by other studies carried out in Taiwan [19] and Japan [20] as a significant clinical sign of BA. The results also showed that 16 infants (80%) experienced increase in their liver enzymes by 2 fold. This finding is in agreement with those of the study carried out in Taiwan by Tang et al. (2007) who stated that elevation of liver enzymes can be utilized to differentiate between biliary atresia and neonatal hepatitis [21].

In the present study, 7 infants (35%) had ultrasound triangular cord sign and 13 (65%) had gallbladder length of less than 1.5 cm. This finding is different from that of the study conducted by Kanegawa et al. (2003) who reported that 27 out of 29 patients (93%) had triangular cord and only 5 patients (17.24%) had small gallbladder shorter than 1.5 cm [22]. This difference may be because of difference in technical facilities and the experience of the practitioners in the center in Japan compared to the different centers in the present study.

In the present study, liver biopsy especially was used for the final decisive diagnosis of BA, and it was used with Lee scoring index to diagnose BA in 14 patients and without Lee scoring index in 6 patients, which proves the accuracy of this diagnostic method. This finding is in line with that of the study conducted by Lee (2009) who reported that the overall diagnostic accuracy of liver biopsy was 92% with Lee scoring system and 88% without the Lee scoring index [23].

The results of the present study indicated that there was a significant relationship between early diagnosis and referral for surgery (1-2 months) and the patients' survival beyond 6 months after Kasai portoenterostomy. Similar results were reported by Narsimhan (2001) [18]. In addition, the results of the present study revealed that there was not a significant association between weight of more than 3.5 kg and prolonged survival after Kasai treatment. This finding was not in agreement with the one reported by Al-Kawaz (2014) who reported that 21 out of 25 patients weighing over 3.5 kg survived longterm and only 4 died [24].

Cholangitis, as the most common complication following Kasai procedure, was observed in 7 out of 8 patients. This finding is similar to the one reported by Lee et al. (2014) who reported that 64% of the patients in their study developed cholangitis after Kasai treatment [25]. But, it is not very similar to the results reported by Ramachandran et al. (2016) who reported a prevalence rate of 35.5% for development of cholangitis after Kasai procedure [26].

The results of the present study revealed that regardless of receiving Kasai treatment or not, most of the patients experienced liver cirrhosis and portal hypertension, but this correlation was not significant. Similarly, in their study, Lee et al. (2009) reported that 47 out of 57 patients with BA developed liver cirrhosis and only 7 had portal hypertension [27].

According to the present study, 19 out of 20 patients with BA died, and there was no significant relationship between mortality and reception or non-reception of Kasai procedure; however, those who underwent Kasai treatment had a longer survival period. In their study carried out in Malaysia, Lee et al. (2009) reported that 34 out of 57 patients died; 9 without any treatment, 23 after Kasai procedure, and 2 after liver transplantation [27]. Unlike the present study, Al-Kawaz (2014) reported that only 10 out of 34 patients (29.4%) who had received Kasai treatment died [24]. This difference can be attributed to various factors including experience of the surgical centers, late diagnosis, postoperative complications, and follow-up measures.

Conclusion

According to the results of the present study, liver biopsy was used to diagnose biliary atresia after the age of 2 months in most of the patients. It was seen that infants who were treated through Kasai procedure had a longer survival duration. Moreover, patients who were diagnosed earlier survived for a longer time. Also, cholangitis was the most common complication of BA regardless of receiving Kasai treatment or not. Therefore, pediatric practitioners are recommended to perform BA evaluations for infants if their neonatal jaundice lasts more than 2 weeks. Moreover, measures should be taken for early diagnosis once the slightest symptoms of BA were observed. In addition, pediatricians are recommended to provide infants with BA with appropriate postoperative care. Finally, pediatric centers should be equipped with advanced facilities, and pediatricians are recommended to develop their experience regarding biliary atresia.

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