INTRODUCTION
Extrahepatic biliary atresia (BA) is the leading hepatobiliary disease worldwide, and it progresses with cholestasis at childhood and requires palliative or radical surgery (liver transplantation) (1). BA is primarily an obliterative cholangiopathy caused by progressive inflammation and fibrosis of the bile duct that is only observed in children.

Materials and Methods:
Medical records of 99 patients who were diagnosed with BA and monitored at our center from 1990 to 2002 (27 patients) and from 2003 to 2015 (72 patients) were analyzed retrospectively. Patients were evaluated for birth weight; age at jaundice onset; age at alcoholic stool detection; age at the time of Kasai portoenterostomy (KPE), if performed; age at admission to our center; age at liver transplantation; duration between KPE and transplantation; pediatric end-stage liver disease (PELD) scores during transplantation; and growth and developmental status. The periods 1990-2002 and 2003-2015 were defined as phases I and II, respectively.

Results:
The median age of the patients at presentation to our hospital was 149 (range: 20-730) days during phase I and 61 (range: 28-720) days during phase II. The median age at jaundice onset was 7 days, and the median age at alcoholic stool detection was 15 days. There was no significant difference between phases I and II in terms of age at jaundice onset, age at alcoholic stool detection, or birth weight. Twenty-five (92.5%) of the 27 patients in the phase I group were admitted to our center after undergoing KPE. Forty-four (61.1%) of the 72 patients in the phase II group (median age at the time of KPE: 47 days) were operated at our center. Median ages of the patients at the time of KPE at our center were 67.5 (range: 25-220) and 47 (range: 28-139) days during phases I and II, respectively. The median age of the 28 patients who were transferred from another center was 70 (range: 45-105) days during phase II. Liver transplantation was performed in 55 of 99 patients (55.5%). Significant differences were observed in the age at transplantation, duration between KPE and transplantation, and PELD scores between patients with BA who underwent KPE at our center and who underwent KPE at other institutes from other institutes.

Conclusion:
These findings demonstrate the importance of a timely diagnosis of BA and undergoing KPE before malnutrition and/or cirrhosis deteriorate the patient’s health. Furthermore, follow-up of patients with BA at a liver transplantation center increased the success of KPE and improved survival rates.

Keywords:
Biliary atresia, follow-up, liver transplantation
cancer can be caused in a short period of 2 months and the prognosis becomes even more serious. BA is lethal without treatment, and the average life expectancy is 8-9 months. Therefore, it is the leading cause of neonatal cholestasis and the primary cause of infant liver transplantation worldwide (2-4).

Childhood hepatobiliary disease that is accompanied by cholestasis and leads to liver transplantation accounts for 40%-60% of the liver transplantation programs (LTPs) for children (5-7). BA accounts for approximately 30% and 70% of liver transplants in Western countries and Japan, respectively, and for 24% of pediatric liver transplants performed at our transplantation center (3-5,8).

Approximately 10% of the patients with BA also suffer from anomalies in other organs such as the heart, esophagus, intestine, spleen, venous veins, and central nervous systems (8-10). BA treatment typically consists of two steps. The first step is a Kasai portoenterostomy (KPE), which facilitates neonatal bile flow and gives the infant valuable time to develop, thus buying time prior to a full liver transplantation, which is often the second step. Transplantation is performed if the success of KPE is inadequate or if complications such as secondary biliary cirrhosis arise (11,12). KPE performed during the early stage helps in reducing complications during a liver transplantation (13-15). Following liver transplantation, the 2-year survival rate is approximately 80%. In this study, we aimed to compare data between patients with BA who were transferred from other centers and those who were diagnosed, treated, and monitored at our center.

MATERIALS AND METHODS
This retrospective study included 99 patients diagnosed with BA who were monitored at our center. Twenty-seven patients (13 male) were monitored between 1990 and 2002 and 72 (38 male) were monitored from 2003 to 2015. The former period was defined as phase I and the latter as phase II.

Patients with BA during both phases were evaluated for birth weight; age of jaundice onset; age at first alcoholic stool detection; age at the time of KPE, if performed; and age at presentation to our center. The patients who underwent KPE at our center during phase II were compared with those who were transferred from other centers with respect to the age at liver transplantation, duration between KPE and transplantation, pediatric end-stage liver disease (PELD) scores during transplantation, and growth and development status. LTP, which was established in March 1997, evaluated patients diagnosed with BA until December 2015. Our study was made in accordance with the declaration of Helsinki. Informed consent could not be obtained due to retrospective design of the study.

Statistical Analysis
Descriptive statistics were used to describe continuous variables (mean, standard deviation, minimum, maximum, and median values). Comparison of two variables was performed by the Student’s t test. Comparison of two independent and abnormally distributed continuous variables was performed by the Mann-Whitney U test.

The \( \chi^2 \) test was used for categorical variables and expressed as observation counts (and percentages). The Kaplan-Meier method was used to calculate survival rates for the overall population. Statistical significance was accepted when \( p=0.05 \).

Statistical analyses were performed using the MedCalc Software version 12.7.7 (MedCalc Software bvba, Ostend, Belgium).

RESULTS
The median time of onset of jaundice was 7 (min-max: 1-30) days, and the median time of detection of alcoholic stool, according to the information provided by the patients’ families, was 15 (min-max: 1-75) days.

The median birth weight of the patients in this series was 3190 g (range: 1500-4300 g). There was no significant difference between phases I and II in terms of the age at jaundice onset, age at the first alcoholic stool detected, or birth weight. The median age of the patients at presentation to our hospital during phases I and II was 149 (range: 20-730) and 61 (range: 28-720) days, respectively. With respect to the weight of the patients at presentation, 14 patients were <3rd weight percentile, 7 patients were in the 3rd-10th weight percentiles, and 6 patients were in the 10th-25th weight percentiles during phase I, whereas 29 (40.2%) of the 72 patients were below the 3rd weight percentile, 22 (30.5%) patients were in the 3rd-10th weight percentile, 12 (16.7%) patients were in the 10th-25th weight percentile, and 9 (12.6%) patients were above the 25th weight percentile during phase II.

During phase I, the median age at the time of KPE was 67.5 (range 25-120) days among 27 patients who underwent KPE at our center and 71.5 (range 30-138) days among patients who underwent KPE at another center. On the other hand, during phase II, the median age at the time of KPE operation was 47 days (range 28-139) among patients who underwent KPE at our center and 70 days (range 45-105) among 28 patients who underwent KPE at another center.

Liver transplantation was performed in 50 of 99 (8 patients from phase I and 42 from phase II) patients with BA during the pediatric LTP. There were significant differences in the age at transplantation, time between KPE and transplantation, and PELD scores between patients with BA who underwent KPE at our center and those patients from other institutes (p<0.05). The survival times of patients with BA who did not receive a transplant are shown in Table 1, 2.

In phase I, none of the patients diagnosed and treated at our hospital underwent liver transplantation, whereas 28 patients...
in phase II underwent liver transplantation. Liver transplantation was performed in 8 and 14 patients coming from another center in phases I and II, respectively. Data from the patients at our center and those from other institutes who underwent transplantation are shown in Table 1, 2. Data of the pediatric LTP and survival rates of patients with BA are shown in Table 3. Table 4 shows the survival rates after liver transplantation because of BA during phases I and II. Statistical analysis could not be performed because of the low number of patients, but there was a statistically significant difference in survival rates between phases I and II. The comparison of survival rates in patients who underwent liver transplantation between phases I and II is shown in Table 4.

Table 1. The status of patients from our center and other institutes during the transplantation phase

<table>
<thead>
<tr>
<th>Institutes</th>
<th>Our center (n=28)</th>
<th>Other institutes (n=22)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transplantation time (months)</td>
<td>34±25.9</td>
<td>16.5±12</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Duration between referral to the hospital and transplantation (months)</td>
<td>23.1±27</td>
<td>6.5±9.1</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>PELD score during transplantation</td>
<td>21 (15-36)</td>
<td>29 (21-45)</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Growth rate during transplantation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Below 3rd percentile</td>
<td>4</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Between 3rd and 10th percentiles</td>
<td>7</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Between 10th and 25th percentiles</td>
<td>8</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Over 25th percentile</td>
<td>9</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Survival without transplantation in patients with biliary atresia

<table>
<thead>
<tr>
<th>Years</th>
<th>% Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st year</td>
<td>53.3</td>
</tr>
<tr>
<td>2nd year</td>
<td>40</td>
</tr>
<tr>
<td>3rd year</td>
<td>40</td>
</tr>
<tr>
<td>5th year</td>
<td>26</td>
</tr>
</tbody>
</table>

Table 3. Pediatric LTP and survival rate in patients with BA

<table>
<thead>
<tr>
<th>Years</th>
<th>% Survival (n=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st year</td>
<td>76.5</td>
</tr>
<tr>
<td>2nd year</td>
<td>72</td>
</tr>
<tr>
<td>5th year</td>
<td>68.5</td>
</tr>
<tr>
<td>10th year</td>
<td>66.6</td>
</tr>
</tbody>
</table>

Table 4. Comparison of survival in patients who underwent liver transplantation during phases I and II

<table>
<thead>
<tr>
<th>Survival</th>
<th>Before year 2002 (n=8)</th>
<th>After year 2002 (n=42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st year</td>
<td>62.2</td>
<td>86.3</td>
</tr>
<tr>
<td>2nd year</td>
<td>50</td>
<td>81</td>
</tr>
<tr>
<td>5th year</td>
<td>37.5</td>
<td>81</td>
</tr>
<tr>
<td>10th year</td>
<td>37.5</td>
<td>78.5</td>
</tr>
</tbody>
</table>

DISCUSSION

Kasai portoenterostomy, ideally before 3 months of age, is the first recommended treatment for managing BA. KPE may preclude the need for LT in approximately 15% children (16,17). In children who do require LT after KPE, KPE allows the child to develop further before performing LT (18,19). The present study aimed to evaluate the management of patients with BA before and after 2002 in our pediatric LTP, one of the top pediatric liver transplantation centers in our country, and to compare our results with those in the literature. Comparing the two study phases in terms of age at the time of KPE showed that the optimal time to perform KPE was not different for patients who were transferred from other centers, whereas the duration between admission and the time of KPE was significantly shorter in our center. This clearly indicates that BA is not being diagnosed early enough in our country; practitioners and pediatricians must be vigilant and knowledgeable about the symptoms of BA to en-
sure early diagnosis. Since the first study on KPE was published in 1959, the 2-year survival rate of patients with BA has increased from 10% to 53%, whereas the 5-year survival rate is currently 60% and the 10-year survival rate is 50% (3). A study conducted by Altman et al. (17) in 1997 determined a 5- and 10-year survival rates of 45% and 35%, respectively. The Japan Biliary Atresia Group reported the most favorable rates thus far as a 5-year survival rate of 59.7% and a 10-year survival rate of 52.8% (9).

According to the literature, nearly half of the patients with BA survive the 1st year, but by the 5th year only one fourth survive without a liver transplantation. Transplantation is essential for long-term survival and these patients should be followed up at transplantation centers (20,21).

According to data collected at our transplantation center, pa-
tients with BA who received a transplant gained a 76.5% sur-
vival advantage in the 1st year and 68.5% in the 5th year. These data show that the survival rate for patients with BA is higher following prompt diagnosis and a good preparation program.

**Survival Rate after 2002**

According to a study performed in Japan, the 5- and 10-year sur-
vival rates of the patients with BA after liver transplantation were 75.8% and 66.7%, respectively (9). In a study of 440 patients be-
tween 1986 and 1996 in France, 226 of whom underwent a liver transplantation after KPE, 5- and 10-year survival rates were 70% and 68%, respectively (8,22). As shown in Table 5, the survival rate of patients diagnosed with BA at our center after 2002 was simi-
lar to that reported in the literature (5,8,14). Clinicians can help in
increasing survival rates by being aware of the symptoms of BA to facilitate early diagnosis. Additionally, they should be knowl-
edgeable about the improvements in prognosis following both
types of surgery. Good management of latent and overt infec-
tion and complete preoperative preparation are also essential;
internists and pediatricians should collaborate closely to man-
age these patients as effectively as possible.

As shown in Table 1, the patients who were transferred from
other clinics were younger with higher body weights and
tended to undergo liver transplantation at an earlier age (aver-
age of 6.5 months) than other patients (average of 23 months).
Malnutrition often necessitates earlier liver transplantation. In
addition to the medical management of cholangitis, portal
hypertension, and metabolic acidosis, many patients require
parenteral nutrition with a special diet and fat-soluble vitamin
supplements. These measures help reduce the incidence of in-
fec tion after transplantation (22). Growth rates of patients who
received no financial support.

Biliary atresia in infants is asymptomatic for the first 15 days of
life because acholic stools and icterus often go unnoticed by
parents and physicians; this condition is not recognized until
malnutrition slows the growth rate of the patient.

When practitioners and pediatricians detect hyperbilirubine-
emia, which does not develop until after 15 days of age, they
should check not only the total bilirubin level but also the direct
and indirect bilirubin levels. If these are concerning, the patient
should be transferred immediately to a pediatric gastroenterol-
ogy department or preferably to a liver transplantation center,
and the color of the stool should be monitored. Our data dem-
onstrate the importance of prompt diagnosis and timely KPE
for patients with BA. Ideally, for the best prognosis, KPE should
be performed before malnutrition and complications, such as
cirrhosis, develop. If necessary, liver transplantation should
then be performed following excellent preoperative prepara-
tion and management to further facilitate healthy growth and
development, thereby improving the prognosis considerably.

**Ethics Committee Approval:** Authors declared that the research was
conducted according to the principles of the World Medical Associa-
tion Declaration of Helsinki “Ethical Principles for Medical Research In-

**Informed Consent:** Informed consent is not necessary due to the re-

trospective nature of this study.

**Peer-review:** Externally peer-reviewed.

**Author contributions:** Concept - S.A., O.E.; Design - M.K., S.A.; Supervi-

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study has re-

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