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The causes of severe jaundice and its complications in newborns admitted to Mofid Children's Hospital, Iran

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ABSTRACT

Background and Objective: Jaundice is one of the most common causes of hospitalization in newborns. The aim of the present study was to determine the causes of severe jaundice and its complications in neonates admitted to Mofid Children's Hospital of Tehran.

Methods: Sixty- five neonates with severe indirect hyperbilirubinemia, admitted to the Neonatal ward of the Mofid Children's Hospital during the years 2018-2019 were investigated. Laboratory data, family socioeconomic status, parental awareness of jaundice and its consequences, neonatal delivery information and their prenatal conditions were collected during hospitalization. The neonates were followed up after discharge from the hospital for complications of jaundice by telephone calls and clinic referrals.

Findings: In the 22 cases (33.8%) of the neonates, the ABO setup, and in the 4 cases (6.2%), the Rh setup between the mother and neonate were observed. A total of 25 neonates (38.5%) had an average of 1.2 times of blood transfusion. Twenty-four neonates (36.9%) had bilirubin level of ≥25 mg/dl. There was a significant relationship between total bilirubin level and delivery type ($P < 0.05$) and between total bilirubin level and type of prenatal care ($P = 0.031$). No complications of jaundice were reported during patient follow-up.

Conclusion: Male gender, vaginal delivery, family delay in diagnosis and treatment of jaundice, positive history of jaundice in a previous baby, and prenatal care by someone other than a gynecologist are associated with more severe hyperbilirubinemia.

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Introduction

Jaundice is one of the most common neonatal diseases. Approximately 60% of term and 80% of preterm babies develop jaundice in the first week of life [1]. Severe jaundice in the neonatal period can be associated with long-term consequences, such as kernicterus (chronic bilirubin-induced encephalopathy) [2-4], which can lead to hypotonia, seizures, motor skills delays, motor disorders, and sensorineural hearing loss (SNHL) in the patient [5]. Hearing loss or hearing impairment, caused by hyperbilirubinemia is still not well known [6-8]. The hearing system is very sensitive to the toxic effects of bilirubin [7], and its high level can damage integrative structures such as the auditory cortex of the brain, spiral ganglion neuron, and auditory nerve fibers [9].

Known risk factors for severe hyperbilirubinemia in newborns include jaundice in the first 24 hours of life, jaundice before discharge, history of jaundice treated with phototherapy in previous pregnancies, gestational age 35 to 36 weeks, Asian race and bruising or Cephalhematoma in the newborn [10-12]. The causes identified in the laboratory include Rh and ABO incompatibility between mother and newborn, and also Glucose-6-phosphate dehydrogenase (G6PD) deficiency [13, 14].

However, timely diagnosis and appropriate treatments have a significant role in reducing the above complications. The progression of postnatal bilirubin is gradual. There are some risk factors such as ABO incompatibility of the mother and the neonate, early discharge from hospital, unawareness of parents about the occurrence of jaundice, the need for an urgent visit in case of suspected jaundice, lack of control of bilirubin before discharge from the hospital, which makes jaundice extremely severe to the extent that the need for blood transfusion in the neonates is necessary. In most cases, the patients have no proper follow-up after treatment of jaundice and discharge from the hospital for its consequences.

Therefore, the present study aimed to determine the causes of severe jaundice and its complications in newborns admitted to the Mofid Children's Hospital by examining the causes proposed to take appropriate measures to diagnose and treat jaundice faster and to prevent severe Complications of jaundice. The neonates were also continuously monitored for bilirubin-induced encephalopathy complications.

Methods

Sampling was by the census method. Initially, total serum bilirubin (TSB) test was performed on all infants with jaundice, referred to the hospital emergency department. Of 326 infants with high bilirubin levels, After removing premature and very sick babies (neonates with sepsis, congenital anomalies, fever, receiving phenobarbital), 65 neonates with severe indirect hyperbilirubinemia (above 95th percentile in the Bhutani curve) were admitted to the Neonatal Ward of the Mofid Hospital (from October 2018 to September 2019) were enrolled in this study.

In addition to laboratory tests, including total serum bilirubin level, complete blood count, Coombs test, peripheral G6PD blood smear, maternal and neonatal Rh, family socioeconomic status, parental awareness of jaundice and its consequences, the information about the neonate's birth and prenatal conditions was collected through a questionnaire during the hospitalization of the newborns. The mentioned neonates were followed up for jaundice related complications (hearing loss and other neurological complications) through telephone calls and clinic visits for one year after discharge from the hospital.

All data were to recorded and entered in SPSS 21, and analyzed using descriptive and inferential statistics. Data were presented using descriptive statistics including mean, standard deviation, number, and percentage. The Shapiro-Wilks test was used to assess the normal distribution of the quantitative data. Since the distribution of all variables was normal, the independent T-test was used to compare the quantitative demographic and clinical characteristics between the two groups. Comparison of qualitative variables was performed using the Chi-Square/Fisher's exact test. Associations between quantitative variables were explored using ordinary linear regression analysis.

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Results

In the current study, 65 neonates with severe indirect hyperbilirubinemia (above 95th percentile in the Bhutani curve) were admitted to the Neonatal Ward of the Mofid Hospital (from October 2018 to September 2019) were enrolled. Based on demographic data, 25 neonates (38.5%) were female and 40 neonates (61.5%) were male. Information on gestational age of mothers, gravidity, parity and age of newborns at hospital discharge, age of newborns with severe jaundice during hospitalization and birth weight of neonates are shown in table 1. Based on the collected data, the mean age of mothers was 28.5 years with a range of 17- 41 years and the mean age of fathers was 33.1 years, with a range of 19-48 years.

Examination of bilirubin and hemoglobin levels in the neonates revealed that the mean total bilirubin level of the newborns was 24.2 mg/dl with a range of 16.22 to 33.9 mg/dl and the mean of neonates' hemoglobin level was 15.2 mg/dl, with a range of 6.6 to 19.7 mg/dl. G6PD deficiency was found in 8 neonates (12.3%), and direct agglutination test was reported 1 neonate (1.5%).

The distribution of blood groups among neonates were A in 18 (27.7%), B in 18 (27.7%), AB in 5 (7.7%), and O in 24 (36.9%). Six neonates (9.2%) were Rh-negative. But, the distribution of blood groups among their mothers were A in 16 (24.6%), B in 12 (18.5%), AB in 1 (1.5%), and O in 36 (55.4%). Also, 6 (9.2%) neonates were Rh-negative. The investigations showed that in 22 cases (33.8%) there was ABO setup between mother and neonate.

All neonates in this study were treated with intensive phototherapy (TOSAN, 8 lamps) and 25 neonates (38.5%) had an average of 1.2 times of blood transfusion.

Studies on the mode and place of delivery indicated that 21 (32.3%) neonates were delivered by vaginal delivery and 44 (67.7%) neonates by cesarean section. One neonate (1.5%) was born at home, 29 neonates (44.6%) in university-affiliated hospitals, 2 neonates (3.1%) in government hospitals and 33 neonates (50.8%) in private hospitals. For evaluation of screening of jaundice in maternity before discharge, 29 (44.6%) neonates were screened, 36 (55.4%) had no screening, and 28 (43.1%) had recommended screening after discharge. fourteen neonates (21.5%), had a history of jaundice. Two cases (3.1%) of them had a history of blood transfusion, but none of them had a history of jaundice complications.

The total serum bilirubin level and all risk factors for jaundice are represented in table 2.

According to the data presented in Table 2, there was a significant relationship between total serum bilirubin level and type of delivery ($P < 0.05$). According to data, there was also a significant relationship between total serum bilirubin level and prenatal care ($P = 0.031$). Of the 65 patients under study, 36 neonates (55.4%) had an auditory test that for 30 cases Auditory Brainstem Response (ABR) method and 6 cases Otoacoustic Emission (OAE) method were administered. Data from patients' follow-up indicated that no cases including hearing loss, kernicterus, and other neurological complications in newborns with severe jaundice were reported.

Table1. Distribution of gestational age, neonates' age at discharge from hospital, and during hospitalization due to severe jaundice and birth weight of neonates

Variables	Mean	SD	Minimum	Maximum
Gestational age (Week)	38.3	1.1	37	41
Gravidity	1.7	0.9	1	4
Parity	1.5	0.7	1	4
Age of neonate when discharge from maternity (Day)	1.9	1.5	1	9
Age of neonates at hospitalization	5.9	2.3	1	12
Birth weight (g)	3280.6	439.1	2400	4560

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Table 2. Total serum bilirubin levels based on the risk factor of jaundice

Variables		TSB≥25 mg/dl	TSB<25 mg/dl	P-value
Gestational age (week)		38.3±1.4	38.2±1.0	0.797
Birth weight (g)		3215.2±490.7	3318.8±407.5	0.364
Age of neonates during hospitalization (day)		5.5±1.9	6.1±2.6	0.366
The age of the neonate at the onset of jaundice (day)		3.9±1.9	3.7±3.1	0.743
Neonate gender	Girl	13 (54.2%)	12 (29.3%)	0.065
	Boy	11 (45.8%)	29 (70.7%)	
Type of delivery	Natural (vaginal)	12 (50%)	9 (22%)	0.028
	Caesarean section	12 (50%)	32 (78%)	
ABO setup	No	30 (73.2%)	13 (54.2%)	0.174
	Yes	11 (26.8%)	11 (45.8%)	
Rh setup	No	38 (92.7%)	23 (25.8%)	1.0
	Yes	3 (7.3%)	1 (4.2%)	
G_6PD Level	Sufficient	35 (85.4%)	22 (91.7%)	0.699
	Deficient	6 (14.6%)	2 (8.3%)	
History of jaundice in the previous neonate	No	33 (80.5%)	18 (75%)	0.756
	Yes	8(19.5%)	6 (25%)	
History of previous exchange transfusions in the previous neonate	No	7 (87.5%)	5 (83.3%)	1.0
	Yes	1 (12.5%)	1 (16.7%)	
Place of delivery	Home	1 (2.4%)	0 (0%)	0.125
	Private Hospital	25 (61%)	8 (33.3%)	
	University Hospital	14 (34.1%)	15 (62.5%)	
	Non- University Government Hospital	1 (2.4%)	1(4.2%)	
Screening of jaundice in maternity ward	Negative	22 (53.7%)	14 (58.3%)	0.799
	Positive	19 (46.3%)	10 (41.7%)	
Recommend to refer again to hospital	Negative	23 (56.1%)	14 (58.3%)	1.0
	Positive	18 (43.9%)	10 (41.7%)	
Prenatal care by…	Obstetrician	37 (90.2%)	15 (62.5%)	0.031
	Midwife	4 (9.8%)	6 (9.8%)	
	Medical professional	0 (0%)	2 (8.3%)	
	No care	0 (0%)	1 (4.2%)	

Discussion

Our study showed the type of delivery and source of prenatal care give (pregnancy care provide) have a significant relation with total serum bilirubin level; and are considered as risk factors for jaundice in neonates. A total of 41 neonates (63.1%) had a bilirubin level of less than 25 mg/del and 24 neonates (36.9%) with a bilirubin level of 25 mg/dl or more. The statistical significance of the total bilirubin level was related to the type of delivery (P<0.05). Etiology study of jaundice revealed that there is a significant relationship between total bilirubin level and the type of prenatal care (P=0.031).

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Jaundice is the most common neonatal problem that occurs in 60% of neonates, and 5 to 10% of these neonates with high levels of bilirubin require hospital admission and treatment [15].

In studies conducted to determine the etiology of neonatal jaundice includes early discharge from the hospital (mother and newborn), the first child of the family, male gender, inadequate breastfeeding and pathological weight loss have been reported as risk factors [16, 17]. However, jaundice enjoys ethnic, cultural and geographical distribution, and therefore each country should improve its follow-up systems [18-20].

The purpose of this study was to determine the risk factors for jaundice in neonates with severe hyperbilirubinemia. Newman et al., [21] reported in a study that the male gender is a risk factor for TSB levels of ≥ 25 mg /dl, although Chou et al. reported TSB≥20 mg /dl [22]. In the present study, as in the study of Bulbul et al., [23], bilirubin levels were higher in males than females, but the sex of neonates with TSB≥25 mg/dl had no significant relationship.

According to studies, the history of previous neonates with jaundice and receiving phototherapy has been accepted as a risk factor for severe hyperbilirubinemia [11, 21, 23]. The findings of the current study are consistent with this issue. As a result of having a history of jaundice in the previous neonate (P<0.001) and blood transfusion (P = 0.044), were identified as risk factors for the development of severe hyperbilirubinemia.

Appropriate postpartum follow-up of mothers with Rh incompatibility with RhoGam injection reduces the need for blood transfusion. ABO incompatibility has been reported to be the most common cause for severe hyperbilirubinemia that leads to neonate's blood transfusion [11, 23]. There were 22 cases (33.8%) of ABO setup and 4 cases (2.6%) of Rh setup between mother and neonate. In the study of Bulbul et al., 8 neonates (0.6%) had G6PD deficiency. In that study, 293 cases (21.9%) had ABO setup, and 70 cases (5.2%) had an Rh setup [23]. Compared to the present study, the study of Gamaleldin et al. had 23.7% of ABO incompatibility, 8.8% had Rh incompatibility and 2.8% had G6PD deficiency [24].

Another interesting finding in this study is the level of awareness in the studied population about jaundice so that 46% of the subjects did not have any information about jaundice and its complications. 71% of the families found jaundice on the third or fourth day of the newborn's life but kept the baby at home for two days. 36% of these neonates remained without treatment, 34% were treated with home treatment (purgative manna and manna), and 17% were treated with the bilineaster drop. Eventually, the neonates were taken to the hospital on the fifth day of their life. According to the findings of Sgro et al., 66% of newborns had also severe hyperbilirubinemia at the time of their first five-day admission.

The results of this study are also in line with the results of Khalesi and Rakhshani [28], Rabiyeepoor et al., [29] and Kashaki et al. [30]. According to the findings of these studies, mothers' knowledge of jaundice detection methods was acceptable, but they did not have enough knowledge about the causes, complications, and methods of prevention. In the study of Davutoğlu et al., the mean age of neonates was 2.2±4.9 days after admission [31]. These findings suggest that neonates with severe hyperbilirubinemia are transferred to the hospital later. Therefore, families must be aware of the symptoms of jaundice and its complications before discharge and recognize the importance of early admission and hospitalization.

In this study 29 (44.6%) neonates had been screening for jaundice before discharge. more than half of the neonates who were born in university hospitals had no screening. Only 28 neonates (43.1%) were recommended to be re-referred after discharge. Meanwhile, in the study of Najib et al., 90.3% of mothers were advised to visit a physician in case of severe jaundice [32].

There have been no cases of jaundice complications, including hearing loss, kernicterus, encephalopathy, seizure and other neurological complications in newborns with severe jaundice in follow-up.

The study results may be affected by the elimination of premature and very sick neonates from the study. These patients were removed from samples due to the homogenization of selected samples in line with the study of the etiological factors. On the other hand, the patients under study did not have a proper follow-up for periodic and long-term examinations as well.

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Conclusion

From the results of this study, it can be concluded that the male gender has a higher risk of developing severe hyperbilirubinemia. Vaginal delivery, a longer interval between discovery in the family and initiation of treatment, a history of jaundice in a previous neonate, and prenatal care by someone other than a gynecologist are associated with more severe hyperbilirubinemia. On the other hand, inadequate awareness of parents about the importance of jaundice and its complications leads to delays in diagnosis and initiation of treatment.

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Ethical Approval

Ethical approval was obtained from the Ethics committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran (Code: IR.SBMU.MSP.REC.1397.12) and informed consent letters were obtained from parents.

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Conflict of interest

All of the authors declare that there are no commercial, personal, political, or other potential conflicting interests related to the submitted manuscript.

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