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Evaluation of Neonatal Jaundice in the First Day of Life

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ABSTRACT

Background: Jaundice in the first day of life is generally considered as pathologic. In this study we aimed to evaluate the etiologies of jaundice in the neonates who were admitted on the first day of life.

Materials and Methods: In this retrospective cross-sectional study, all the neonates with gestational age of more than 35 weeks with jaundice in the first day of life who were admitted in Vali-e-Asr Hospital, Tehran, Iran, during 2015-2018 were investigated. Data including gestational age, delivery type, birth weight, sex, neonatal age (hours), maternal disease, maternal age, parity, maternal and neonatal blood group, serum levels of bilirubin and haemoglobin, reticulocyte count, peripheral blood smear results, glucose-6-phosphate dehydrogenase (G6PD) activity and therapeutic interventions were evaluated.

Results: Of the 1512 neonates who were admitted for neonatal jaundice, 230 had first-day jaundice (15.6%). Of 230 neonates 46.1% were male, 73.9% were delivered by cesarean section, 40% of their mothers had an underlying disease. The mean birth weight and bilirubin level were 3040 ± 6.02 gr and 7.87± 2.73 mg/dl, respectively.

Most common etiologies were ABO incompatibility 41%, Rh incompatibility 14.3%, simultaneous ABO and Rh incompatibility 3.4%, caput succidanum and cephalohematoma 4.9%, G6PD deficiency 2.6%, sepsis 2.1% and others 2%.

All patients received phototherapy, 1.3% received intravenous immunoglobulin (IVIG), 1.7% underwent exchange transfusion and 2.6% received both IVIG and exchange transfusion.

Conclusions: In the present study, ABO incompatibility was the commonest etiology for the first day jaundice and the main reason for exchange transfusion in neonates. Blood type screening at the antenatal period and by cord blood sampling may result in early diagnosis and prompt treatment and can prevent the serious complications of jaundice in the neonates.

Key words: First day, Jaundice, Neonates, Treatment

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INTRODUCTION

Neonatal jaundice a yellowish discoloration of skin, sclera, and mucous membranes, is a common finding in neonates. It occurs in 60% of term and 80% of preterm infants. Jaundice is usually a physiologic event because infants naturally produce 6 to 10 mg/kg of bilirubin per day and their liver cannot clear this load of bilirubin rapidly from the blood. In most cases it disappears after a few days without treatment. In several neonate ' s pathologic jaundice may occur which requiring evaluation and intervention because bilirubin is potentially toxic to the central nervous system [1-3].

Jaundice in the first day of life is generally regarded as pathologic and is one the risk factors for developing severe hyperbilirubinemia. It needs timely diagnosis and appropriate treatment. If overlooked the bilirubin may pass through the blood-brain barrier and accumulate in basal ganglia and brain stem nuclei that may lead to acute or chronic neurologic dysfunction or even death. The common causes of jaundice in the first day of life are hemolysis, concealed hemorrhages, sepsis and intrauterine infections [3-5]. The treatment modalities for hyperbilirubinemia are phototherapy, exchange transfusion and pharmacologic therapies such as high dose IVIG for isoimmune hemolytic jaundice [5,6].

Considering the importance of the first day jaundice and few studies carried out on this topic, this study was conducted on newborns with jaundice in the first 24 hours of life who were admitted to Vali-e-Asr Hospital, Tehran, Iran.

MATERIALS AND METHODS

In this retrospective cross-sectional study neonates with gestational age of more than 35 weeks who were admitted for jaundice in the first day of life in Vali-e- Asr hospital (Tehran-Iran) from 2015 to 2018 were evaluated. The study was approved by the local ethics committee of Tehran University of Medical Sciences. The sampling method was non-random, and census based. Neonates with gestational age of less than 35 weeks, congenital anomalies, direct hyperbilirubinemia, incomplete medical records were excluded from the study. Data including gestational age, mode of delivery, birth weight, sex, neonatal age (hours), maternal diseases (preterm rupture of membrane, hypothyroidism, gestational diabetes mellitus, preeclampsia, hypertension and HELLP syndrome), maternal age, parity, maternal and neonatal blood group, levels of bilirubin and hemoglobin, reticulocyte count, peripheral blood smear , direct Coombs results, glucose-6-phosphate dehydrogenase (G6PD) activity, treatment modalities were extracted from the medical records and analyzed.

Statistical analysis

The results for quantitative variables were expressed as mean and standard deviation (mean ± SD) and qualitative categorical variables were expressed as percentages. A comparison of quantitative variables was performed by the t-test or Mann-Whitney test based on normal or abnormal distributions, respectively. The comparison between qualitative variables was performed using the Chi-square test or Fisher's exact test. In determining factors related to patient outcomes and in the presence of basic characteristics of patients as confounding factors, regression analysis was performed, and the results were expressed as odds ratios (95% confidence interval). Data were analysed using SPSS version 24 and SAS version 9.1. The significance level was considered at less than 0.05.

RESULTS

During the study period 1512 neonates were admitted for jaundice of whom 230 had first day jaundice with an incidence of 15.6%. Of the 230 neonates 46.1% were male, 73.9% were delivered by cesarean section. The mean birth weight, neonatal age and maternal age were 3040 ± 6.02 gr, 18.3 ± 5.49 hours, and 30.57 ± 6.10 years, respectively. About 40% of mothers had underlying diseases. Gestational diabetes mellitus in 11.3% and pre-eclapmsia in 10.7% were the two most common morbidities (Table 1).

Table 1: Characteristics of the neonates and their mothers.

Variable		Frequency	Percent
Demographic characteristics			
Sex	Male	106	46.1
	Female	124	53.9
Birthweight (gr)	<2499	38	16.5
	2500-4000	179	77.8
	>4000	13	5.6
Maternal age (yr)	<25	61	26.5
	≥ 25	166	72.1
Delivery type	NVD[a]	60	26.1
	C/S[b]	170	73.9
Gestational age (weeks)	35- (36+6[d])	64	27.8
	37- 40	169	69.1
	>40	7	3
Gravid	1	77	33.5
	2	51	22.2
	3	66	28.7
	≥ 4	36	15.7
Maternal disease	PROM[c]	10	4.3
	hypothyroidism	12	5.2
	GDM[d]	26	11.3
	preeclampsia	11	10.7

	HTN[e]	7	4.8
	GDM + hypothyroidism	12	5.2
	HELLP	4	1.7
	GDM+HTN	5	3
Lab data			
Peripheral blood smear	Normal	206	89.6
	Abnormal	24	10.4
G6PD	Sufficient	225	97.8
	Deficient	5	2.2
Direct coombs	Positive	6	2.6
	Negative	224	97.4
Reticulocyte count>5%	Yes	71	30.8
	No	159	69.2
Treatments			
Exchange		4	1.7
IVIG f		3	1.3
Exchange + IVIG		6	2.6

a: Normal vaginal delivery, b: Cesarean section, c: Preterm rupture of membrane, d: Gestational diabetes mellitus, e: Hypertension, f: Intravenous Immunoglobulin

The mean bilirubin, hemoglobin and reticulocyte count in neonates were 7.87 ± 2.73 mg/dl, 16.34 ± 3.01g/dl, and 4.81 ± 3.53 percent, respectively. Direct Coombs test was positive in 2.6% of cases, 2.1% in Rh and 0.5% in ABO incompatibilities. The most common blood group in the mothers and neonates were O (50.4%) and A (32.2%) respectively and the least common was AB in both.

In our study the most common etiology for the first day jaundice was blood group incompatibilities. ABO incompatibility was found in 94 (41%), Rh incompatibility in 33(14.3%) of cases. Simultaneous ABO and Rh incompatibility were seen in 3.4% of neonates followed by caput succidanum and cephalohematoma (4.9%), G6PD deficiency (2.6%), sepsis (2.1%), and other causes (2%).

Phototherapy with a mean duration of 51.2 ± 40.20 hours was established for all patients. Three neonates (1.3%) received intravenous immunoglobulin (IVIG), exchange transfusion

was performed for 4 patients (1.7%) and 6 neonates (2.6%) received both IVIG and exchange transfusion (Table 2).

Table 2: The frequency of exchange transfusion and IVIG administration in 13 patients with first day jaundice.

Patient	Etiology	Number of exchange transfusion	IVIG therapy
1	Unknown	3	+
2	Rh incompatibility	3	+
3	Sepsis	3	-
4	Unknown	3	-
5	ABO incompatibility	2	+
6	ABO Incompatibility	2	+
7	Unknown	2	+
8	ABO Incompatibility	2	-
9	ABO Incompatibility	1	+
10	ABO Incompatibility	1	-
11	ABO Incompatibility	-	+

12	ABO incompatibility	-	+
13	Unknown	-	+

DISCUSSION

Hyperbilirubinemia is a common problem in neonates. Jaundice occurring in the first 24 hours of life is abnormal and needs evaluation. The prevalence of jaundice on the first day of birth and its causes has not been widely studied. The prevalence of first day jaundice in our study was 15.6%. In a study conducted by Najib et al the prevalence of jaundice at the first 24 hour of life was 11.4% [7], another study from Nigeria reported a prevalence of 9.6% [8]. A prevalence of 8.8% was stated by Alkhotani et al from Saudi Arabia [9]. Other studies showed prevalences of 6.7% and 5.8% [10, 11]. These variations in the prevalence of neonatal jaundice could be related to ethnic and genetic differences in bilirubin metabolism [7-10].

Many researchers mentioned that maternal risk factors including maternal age (≥25 years), hypertensive disorders, diabetes, preterm delivery might play an important role in the development of neonatal jaundice. In the present study, the age of 73.1% of the mothers was more than 25 years. This result is in line with the study of Saber et al and Najib et al which reported the age of 65.9% and 52.6% of the mothers were more than 25 years old respectively [7,12]. But Scrafford demonstrated that the probability of newborn's admission due to jaundice was higher for mothers under 20 years of age than older mothers [13]. Another study from Greece reported 38.9% of mothers were in the age range of 21-25 [14].

Regarding perinatal complications, 11.6% and 10.7% of neonates with first day jaundice were born from mothers with gestational diabetes and preeclampsia, respectively. Several studies demonstrated that gestational diabetes mellitus with a range of 1-17% and pregnancy induced hypertension with a range of 4.7-19%, are predisposing risk factors for developing jaundice in neonates [15, 16].

The mean value of serum bilirubin, hemoglobin and reticulocyte counts in our study was like previous studies [15].

In the current study the most common etiologies for neonatal jaundice were as follows:

ABO incompatibility (40.9%), Rh incompatibility (14.3%), caput succedaneum and cephalohematoma (5%), both ABO and Rh incompatibility (3.4%), G6PD deficiency (2.6%), sepsis (2.5%). The etiology was unknown in about 30% of cases. Therefore, the most common causes of jaundice on the first day were incompatibilities in ABO and Rh, respectively. In agreement with our results, Mosayebi et al reported the most common causes of jaundice on the first 24 hour of life were ABO incompatibility (48.1%), sepsis (16.6%), ABO incompatibility and sepsis (13%), Rh incompatibility (7.4%), ABO and Rh incompatibility (3.7%), cephalic hematoma (1.9%) and G6PD deficiency (1.9%), respectively. In study, no specific cause was found for jaundice in 7.4% of infants [17]. In another study from Iran, the most common causes of hyperbilirubinemia in the first 24 hours of birth was mentioned as ABO incompatibility, early onset infections, G6PD deficiency, cephalic hematoma, asphyxia, and Rh incompatibility, respectively [11]. In the study conducted by Saadat et al, ABO incompatibility (36.6%), G6PD deficiency (30.8%), prematurity (26.2%), gestational diabetes mellitus (15.9%), Rh incompatibility (6.2%) and Apgar score less than 6 (3.7%) were the major risk factors for severe jaundice in the first day [15]. Similar studies indicated that incompatibilities in blood groups including ABO (13.1%) and Rh (44%) incompatibilities were the most common causes for first day hyperbilirubinemia [8]. The most common etiologies for jaundice in the first day were septicemia, prematurity, cephalohematoma and ABO incompatibility in Onyearugha's study [18]. Ethnicity and geographic factors may be responsible for these different etiologies.

Phototherapy is the first line of treatment for hyperbilirubinemia. It has been shown IVIG is effective in the treatment of isoimmune hemolytic jaundice and may reduce the need for invasive therapies such as exchange transfusion. When phototherapy has failed to reduce the rise of bilirubin or if there are signs of bilirubin encephalopathy exchange transfusion will be the gold standard for effective treatment [1,7].

Several studies revealed the use of IVIG for treatment of hemolytic diseases of newborn mainly blood group incompatibilities. In our study the major reason for administration of IVIG was ABO incompatibility, followed by unknown etiology which was in line with other studies.

Administration of IVIG is recommended by American Academy of Pediatrics if the serum bilirubin level is rising despite intensive phototherapy or the bilirubin level is within 2-3 mg/dL of the exchange level [1, 5)]. The use of IVIG with phototherapy in the treatment of hemolytic jaundice may shorten the duration of phototherapy and decrease the requirement for exchange transfusion.

According to our study ABO incompatibility, sepsis and unknown etiology were the major causes for exchange transfusion which was compatible to several studies. Sgro et al from Canada reported ABO incompatibility and jaundice with unknown origin as the major causes of exchange transfusion [19] which was compatible with our study. Moreover, a study conducted in Mashhad showed ABO incompatibility was the most common cause of exchange transfusion [20]. Most cases of exchange transfusion were in patients with ABO incompatibility in Mosayebi et al study [17]. In another

study the main causes for exchange transfusion were idiopathic, sepsis and hemolysis [21].

Timely recognition and appropriate treatment should be considered for pathologic neonatal hyperbilirubinemia especially for the first day jaundice to prevent the subsequent and serious complications of hyperbilirubinemia.

The most limitation of our study was the scarce available data in the literature regarding first day jaundice, affecting our ability to compare our results with other published studies. Therefore, further and multicenter studies concerning this important issue is warranted.

CONCLUSION

According to the results of this study, the most common causes of jaundice in the first day of life were ABO and Rh incompatibilities and the most common reason for exchange transfusion was ABO incompatibility as well. It is important to recognize the infants who are at risk of increased bilirubin production. So, blood typing at antenatal period and screening cord blood when maternal blood group is O and negative maternal Rh exists may result in timely diagnosis, prompt evaluation and accurate treatment for neonates who are at risk of pathologic hyperbilirubinemia.

CONFLICT OF INTEREST

None to declare.

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