

Maternal risk factors for neonatal jaundice: a hospital-based cross-sectional study in Tehran

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Abstract

Diagnosis and timely treatment of neonatal jaundice is critical to preventing its dangerous side effects. Knowing the predisposing factors of neonatal jaundice is still a serious debate, which can be effective in controlling jaundice and the primary problem. The aim of this study was to evaluate maternal risk factors that contribute to the Hyperbilirubinemia among newborns admitted to Imam Khomeini and Ziaeean hospitals during 2015. We collected random samplings for the current study. Medical records for all newborns with jaundice were examined for risk factors associated with Hyperbilirubinemia. All variables were analyzed by SPSS software, version 19. Chi-square test and T-test were applied to evaluate qualitative and quantitative data, respectively. Our findings revealed that maternal age, weight, BMI, WBC, Hb, PLT, birth in the first pregnancy, numbers of pregnancies and prolonged delivery were significantly associated with bilirubin levels. Preventing the risk correlated with maternal factors or identifying neonates with these risk factors is important in effective management of infants. Therefore, the evaluation of neonatal jaundice in health care services should always be considered as a fundamental policy.

Key Words: Neonatal jaundice, bilirubin, pregnancy, risk factors, health care

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Neonatal jaundice is a common condition that occurs during the transitional period after birth.¹⁻³ This unpreventable condition occurs in 60% of term and 80% of preterm neonates all over the world. Jaundice is one of the most common causes of neonatal readmission to hospital.¹ It usually begins on the second day after birth and lasts two to three days to reach normal levels of bilirubin in most cases without treatments.^{4,5} On the other hand, neonate population may show severe jaundice, or even jaundice that develops into acute bilirubin encephalopathy or kernicterus.^{6,7} Hyperbilirubinemia is primarily important because there is a close relationship between the increase in unconjugated bilirubin levels and neurotoxic effects that can lead to long-term complications such as cerebral palsy, kernicterus and hearing impairment.⁸⁻¹⁰ Severe jaundice is a serious life-threatening problem, and several factors interfere with the development of severe

jaundice, which can be related to genetic and/or geographic variables.⁷ Early diagnosis of infants at high risk of severe hyperbilirubinemia plays an important role in facilitating the timely and appropriate prevention of disease within the first 14 days of birth.^{7,11} Clinical symptoms of hyperbilirubinemia are primarily seen in the head and face, and then affect the organs of the trunk and the limb due to increased serum levels of bilirubin. It is noteworthy that increasing hemoglobin release from breakdown of red cells due to high hemoglobin leads to jaundice at birth.^{12,13} This disease may also be due to decreased hepatic excretion of bilirubin.^{14,15} Since jaundice may have serious side effects on the health of infants, consideration should be given to its associated factors in newborns. Kernicterus is one of the most important diseases that complications of the disease are sometimes so dangerous. Considering the fact that jaundice is one of the common causes of

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Table 1. Association of some maternal factors with the level of bilirubin

Bilirubin		Mother's age	Mother's breathing number	Mother's heart rate	Weight	Height	BMI
	p-value	0.02	0.44	0.85	0.001	0.19	0.01
10-14.9	Mean	29.37	14.93	89.04	80.43	162.65	30.42
	SD	6.21	2.91	6.04	7.42	4.09	2.94
15-19.9	Mean	25.94	14.48	88.42	75.03	161.45	28.78
	SD	5.91	2.39	6.13	5.48	3.54	1.89
20-24.9	Mean	28.17	13.67	88.33	78.50	160.83	30.43
	SD	5.71	2.73	1.63	7.18	3.06	3.55
Total	Mean	28.81	14.82	88.92	79.54	162.41	30.17
	SD	6.24	2.83	5.96	7.38	4.00	2.87

SD, Standard Deviation

hospitalization of newborns, attention can be paid to timely diagnosis and prevention of it. On the other hand, the rapid treatment of jaundice or timely prevention will be cost-effective in annual costs due to reduced hospitalization of newborns. To the best of our knowledge, the evaluation of the causes and risk factors of neonatal jaundice in newborns has not been comprehensively performed in Iran, while we are confronted with the spread of the disease among the newborns. Therefore, it is advisable to have a systematic and effective program for evaluation of causes and risk factors of jaundice in newborns. Prevention of jaundice risks requires extensive and accurate analyses that should be continuously and repeatedly performed. The present study was set out to assess the effects of maternal factors on neonatal jaundice with the aim of determining modifiable risk factors to reduce occurrence and consequences of severe jaundice in newborns.

Materials and Methods

Ethical considerations

All ethical principles of the Helsinki II declaration were followed. Newborns' parents were informed and written consent forms were collected.

Data Collection

This cross-sectional study was performed on 2207 term newborns (<15 days) with hyperbilirubinemia (>15 mg/dl), who admitted to the neonatal intensive unit of the Ziaeean and Imam Khomeini Hospitals, Tehran, Iran, from April 2010 to May 2016. The records of all infants in terms of the maternal risk factors for neonatal jaundice have been investigated. Neonates born with jaundice in the birth admission were selected based on the neonatal outcome indicator. Data were obtained from medical records and interview sessions with the mothers by study staff. A checklist consisting of

maternal demographic data and other data was provided for collecting data. Maternal information

Maternal information, including maternal age during pregnancy (over 35 and under the age of 18), first pregnancy, number of pregnancy, inter-pregnancy intervals of 3 years, type of delivery, Oxytocin Induction of labor, premature rupture of membranes (PROM), prolonged labor, cesarean section, multiple birth in the current pregnancy, respiratory rate during pregnancy, number of heart beats during pregnancy, maternal weight during pregnancy, body mass index, losing weight during pregnancy, history of abortion, were obtained from all mothers.

Inclusion criteria: Getting jaundice.

Exclusion criteria: Exclusion criteria included incomplete medical records that were beyond the control of the researcher; however, the additional sample size was considered to be about 20%.

Sample size calculation

alfa=	0.05	$Z_{1-\alpha/2}$ =	1.961150776
d=	0.03		
p=	0.96	n=	165

$$n = \frac{Z_{1-\frac{\alpha}{2}}^2 pq}{d^2}$$

An additional 20 percent sample size was added to prevent loss and withdrawal. p = first pregnancy as previously described.^{24,25} The sample size was finally calculated as 200. The data were subsequently collected and entered in the questionnaire, followed by statistical analysis based on SPSS software version 19. The obtained data was entered into cod sheet and master sheet. Qualitative variables were presented as frequency, while quantitative variables were calculated as mean, range, and standard deviation. Chi-square test was applied to examine qualitative data, while

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Table 2. Relationship of first pregnancy with neonatal jaundice based on the different bilirubin levels

		P=0.01		Bilirubin			Total
				10-14.9	15-19.9	20-24.9	
First/child	Yes	Number	49	18	2	69	
		Percent	30.1%	58.1%	33.3%	34.5%	
	No	Number	114	13	4	131	
		Percent	69.9%	41.9%	66.7%	65.5%	
Total		Number	163	31	6	200	
		Percent	100.0%	100.0%	100.0%	100.0%	

Relationship of some maternal blood factors with jaundice						
Bilirubin		Maternal white blood cells	Hemoglobin	Mean corpuscular volume	Platelet	Hematocrit
p-value		0.001	0.04	0.77	0.001	0.88
10-14.9	Mean	12.26	12.09	87.33	222.72	34.09
	SD	4.03	1.79	5.93	72.61	4.03
15-19.9	Mean	10.04	12.79	86.51	281.77	34.22
	SD	2.48	1.40	5.08	62.72	2.28
20-24.9	Mean	9.10	13.27	87.17	243.67	33.35
	SD	1.53	1.37	2.81	60.48	1.27
Total	Mean	11.82	12.24	87.20	232.50	34.09
	SD	3.88	1.75	5.72	73.74	3.75

SD, Standard Deviation

quantitative data were statically analyzed by T-test, $p < 0.05$ was considered statistically significant.

Results and Discussion

A list of maternal data is provided in Table 1. Regarding the mean age of the mother, the maternal age was significantly associated with different levels of bilirubin ($p = 0.02$), indicating a significant correlation of maternal age with incidence of jaundice. Maternal weight, and BMI showed also significant differences among different levels of bilirubin ($p = 0.001$; $p = 0.01$). As matter of fact, our findings suggest that the aforementioned variables were associated with neonatal jaundice. Respiratory rate at delivery, maternal heart rate and height had a significant difference at various levels of bilirubin, and were found to be linked to incidence of jaundice ($p = 0.44$; $p = 0.85$ $p = 0.19$). Table 2 shows the association of some maternal blood factors with jaundice. The statistical analysis revealed that maternal WBC, PLT and Hb had a significant relationship with jaundice ($p = 0.001$; $p = 0.001$; $p = 0.04$), but maternal MCV, and HCT did not show significant correlation with bilirubin levels ($p = 0.77$; $P = 0.88$). There is a significant difference in terms of birth in the first pregnancy among neonates with different levels of bilirubin ($p = 0.01$; Table 2). Our findings also indicate that the numbers of pregnancies were more likely to be referred for bilirubin levels ($p=0.00$; Table3). In addition, interpregnancy interval of less than 3 years was not found to be linked to hyperbilirubinemia ($p= 0.9$; Table 3). Table 4 shows

that 30.1% of infants in the first maternal delivery had a bilirubin level of 10 to 14.9, followed by bilirubin levels of 15-19.9 (58.1%) and bilirubin levels of 20- 24.9 (33.3%). Table 4 demonstrates that 38.7% of natural childbirth (Vaginal delivery) was categorized to the bilirubin level, where ranged from 10-14.9; while the bilirubin level in the range of 15-19.9 mg/dL was attributed to a frequency of 54.8% ; Furthermore, bilirubin values ranged from 20- 24.9 mg/dL in 33.3% of neonates. The delivery mode was not associated with the incidence of hyperbilirubinemia ($p = 0.2$; Table 4). Regarding to oxytocin infusion, there was no significant difference between oxytocin infusion and disease incidence ($p = 0.5$; Table 4). According to the data of this study, there was a significant relationship between prolonged delivery and the incidence of neonatal jaundice ($p= 0.03$, Table 4). Moreover, 46.6% of infants, who showed premature rupture of membranes (PROM), had a bilirubin level in the range of 10-14.9 mg/dL, followed by bilirubin levels in the range of 15-19.9 (61.3%) and 20- 24.9 mg/dL (33.3%). No association was found between PROM and different levels of bilirubin ($p = 0.2$, Table 4). ,Om the ther hand neonates with different levels of bilirubin had no significant difference in maternal cesarean section ($p = 0.1$, Table 5). As shown in Table 5, 16% of infants delivered by a multiple pregnancy showed a bilirubin level between 10-14 mg/dL. 10-14.9; while the bilirubin level in the range of 15-19.9 mg/dL was attributed to a frequency of 6.5% and bilirubin values ranged from 20-24.9 mg/dL in 0% of neonates. It is noteworthy that no

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Table 3. Correlation of numbers of pregnancies with neonatal jaundice based on the different bilirubin levels

		P=0.001	Bilirubin			Total
			10-14.9	15-19.9	20-24.9	
number/of/pregnancy	1.00	Number of (first pregnancy)	49	18	2	69
		Percent	30.1%	58.1%	33.3%	34.5%
	2.00	Number of (second pregnancy)	57	5	1	63
		Percent	35.0%	16.1%	16.7%	31.5%
	3.00	Number of (third pregnancy)	32	6	2	40
		Percent	19.6%	19.4%	33.3%	20.0%
	4.00	Number of (fourth pregnancy)	21	0	0	21
		Percent	12.9%	0%	0%	10.5%
	5.00	Number of (fifth pregnancy)	0	2	1	3
		Percent	0%	6.5%	16.7%	1.5%
	6.00	Number of (sixth pregnancy)	3	0	0	3
		Percent	1.8%	0%	0%	1.5%
	8.00	Number of (seventh pregnancy)	1	0	0	1
		Percent	0.6%	0%	0%	0.5%
Total		Number	163	31	6	200
		Percent	100.0%	100.0%	100.0%	100.0%
Relationship between the number of pregnancies and neonatal jaundice						
		P=0.9	Bilirubin			Total
			10-14.9	15-19.9	20-24.9	
interpregnancy interval of less than 3 years	No	Number	106	20	4	130
		Percent	65.0%	64.5%	66.7%	65.0%
	Yes	Number	57	11	2	70
		Percent	35.0%	35.5%	33.3%	35.0%
Total		Number	163	31	6	200
		Percent	100.0%	100.0%	100.0%	100.0%

significant difference was found between twins and disease incidence among neonates with different levels of bilirubin ($p=0.2$). The history of abortion did not show a significant relationship with the incidence of disease ($p=0.2$; Table 5).

Jaundice is a complication that may lead to death in the first month of birth and infants who are still alive suffer from many disorders including mental retardation (Intellectual disability), mobility and balance disorders, seizures, hearing loss at high frequencies, and speech impairment. Protecting and promoting the health of infants as a vulnerable group in the health services has a special place. Therefore, evaluation of neonatal jaundice in health care services should always be considered as a fundamental policy. Nearby, early detection of its risk factors can be effective in preventing disease in high-risk mothers-infants. Our study showed that maternal age, weight, BMI, WBC, Hb, PLT, birth in the first pregnancy, numbers of pregnancies and prolonged delivery were significantly correlated with bilirubin levels. Maternal age was found to be statistically significant in statistical analysis. Srivastav et al., found

higher serum bilirubin levels in neonates of younger mothers.¹⁶ A previous study has also suggested that maternal age ≥ 30 years can be linked to increased risk for neonates.¹⁷ Another study by Özdek et al. demonstrated that mothers who have more weight than the advised amount may be at risk of neonatal jaundice.¹⁸ Conversely, many studies have reported that this variable was not correlated with hyperbilirubinemia.^{19,20} In the present study, the mean age of mothers in patients was determined as 28.8 years (Maximum: 43 years; Minimum: 17 years). Based on the findings, the mean age of mothers in newborns with moderate jaundice was lower than other forms of disease and the most cases of jaundice were observed in the first pregnancy (34.5%, 69 cases). In other studies, CBC level and its related parameters have not been studied in the mother. One of the strengths of this study is to examine the level of maternal blood parameters. It seems that the levels of WBC, Hb, and PLT have a significant correlation with the incidence of neonatal jaundice. However, it was found that there was not an increasing risk for neonatal jaundice with maternal

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Table 4. Relationship between delivery method and jaundice in different levels of bilirubin

P=0.2			Bilirubin			Total
			10-14.9	15-19.9	20-24.9	
Type of delivery	Normal vaginal delivery (NVD)	Number	63	17	2	82
		Percent	38.7%	54.8%	33.3%	41.0%
	Caesarean section (CS)	Number	100	14	4	118
		Percent	61.3%	45.2%	66.7%	59.0%
Total		Number	163	31	6	200
		Percent	100.0%	100.0%	100.0%	100.0%
Relationship between oxytocin infusion and jaundice in different levels of bilirubin						
P=0.5			Bilirubin			Total
			10-14.9	15-19.9	20-24.9	
Oxytosin injection	Yes	Number	147	26	5	178
		Percent	90.2%	83.9%	83.3%	89.0%
	No	Number	16	5	1	22
		Percent	9.8%	16.1%	16.7%	11.0%
Total		Number	163	31	6	200
		Percent	100.0%	100.0%	100.0%	100.0%
Association between prolonged delivery and incidence of jaundice in different levels of bilirubin						
P=0.03			Bilirubin			Total
			10-14.9	15-19.9	20-24.9	
Prolonged	Yes	Number	72	20	1	93
		Percent	44.2%	64.5%	16.7%	46.5%
	No	Number	91	11	5	107
		Percent	55.8%	35.5%	83.3%	53.5%
Total		Number	163	31	6	200
		Percent	100.0%	100.0%	100.0%	100.0%
Association between PROM and neonatal jaundice in different levels of bilirubin						
P=0.2			Bilirubin			Total
			10-14.9	15-19.9	20-24.9	
PROM	Yes	Number	76	19	2	97
		Percent	46.6%	61.3%	33.3%	48.5%
	No	Number	87	12	4	103
		Percent	53.4%	38.7%	66.7%	51.5%
Total		Number	163	31	6	200
		Percent	100.0%	100.0%	100.0%	100.0%

MCV, and HCT. Nevertheless, conversely, a study indicated that maternal haemoglobin was not demonstrated to affect the bilirubin levels in physiological jaundice.¹⁹ Further studies are needed to clarify the role of blood factors mentioned in the current study. Our finding suggested that birth in the first pregnancy, numbers of pregnancies and prolonged labor could be important risk factors in current study population. In our study population, some factors such

as delivery mods, twins, interpregnancy interval of less than 3 years were found to be associated with neonatal jaundice. In agreements with previous studies, there was no an increasing risk for neonatal jaundice with the delivery mode, where was not correlated with the incidence of hyperbilirubinemia.

It has been previously reported that mode of delivery could be liked to jaundice and its severity^{19,20-24} Contrary, it has been previously revealed that naturally

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Table 5. Association between neonatal hyperbilirubinemia and cesarean section

P=0.1			Bilirubin			Total
			10-14.9	15-19.9	20-24.9	
History of cesarean section (CS)	Yes	Number	58	6	3	67
		Percent	35.6%	19.4%	50.0%	33.5%
	No	Number	105	25	3	133
		Percent	64.4%	80.6%	50.0%	66.5%
Total		Number	163	31	6	200
		Percent	100.0%	100.0%	100.0%	100.0%
Correlation between neonatal hyperbilirubinemia and multiple births in the current pregnancy (twin)						
P=0.2			Bilirubin			Total
			10-14.9	15-19.9	20-24.9	
Multiple birth in the current pregnancy (twin)	YES	Number	26	2	0	28
		Percent	16.0%	6.5%	0%	14.0%
	NO	Number	137	29	6	172
		Percent	84.0%	93.5%	100.0%	86.0%
Total		Number	163	31	6	200
		Percent	100.0%	100.0%	100.0%	100.0%
History of abortion and risk of hyperbilirubinemia						
P=0.2			Bilirubin			Total
			10-14.9	15-19.9	20-24.9	
History of abortion	Yes	Number	81	11	4	96
		Percent	49.7%	35.5%	66.7%	48.0%
	No	Number	82	20	2	104
		Percent	50.3%	64.5%	33.3%	52.0%
Total		Number	163	31	6	200
		Percent	100.0%	100.0%	100.0%	100.0%

delivered subjects are likely to be at higher risk for neonatal jaundice, when comparing with those born by cesarean section, indicating the importance of delivery mode as a risk factors for jaundice.^{25,26} The conflicting findings could be linked to types of variables, types of study, sample size and study condition, where can affect to data analysis. On the other hand, no significant difference was found between oxytocin infusion and disease incidence, while oxytocin is involved in bilirubin metabolism and has been described to be a risk factor for the development of neonatal jaundice, induction of labor with oxytocin may associated with hypoosmotic and lytic effects (increased red blood cell lysis), resulting in hyperbilirubinemia²⁶⁻²⁸. However, it is recommended that this factor be assessed with a higher sample size. Excessive application of oxytocin during labor and cesarean section have been defined as risk factors.^{25, 26} In the present study, cesarean section was not found to be associated with hyperbilirubinemia. Hyperbilirubinemia might be exacerbated by cesarean section, in comparison to natural births¹¹. On the other hand, mode of delivery has been not found to be significantly associated with incidence of hyperbilirubinemia.²⁹ As mentioned in results, prolonged labor remained obviously linked to

neonatal jaundice in our study population. In consist with the current study, Scrafford, et al, reported a significant association of prolonged labor with jaundice, possibly the clinical relationship between longer labor and cephalohematoma may play a role in this event.^{10,30} Furthermore, no significant association was found between PROM and neonatal jaundice, however PROM has been described to affect some of the parameters involved in the health of fetuses and infants, such as neonatal jaundice, platelet parameters and erythrocyte parameters³¹, Further evaluation are required to clarify the role some of mentioned variable that were not showed correlation with neonatal jaundice. Twins was not important risk factors in the current study, several reported risk factors were not found in the current study to be correlated with jaundice in neonates such as twins³²⁻³⁵. As matter of fact twins was found to be correlated with hyperbilirubinemia in some investigations, but we did not find such association in our studies. In consist with our study, Scrafford et al. did not demonstrate correlation between twins and hyperbilirubinemia.¹⁰ The number of multiple births was very low in the current study (N=28), whereas caution should be observed in its interpretation; thereby, may reduce the statistical power for determining the statistically strong association

between twins and jaundice in newborns.¹⁰ Preventing the risk correlated with maternal factors or identifying neonates with these risk factors is firstly important in effective management of infants, which can be taken into account by improving maternal and public health education.^{10, 36, 37}

The findings of this study indicated that there is a need for more epidemiological studies on characteristics of infants, and identifying the risk factors for hyperbilirubinemia. The history of abortion stillbirth or abortion did not show a significant relationship with the incidence of disease. History of stillbirth or abortion has been previously reported to be associated risk factor for neonatal hyperbilirubinemia,^{38,39} which are in agreement with our study. Further assessment of community-based detection of abortion history should be investigated in neonates. In future studies, the variables should be further evaluated in higher sample size. Finally, in order to promote health of infants, evaluation of neonatal jaundice should always be considered at all levels of health services.

List of acronyms

BMI - Body mass index
 CS - Cesarean section
 HB - Haemoglobin,
 HCT - Hematocrit
 MCV - Mean corpuscular volume
 NVD - Normal vaginal delivery
 PLT - Platelets
 PROM - Premature rupture of membranes
 WBC - White blood cells
 SD – Standard deviation

Author's contributions

Each author contributed in equal part to the manuscript.

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Conflict of Interest

The authors declare no conflicts of interests.

Ethical Publication Statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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