Arch Iran Med. February 2020;23(2):128-140

http www.aimjournal.ir

ARCHIVES OF IRANIAN MEDICINE

Open Access

Systematic Review

Evaluation of Maternal Risk Factors in Neonatal Hyperbilirubinemia

Hassan Boskabadi, MD[1]; Forough Rakhshanizadeh, MD[1]; Maryam Zakerihamidi, PhD[2*]

[1]Department of Pediatrics, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
[2]Department of Midwifery, School of Medical Scienses, Tonekabon Branch, Islamic Azad University, Tonekabon, Iran

Abstract

Background: Diagnosis and timely treatment of neonatal jaundice and prevention of dangerous side effects of pathologic neonatal jaundice remain a serious debate. The first step in prevention of jaundice is the identification of predisposing factors. The present study aims to systematically review the maternal risk factors of neonatal hyperbilirubinemia.

Methods: For this study, we searched databases including Science Direct, Cochrane Library, ISI, PubMed and Google Scholar from 1993 to 2017. The keywords searched based on MESH included hyperbilirubinemia, jaundice, infants, mothers and risk factors. The present systematic review was conducted on studies reporting maternal risk factors for neonatal jaundice. The inclusion criteria were: study on neonates; examination of maternal factors or both maternal and neonatal factors. Papers associated with the diagnosis and treatment of neonatal jaundice were excluded from the study, as well as those articles for which only abstracts were available. The limitations of this study include lack of access to all relevant articles, lack of qualified reports in some papers, and the limitation in number of articles related to maternal risk factors, and therefore inability to judge accurately about their effects on neonatal jaundice.

Results: Of 500 searched articles, 17 articles (1 prospective article, 2 retrospective papers, 12 cross-sectional papers and 2 historical cohort articles) were finally investigated. Maternal risk factors included hypertension, diabetes, type of delivery, vaginal bleeding, premature rupture of membranes (PROM), maternal age, lack of initiation of feeding during the first hours of life, inappropriate breastfeeding techniques and presence of maternal breast problems.

Conclusion: The most common maternal risk factors for neonatal jaundice were prematurity, blood type incompatibilities, preeclampsia, hypertension, diabetes mellitus, vaginal bleeding, delivery problems (type of delivery, labor injuries, delivery at home, skin ecchymosis, and cephalohematoma), mothers and community cultural beliefs (use of traditional supplements), breast problems, and decrease in breastfeeding.

Keywords: Breast problems, Delivery, Hyperbilirubinemia, Jaundice, Maternal risk factors, Neonates, Pregnancy

Cite this article as: Boskabadi H, Rakhshanizadeh F, Zakerihamidi M. Evaluation of maternal risk factors in neonatal hyperbilirubinemia. Arch Iran Med. 2020;23(2):128–140.

Received: February 23, 2019, Accepted: September 18, 2019, ePublished: February 1, 2020

Introduction

Neonatal hyperbilirubinemia is the most common cause of hospitalization in the newborn (17%–19%).[1] Neonatal hyperbilirubinemia occurs when the serum bilirubin level reaches more than 5 mg/dL (86 µmol/L).[2] Neonatal physiologic jaundice occurs on the second to fourth day after birth and reaches its peak on the fourth to sixth day. It improves spontaneously on the 10th to 14th day after birth, but in 8–11% of cases, the bilirubin level progresses to higher than the 95th percentile and it needs to be evaluated and treated.[3] It can be a sign of a serious condition and lead to severe complications such as kernicterus, which causes life-long disability.[4] In a study, 13% of neonates with bilirubin above 20 mg/dL suffered from jaundice complications, the most important of which were hearing loss and developmental delay.[5]

Identifying the predisposing factors of neonatal jaundice remains a serious discussion and it can be effective in controlling jaundice and the underlying problem.[6] The risk of pathologic jaundice is 1% in the absence of risk factors for hyperbilirubinemia and up to 59% in the presence of risk factors.[7] Maternal risk factors for hyperbilirubinemia include: maternal diabetes, mother's age over 25 years, TORCH syndrome,[8,9] hypertension and preeclampsia,[10] premature rupture of membranes (PROM),[11] type of delivery,[9,12] and inadequate breastfeeding.[13] Maternal causes of inadequate breastfeeding include breast congestion, nipple fissure, mastitis, inverted nipples, maternal fatigue, lack of support by relatives for breast feeding, inadequate maternal nutrition during breastfeeding, inadequate education about breastfeeding during pregnancy and postpartum.[14,15] Therefore, the importance and necessity of careful monitoring of breast feeding education for mothers and the evaluation of appropriate lactation technique should be considered. In this regard, the results of a study by Chen et al showed that a proper lactation

*Corresponding Author: Maryam Zakerihamidi, PhD; Department of Midwifery, School of Medical Scienses, Tonekabon Branch, Islamic Azad University, Tonekabon, Iran. Email:maryamzakerihamidi@yahoo.co.nz

technique and its observation play an important role in successful lactation and decreased jaundice.[16] For primary prevention of neonatal jaundice, 8–12 times of lactation per day are recommended during the first days after birth.[17] As increased breastfeeding decreases the possibility of severe jaundice, appropriate support and breastfeeding counseling for mothers result in successful breastfeeding (the infant receiving enough milk) and decrease the risk of hyperbilirubinemia.[17]

Given that jaundice is a common problem in Asian countries such as Iran, accounting for about 21% of causes of neonatal hospitalization with serious side effects including kernicterus, and given that identifying the predisposing factors can be suggested as markers for prevention of jaundice and its rapid diagnosis in order to provide better treatment care and improve outcomes, the present study aims to systematically review the maternal risk factors for neonatal jaundice.

Materials and Methods

Selection of Maternal Risk Factors for Neonatal Jaundice Development

After preliminary review of papers, a list of maternal, or maternal/neonatal risk factors for jaundice was prepared for systematic review, and articles that only examined maternal risk factors or the combination of maternal and neonatal jaundice risk factors were studied. In this regard, articles including maternal risk factors (7 articles), or a combination of maternal and neonatal risk factors for neonatal jaundice (10 articles) were included in our study.

Search Strategy

In order to perform the systematic review and find the studies addressing neonatal jaundice maternal risk factors, the Science Direct (97 articles), Cochrane Library (24 articles), PubMed (43 articles), ISI (136 articles) and Google Scholar (200 articles) databases were searched from 1993 to 2017. "Maternal risk factors", "jaundice", "mothers", "Maternal risk factors and jaundice", "jaundice and mothers" and "jaundice or hyperbilirubinemia" were used as the key words to search for the articles. The risk factors were considered within a paper based on the conclusion of the papers.

A total of 500 studies included the entry criteria, and they were collected using the EndNote software in a separate library file. There were 200 duplicate articles which were deleted. The articles were evaluated in terms of title and abstract and 75 articles were eliminated in this stage. Of 175 remaining papers, 160 papers were deleted due to incomplete data, lack of full text, adult evaluation, uncertainty of study type, and target group. Finally, 17 articles related to the research subject were studied (Figure 1).

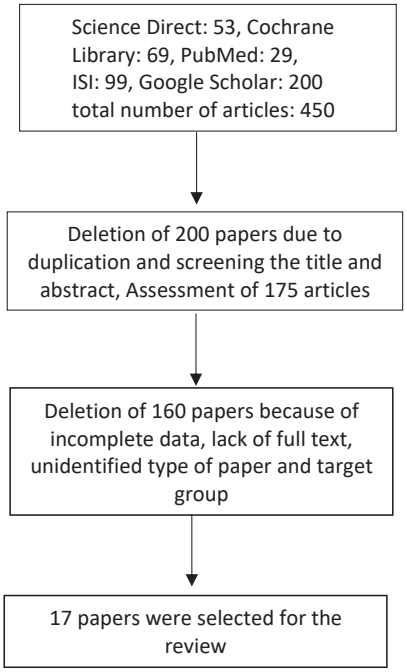

Figure 1. Search Strategy and Selected Articles.

Inclusion Criteria

Papers were selected based on the following criteria: (1) studied population should be neonates. (2) Neonatal jaundice is identified. (3) Maternal factors, or both maternal and neonatal factors are investigated. (4) Availability of sufficient information about the results of studies.

Exclusion Criteria

The following articles were excluded from the study so that only proper and relevant articles were reviewed: (1) Papers that addressed adults. (2) Papers related to the diagnosis and treatment of neonatal jaundice. (3) Papers that were only available in abstract.

Data Extraction and Evaluation of Article Quality

Papers with full text were obtained from the aforementioned databases and the extracted data were entered in Excel software with the following details: author's name; year; method of study; location of study; number of samples, type of risk factor, and results from research and conclusion. We assessed the methodological quality of papers using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) – a quality control tool for diagnostic accuracy. This tool consists of 14 questions; replies including "yes", "no" and "unspecified" were scored 1, -1 and 0, respectively, and the maximum score was 14.[18]

Results

Among 500 papers, 17 papers with a sample size of 52,719 neonates with jaundice were examined (Table 1).

Table 1. Summary of Studies on Neonatal Jaundice Risk Factors

Author/year	Method of study	Location	Results	Case Group	Control Group	Risk factors	Prevalence of Risk Factors	QUADAS Score
Boskabadi et al (2012)	Cross-sectional	Iran	A quarter of neonates with jaundice had a history of maternal risk factors. The most common maternal predisposing factor was hypertension (4.7%) and other factors included in terms of frequency: vaginal bleeding, diabetes, urinary tract infections and PROM.	2796 term neonates, 3- 29 days old, with jaundice		Maternal	Hypertension (4.7%), vaginal bleeding (3. 3%), diabetes (2.78%), PROM (2.7%), urinary tract infection (0.8%),	12
Boskabadi et al (2011)	Cross-sectional	Iran	There were no relationship between type of delivery and mean bilirubin level and jaundice	1847 neonates 3-29 days old with jaundice		Maternal	The cause of jaundice was clear in 690 infants, and was unknown in 797 newborns with jaundice. Neonates were divided into two groups of NVD and cesarean section according to delivery type. The predisposing factors, pregnancy and delivery problems, and neonatal status were compared in these two groups. 41.9% of newborns with jaundice were born through cesarean section.	
Alizadeh Taheri et al (2013)	Case-control prospective	Iran	The results of this study call for greater attention and better follow-up of mothers of newborns who are at risk of breastfeeding jaundice, especially mothers with abnormal breast problems such as inverted nipple or inadequate breastfeeding training. In this study, the earliest possible initiation of breastfeeding, especially in the first hour after birth, was one of the most important factors in reducing the incidence of jaundice.	75 term infants with breastfeeding jaundice	75 normal term infants	Maternal	Lack of initiation of breastfeeding in the first hours after birth, inappropriate breastfeeding techniques and maternal breast disorders were significantly higher in the case group than the control group.	
Norman et al (2015)	Cross-sectional	Sweden	The maternal and obstetric risk factors cause a difference of more than 100-fold in the incidence of neonatal jaundice	Neonates diagnosed with jaundice (23,711 cases)		Maternal and obstetric	Maternal factors associated with an increased risk of neonatal jaundice included Asian race, age over 30, maternal overweight or obesity and diabetes. Obstetric factors included first pregnancy, induction, instrumental delivery, and delivery at 37 to 38 weeks of gestation. Cesarean delivery section (emergency or elective) and gestational age higher than 41 weeks were associated with a reduction in the risk of neonatal jaundice.	
Mansouri et al (2014)	Case-control	Iran	Maternal underweight during pregnancy, maternal age above 35 years during pregnancy, and family history of diabetes were the maternal risk factor for neonatal jaundice.	197 neonates with jaundice	250 neonates as control	Maternal	Maternal underweight during pregnancy increases the chances of having a baby with jaundice by more than 2.5 times and family history of diabetes by more than 1.5 times.	12
Boskabadi et al (2011)	Cross-sectional	Iran	Infant's gender, maternal gestational age, serum T4 level, maternal hypertension, preeclampsia and diabetes can play a role in jaundice.	140 neonates with jaundice		Maternal	The most common perinatal complications among neonates with jaundice were maternal hypertension (19%), preeclampsia (14.3%) and diabetes (9.5%). Also, the incidence and severity of jaundice was significantly related to the infant's gender, maternal gestational age and serum T4 level.	12

Table 1. Continued

Author/year	Method of study	Location	Results	Case Group	Control Group	Risk factors	Prevalence of Risk Factors	QUADAS Score
Boskabadi et al (2017)	Cross-sectional	Iran	With increasing frequency of breastfeeding, the severity of neonatal hyperbilirubinemia decreases. Accelerating weight gain and increasing frequency of stools also reduce the severity of neonatal jaundice. Hence, breastfeeding training is helpful in reducing the severity of jaundice, insisting on the frequency of infants' feeding.	634 infants with jaundice hospitalized in emergency department, infants or neonatal clinics		Maternal	At bilirubin levels of 1–12, 12.1–16, 16.1–20 and 20.1–39 mg/dL, the mean frequency of breastfeeding was 10.66, 9.83, 9.19 and 7.5 times / day, respectively. The mean serum bilirubin level in infants with fewer than 7 times breastfeeding daily (19 mg/dL) is higher than that of infants with a frequency of feeding more than 7 times (16 mg/dL). With increasing frequency of feeding, the percentage of weight loss was lower. In neonates with bilirubin less than 20 mg/dL, the severity of hyperbilirubinemia decreased with decreasing amount and percentage of daily weight and increasing frequency of stools.	
Devi et al (2016)	Case control	India	The presence of pregnancy problems such as GDM, hypertension and IUGR is associated with the occurrence of neonatal jaundice.	140 neonates with bilirubin higher than 10 mg / dL		Maternal and neonatal	74% of newborns with jaundice were born through natural vaginal delivery and 25% through cesarean section, but the difference was not significant. The results of this study showed a significant relationship between hyperbilirubinemia and LBW, preterm delivery, PROM, breastfeeding, infant infections, instrumental delivery, gestational diabetes, abortion history and IUGR.	12
Mahmoudi et al (2016)	Cross-sectional	Iran	In this study, the prevalence of jaundice was 16.72%, which was mostly due to ABO incompatibility and G6PD deficiency.	579 neonates admitted to Neonatal Department of Imam Sajjad Hospital in Yasuj		Maternal and neonatal	In this study, 16.72% of the cases were affected by jaundice. G6PD deficiency was present in 12.95% of neonates with jaundice. The common risk factors of premature jaundice was as follows: ABO incompatibility and G6PD deficiency, prematurity, cephalohematoma , RH incompatibility. Of 579 infants, 58.2% had normal delivery, and the rest were caesarean section. Also, 53.2% of cases were male and the rest were female. The most common blood type of neonates was A followed by AB; the most common type of maternal blood was O. Of neonates with jaundice, 9.15% were premature (35–37 weeks) and 20 infants (3.45%) had neonatal infections due to maternal infections during pregnancy. There was a significant relationship between frequency of breastfeeding, prematurity, ABO incompatibility, G6PD deficiency and jaundice prevalence.	
Bulbul et al (2014)	Retrospective	Turkey	Neonates who came later had more severe hyperbilirubinemia.	137 patients in group 1 (with bilirubin 25 mg/dL and higher)	1198 neonates in group 2 (with bilirubin 25 mg/dL and lower)	Maternal and neonatal	Pathologic weight loss, NVD, supplementary feeding, and second child of family ($P < 0.001$, $P < 0.001$, $P = 0.04$, $P = 0.002$) were the risk factors for severe hyperbilirubinemia.	11

Table 1. Continued

Author/year	Method of study	Location	Results	Case Group	Control Group	Risk factors	Prevalence of Risk Factors	QUADAS Score
Najib et al (2013)	Cross-sectional, prospective	Iran	Indirect severe hyperbilirubinemia has a high prevalence in Fars province, and reforming maternal ethic and cultural beliefs by education could be effective in preventing hyperbilirubinemia complications.	170 infants more than 28 days with indirect severe hyperbilirubinemia		Maternal and neonatal	The most common causes of severe indirect hyperbilirubinemia were blood group incompatibility (5.9%), G6PD deficiency (25.5%), sepsis (12%) and unknown causes (53.1%). Risk factors for severe hyperbilirubinemia included male gender (58.2%), history of severe hyperbilirubinemia in previous sibling (27.9%), early discharge, NVD (73.5%), exclusive breastfeeding (91%), and mothers' cultural beliefs about taking herbal drugs rather than referring to the doctor in case of jaundice (69.4%).	13
Scrafford et al (2013)	Historical-cohort	Nepal	Exclusive breastfeeding is considered as a risk factor for neonatal jaundice. While in infants without nutritional problems, this type of nutrition plays a protective role against neonatal hyperbilirubinemia.	18,985 infants born in Nepal		Maternal and neonatal	Male gender, birth weight 3000 g and higher, infants with nutritional problems, newborns receiving Colostrum, delivery in labor facilities, delivery by a trained person, skin ecchymosis during childbirth, presence of childbirth injuries, maternal vaginal bleeding 7 days before labor and prolonged labor increase the risk of referral due to neonatal jaundice.	12
Zabeen et al (2010)	Cross-sectional	Bangladesh	Diabetes and septicemia were the most common cause of neonatal jaundice. Hemolytic causes such as incompability of ABO, Rh and G6PD deficiency were reported to be irrelevant. Infants who died showed septicemia.	60 neonates with hyperbilirubinemia requiring phototherapy or exchange		Maternal and neonatal	35% of infants were born with gestational age under 32 weeks, and 32% of them with 35 weeks and higher. 83.3% of newborns were born though cesarean section. There was incompability for both ABO and Rh in 13.3% and 3.3% of cases, respectively. 26.7% of neonates showed septicemia and 20% of newborns had positive blood cultures. Septicemia was more prevalent in infants under 32 weeks of age than those with 35 weeks and more (68.8% versus 12.5%). Prematurity in 73.3% of cases, diabetes in 35%, septicemia in 26.6% were observed among neonates with hyperbilirubinemia. G6PD deficiency was seen in 1.7% of infants. A significant number of neonates with jaundice were associated with lower gestational age, and lower gestational age was associated with septicemia and possibly hyperbilirubinemia.	12
Korejo et al (2010)	Cross-sectional	Pakistan	Most of neonates with kernicterus were born at home. Infection, prematurity, and LBW were common risk factors.	100 infants with kernicterus		Maternal and neonatal	62% of all cases were male and 38% were female. The infant age range was 1–15 days, and 56 newborns were under 5 days of age. Prematurity was observed among 39%, LBW in 55%, hypothermia in 44%, delivery at home in 60%, hemolysis in 30%, and sepsis in 52% of infants. In 5 infants, there were 5 risk factors, in 21 infants 4 risk factors, in 30 infants 3 risk factors,in 26 infants 2 risk factors and in 16 infants there was 1 risk factor. The mean bilirubin level was 27.4 mg/dL.	13

Table 1. Continued

Author/year	Method of study	Location	Results	Case Group	Control Group	Risk factors	Prevalence of Risk Factors	QUADAS Score
Aiswarya et al (2016)	Prospective	Greece	Jaundice is one of the main causes of hospitalization among newborns. Several maternal and neonatal factors cause neonatal jaundice, and the severity of jaundice increases with decreased or lack of breastfeeding.	231 infants admitted for jaundice in the neonatal intensive care unit		Maternal and neonatal	38.9% of mothers were aged 21–25 years . 65.36% of mothers consumed 3 to 4 cups of coffee / tea daily. 75.32% of mothers smoked. 54.97% of infants were male. 67.34% of infants had jaundice with or without risk factors. 19.04% of the infants were immature and 54.11% of infants showed jaundice in the first 3 or 4 days of life. 48.48% of the neonates were born through natural vaginal delivery and 45.88% of the cases were born through cesarean section. 29.43% of all reasons for jaundice were due to incompatibility of the OA group, 18.61% due to OB incompatibility, and 10.82% of the other cases of jaundice were due to Rh incompatibility. 21.21% of cases of jaundice were associated with a decrease in breastfeeding in the neonatal intensive care unit. Causes of jaundice were LBW (58.44%), incompatibility of the blood groups (58.86%), infections (33.33%), hypoxia (22.07%), and nutritional problems (18.61%).	13
Shetty et al (2014)	Retrospective	India	ABO Incompatibility, premature birth, first delivery, and LBW are risk factors for neonatal jaundice.	753 newborns treated for jaundice		Maternal and neonatal	13.47% of neonates with jaundice needed to be hospitalized. Maternal and neonatal characteristics of these infants were investigated. 53.5% of all infants with jaundice were male. 65.1% of cases were the first child of family. 44.2% of newborns were born through cesarean section ABO blood type incompatibility was the most common cause of hyperbilirubinemia (42.5%). The researchers conclude that Rh group incompatibility (9.4%), sepsis (11.6%) and cephalohematoma (4.6%) were the other most common causes of hyperbilirubinemia. The causes of neonatal jaundice were unclear in one third of cases. Preterm delivery and LBW were also other causes of neonatal jaundice.	13
Phuapradit W et al (1993)	Historical cohort	Thailand		638 neonates with hyperbilirubinemia more than 15 mg/dL			The results of this study showed a significant relationship between neonatal hyperbilirubinemia and delivery by vacuum (2.7 times), preterm labor (2.1 times), LBW (2 time), complications during pregnancy (1.7 times), complications during labor (1.5 times), delivery by forceps (1.4 times) and induction (1.3 times).	

ABO, ABO blood group system; G6PD, Glucose-6-phosphate dehydrogenase deficiency; LBW, Low birth weight; IUGR, Intrauterine growth restriction; PROM, Premature rupture of membranes

Prevalence of Studies on Maternal Risk Factors for Neonatal Jaundice

A review of related studies conducted between 1993–2017 shows 7 (37.5%) articles were about maternal risk factors while 10 (62.5%) were related to the combination of maternal and neonatal risk factors. Seventeen studied articles included 1 prospective article, 2 retrospective papers, 12 cross-sectional studies, and 2 historical cohort articles. Most of the studies (8 articles, 47%) were related to Iran.

Inhomogeneity of Studies

All searched studies about maternal risks for neonatal jaundice were different in terms of inclusion criteria for neonates, sample size, place of study, and results.

Global Distribution of Jaundice-Related Studies

Studies on neonatal jaundice risk factors were carried out in Iran (8 studies, 50%), India (2 studies, 12.5%), Bangladesh (1 study, 6.25%), Turkey (1 study, 6.25%), Greece (1 study, 6.25%), Nigeria (1 study, 6.25%) Nepal (1 study, 6.25%), Sweden (1 study, 6.25%), Thailand (1 study, 6.25%), and Pakistan (1 study, 6.25%).

Maternal Risk Factors For Neonatal Jaundice (7 Articles)

In a study by Boskabadi et al, maternal predisposing factors in incidence of neonatal jaundice were studied. This study was performed on 2796 term neonates from 3 to 29 days of age. After confirmation of diagnosis of jaundice in neonates, based on laboratory results and comments of neonatal subspecialists, a questionnaire was completed including maternal demographic information, infant characteristics, maternal complications during pregnancy and delivery. Among these term infants with jaundice, 21% had a history of gestational problems and 79% had a normal pregnancy history. The results of this study showed that 1146 (41%) neonates had a history of maternal predisposing factors including hypertension (4.7%), vaginal bleeding (3. 3%), diabetes (2.78%), PROM (2.7%) and urinary tract infection (0.8%).[18]

In a case-control study by Mansouri et al conducted on 197 neonates with jaundice and 250 control neonates under supervision at Isfahan Health Center, maternal underweight during pregnancy and a family history of diabetes were two independent risk factors for neonatal Jaundice. Mother's underweight during pregnancy increased the chance of having a baby with jaundice by more than 2.5 times, and a family history of diabetes increased the chance of jaundice by more than 1.5 times.[19]

In Boskabadi et al study, 1847 newborns hospitalized due to jaundice in a cross-sectional study. In 690 infants (37%), the cause of jaundice was determined. All cases were divided based on delivery type into two groups of normal delivery and delivery by cesarean section. The predisposing factors, pregnancy and delivery problems, and neonatal status were compared between these two groups. In total, 41.9% of newborns with jaundice were born through cesarean section. The results of the study showed no relationship between type of delivery with mean bilirubin and jaundice severity.[20]

Boskabadi et al conducted a cross-sectional study on 140 neonates with jaundice. The most common perinatal complications among neonates with jaundice were maternal hypertension (19%), preeclampsia (14.3%) and diabetes (9.5%), respectively. Also, the incidence and severity of jaundice were related to the neonate's gender and gestational age.[10]

Alizadeh Taheri et al identified the maternal risk factors affecting breastfeeding jaundice. This study was conducted in the neonatal ward of the Bahrami pediatric hospital in Tehran. Seventy-five term neonates with breastfeeding jaundice were selected as the case group by considering weight loss more than 7% of birth weight and one of the laboratory signs of dehydration as urine specific gravity <1012, serum sodium higher than 150 mEq/L and urea ≥40 mEq/L. Also, 75 term neonates hospitalized for jaundice were selected as control group who had weight loss less than 7% of birth weight and other causes of jaundice. The results of this study showed that lack of initiation of breastfeeding in the first hour of life, inappropriate breastfeeding techniques and the presence of maternal breast problems were significantly higher in the case group than the control group. The researches of this study recommended greater attention and better follow-up of mothers of breast-fed infants who are at higher risk of breastfeeding jaundice, especially mothers with breast disorders such as inverted nipple or inadequate breastfeeding education. In this study, initiation of breastfeeding after delivery as soon as possible, especially in the first hour, was one of the most important factors in reducing breastfeeding jaundice.[21]

Norman et al examined the maternal and obstetric risk factors in neonates with jaundice. This study was conducted on data from the Swedish Birth Registration Center from 1999 to 2012, including 126,198 newborns. Neonates diagnosed with jaundice (23711) were included and neonates with hemolytic jaundice were excluded from the study. The results of the study showed that maternal factors associated with an increased neonatal jaundice risk included Asian race, age over 30 years, maternal overweight or obesity and diabetes. Age below 20 years was associated with a reduction in risk of neonatal jaundice. Obstetric factors also included first pregnancy, induction, instrumental delivery, and delivery at 37 to 38 weeks of gestation, while delivery by cesarean section (emergency and elective), and gestational age greater than 41 weeks were associated with reduction in the risk of neonatal jaundice. They noticed that the set of maternal and obstetric risk factors caused a difference in the incidence of neonatal jaundice.[22]

Boskabadi et al conducted a cross-sectional study on 634 infants with jaundice at the emergency department and neonates or neonatal clinic of Ghaem hospital in Mashhad. They studied the frequency and duration of breastfeeding and the severity of hyperbilirubinemia among the neonates. Data collection was done using a researcher-made questionnaire. Then, the infants were studied based on frequency and duration of breastfeeding and hyperbilirubinemia severity. According to the results of this study, at the bilirubin levels of 1–12, 12.1–16, 16.1–20 and 20.1–39 mg/dL, the mean frequency of breastfeeding was 10.66, 9.83, 9.19 and 7.5 times per day, respectively. The mean serum bilirubin level in infants fed equal or fewer than 7 times daily (19 mg/dL) was more than those with a frequency of feeding more than 7 times per day (16 mg/dL). With increasing frequency of feeding, the percentage of weight loss was lower. In neonates with bilirubin less than 20 mg/dL, with increasing amount and percentage of daily weight gain and increasing the frequency of stools, the severity of hyperbilirubinemia decreased. The researchers concluded that increasing the frequency of breastfeeding reduced the severity of neonatal hyperbilirubinemia. Accelerating weight gain and increasing frequency of stools also reduced the severity of jaundice in infants. Therefore, breastfeeding training and insisting on increasing the frequency of feeding are helpful in reduction of the severity and side effects of hyperbilirubinemia.[17]

Studies About Both Maternal and Neonatal Risk Factors for Neonatal Jaundice (10 Articles)

Devi et al conducted a case-control study to evaluate the maternal and neonatal risk factors of neonatal jaundice in 140 neonates with bilirubin above 10 mg/dL in India. According to the results of this study, 74% of neonates were born by natural delivery and 25% of those by cesarean section developed jaundice, but the difference was not significant. The results of this study showed a significant relationship between hyperbilirubinemia and low birth weight (LBW), preterm delivery, PROM, breastfeeding, neonatal infections, instrumental delivery, gestational diabetes, intrauterine growth restriction (IUGR) and abortion history. The researchers concluded that pregnancy problems such as gestational diabetes mellitus (GDM), hypertension, and LBW are related to the occurrence of neonatal jaundice.[23]

Mahmodi et al conducted a cross-sectional study in Iran to evaluate the maternal and neonatal risk factors of neonatal jaundice in 579 infants who were admitted to the Neonatal Department of Imam Sajjad hospital in Yasuj. The results of this study showed that 72.16% of infants were affected by jaundice. The common risk factors of premature jaundice were as follows: ABO incompatibility and glucose-6-phosphate dehydrogenase (G6PD) enzyme deficiency, prematurity, cephalohematoma, and RH incompatibility. Of 579 infants, 58.2% had normal delivery, and the others had caesarean section. 53.2% of them were male. The most common type of neonatal blood group was A, followed by AB and the most common type of maternal blood group was O. Of neonates with jaundice, 9.15% were premature (35–37 weeks) and 20 infants (3.45%) showed neonatal infections due to maternal infections during pregnancy. There was a significant relationship between the frequency of breastfeeding, prematurity, ABO incompatibility and G6PD deficiency with jaundice prevalence.[24]

Bulbul et al conducted a retrospective study on neonates 35 weeks and older who underwent phototherapy in Turkey during a 10-year period from 2000 to 2009. The research subjects were divided into two groups, and clinical manifestations, etiology and jaundice risk factors were compared. Group 1 included infants with bilirubin levels of 25 mg/dL or higher (severe hyperbilirubinemia) and group 2 were infants with bilirubin levels less than 25 mg/dL. During the research, 1335 neonates were evaluated. Severe Hyperbilirubinemia was found in 137 (10.3%) of infants. Serum bilirubin level was 29.7 ± 4.7 mg/dL in group 1 and 18.9 ± 3.5 mg/dL in group 2. Pathologic weight loss, normal vaginal delivery (NVD), complementary feeding and second child afterwards ($P < 0.001$, $P < 0.001$, $P = 0.04$, $P = 0.002$, respectively) were important risk factors for hyperbilirubinemia. The time of jaundice detection by the family, and the age of referral were significantly higher in group 1. A history of previous sibling receiving phototherapy and being second child or later were more common in group 1.[25]

Najib et al carried out a prospective cross-sectional study in Fars province, Iran to assess the incidence, causes and risk factors for severe neonatal jaundice. Neonates who were under 28 days of age and referred due to severe indirect hyperbilirubinemia were included in the study. The results of this study showed that the most common cause of severe indirect hyperbilirubinemia included blood type incompatibility (5.9%), G6PD deficiency (25.5%), sepsis (12%), and unknown (53.1%). Risk factors for severe hyperbilirubinemia included male gender (58.2%), history of severe hyperbilirubinemia in previous sibling (27.9%), early discharge (73.5%), normal delivery (73.5%), breastfeeding (91%) and mothers' cultural beliefs (69.4%). The researchers concluded that there was a high prevalence of severe indirect hyperbilirubinemia in Fars province. Reforming ethnic and cultural beliefs of mothers by education could be effective in preventing the hyperbilirubinemia complications.[26]

Scrafford et al conducted a historical cohort study in Nepal on 18 985 neonates with a mean age of 6 days from 2003 to 2006 to determine the incidence and risk factors for neonatal jaundice. Almost half (55.8%) of neonatal jaundice occurred in the first week of birth. Sampling was performed by random-cluster method. The results of this

study showed that the incidence of neonatal jaundice was 29.3 in 1000 live births. Probability of referral for neonatal jaundice increased by male gender of neonate, 3000 g birth weight or higher, infants with nutritional problems, accelerated delivery, skin ecchymosis during birth, presence of labor injuries, vaginal bleeding in mother 7 days before delivery and prolonged labor. Neonates who were born in warm seasons were at higher risk for jaundice. For each 1 degree increase in air temperature, the risk of neonatal jaundice increased by 3%. In neonates with nutritional problems, exclusive breastfeeding was considered a risk factor for neonatal jaundice, while in infants without nutritional problems, this type of nutrition played a protective role against neonatal hyperbilirubinemia.[27]

Zabeen et al in Bangladesh performed a cross-sectional study on 60 neonates with hyperbilirubinemia requiring phototherapy or exchange transfusion. In this study, maternal and neonatal risk factors for jaundice, characteristics and outcome of hyperbilirubinemia in newborns were investigated. Type of delivery, gestational age, birth weight, CBC (complete blood count), ABO and Rh incompatibility, TSH (thyroid stimulating hormone) and serum bilirubin level, G6PD deficiency, and brain ultrasonography were assessed. Thirty-five percent of infants were born with a gestational age under 32 weeks, and 32% of them with 35 weeks and higher. Eighty-three percent of cases were born through cesarean section. Incompatibility for ABO and Rh was observed in 13.3% and 3.3% of cases, respectively. Prematurity was observed among 73.3%, maternal diabetes in 35% and septicemia in 26.6% of neonates with hyperbilirubinemia.[28]

Korejo et al performed a cross-sectional study in a neonatal intensive care unit in Pakistan. In this study, risk factors for neonatal jaundice were examined on 100 neonates with kernicterus by objective-sampling method. Among these, 62 cases were male and 38 were female. The infant's age was between 1 to 15 days. In total, 39 infants were premature, 55 cases had LBW and 44 neonates had a history of hypothermia. Delivery at home was recorded for 60 cases, and hemolysis occurred in 30 infants. The mean bilirubin level was 27.4 mg/dL. There were five risk factors in 5 infants, four risk factors in 21 infants, three risk factors in 30 infants, two risk factors in 26 infants, and one risk factor in 16 infants. The researchers concluded that the majority of kernicterus cases were neonates who were born at home. Neonatal infections, prematurity, and LBW were also common risk factors.[29]

Aiswarya et al conducted a prospective study on 231 neonates admitted for jaundice in a neonatal intensive care unit in Greece. The purpose of this study was to determine the incidence, risk factors and neonatal jaundice control. In this study, 38.9% of mothers were aged 21–25 years, and 54.97% of the neonates were male. In total, 67.34% of infants showed jaundice with or without risk factors. Also, 19.04% of the infants were premature and 54.1% of them were diagnosed for jaundice in the first 3 or 4 days of life. Moreover, 48.48% of neonates were born through natural vaginal delivery. Causes of jaundice were LBW (58.44%), incompatibility of blood group (58.86%), neonatal infections (33.33%), hypoxia (22.07%), and nutritional problems (18.61%). The researchers concluded that jaundice is the common reason for hospitalization of infants, and the intensity of jaundice increases with the decrease or lack of breastfeeding.[30]

In a retrospective study, Shetty et al examined the incidence, etiology, and neonatal jaundice risk factors in a tertiary health care facility in India. Of all 5589 cases, 753 infants were treated for jaundice. Males constituted 53.5% of neonates with jaundice, and 65.1% of cases were the first child of the family. Also, 44.2% of infants were born though cesarean section. The incompatibility of ABO blood group (42.5%) and Rh (9.4%), sepsis (11.6%) and cephalohematoma (4.6%) were the most common causes for hyperbilirubinemia. Preterm delivery (32.9%) and LBW (27.7%) were other reasons for neonatal jaundice.[31]

The most common maternal risk factors for neonatal jaundice include prematurity, blood type incompatibilities, preeclampsia, hypertension, diabetes and vaginal bleeding (Table 2).

Discussion

Reviewing the studies about maternal risk factors for neonatal jaundice has shown that the maternal risk factors play a role in neonatal jaundice incidence. Maternal risk factors for neonatal jaundice include: maternal diseases (diabetes, hypertension, preeclampsia, gestational infection), pregnancy problems (prematurity, premature rupture membrane history, blood group O and negative maternal RH, etc), labor problems (type of delivery, complications and problems during labor, delivery by forceps or vacuums and induction, accelerated delivery, skin ecchymosis during labor, vaginal bleeding, delayed labor, delivery at home, delivery trauma, cephalohematoma), breastfeeding difficulties (breast problems, reduced amount or frequency of breastfeeding, inappropriate breastfeeding techniques and type of nutrition), mother and community cultural beliefs (traditional dietary practice), and miscellaneous factors (maternal age, first delivery and abortion history).

Maternal Disease

According to our results, about 6% of icteric newborns were born to diabetic mothers. In numerous studies, between 1–17% of causes of neonatal jaundice pertained to neonates of diabetic mothers.[32] In a study by Mohammad-Beigi et al, the chance of jaundice in neonates of diabetic mothers was three times higher in comparison with the control group.[33] There are several causes for the occurrence of jaundice in newborns of diabetic mothers, including prematurity, polycythemia, macrosomia and an increase in

Table 2. Average Incidence of Risk Factors for Neonatal Jaundice

Mean of Incidence	Incidence Range	Incidence of Risk Factor
Hypertension (11.85%)	Hypertension (4.7–19%)	Hypertension (4.7%), hypertension (19%)
Preeclampsia (14.3%)	Preeclampsia (14.3%)	Preeclampsia (14.3%)
Vaginal bleeding (3.3%)	Vaginal bleeding (3.3%)	Vaginal bleeding (3.3%)
Diabetes (6.14%)	Diabetes (2.78–9.5%)	Diabetes (2.78%), diabetes (9.5%)
Premature rupture of membranes (2.7%)	Premature rupture of membranes (2.7%)	Premature rupture of membranes (2.7%)
Natural vaginal delivery (45.85%)	Natural vaginal delivery (16.7–75%)	Natural vaginal delivery (58.1%), NVD (75%), NVD (58.2%), NVD (73.5%), NVD (16.7%), NVD (48.48%), NVD (58%)
Maternal infections (3.45 %)	Maternal infections (3.45 %)	Maternal infections (3.45 %)
Preterm delivery (33.3%)	Preterm delivery (32–35%)	Preterm delivery (32.9%), gestational age under 32 weeks (35%), gestational age 35 weeks and higher (32%)
Use of herbal medicines based on maternal cultural beliefs (69.4%)	Use of herbal medicines based on maternal cultural beliefs (69.4%)	Use of herbal medicines based on maternal cultural beliefs (69.4%)
Reduction in breastfeeding rate (21.21%)	Reduction in breastfeeding rate (21.21%)	Breastfeeding (91%)

NVD, normal vaginal delivery.

enterohepatic cycle.[34,35]

One of the maternal risk factors for neonatal jaundice is maternal hypertension during pregnancy. In several studies, hypertension was the most common maternal problem with neonatal jaundice (4.7%–19%).[10,18,36,37] Maternal high blood pressure is an important factor in premature delivery, and preterm infants are at high risk for jaundice due to liver immaturity and high red blood cell count.

Pregnancy Problems

One of the maternal problems that affects neonatal jaundice incidence, is premature delivery and also premature birth. In a study, 30% of cases of neonatal jaundice were due to prematurity. Uridine diphosphoglucuronide acid-glucuronyl transferase (UDPGT) enzyme maturity is related to gestational age: the activity of this enzyme is one third among infants with 32 weeks of gestational age compared to term neonates, and as a result, the possibility of jaundice and its complications is increased in premature infants. On the other hand, delay in milk production and weakness of infant sucking lead to decreased caloric intake, dehydration and increase in enterohepatic circulation of bilirubin, thus resulting in increased concentration of bilirubin.[17,35,38]

PROM was also a maternal risk factor. In previous studies, the history of PROM in pregnancy was observed in 1.7%–4.8% of infants with jaundice.[18] In a study by Kern et al, prolonged rupture of membrane was one of the maternal predisposing factors relevant to neonatal jaundice.[25] In 40% of premature cases, there is a history of PROM. Thus, prematurity may be the main cause of jaundice in newborns with PROM.

Another risk factor for neonatal jaundice is ABO incompatibility, the result of mother's O blood group and nenonate's A or B blood group. According to Mahmodi et al, ABO incompatibility, G6PD enzyme deficiency, prematurity, cephalohematoma, and RH incompatibility were the most prevalent risk factors for early neonatal jaundice. Also, there was a significant correlation between ABO incompatibility and jaundice prevalence.[24] In the study by Zabeen et al, ABO and Rh incompatibility were found in 13.3% and 3.3% of cases, respectively.[28]

Type of Delivery

Delivery type is one of the risk factors for neonatal jaundice. However, there is still disagreement which type would reduce jaundice. In several studies, 16.7%–75% of neonates with jaundice were naturally delivered, while 40% of them were born through cesarean section.[9,12,18,35,39,40] In one study, the bilirubin level in the first two days after birth was lower in newborns with cesarean delivery compared to those with normal delivery, although afterwards, this ratio was reversed. The reason is that these infants undergo stress before birth and during normal delivery, resulting in an increase in UDPGT enzyme levels.[41] The results of one study showed that cesarean delivery reduces the risk of neonatal jaundice. According to the researchers, the reason was longer hospitalization of mother (48 to 72 hours) after cesarean section, and therefore more opportunity to establish appropriate and adequate breastfeeding.[42] Based on the results of one study, with increasing maternal hospitalization, the serum bilirubin level, the rate and percentage of daily weight loss decreased among neonates.[43] It is still not well understood which delivery type reduces the risk of jaundice, but elective caesarean increases the incidence of jaundice probably by increasing the risk of prematurity. On the other hand, natural vaginal delivery is still the preferred type due to its many benefits for maternal and neonatal health.

Among other maternal problems associated with jaundice is maternal vaginal bleeding during labor. In a study by Yin et al, bilirubin levels were higher in infants of mothers with placental abruption than the control group neonates, although the difference was not significant. The cause of jaundice in this case was unknown.[44]

Trauma during delivery may lead to subcutaneous hemorrhage, cephalohematoma and bleeding in other organs. Absorption of this bleeding leads to more severe jaundice in newborns. In a study by Zarrinkoub et al, the prevalence of cephalohematoma was reported as a risk factor for neonatal jaundice.[9]

It has been reported that 58%–81.4% of infants who had severe hyperbilirubinemia were fed exclusively or predominantly by breastfeeding.[43] According to the results of Chen et al, breastfeeding in the first days after birth has an important effect on severity of jaundice and the frequency of urination and feces.[16] The results of Cheng et al showed that the incidence of hyperbilirubinemia was significantly smaller in infants who were breastfed eight times or more per day, than those who received breastfeeding fewer than eight times a day.[45] In another study, it was shown that with increasing frequency of feeding (more than seven times in 24 hours), serum bilirubin levels and the percentage of weight loss in newborns decreased.[17] Therefore, education to mothers about repeated breastfeeding (at least 8 times per a day) can reduce the incidence of hyperbilirubinemia. The American Academy of Pediatrics has recommended that the frequency of breastfeeding should be between 8 and 12 times daily during the first weeks of birth[46]. In another study, exclusive breastfeeding in infants with nutritional problems was suggested as a risk factor for neonatal jaundice. In infants without nutritional problems, this type of nutrition shows a protective effect against neonatal hyperbilirubinemia. Interference between exclusive breastfeeding and nutritional problems or reduced calorie intake can explain the mechanism of neonatal jaundice in these cases.[27] Bulbul et al showed that the risk of severe hyperbilirubinemia was 1.4 times higher in complementary nutrition group than the breastfeeding group[25]. In the study by Salas et al, 60% of newborns with early jaundice caused by lack of breastfeeding showed more than 10% weight loss, and a significant difference was found between serum bilirubin levels and weight loss.[41]

In another study, mean serum bilirubin levels were higher in the group with a frequency of feeding seven times per day or fewer (19 mg/dL) than the group fed more than seven times per day (16 mg/dL). With increasing frequency of feeding, the percentage of weight loss was lower. In neonates with serum bilirubin levels under 20 mg/dL, with reduction in daily percentage weight loss and increased stool frequency, the severity of hyperbilirubinemia decreased.[17] One study showed that neonatal complications of breast problems (and therefore, reduced breastfeeding rates) were pathological weight loss, reduced urinary intervals and increased risk of jaundice.[47] Also, according to the results of one study, about one-third of infants with idiopathic jaundice suffered from severe weight loss and severe hyperbilirubinemia. The mean body weight loss was three times higher in newborns with severe jaundice (serum bilirubin level above 20 mg/dL) than neonates with moderate jaundice (under 20 mg/dL).[48] One of the serious concerns of mothers in the first days of neonatal life is reducted amount of milk; they repeatedly complain of this problem and they often blame themselves. However, the results of studies indicate that breastfeeding duration has no clear effect on reduction of jaundice, while the frequency of breastfeeding is much more important and effective. Perhaps frequent breastfeeding leads to faster stabilization of breastfeeding, and also early maturity of hepatic conjugating enzyme of bilirubin decreases the absorption of bilirubin through the enterohepatic cycle, and it reduces the severity of hyperbilirubinemia in infants with unknown jaundice.[17,35]

According to the results of Riordan's study, the reduction in calorie intake of infant due to reduced breastfeeding intervals or feeding with water, sugar juice and formula often leads to an increase in jaundice in the first three days after birth. Reduction in calorie is associated with release of fatty acids and their competition in bilirubin conjugation and prevents the conversion of indirect bilirubin to direct bilirubin and increases the serum indirect bilirubin concentration.[49] In one study, use of Manna and *Sisymbrium irio* were the major risk factors for jaundice.[5] Tarhani et al examined this issue based on the Iranian native culture, especially in Lorestan province, where people use the Manna as a reducer agent for newborn jaundice. The results of the study showed that despite the native belief regarding the effect of Manna in reducing neonatal jaundice, administration of this substance has no significant effect on treatment of jaundice; thus, it is not recommended a treatment for neonatal jaundice.[50]

Another maternal risk factor was maternal age. In the study by Boskabadi et al, mean bilirubin levels were significantly higher in neonate of mothers older than 30 years of age in comparison with those aged 30 years and below.[20] In a study by Scrafford et al, the probability of newborns' referral due to jaundice was higher for mothers under 20 years of age than older mothers.[27] This difference in maternal age range can be due to different communities studied or other underlying causes.

One of the strengths of the present study is the collection of maternal risk factors of neonatal jaundice in several studies and the determination of average incidence of each risk with purpose of assessing the most common neonatal jaundice risk factors. The limitations of this study include lack of access to all relevant articles, lack of qualified and usable reports for some papers, and the limitation in number of articles related to maternal risk factors, and therefore, the inability to judge accurately about their effects on neonatal jaundice. Considering the importance of identifying neonatal jaundice risk factors and appropriate and timely treatment to prevent adverse outcomes in neonates, further studies are required to learn more about risk factors for neonatal jaundice and determine the predictive value of each risk factor.

Conclusion

In conclusion, reviewing studies addressing maternal risk factors for neonatal jaundice has shown that maternal risk factors play an important role in the incidence of neonatal jaundice. These risk factors included maternal age, hypertension, diabetes, cesarean section, birth order, PROM, preterm delivery, LBW, frequency of breastfeeding and neonatal weight loss. Based on the average incidence of maternal risk factors for neonatal jaundice, the most common factor was hypertension (11.85%).

Therefore, regular and effective care seems to be necessary during pregnancy including training about the harmful effects of some herbal medicines, proper nutrition for the mother and normal delivery, and moreover, following-up the baby in case of complications such as PROM, GDM, high blood pressure and preeclampsia during pregnancy in order to prevent premature birth and neonatal sepsis, which are important causes of hyperbilirubinemia. Also, the optimal training techniques of breastfeeding, preventing early discharge, and a general screening of preterm or low-birth weight infants by assessing blood or cutaneous bilirubin levels before discharge and following them in a safe and cost-effective manner are helpful.

Authors' Contribution

HB conceptualized and designed the study, drafted the initial manuscript, initial analyses, reviewed and revised the manuscript, and approved the final manuscript as submitted. FR designed the study and carried out the initial analyses, reviewed and revised the manuscript, and approved the final manuscript as submitted. MZ designed the data collection instruments, and coordinated and supervised data collection at two of the four sites, critically reviewed the manuscript, and approved the final manuscript as submitted. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Conflict of Interest Disclosures

None.

Ethical Statement

Not applicable.

References

1. Khatami F, Soltani M. Home phototherapy; an alternative method for treatment of jaundice in healthy-term newborns. Iran J Pediatr. 2007;17(suppl 2):193-8.
2. Kliegman R, Behrman RE, Jenson HB, Stanton BF. Nelson Textbook of Pediatrics. Switzerland: Elsevier/Saunders; 2012.
3. Boskabadi H, Omidian M, Mafinejad S. Prevalence and clinical manifestation of glucose-6-phosphate dehydrogenase deficiency in newborns with hyperbilirubinemia in Mashhad, Iran. Macedonian Journal of Medical Sciences. 2010;3(4):383-7.
4. Boskabadi H, Maamouri G, Mafinejad S. The effect of traditional remedies (Camel's Thorn, Flixweed and Sugar Water) on idiopathic neonatal jaundice. Iran J Pediatr. 2011 Sep;21(3):325-30.
5. Boskabadi H, Ashrafzadeh F, Azarkish F, Khakshour A. Complications of Neonatal Jaundice and the Predisposing Factors in Newborns. Journal of Babol University of Medical Sciences. 2015;17(9):7-13.
6. Boskabadi H, Maamouri G, Kiani M, Abdollahi A. Evaluation of urinary tract infections following Neonatal hyperbilirubinemia. Journal of Shahrekord University of Medical Sciences. 2010;12(2):95-101.
7. Behrman R, Kliegman R, Jenson H. Behrman: Nelson Textbook of Pediatrics. Philadelphia, Pa: WB Saunders; 2004.
8. Javadi T, Mohsen Zadeh A. Examine the causes of jaundice in newborns admitted in Hospital of Shahidmadani Khoramabad in 2000. Journal of Lorestan University of Medical Sciences. 2005;3(7):73-8.
9. Zarrinkoub F, Beigi A. Epidemiology of hyperbilirubinemia in the first 24 hours after birth. Tehran University Medical Journal. 2007;65(6):54-9.
10. Boskabadi H, Khakshoor A, Khorashadizadeh F, Taherpour M, Esmaeili H. Prenatal complications causing neonatal jaundicein Ghaem hospital, Mashhad- Iran. J North Khorasan Univ Med Sci. 2011;3(2):7-12.
11. Kurjak A, Chervenak FA. Textbook of Perinatal Medicine. Abingdon: Informa Healthcare; 2006.
12. Tamook A, Salehzadeh F, Aminisani N, Moghaddam Yeganeh J. Etiology of neonatal hyperbilirubinemia at Ardabil Sabalan Hospital. J Ardabil Univ Med Sci. 2006;5(4):316-20.
13. Ambalavanan N, Carlo WA. Jaundice and Hyperbilirubinemia. In: Ambalavanan N, Carlo WA, eds. Nelson Textbook of Pediatrics. Philadelphia: Elsevier; 2016.
14. Kaplan M, Wong RJ, Sibley E, Stevenson DK. Neonatal jaundice and liver disease. In: Martin RJ, Fanaroff AA, Walsh MC, eds. Neonatal-Perinatal Medicine: Diseases of the Fetus and Infant. 9th ed, Vol 2. St. Louis: Elsevier Mosby; 2011:1443-96.
15. Huang A, Tai BC, Wong LY, Lee J, Yong EL. Differential risk for early breastfeeding jaundice in a multi-ethnic Asian cohort. Ann Acad Med Singapore. 2009;38(3):217-24.
16. Chen CF, Hsu MC, Shen CH, Wang CL, Chang SC, Wu KG, et al. Influence of breast-feeding on weight loss, jaundice, and waste elimination in neonates. Pediatr Neonatol. 2011;52(2):85-92. doi: 10.1016/j.pedneo.2011.02.010.
17. Boskabadi H, Zakerihamidi M. The correlation between Frequency and Duration of Breastfeeding and the Severity of Neonatal Hyperbilirubinemia. J Matern Fetal Neonatal Med. 2018;31(4):457-463. doi: 10.1080/14767058.2017.1287897.
18. Boskabadi H, Zakeri Hamidi M, Goudarzi M. Investigating the effect of maternal risk factors in incidence of neonatal jaundice. The Iranian Journal of Obstetrics, Gynecology and Infertility. 2013;15(34):1-6.
19. Mansouri A, Ghaderpanahi M, Kazemi-Galougahi MH, Moradzadeh R, Tolide-ie HR, Akbarpour S, et al. A Case-Control study on prenatal factors of newborns' mild jaundice. Journal of Nurse and Physician within War. 2014;1(1):17-23.
20. Boskabadi H, Navaei M. Relationship between delivery type and jaundice severity among newborns referred to Ghaem hospital within a 6-year period in Mashhad. 2011;14(4):15-21.
21. Alizadeh Taheri P, Sepahran M, Shariat M. Maternal factors in newborns breast feeding jaundice: a case control study. Tehran University Medical Journal. 2013;70(12):768-73.
22. Norman M, Åberg K, Holmsten K, Weibel V, Ekéus C. Predicting nonhemolytic neonatal hyperbilirubinemia. Pediatrics. 2015;136(6):1087-94. doi: 10.1542/peds.2015-2001.
23. Devi DS, Vijaykumar B. Risk factors for neonatal hyperbilirubinemia: a case control study. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2016;6(1):198-202. doi: 10.18203/2320-1770.ijrcog20164657
24. Mahmodi Z, Mahmodi F. Epidemiology and Risk Factors for Neonatal Jaundice in Infants Admitted to NICU of Imam Sajjad hospital, Yasooj. Scientific Journal of Hamadan University of Medical Sciences. 2016;22(4):346-52.
25. Bulbul A, Cayonu N, Sanli ME, Uslu S. Evaluation of risk factors

for development of severe hyperbilirubinemia in term and near term infants in Turkey. Pak J Med Sci. 2014;30(5):1113-8. doi: 10.12669/pjms.305.5080.
26. Najib KS, Saki F, Hemmati F, Inaloo S. Incidence, risk factors and causes of severe neonatal hyperbilirubinemia in the south of iran (fars province). Iran Red Crescent Med J. 2013;15(3):260-3. doi: 10.5812/ircmj.3337
27. Scrafford CG, Mullany LC, Katz J, Khatry SK, LeClerq SC, Darmstadt GL, et al. Incidence of and risk factors for neonatal jaundice among newborns in southern Nepal. Trop Med Int Health. 2013;18(11):1317-28. doi: 10.1111/tmi.12189.
28. Zabeen B, Nahar J, Nabi N, Baki A, Tayyeb S, Azad K, et al. Risk factors and outcome of neonatal jaundice in a tertiary hospital. Ibrahim Medical College Journal. 2010;4(2):70-3.
29. Korejo HB, Bhurgri GR, Bhand S, Qureshi MA, Dahri GM, Chohan RK. Risk factors for kernicterus in neonatal jaundice. Gomal Journal of Medical Sciences. 2010;8(1):1881-7.
30. Aiswarya AT, Sajeeth CI. The incidence, risk factors and management of neonatal jaundice in a government hospital, Palakkad District, Kerala. IJHSR. 2016;6(6):123-9.
31. Shetty A, Kumar BS. A study of neonatal hyperbilirubinemia in a tertiary care hospital. Kathmandu Univ Med J. 2015;13(50):102-8. doi: 10.3126/kumj.v13i2.16781
32. Javadi Kalateh Jafaeabadi T, Mohsenzadeh A. Evaluation of the causes of jaundice in neonates admitted to Madani hospital of Khorram Abad in 2002. Yafte. 2006;7(4):73-8.
33. Mohammad-Beigi A, Tabatabaee SHR, Yazdani M, Mohammad-Salehi N. Gestational diabetes related unpleasant outcomes of pregnancy [Persian]. Feyz Journals of Kashan University of Medical Sciences. 2007;11(1):1-6.
34. Gleason CA, Devaskar S. Avery's Diseases of the Newborn. Switzerland: Elsevier Health Sciences; 2011.
35. Maamouri G, Boskabadi H, Mafinejad S, Bozorgnia Y, khakshur A. Efficacy of Oral Zinc Sulfate Intake in Prevention of Neonatal Jaundice Iranian Journal of neonatology 2014;4(4):11-6.36.
36. Oladokun A, Otegbayo J, Adeniyi A. Maternal and fetal out comes of jaundice in pregnancy at the University College Hospital, Ibadan. Nigerian Journal of Clinical Ppractice. 2009;12(3):277-80.
37. Boskabadi H, Zakerihamidi M. Effect of maternal risk factors in the incidence of neonatal jaundice. Iran J Neonatol. 2012;3(3,4):4-5.
38. Bratton S, Stern M. Breast Milk Jaundice. Treasure Island (FL): StatPearls Publishing LLC.; 2020.
39. Saber A, Ferdowsi S, Askari F, Farsi L. Epidemiology of pathological jaundice and its association with demographic factors in infants born in the 22 Bahman Hospital in Gonabad, 2011. Razi Journal of Medical Sciences. 2013;20(114):42-8.
40. Agarwal V, Singh V, Goel S, Gupta B. Short communication maternal and neonatal factors affecting physiological jaundice in Western up. Indian J Physiol Pharmacol. 2007;51(2):203-6.
41. Salas AA, Salazar J, Burgoa CV, De-Villegas CA, Quevedo V, Soliz A. Significant weight loss in breastfed term infants readmitted for hyperbilirubinemia. BMC Pediatr. 2009;9:82. doi: 10.1186/1471-2431-9-82.
42. Boskabadi H, Zakerihamidi M. The effect of maternal hospitalization duration on neonatal bilirubin level. Tehran University Medical Journal. 2018;75(10):715-21.
43. Sgro M, Campbell D, Shah V. Incidence and causes of severe neonatal hyperbilirubinemia in Canada. CMAJ. 2006 Sep 12;175(6):587-90. doi: 10.1503/cmaj.060328.
44. Yin X, Chen Z, Yang L, Shao Q, Chen C, Feng Z. Coagulation function and placental pathology in neonates with placental abruption. Int J Clin Exp Pathol. 2018;11(2):604-13.
45. Chen YJ, Yeh TF, Chen CM. Effect of breast-feeding frequency on hyperbilirubinemia in breast-fed term neonate. Pediatr Int. 2015;57(6):1121-5. doi: 10.1111/ped.12667.
46. Gartner LM, Morton J, Lawrence RA, Naylor AJ, O'Hare D, Schanler RJ, et al. Breastfeeding and the use of human milk. Pediatrics. 2005;115(2):496-506. doi: 10.1542/peds.2004-2491
47. Boskabadi H, Ramazanzadeh M, Zakerihamidi M, Omran FR. Risk factors of breast problems in mothers and its effects on newborns. Iran Red Crescent Med J. 2014;16(6):e8582..
48. Boskabadi H, Maamouri G, Bagheri S. Significant neonatal weight loss related to idiopathic neonatal hyperbilirubinemia. Int J Pediatr. 2014;2(4.1):225-31.
49. Riordan J, Wambach K. Breastfeeding and Human Lactation. Sudbury, MA: Jones & Bartlett Learning; 2010.
50. Tarhani f, Momennasab m, Delfan b, Zendehkar a, Zaman m. A study of oral Taranjabin effects on reducing neonat's hyprebilirubinemia. Yafte. 2004;6(3):55-9.