

# Comparison of bilirubin level in term infants born by vaginal delivery and cesarean section

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## ABSTRACT

**Background:** Given the overriding importance of neonatal jaundice and scarcity of studies on the role of route of delivery on its occurrence, this study aimed to investigate the association between neonatal bilirubin level and the route of delivery (i.e., normal vaginal delivery [NVD] and cesarean section [CS]).

**Methods:** This prospective, cross-sectional study was conducted in 2012 in Imam Reza Hospital of Mashhad, Iran, 2012. In all term infants, who met the inclusion criteria, serum bilirubin level was measured by the bili-test device between the second and seventh days after birth. In cases with skin bilirubin level >5 mg/dl, serum bilirubin was also checked. The collected data were analyzed using SPSS, version 16.

**Results:** A total of 182 neonates were enrolled in the study, 56% of whom were male. The mean bilirubin levels in the NVD and CS groups were  $9.4 \pm 2.9$  mg/dl and  $9.8 \pm 3.4$  mg/dl, respectively ( $P=0.53$ ). Additionally, comparison of the mean bilirubin levels between the two groups based of demographic characteristics demonstrated no significant differences.

**Conclusion:** This study showed no significant correlation between neonatal jaundice in term infants and the route of delivery.

**Keywords:** Cesarean section, Hyperbilirubinemia, Neonatal jaundice, Normal vaginal delivery

## Introduction

Hyperbilirubinemia is one of the common findings during the first days of life, which is considered as a benign condition and is observed in 60% of term and 80% of preterm infants (1, 2). Neonatal hyperbilirubinemia is defined as total serum bilirubin level of more than 5 mg/dl (86  $\mu\text{mol/L}$ ) (3). The causes of this disorder can be

classified into overproduction of bilirubin, reduced bilirubin conjugation, and bilirubin excretion disturbance.

Bilirubin is one of the end products of hemoglobin catabolism, and its deposition in the skin and mucous membranes can result in icterus (4). In case of brain bilirubin deposition and its

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lack of early diagnosis and treatment, it can lead to major complications such as kernicterus. This condition can be fatal during the first months of life or might cause mental retardation, movement and balance disorders, seizure, high-frequency hearing loss, and speech disorders in survivors (2, 5). Therefore, early diagnosis and treatment of neonatal jaundice is vital to prevent such serious complications (6).

In a study by Olusanya et al., one-fourth of neonates with icterus had predisposing maternal factors. The most important parameters were hypertension followed by vaginal bleeding, diabetes, urinary infection, and premature rupture of membranes (PROM), maternal diabetes, East Asian race, prematurity, drug consumption, living in highlands, polycythemia, male gender, trisomy 21, cyanosis, cephalohematoma, oxytocin injection for delivery, breast feeding, weight loss (dehydration or calorie deprivation), delay in bowel movements, and history of neonatal jaundice in the siblings (7). In term neonates, the indirect bilirubin level reaches adult values normally within 10-14 days (8).

Given the paramount importance of neonatal jaundice and the paucity of studies on the role of the route of delivery in this condition, and considering the high demand of Iranian mothers for cesarean section (CS) delivery, this study was designed to determine the relationship between occurrence of neonatal jaundice and the route of delivery.

## Methods

This prospective, cross-sectional study was conducted in 2012 in Department of Gynecology of Imam Reza University Hospital, Mashhad, Iran. All the singleton term neonates (37-42 weeks of gestation) delivered in Imam Reza Hospital, who had no risk factors for neonatal jaundice, were enrolled in the study.

The exclusion criteria were parental income-pliance, fetal and neonatal complications such as congenital anomaly, abnormal presentation of the fetus in the uterus, hormonal and genetic disorders, cephalohematoma, asphyxia, intrauterine growth retardation, hemolytic disorders, blood incompatibility, neonatal infection, premature or post-term delivery, and maternal disorders including multiple pregnancies, meconium in the amniotic fluid, maternal diabetes (diabetes mellitus or pregnancy-induced diabetes), urinary infection, premature rupture of membranes, placental abruption, operative vaginal delivery (vacuum and forceps), abnormal labor process (rapid or prolonged labor), need for labor induction, poly-

hydramnios, and oligohydramnios. Neonates who were fed with formula, those with icterus (jaundice) on the first day of birth or with a total serum bilirubin level of  $15 \leq$  mg/dl and a direct serum bilirubin level of  $1.5 \leq$  mg/dl were excluded from the study.

The neonates were divided into two groups of normal vaginal delivery (NVD) and CS. Targeted sampling was performed, taking into account the confounding factors along with matching of probable factors. The two groups were also matched for confounding maternal (age, parity, and positive history of neonatal jaundice) and neonatal factors (age and sex).

After obtaining written informed consent from the neonates' parents, demographic data of the neonates and their mothers were recorded in a checklist. The infants were visited by an expert neonatologist in the clinic within 2-7 days after birth, and bilirubin level was checked by a jaundice meter (DAVID Ltd, Germany) on the forehead skin. A trained nurse performed all the measurements in the clinic by a single bili-test device. The necessary arrangements were made with medical equipment department to calibrate the device if required (standard colored sticks were used to find this necessity [yellow one=22, white one=0.1]). In case of skin bilirubin level of higher than 5 mg/dl, the serum bilirubin level was also checked. In the blood test, the total and direct bilirubin levels of the neonates were measured.

The data were analyzed using SPSS, version 16. Chi-square test was performed for qualitative data, and Mann-Whitney U test was applied for quantitative variables. P-value less than 0.05 was considered statistically significant.

## Results

Out of the 182 neonates, 91 (50%) were born by NVD and the remaining 91 through CS. The mean age of the mothers was  $26.6 \pm 4.1$  years (age range: 19-39 years). The age of 11 mothers was below 20 years, 163 were aged between 20 and 35 years, while nine mothers were aged over 35 years. Their mean number of children was  $1.7 \pm 1.6$  and the mean number of previous parities was 1.76 (range: 0-7).

The mean neonatal bilirubin level was 9.60 mg/dl (range: 2-21 mg/dl). Table 1 demonstrates the mean bilirubin level regarding route of delivery. The mean serum bilirubin levels in the NVD and CS groups were  $9.4 \pm 2.9$  mg/dl and  $9.8 \pm 3.4$  mg/dl, respectively.

**Table 1.** Comparison of the mean bilirubin level regarding route of delivery

	Bilirubin level (mg/dl) <sup>a</sup>	P-value*
Elective cesarean section	9.6±4	
Emergency cesarean section	10±2.9	0.510
Vaginal delivery	9.4±2.9	

a: mean±SD, \*: One-way ANOVA test

**Table 2.** The comparison between the mean bilirubin levels of cesarean section and vaginal delivery groups based on characteristics of the neonates

Characteristics	Bilirubin level (mg/dl) <sup>a</sup>		P-value*
	Cesarean section	Normal vaginal delivery	
Female	9.9±3.2	10.2±3.7	0.546
Male	9.8±3.8	8.8±2.8	0.220
Primigravid	9.2±3.1	8.7±3.0	0.509
Multigravid	10.2±3.5	9.9±2.7	0.581
History of neonatal jaundice in siblings	12.2±2.8	11.4±3.3	0.538
Mother's age<20 years	11.1±4.0	8.3±5.5	0.377
Mother's age 20-35 years	9.6±3.4	9.3±2.7	0.639
Mother's age>35 years	11.6±8.1	14.0±2.8	0.083

a: mean±SD, \*: Mann-Whitney U test

Moreover, the correlation between the bilirubin level and need for CS was significant ( $P=0.01$ ); as the highest bilirubin level was obtained in the failed labor induction group while the lowest rate belonged to the cephalopelvic disproportion (CPD) group. Table 2 demonstrates the comparison of the mean bilirubin levels between CS and NVD groups based on demographics of the neonates. In addition, the rate of clinical hyperbilirubinemia (bilirubin more than 5 mg/dl) was 72.2% in neonates delivered through NVD and 74.1% in the CS group, which was not significantly different ( $P=0.58$ ).

## Discussion

In our study, the bilirubin level of term infants delivered by CS was slightly higher than that of neonates delivered through NVD, yet this difference was not statistically significant. In a study by Feldmann et al. in 2012, neonatal jaundice showed a significant difference between preterm and term neonates, while no difference was noted regarding route of delivery (9).

In the present study, the mean bilirubin level was marginally higher in boys compared to girls, while it may become significant in a larger

population. Similarly, Boskabadi et al. in 2014 reported higher bilirubin level among boys (10). In a study by Gale et al., higher bilirubin level was significantly associated with male gender (11).

In the present study, investigation of the relationship between maternal age and bilirubin level revealed that the highest level was obtained from the 20-35 year age group. Similar results were reported by Boskabadi et al. (10); moreover, Gale et al. asserted that high bilirubin levels were remarkably associated with increased maternal age (11). Whereas, in a study by Zanjani et al., no significant correlation was found between bilirubin level and maternal age (12).

Moreover, a significantly higher bilirubin level was found in infants with a history of jaundice in other siblings. Gale et al. also reported that high bilirubin levels were strongly correlated with positive history of neonatal jaundice in a sibling (11).

In our study, bilirubin level was significantly lower in the primigravid group compared to the multigravid group. However, Zanjani et al. in 2008 concluded that hyperbilirubinemia is more common among neonates of primigravid mothers (12).

Although in the current study there was a marginally significant association between neonatal bilirubin level and maternal age, the infant's gender, and route of delivery, the relationship may become significant in a larger study population.

In addition, no significant correlation was obtained between the level of neonatal hyperbilirubinemia and the route of delivery. This finding is consistent with the study of Saber et al. in 2013 and Boskabadi et al., both having reported no such correlation (10, 13). Agrawal et al. in 2007 also concluded that the route of delivery does not affect neonatal bilirubin level (14).

Nevertheless, Yamunchi et al. stated that the bilirubin measured through skin in the first week of life in term infants was lower among neonates born by CS compared to those delivered by non-complicated NVD (15). Bertini et al. in 2001 found that CS significantly decreased the risk of hyperbilirubinemia (16). Bulbul et al. in 2014 also proposed NVD as a risk factor for severe hyperbilirubinemia ( $Bili>25$  mg/dL) (17). On the other hand, Gale et al. reported this correlation in favor of NVD (11), while Geller et al. in 2010 reported NVD to be correlated with lower rates of neonatal jaundice (18). Resende et al. in 2014 revealed a higher risk of hyperbilirubinemia among neonates delivered by CS, especially when it was performed before the 39th week of gestation (19).

Furthermore, Vidic et al. in 2015 asserted that with accurate determination of the exact

gestational age in CS candidates, the rate of hyperbilirubinemia could be reduced from 12% in neonates born in the 37th gestational week to 4% in those delivered in the 40th week of gestation (20). Certain studies have mentioned that glucuronyl transferase increases during NVD resulting in lower bilirubin levels after three days of birth. Other studies reported lower rates of hyperbilirubinemia among neonates delivered through CS, which may be due to sufficient breastfeeding training in such mothers as a result of longer hospitalization.

It should be borne in mind that neonatal complications associated with NVD such as cephalohematoma can result in high bilirubin levels. Accordingly, reduced calorie intake and the following weight loss are serious problems among such infants, which can aggravate neonatal jaundice. Armanian et al. in 2015 compared full-term and near-term neonates with regard to hyperbilirubinemia, showing higher bilirubin levels in the fifth to seventh days of birth in near-term neonates. These neonates were 2.4 times more likely to suffer from neonatal jaundice in comparison with the full-term neonates (21). In a study by Belgin et al. in 2013, neonatal jaundice had a significantly stronger association with CS compared to NVD, which was mostly attributed to the drugs used for anesthesia induction (22).

## Conclusion

In the current study, neonatal bilirubin level was significantly higher among mothers with previous history of neonatal jaundice in their other offspring and in those who underwent CS due to induction failure. Therefore, we highly recommend screening such infants for icterus.

We found no significant association between neonatal jaundice in term infants based on the route of delivery (NVD or CS). However, conducting further studies with larger sample sizes is recommended to achieve more definitive results. According to our findings, the route of delivery in maternal age of older than 35 years is a risk factor for neonatal hyperbilirubinemia; thus, we recommend to check neonatal bilirubin in infants of these mothers.

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## Conflicts of interests

None declared.

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