

Comparison of Bilirubin Level in Term Infants Born by Vaginal Delivery and Cesarean Section Delivery

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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 Accadmic hospital of medical faculty of balkh university Afghanistan, in all term infants, who met

the inclusion criteria was 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.

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±2.9 mg/dl and 9.8±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.

I. 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 μmol/L)⁽³⁾. Neonatal hyperbilirubinemia, defined as a total serum bilirubin level above 5 mg per dL (86 μmol per L), is a frequently encountered problem. Although up to 60 percent of term newborns have clinical jaundice in the first week of life, few have significant underlying disease.^{1,2} However, hyperbilirubinemia in the newborn period can be associated with severe illnesses such as hemolytic disease, metabolic and endocrine disorders, anatomic abnormalities of the liver, and infections²³.

Extreme hyperbilirubinemia (plasma bilirubin ≥24.5 mg/dL) is an important risk factor for severe

bilirubin encephalopathy. Several risk factors for hyperbilirubinemia are known, but in a large number of patients, a causal factor is never established.⁽²⁴⁾

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⁾.

Case of brain bilirubin deposition and its Comparison of vaginal delivery and Cesarean section delivery regarding bilirubin level 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, Living in highlands such as Badakhshan district of Afghanistan and Pamir Badakhshan 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⁾.

Importance of Research:

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 Afghanistan north part mothers for Cesarean section delivery (CS D), this study was designed to determine the relationship between occurrence of neonatal jaundice and the route of delivery.

II. METHODS

This prospective, cross-sectional study was conducted in 2019 in Accademic hospital of medical faculty of balkh university Afghanistan:

Inclusion criteria in the study: All the singleton term neonates (37-42 weeks of gestation), age mother contain research who had no risk factors for neonatal jaundice, were enrolled in the study.

The exclusion criteria: were parental incomepliance, 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 incompatability, 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 $\geq 15\text{mg/dl}$ and a direct serum bilirubin level of $\geq 1.5\text{mg/dl}$ were excluded from the study. Data collected throughout the whole year of 2012.

Two hundred cases of cesarean section were performed in the hospital, 91 cases were included in the study. 109 cases were excluded from the study.

The neonates were divided into two groups of normal vaginal delivery (NVD) and CS. Birth cesarean section is divided into two groups **Elective sesarean and section Emergency sesarean section.**

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 ethics verification committee has been observed in this investigating

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.

III. A REVIEW OF THE LITERATURE OR ARTICLES

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 breast-feeding 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 2012 compared full-term and near-term neonates with regard to hyper-bilirubinemia, 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⁾.

In a study by Olusanya et al., one-fourth of neonates with icterus had predisposing maternal factors.

Extreme neonatal hyperbilirubinemia was defined as maximum total serum bilirubin (TSB_{max}) level ≥ 450 $\mu\text{mol/L}$ and a ratio of conjugated serum bilirubin/TSB < 0.30 .⁽²⁵⁾

Extreme neonatal hyperbilirubinemia (median [range] TSB_{max} level: 491 [456-756] $\mu\text{mol/L}$), accounting for 1.7% of all extreme neonatal hyperbilirubinemia cases. During the first 10 days of life, hyperbilirubinemia was predominantly of unconjugated type.⁽²⁵⁾

Galactosemia is a potential cause of extreme neonatal hyperbilirubinemia, Thus it is important that galactosemia is part of the work up for unconjugated hyperbilirubinemia.⁽²⁵⁾

Extreme hyperbilirubinemia (plasma bilirubin ≥ 24.5 mg/dL) is an important risk factor for severe bilirubin encephalopathy. Several risk factors for hyperbilirubinemia are known, but in a large number of patients, a causal factor is never established. UGT1A1 is the rate-limiting enzyme in bilirubin's metabolism.⁽²⁶⁾

Hyperbilirubinemia arises from an imbalance between production and elimination of bilirubin.¹ Among newborn infants, it is almost universal and generally benign, but may in rare instances cause severe bilirubin encephalopathy. This condition is primarily seen with extreme hyperbilirubinemia (ie, plasma bilirubin values ≥ 24.5 mg/dL).⁽²⁶⁾

IV. 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 ± 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 ± 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 ± 2.9 mg/dl and 9.8 ± 3.4 mg/dl, respectively.

Table1.comparison of the mean bilirubin level regarding route of delivery

Number Delivery		Bilirubin level (mg. dl)	p-value *
51	Elective sesarean section	9.6+_ 4	P> .05
40	Emergency sesarean section	10+_ 2.90	P=0.53
91	Vaginal delivery	9.4 +_ 2.9	P=0.58

Table 2. The camparision between the mean bilirubin level of sesarin section and vaginal delivery groups

Number Children	Characteristic	Bilirubin level (mg . dl)	Bilirubin level (mg . dl)	p---value
		sesarean section delivery	Vaginal delivery	
11	Female	9.9 +_ 3.2	9.2 +_ 3.7	P> .05
12	Male	9.8 +_ 3.8	8.8 +_ 2.8	P> .005
10	Primigravid	9.2 +_ 3.2	8.7+_ 3.0	P> .05
10	Multigravid	10.2 +_ 3.5	9.9+_ 2.7	P> .05
20	History of neonatal jaundice Sibilings	12.2+_ 2.8	11.4 +_ 3.3	P> .05
10	Mothers age -20 years	11.1+_ 4.00	8.3 +_ 5.5	P> .02
10	Mother age 20 –35 years	9.6 +_ 3.4	9.3 +_ 2.7	P> .005
8	Mother age more than 35 years	11.6 +_ 8.1	10.0 +_ 2.8	P> .001

Table .3. The comparison between the mean bilirubin level of cesarean section without fight stress and cesarean section under fight of stress in Afghanistan Based on characteristic of neonates and under effect of fight stress in Afghanistan

Number of children	Characteristic	Bilirubin level (mg . dl)	Bilirubin level (mg. dl)	p---value
		cesarean section delivery without fight stress	cesarean section delivery under fight stress	
11	Female	9.9 +_ 3.2	11.2+_ 2	P> =.05
12	Male	9.8 +_ 3.8	9.9 +_ 1	P> 005
10	Primigravid	9.2 +_ 3.2	9.5+_ 2	P> .05
10	Multigravid	10.2 +_ 3.5	11+_ 1	P> .05
20	History of neonatal jaundice sibilings	12.2+_ 2.8	12+_ 3	P> .05
10	Mothers age -20 years	11.1+_ 4.00	11.1+_ 5	P> .02
10	Mother age 20 –35 years	9.6 +_ 3.4	11.8 +_ 2.1	P> .005
8	Mother age more than 35 years	11.6 +_ 8.1	12+_ 3	P=0.01

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).

Final results:

In the present study, in the conditions of without stress, children born to Cesarean section delivery newborn children had high bilirubin assets, which are the results of the table:2.

In our study, 91 mothers without under war stress were born by cesarean section .Their demographic characteristics and results were as follows.

1- The girl child was 11 silver. Their average bilirubin level was average 9.9 +_ 3.2**mg. Dl** was found in Mazar-e-Sharif laboratory in Balkh, Afghanistan. P> =.05

2. The number of children or boys was 12. Their mean bilirubin level was found to be 9.8 ± 3.8 mg. dl on average. $P > .005$

3- The first child was from the mother of Primigravid 10 children Their bilirubin level was found to be 9.2 ± 3.2 mg. dl on average. $P > .05$

4-- The first child was from the mother of Multigravid 10 children. Their bilirubin level was found to be on 10.2 ± 3.5 mg. dl average. $P > .05$

5 - From mothers with a history of siblings with neonatal jaundice to 20 Children had an average bilirubin level of 12.2 ± 2.8 mg. dl. $P > .05$

6- The age of 20-year-old mothers was 10 children. Their average bilirubin level was found to average 11.1 ± 4 mg. dl. $P > .02$

7- The age of mothers was between 20 to 35 with 10 children. Their bilirubin level was found to average 9.6 ± 3 mg. dl. $P > .005$

8-Mothers with age over 35 were found to have 8 children with a bilirubin level of 11.6 ± 8.1 mg. dl. $P = 0.01$

In the present study, in the conditions of war stress, children born to Cesarean section delivery newborn children had high bilirubin assets, which are the results of the table 3.

In our study, 91 mothers under war stress were born by cesarean section. Their demographic characteristics and results were as follows:

1- The girl child was 11 silver. Their average bilirubin level was average 11.2 ± 2 mg. dl was found in Mazar-e-Sharif laboratory in Balkh, Afghanistan. $P = .05$

2. The number of children or boys was 12. Their mean bilirubin level was found to be 9.9 ± 1 mg. dl on average. $P > .005$

3- The first child was from the mother of Primigravid 10 children Their bilirubin level was found to be 9.5 ± 2 mg. dl on average. $P > .05$

4- The first child was from the mother of Multigravid 10 children. Their bilirubin level was found to be on 11 ± 1 mg. dl average. $P > .05$

5- from mothers with a history of siblings with neonatal jaundice to 20 Children had an average bilirubin level of 12 ± 3 mg. dl. $P > .05$

6- The age of 20-year-old mothers was 10 children. Their average bilirubin level was found to average 11.1 ± 5 mg. dl $P > .02$

7- The age of mothers was between 20 to 35 with 10 children. Their bilirubin level was found to average 11.8 ± 2.1 mg. dl. $P > .005$

8- Mothers with age over 35 were found to have 8 children with a bilirubin level of 12 ± 3 mg. dl. $P = 0.01$

V. DISCUSSION

In our study Pediatric bilirubin level was received in women with cesarean section births compared with vaginal births finding high. The explanation is in Table 2

Bilirubin level was given to infants born by cesarean section under stress and warfare compared to children born without high stress and warfare finding high. The explanation is in Table 3.

VI. 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 significant association between neonatal jaundice in term infants based 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.

VII. prerequisites

In the conditions of Afghanistan, I have the following prerequisites

Children are the flowers of nature, efforts should be made to nurture them in the mother's womb so that we can present a healthy future generation to the society

1-Pregnant women should be kept away from stress and always receive psychotherapy.

2- Avoid unwanted cesarean sections

3- Try to give birth naturally so that a healthier child is born

4- To prevent violence and family stress during pregnancy as much as possible

5- I recommend exercise during pregnancy, it is anti-stress

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