

Original article

Risk Factors for Severe Hyperbilirubinemia and Exchange Transfusion in Neonates

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Abstract:

- **Background:** Neonatal jaundice is a frequent cause of hospital admission. Its incidence has increased in the last decade, affecting 65% of term babies and 80% of preterm babies. This study aims to identify risk factors for severe hyperbilirubinemia and exchange transfusion in neonates.
- **Methods:** In Kirkuk city, a prospective follow-up study was conducted in the neonatal care unit (NCU) of Azadi Teaching Hospital from 1st June 2019, to 1st June 2020. One hundred and sixty-four neonates with hyperbilirubinemia were enrolled. Relevant data were collected upon hospital admission, and patient management followed by American Academy of Pediatrics (AAP) guidelines, utilizing either phototherapy or exchange transfusion with phototherapy.
- **Result:** Among 164 cases, the mean TSB level was 16.6 mg/dL. Significant TSB elevations were seen in male neonates, Rh-negative mothers with Rh-positive babies, >37 weeks' gestation, admission after 72 hours, history of affected siblings or received phototherapy, and family history of hemolytic diseases. Mode of delivery, birth weight, cephalohematoma, infants of diabetic mothers, and feeding types were not significant. Phototherapy was primary treatment. Infants needing exchange transfusion had mean age 4.97 ± 2.24 days at NCU admission, TSB level 20.2 ± 2.84 mg/dL. Leading causes for ET were early maternity discharge and delayed NCU admission (72.4%).
- **Conclusions:** Neonatal severe hyperbilirubinemia was more prevalent in male neonates born >37 weeks, with Rh-negative mothers and Rh-positive babies, admitted after 72 hours, with a family history of hemolytic diseases, affected siblings, or received phototherapy. Phototherapy was the primary treatment, while the leading cause of ET was early maternity discharge and delayed NCU admission.
- **Keywords:** Neonatal hyperbilirubinemia, Risk factors, Exchange transfusion.

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INTRODUCTION

Neonatal jaundice within the first week of birth is a common cause of hospitalization ^(1,2), with 80% of premature babies exhibiting clinical symptoms such as yellowish skin and sclera due to elevated TSB levels ⁽³⁻⁵⁾. While most cases resolve spontaneously after 48 hours ^(6,7), extremely high TSB levels may lead to kernicterus and permanent brain damage ⁽⁸⁾. Early diagnosis and treatment of severe hyperbilirubinemia are crucial for neonatal health ⁽⁸⁾. Breastfed infants may experience higher indirect bilirubin levels compared to bottle-fed babies due to decreased fluid intake ⁽³⁾. Prolonged jaundice lasting more than 14 days can also occur ⁽⁶⁾. Pathological jaundice typically presents on the first day of life and can result from hemolysis, infection, or internal hemorrhage ^(9,10). Evaluating risk factors, such as maternal diabetes, medications during pregnancy, gestational age, male gender, cephalohematoma, delayed meconium passage, low birth weight, breast milk feeding, and family history of neonatal jaundice and hemolytic diseases, is important in disease management ⁽¹¹⁻¹⁶⁾. Exchange transfusion (ET) may be necessary when intensive phototherapy fails or in cases of excessive hemolysis or kernicterus ^(16,17). This study aims to identify maternal and neonatal factors associated with severe hyperbilirubinemia in neonates admitted to NCU in Azadi Teaching Hospital and to determine the predisposing factors for ET, thereby reducing the morbidity and mortality rate of severe hyperbilirubinemia.

PATIENT and METHOD

Ethical approval was obtained, and a prospective study was conducted in Azadi Teaching Hospital over one year, from June 1, 2019, to June 1, 2020. Out of 476 Neonatal Care Unit admissions, 164 babies were enrolled based on inclusion and exclusion criteria. Inclusion criteria covered neonates admitted with severe hyperbilirubinemia, while exclusion criteria excluded those with severe cardiorespiratory problems, congenital malformations, surgical conditions, or sepsis.

The method involved defining neonatal severe hyperbilirubinemia as a high TSB requiring phototherapy or exchange transfusion based on AAP guidelines. Detailed history and gestational age assessment were conducted using obstetric ultrasound reports. TSB levels, blood grouping, and Rh of mother and baby were determined.

Phototherapy was administered to babies lying supine in incubators with eyes and genitals covered while encouraging feeding. Phototherapy was discontinued when TSB levels fell below 12 mg/dL. Exchange transfusion involved umbilical vein catheterization and replacement of baby's blood with donor blood.

Maternal and neonatal data were collected, and statistical analysis was performed using SPSS version 21 and Microsoft Window. Continuous variables were expressed as mean, and descriptive data as percentages (%). Chi-square was used for comparison between different groups, with significance test when p-value <0.05.

RESULTS

In this study, one hundred and sixty four neonates with severe hyperbilirubinemia were analyzed. Males babies (42.7%), Rh+ve babies with Rh- mothers (15.2%), term babies(62.8%), babies with late admission(89.6%), babies with family history of hemolytic diseases (18.3%) and previous siblings affected with jaundice(40.2%) and or received phototherapy(27.4%) were having significantly higher mean of serum bilirubin levels (17.1, 18.6, 17, 16.8, 17.8, 17.3, 17.7) mg/dL respectively with P-value <0.05.

Babies had cephalohematoma (15.9%), babies with O+ve mothers (34.8%), babies of diabetic mothers (22%), babies with a birth weight > 2.5 kgs (83.5%), babies delivered by LSCS (64%) and babies with breast feeding (54.3%) were having more mean bilirubin level(17.5, 17, 16.9, 16.8, 16.8 & 16.7)mg/dL respectively but these relations were statistically not significant.

Table 1.

Table -1- Risk factors of neonatal hyperbilirubinemia

variables		No.	Percentage	Mean of TSB (mg/dl)	P-value
Sex	Male	70	42.7%	17.1	0.045*
	Female	94	57.3%	16.3	
Weight	<2.5kg	27	16.5%	15.9	0.102
	≥2.5kg	137	83.5%	16.8	
O+ve mothers		57	34.8%	17	0.148
Rh-ve mothers & Rh+ve babies		25	15.2%	18.6	<0.001*
Gestational age	≤37wks	61	37.2%	15.9	0.012*
	>37wks	103	62.8%	17	
Time of admission	≤3days	17	10.4%	15.3	0.028*
	>3days	147	89.6%	16.8	
Hx. of sibling affected with jaundice		66	40.2%	17.3	0.01*
Hx. of sibling recieved phototherapy		45	27.4%	17.7	0.002*

FHx. of hemolytic diseases		30	18.3%	17.8	0.009*
Type of delivery	NVD	59	36%	16.4	0.4
	S.C	105	64%	16.8	
Cephalohematoma		26	15.9%	17.5	0.06
Maternal D.M.		36	22%	16.9	0.52
Feeding	Breast F.	89	54.3%	16.7	0.141
	Bottle F.	62	37.8%	16.4	
	Mixed F.	13	7.9%	16.5	

* Significant (p-value < 0.05)

Phototherapy was the commonest mode of treatment used in (82.3%) of cases with mean TSB level not exceed 16mg/dL, while exchange transfusion was used only in (17.7%)of cases with mean TSB level was 20.2mg/dL. Table2.

Table -2- Treatment modalities in hyperbilirubinemia

Variables	No.	Mean of TSB (mg/dl)	Percentage
Phototherapy	135	15.9	82.3%
Exchange transfusion	29	20.2	17.7%

Out of the 164 patients, only 29 cases their TSB remained at high levels despite intensive phototherapy and treated by exchange transfusion. The most common cause for ET was early discharge from the maternity unit & late admission to the NCU (72.4%) which was significant. Although other causes included S.C delivery (69%), family history of previous siblings affected with jaundice (62.1%)and or received phototherapy(58%), female gender(51.7%), breast feeding(44.8%), ABO & Rh incompatibility(41.4%), preterm babies(34.8%) with low birth weight(27.6%) associated with high rate of ET but there were statistically not significant. Figure 1.

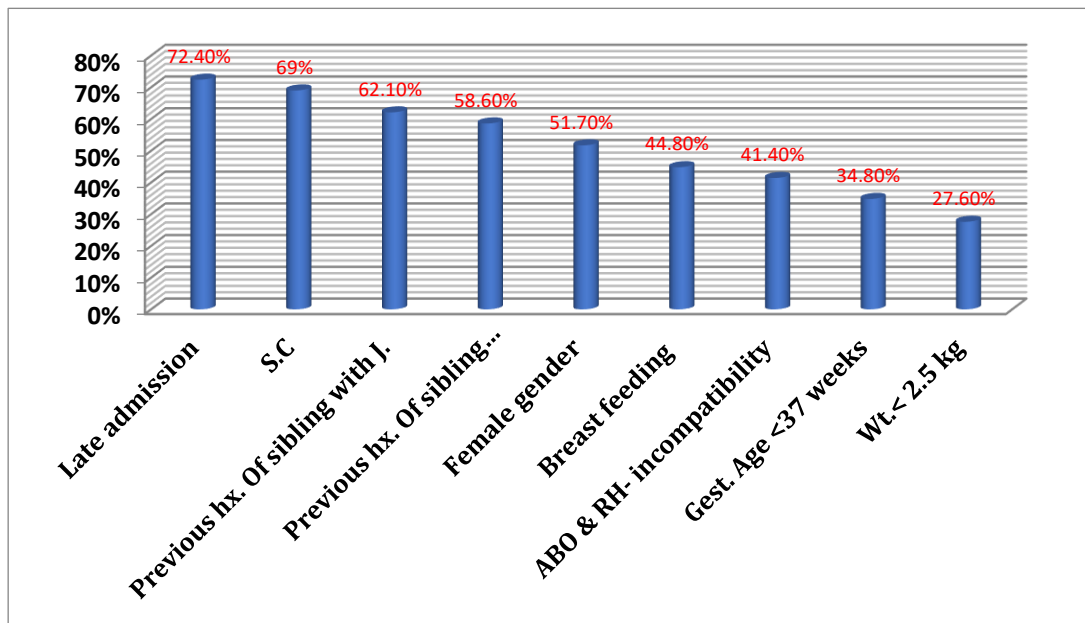


Figure-1- Risk factors of Exchange Transfusion in neonates

DISCUSSION

This study highlights the risk factors associated with neonatal severe hyperbilirubinemia. Hospital readmission rates and kernicterus cases have increased due to early discharge of healthy neonates from maternity units ^(18,19). Male gender is a risk factor for severe hyperbilirubinemia, consistent with previous studies ^(4,5). In our study, although more females (57%) were affected, males had significantly higher mean TSB levels.

Greater birth weight showed a linear relation with severe hyperbilirubinemia in many studies ^(5,6). In our study, babies with birth weight >2.5 kg had higher TSB levels, but this was not statistically significant. Rh incompatibility was associated with severe hyperbilirubinemia in our study, contrary to other research ⁽²²⁾. Rh-incompatible babies had significantly higher mean TSB levels.

Gestational age was another significant factor, with full-term babies having a higher incidence of severe hyperbilirubinemia ^(4,5,15). In our study, babies with gestation >37 weeks had significantly higher TSB levels. Late admission (after 72 hrs) was linked to higher TSB levels, consistent with previous findings ^(13,19)

A history of previous siblings affected by jaundice and receiving phototherapy was associated with higher TSB levels ^(10,11). Similarly, cases with a family history of hemolytic diseases had significantly higher TSB levels.^(9,10)

Mode of delivery did not show a significant association with severe hyperbilirubinemia in our study, differing from other researchs ^(13,24). Exclusive breastfeeding was not significantly associated with higher TSB levels, consistent with other studies ^(20,21). Infants of diabetic mothers had higher TSB levels, but the difference was not statistically significant, contrary to other findings.^(5,6,13)

Phototherapy was the primary treatment modality in most cases (82.3%), with only 17.7% requiring exchange transfusion along with phototherapy ⁽³⁾. The leading cause for exchange transfusion was early maternity discharge and late NCU admission (72.4%), aligning with other studies ^(16,17,23)

CONCLUSION

Severe hyperbilirubinemia is influenced by several predisposing risk factors. Male gender, full-term birth, and Rh incompatibility were associated with higher TSB levels. Babies admitted to the hospital after 72 hours of life exhibited elevated serum bilirubin levels and were more likely to require exchange transfusion (ET) and face readmission. Conversely, mode of delivery, birth weight, type of feeding, and maternal diabetes did not play a significant role in severe hyperbilirubinemia development.

Phototherapy emerged as the most commonly utilized treatment modality. The leading cause for ET was early discharge from maternity units and late admission to the NCU. Recognizing these risk factors before discharge and ensuring proper follow-up may prevent the development of severe hyperbilirubinemia and reduce irreversible complications. Ensuring vigilance and timely intervention during the neonatal period is crucial for the well-being of these infants.

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Ethical Clearance:

In accordance with the 2013 WMA Helsinki Declaration, all ethical aspects of this study were approved. Before enrolling the participants, an informed oral consent was obtained from their families as an ethical agreement. Additionally, approval from the hospital administrator was obtained, following document number 20 on 18th December 2022.

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Nil.

Conflicts of interest:

There are no conflicts of interest.

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