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Risk Factors and Outcome of Neonatal Hyperbilirubinaemia in a Tertiary Care Hospital

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ABSTRACT

Neonatal hyperbilirubinaemia is one of the commonest problems in the early days of life. Hyperbilirubinaemia occur in 80% of preterm and 60% of term infants in the first week of life. It is a significant cause of morbidity among neonates worldwide. So, the study aims to determine the risk factors of neonatal hyperbilirubinaemia and its outcome in a tertiary care setting. This cross-sectional type of descriptive study was conducted in the neonatal unit of the paediatrics department of Jalalabad Ragib-Rabeya Medical College Hospital, Sylhet, from September 2018 to February 2019. A total of 100 clinically jaundiced neonates were enrolled in the study. Data were collected by using a structured questionnaire. Study results revealed that 63% were male, and 61% babies were 1-3 days of age, with the majority (52%) had a birth weight ≥ 2500 grams. The majority (61%) of the patients were >37 weeks gestational age, and most (87%) of them belonged to middle socioeconomic conditions. Fifty-four percent of babies had the features of sepsis. Among the neonates, 12% had serum bilirubin levels of 20 mg/dl or more and 93% of patients were treated with phototherapy. Exchange transfusion was conducted in 8% of cases. Fifty-four percent of neonates were discharged within 5 days of admission. Seven percent (7%) of patients were discharged on request and 93% were discharged with advice after recovery. In conclusion, the present study found that 1-3 days of male babies with a birth weight ≥2500 grams and a gestational age >37 weeks having features of sepsis developed neonatal hyperbilirubinaemia. All of the neonates admitted in the hospital were improved at discharge.

Keywords: *Neonatal hyperbilirubinaemia, Risk factors, Outcome.*

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INTRODUCTION

Hyperbilirubinaemia in neonates is a common problem. About 5-10% of neonates have jaundice significant enough to require treatment[1]. Hyperbilirubinaemia occurs when there is an imbalance between the production and elimination of bilirubin in the body[2]. Jaundice is present in approximately 60% of term and 80% of preterm infants during the first week of life[3].

The accumulation of lipid-soluble, non-polar bilirubin pigment in the skin results in the yellow colouration[3]. A total serum bilirubin (TSB) of 5 mg/dL in neonates is usually recognised as jaundice[4]. A TSB of at least 20-25 mg/dL in term neonates may result in severe neonatal jaundice[5]. Hyperbilirubinaemia may result in a severe complication referred to as bilirubin encephalopathy or kernicterus when it reaches a toxic level. The Eunice Kennedy Shriver National Institute of Child Health and

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Human Development sponsored a conference in 2003 that proposed 'hazardous' hyperbilirubinaemia when bilirubin levels reach ≥30 mg/dL because of the perceived higher risk of neurologic injury[6].

The American Academy of Paediatrics (AAP) stated risk factors for hyperbilirubinaemia including blood group incompatibility (most commonly Rhesus or ABO incompatibility), prematurity, maternal age ≥25 years, history of a sibling receiving phototherapy, cephalohaematoma or significant bruising, male gender and discharge from the hospital within 72 hours[7].

Hyperbilirubinaemia usually resolves within 3-5 days without significant complications in the absence of haemolysis, sepsis, birth trauma or prematurity. However, epidemiological evidence suggests that severe neonatal jaundice (SNJ) results in substantial morbidity and mortality[7]. SNJ has been recognised as a significant cause of long-term neurocognitive sequelae, cerebral palsy, non-syndromic auditory neuropathy, deafness and learning difficulties[8]. The burden is higher in low-income and middle-income countries (LMICs) and has prompted calls for intense scrutiny and attention[9].

Ah et al.[9] obtained in their study that drugs may cause hyperbilirubinaemia and/or associated adverse effects. Certain drugs act as substrates or inhibitors of the enzymes and/or transporters involved in bilirubin excretion. Therefore, functional inhibition by drugs of the proteins responsible for the metabolism and excretion of bilirubin may directly and indirectly result in hyperbilirubinaemia. In this sense, as for drugs with a high hyperbilirubinaemic risk, caution should be taken in clinical practice to see whether or not they manifest hyperbilirubinaemia and its resultant side effects[10]. Drugs such as oxytocin (in the mother) and chemicals used in the nursery, such as phenolic detergents, may also produce unconjugated hyperbilirubinaemia[11].

Maamouri et al.[10] in a study found evidence for sepsis in 1.7% of neonates with hyperbilirubinaemia and 95% of the jaundiced neonates with sepsis were symptomatic (poor feeding, fever, respiratory distress). Sepsis should be considered as a probable cause of jaundice among neonates, especially in symptomatic cases. The mechanism of jaundice in neonatal sepsis may be related to liver involvement by infection or haemolysis, although this mechanism is not well known. Conjugated hyperbilirubinaemia was reported in 17% of cases, which were raised over 20% of total bilirubin. Maamouri et al.[10] indicated that urinary tract infections after and before sepsis during the first week of life may be associated with jaundice.

The most common treatment modalities for neonatal hyperbilirubinaemia are phototherapy, exchange transfusion (ET) and intravenous immunoglobulin[12]. However, due to constrained resources, devices for measuring bilirubin and effective phototherapy are lacking in LMICs, together with higher prevalence of blood group incompatibilities, late referrals and delayed recognition of excessive bilirubin levels in LMICs has necessitated excessive use of ETs[12]. Whereas the requirement for ET in developed countries has declined largely due to improved surveillance of infants with clinically significant jaundice, routine use of rhesus immunoglobulin prophylaxis to prevent primary isoimmunization of Rh-negative women and optimisation of blue light phototherapy[13].

One study examined the outcomes of various treatments for neonatal hyperbilirubinaemia where ABO incompatibility was found to be twice as common as Rh incompatibility. The majority of kernicterus patients died in the acute phase[14]. The incidence of Rh isoimmunization has decreased as a result of the introduction of Rh (D) immunoglobulin to Rh-negative mothers. Although neonatal hyperbilirubinaemia is a common event, it is of interest because of its extreme consequences and it also can be a source of considerable potential concern. Now with emerging affordable technologies, the worldwide prevention and management of neonatal hyperbilirubinaemia can more feasibly reach those at risk even in low-income settings[15].

Current evidence suggests that low and middle-income countries (LMICs) disproportionately bear the burden of severe neonatal hyperbilirubinaemia[14]. Another systematic review found that LMICs consistently report substantially higher rates of exchange transfusion and bilirubin-induced neurologic dysfunctions (acute bilirubin encephalopathy and chronic bilirubin encephalopathy or kernicterus) than in high-income countries[14]. So, the main thrust of interventions to curtail the burden of neonatal jaundice must be two fold, firstly to identify the infants with the most prevalent and readily detectable risk factors and secondly to reduce to the barest minimum avoidable delays to effective recognition, timely detection and treatment of infants with hyperbilirubinaemia[14]. So, the study aims to determine the risk factors of neonatal hyperbilirubinaemia and its outcome in a tertiary care setting.

MATERIALS AND METHODS

This was a cross-sectional type of descriptive study conducted in the neonatal unit of the paediatrics ward of Jalalabad Ragib-Rabeya Medical College Hospital, Sylhet, during the period of September 2018 to February 2019. Ethical clearance was duly obtained. Informed written consent was obtained before commencing the study. All the admitted neonates who were jaundiced with gestational age >28 weeks and birth weight >1000 grams were

enrolled in the study. Data were collected by using a structured questionnaire. Maternal age, occupation, education, presence of diabetes, consanguinity in marriage, and use of oxytocin during labour were considered as maternal risk factors. Gestational age of the infants, birth weight, blood group incompatibility, perinatal asphyxia, and birth trauma were considered as neonatal risk factors. Detailed neonatal and maternal information and progress of babies was noted regularly until discharge or death. All of the patients with clinical jaundice, regardless of the severity, were assessed for serum bilirubin. Socio-economic classifications in this study were made according to July 2017 per capita Gross National Income by World Bank calculations[16]. Statistical data was calculated by using Microsoft Excel. Categorical data was presented as frequency and percentage, and continuous variables were expressed as mean and standard deviation.

RESULTS

In our study, a total of 100 patients were taken; among them, the majority (61%) belonged to the 1-3 days age group. The mean age was 3.44±1.63 days, which ranged from 1 to 7 days. Among the study neonates, 63% were male and 37% were female. Most (80%) of the patients came from rural areas, and 20% were urban. Sixty-seven percent of the mothers were in the age group of 18 to 25 years. The mean mother's age was 24.86±4.42 years, which ranged from 18 to 38 years. Most (87%) of the family's monthly income was in the middle-income range, and 13% was in the lower-income range (table-I).

Regarding maternal risk factors of the study patients, the majority (32%) of the mothers were blood group A+ve. Seven percent of mothers received oxytocin during labour. Eight percent of patients had consanguineous parents. Five percent of patients had maternal diabetes mellitus. Most (77%) of the patients were delivered by LUCS (table-II).

Table-I: *Distribution of study patients by demographic profile.*

Demographic profile		Frequency	Percentage
Age (days)	1-3	61	61
	>3	39	39
Mean age (±SD) days		3.44±1.63	
Sex	Male	63	63
	Female	37	37
Residence	Rural	80	80
	Urban	20	20
Mother's age (in years)	18-25	67	67
Mother's education	>25	33	33
	Illiterate	26	26
	<SSC	42	42
	>SSC	21	21
	Post Graduate	11	11
Monthly family income (in BDT)	Middle income	87	87
	Low income	13	13

Table-II: *Distribution of study patients by maternal risk factors.*

Risk factors		Frequency	Percentage
Mother's blood group	A+ ve	32	32
	A-ve	1	1
	B+ve	30	30
	B-ve	1	1
	AB+ve	4	4
	O+ve	30	30
	O-ve	2	2
Oxytocin during labour	Yes	7	7
	No	93	93
Consanguinity	Yes	8	8
	No	92	92
Maternal diabetes mellitus	Yes	5	5
	No	95	95
Mode of delivery	NVD	13	13
	LUCS	77	77

Table-III: *Distribution of study patients by perinatal risk factors.*

Risk factors		Frequency	Percentage
Perinatal asphyxia	Present	21	21
	Absent	79	79
Multiple gestation	Present	05	05
	Absent	95	95
Sepsis	Present	31	31
	Absent	69	69
Cephalohaematoma	Present	02	02
	Absent	98	98
Gestational age (weeks)	28-32	04	04
	33-37	35	35
	>37	61	61
Birth weight (grams)	1000-1499	09	09
	1500-2499	39	39
	>2500	52	52

Table-IV: *Distribution of study patients by bilirubin level.*

Risk factors	Frequency	Percentage
10-<15	47	47
15-<20	41	41
≥20	12	12

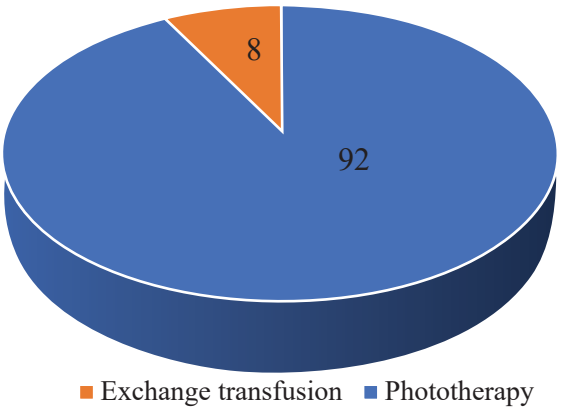

Figure-I: *Treatment of hyperbilirubinaemia.*

Table-V: *Distribution of study patients by duration of hospital stay.*

Hospital stay (days)	Frequency	Percentage	Mean
<5	54	54	
≥5	46	46	6.98±2.76

Table-VI: *Distribution of study patients by outcome.*

Outcome	Frequency	Percentage
Discharge with advice	93	93
Discharge on request	7	7

Perinatal risk factors of the study patients demonstrated that twenty-one percent of patients had birth asphyxia. Five percent of patients were of multiple gestation. Thirty-one percent of patients had sepsis. More than half (52%) of neonates belonged to the weight on admission of ≥2500 gm. Mean weight on admission was 2686.5±2434.2 grams, with a range from 1200 to 2600 grams. Sixty-one percent of patients belonged to gestational age >37 weeks (table-III).

Most of the patients (47%) had serum bilirubin below 15 mg/dL and 12% had 20 mg/dL or more (Table-IV). Regarding treatment of the study patients, it was observed that the majority (92%) patients improved with phototherapy, and only eight percent needed exchange transfusion (figure-1). Fifty-four (54%) patients had a hospital stay of <5 days. The mean hospital stay was 6.98±2.76 days, which ranged from 2 to 15 days (table-V). The majority of the patients (93%) were discharged after improvement (table-VI).

DISCUSSION

This study was carried out in the neonatal ward of Jalalabad Ragib-Rabeya Medical College Hospital, Sylhet. One hundred neonates with hyperbilirubinaemia were enrolled in the study. Mean age was 3.44±1.63 days. This finding is similar to Mostafa et al.[11] who found jaundice appeared in 2.89 days of the neonates. But Iskander et al.[7] study showed that the mean age of jaundiced neonates was 4.1 days of life. In another study, Onyearugha et al.[17] found the median age of the jaundiced infants was 11 days at the time of visiting the hospital. In this study, 63% of neonates were male and 37% were female who were suffering from hyperbilirubinaemia. Iskander et al.[7] studied 130 neonates to identify root causes for late presentation of severe neonatal hyperbilirubinaemia. Among 130 neonates, 89 were males and 41 were females. Similar observations regarding male predominance were also observed by several other investigators[4,18]. But Garosi et al.[19] found more female neonates are suffering with hyperbilirubinaemia in their study.

We found in our study that the mean age of mothers was 24.86±4.42 years. The mother's age of 67% ranged between 18-25 years. Mostafa et al.[11] found the mean age of mothers was 26.74±6.188 years, and Devi and Vijaykumar[20] observed that the mean maternal age was 25.6 years. In this study, 87% belonged to middle socioeconomic status. Whereas Mostafa et al.[11] found the majority (64.4%) of the patients belonged to low socioeconomic status.

In this present study, it was observed that 42% of mothers were under SSC level and 11% completed post-graduation. This finding was contradictory with Mostofa et al[11]. They found 11.1% did not finish secondary school, and 42.2% were university degree holders. Neonates with underaged, illiterate or semiliterate mothers, those who belong to low-income families, are found with hyperbilirubinaemia because of the unawareness of their mothers and family.

In this present study, 61 patients belonged to gestational age >37 weeks, which is supported by Kale et al[21]. They mentioned a statistically significant correlation between higher bilirubin levels and higher gestational ages. Watchko et al.[22] and Najib et al.[8] also found that a higher incidence of significant hyperbilirubinaemia was seen in babies with full-term gestation of more than 38 weeks. Kumar et al.[18] reported that the incidence of neonatal hyperbilirubinaemia was significantly higher (62.5%) in those newborns whose gestational age was <38 weeks as compared to those whose gestational age was ≥38 weeks, which contradicts the finding of our study.

Ah et al.[9] found no significant correlation between the mode of delivery and use of oxytocin with the development of hyperbilirubinaemia which is consistent with the finding of our study. But Garosi et al.[19] mentioned that bilirubin level was higher among naturally delivered babies in comparison to caesarean babies.

Sepsis was detected as a significant determinant of hyperbilirubinaemia in neonates by Kalakheti et al.[23] which contradicts the finding of the present study.

In this study, 54% of neonates stayed in the hospital for <5 days, and 46% of neonates stayed in the hospital for about 10-15 days. Our finding is closely similar to Sharma S[24] who found that 67.6% of patients stayed <4 days and 32.4% stayed >4 days in the hospital. Regarding discharge from the hospital in the current study, 93% were discharged after recovery, and 7% were discharged on request. No patients died during the study. Similarly, Sharma S[24] revealed that 86.2 percent of neonates were discharged after recovery, and 6.2 percent were referred to better centres; death was observed in only 0.7 percent of neonates in their study. Rasul et al.[14] found 4 (0.9%) neonates were discharged with neurological abnormality, and 12 (2.8%) patients in this study died in the hospital.

CONCLUSION

Neonatal hyperbilirubinaemia is one of the most common problems in the neonates with male predominance. Perinatal asphyxia, sepsis, prematurity, low birth weight, and the use of oxytocin during delivery and caesarean delivery are common perinatal and maternal risk factors. The most commonly used treatment modality was phototherapy, though exchange transfusion was needed in some cases. With prompt diagnosis and appropriate treatment, there is no risk of long-term morbidity and mortality in newborns with hyperbilirubinaemia.

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