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ETIOLOGICAL FACTORS OF NEONATAL HYPERBILIRUBINEMIA IN TRIBAL COMMUNITY OF MEGHALAYA, INDIA - A CROSS-SECTIONAL STUDY

Paediatrics

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ABSTRACT

Objective: To identify the etiological factors of neonatal hyperbilirubinemia in tribal population of Meghalaya, India.
Design: Cross sectional study.
Setting: Neonatal intensive care unit under (level II NICU) Department of Paediatrics and Neonatology of Nazareth Hospital, Meghalaya, India.
Participants: Neonates of Khasi, Jaintia and Garo tribes with neonatal jaundice admitted in NICU of Nazareth Hospital, Meghalaya, India.
Main Outcome Measures: Demographic variables of the study population, Mean TSB values of various etiological factors, Effect of various etiological factors in early onset neonatal jaundice, Nature and duration of interventions needed for the neonates studied.
Results: In 58.9% of the 409 neonates studied, no cause could be assigned for the development of jaundice. Of the remaining, 19.8% was attributed to low birth weight whereas 19% had ABO incompatibility and 10.8% were premature. 9.3% had sepsis, 8.5% had G6PD deficiency while 3.2% were born to mothers with diabetes mellitus. Rh incompatibility was the causative factor in 1.7%. In 1.7%, pre-lacteal feed was associated with jaundice. In 62.3% of cases delayed cord clamping was found to be associated.
Conclusions: Total serum bilirubin tends to be higher in female neonates, of term gestation, with birth weight 2500 g or above and with ABO incompatibility. Delayed initiation of breast feeding, those with positive history of neonatal jaundice in older siblings and those with proven neonatal sepsis were also found to have higher levels of bilirubin. Neonates who were given pre-lacteals and those born to diabetic mothers show lower mean total serum bilirubin levels. Most neonates who developed jaundice within 24 hours of life (early onset jaundice) had ABO incompatibility.

KEYWORDS

Etiological factors, Meghalaya, Neonatal jaundice, Tribal community.

In approximately 60% of term infants and 80% preterm infants jaundice is observed during the 1st week of life [1]. It is usually due to the deposition of unconjugated bilirubin in the skin. It can also be partly caused by deposition of conjugated bilirubin which is produced from the conjugation of unconjugated bilirubin in the liver cell microsome by the enzyme uridine diphosphoglucuronic acid (UDP)-glucuronyl transferase [1]. In most cases neonatal hyperbilirubinemia is a benign problem. Physiological role of bilirubin as an antioxidant has been well established. But high levels of unconjugated bilirubin can be toxic to the developing central nervous system of new born and it can cause neurological impairment even if the baby is born term. The present study assessed the factors that may influence neonatal hyperbilirubinemia and its prevalence in tribal infants born in a tertiary care centre of Meghalaya.

METHODS

This study was a hospital-based cross sectional study conducted in the neonatal intensive care unit of a tertiary care centre in Meghalaya. Data of all neonates belonging to Khasi, Jaintia and Garo tribes with neonatal jaundice who got admitted from 3rd September 2018 to 2nd September 2019 were included in study.

Need for hospitalization and nature of intervention were decided based on hour specific TSB nomogram for term neonates and birth weight specific cut-off values for those neonates born within 35 weeks of gestation or weigh less than 2500 gm. Neonates were enrolled by consecutive sampling. The data were collected and recorded in a pretested proforma after obtaining informed consent from the parents or guardian. Total number of NICU admissions with neonatal hyperbilirubinemia during the present study period was 442. Out of these, 33 babies were not enrolled in the study since one or both of their parents did not belong to the tribal populations of Meghalaya, viz; Khasi, Garo, Jaintia. Hence a total of 409 babies were enrolled into the present study.

Gender, maturity, birth weight, tribe, hours of life, hour specific TSB and hemoglobin, blood group of newborn and mother, family history of sibling requiring intervention for neonatal jaundice, mode of delivery, use of oxytocin during delivery, maternal illnesses, time of initiation of breast feeding, type of feeding, administration of prelacteals and duration of phototherapy were the parameters observed among studied neonates. DCT, sepsis screen, cell morphology, reticulocyte count, blood culture, serum albumin, ABG, serum electrolytes, G6PD level, TFT and urine culture were the additional tests performed when indicated.

Demographic variables, mean TSB values of various etiological factors, effect of various etiological factors in early onset neonatal jaundice, nature and duration of interventions needed were the outcomes studied.

Table I. Demographic Variables Of Study Population

Variable		No. of Cases	Percentage
Tribe	Khasi	267	65.3
	Garo	17	4.2
	Jaintia	82	20
	Mixed	43	10.5
Gender	Male	188	45.9
	Female	221	54.1
Gestation	Term	365	89.2
	Preterm	44	10.8
Birth weight	< 2500 g	81	19.8
	2500 g and above	328	80.1
Age at admission	Below 24 hours	26	6.4
	24 to 72 hours	173	42.3
	Beyond 72 hours	210	51.3

Mode of delivery	Normal delivery	184	45
	Instrumental delivery	35	8.6
	LSCS	190	46.4

RESULTS

409 neonates with jaundice whose both parents belonged to one of the three tribal populations of Meghalaya were enrolled into the study after obtaining due consent from guardian/attendant.

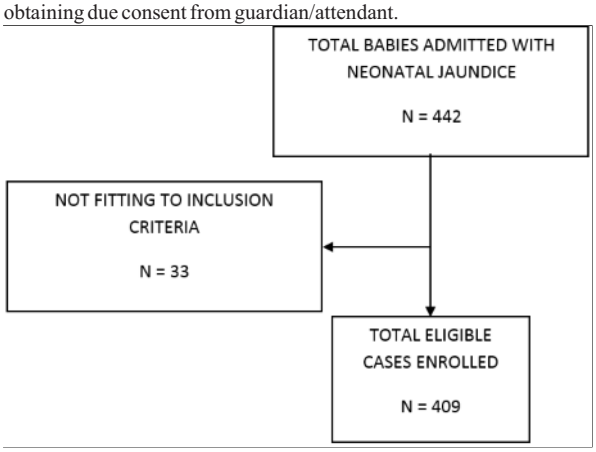

Figure I. Flow Diagram Of The Cases Of The Present Study

The mean initial TSB range was between 19.49 mg/dl to 19.96 mg/dl among neonates born to parents of various tribes. Neonates born to Khasi parents formed a statistically significant higher percentage of case in the initial TSB ranges of 10-14.9 mg/dl **(p < 0.001)** , 15-19.9 mg/dl **(p <0.01)** and 20-24.9 mg/dl **(p-value <0.01).**

Out of total 409 neonates, 188 were males and 221 were females. Female neonates showed a higher mean initial TSB among (mean TSB: 20.69mg/dl; SD: 8.28mg/dl) compared to male neonates (mean TSB: 18.37 mg/dl; SD: 3.49 mg/dl **(p <0.001).**

A statistically significant higher mean initial TSB value was observed among babies born with birth weight 2500 g and above (mean TSB: 20.31 mg/dl; SD:6.87 mg/dl) compared to those with a birth weight below 2500 g (mean TSB: 16.83 mg/dl; SD:4.58 mg/dl) **(p <0.001).**

7% (26/409) of neonates studied developed jaundice within 24 hours of life, of which 76.9% had ABO incompatibility. **(p <0.001).**

Neonates born by normal delivery showed a statistically significant higher number of cases among those who presented with initial TSB of 10-14.9 mg/dl **(p <0.0001)** whereas neonates born by LSCS showed a statistically significant number of cases among those who presented with initial TSB of 15 - 19.9 mg/dl **(p <0.001)**

19% (79/409) of all neonates enrolled had ABO incompatibility, which was associated with a statistically significant higher mean initial TSB value **(p : 0.001).** 14.9% of all neonates with initial TSB between 15 to 19.9 mg/dl **(p = 0.008)**, 83.3% of all neonates with initial TSB between 35 to 39.9 mg/dl **(p = 0.00006)** and 41.7% o of all neonates with initial TSB 40 mg/dl and above had ABO incompatibility **(p = 0.0465)**.

2% (7/409) of all cases had Rh incompatibility. 2% (7/409) of all cases studied received pre-lacteals. **(p = 0.032).** At the same time the study also revealed that 12.5% of all neonates with initial TSB of 10 to 14.9 mg/dl received prelacteals, which is statistically significant. **(p <0.001).**

38% (154/409) of all neonates studied were initiated on breastfeeding within one hour of life and it is seen that neonates for whom breastfeeding was initiated within 30 minutes of delivery showed a statistically significant low mean initial TSB levels. **(p = 0.003)**

9% (38/409) of all neonates studied had an older sibling with neonatal jaundice. **(p = 0.002)**.

Only 3% (13/409) of all neonates enrolled in the study were born to mothers with diabetes mellitus. Such neonates showed a statistically significant higher mean initial TSB value **(p = 0.03)**. But 10.7 % of neonates with initial TSB 10-14.9 mg/dl were born to mothers with diabetes mellitus. **(p = 0.00054)**

5% (22/409) of all neonates had proven sepsis. **(p = 0.002)**

5% (22/409) of all cases received both phototherapy and double volume exchange transfusion. The mean initial TSB value for neonates who received both interventions was markedly higher than those neonates who received only phototherapy **(p <0.001)**

Table II. Incidence Of Different Etiological Factors In The Development Of Neonatal Hyperbilirubinemia

Etiological factors	Number of patients	Percentage	Mean TSB +/- SD (mg/dl)
Idiopathic	241	58.9	18.21 +/- 3.28
Prematurity	44	10.8	17.58 +/- 4.75
Low birth weight	81	19.8	16.83 +/- 4.58
ABO incompatibility	79	19	21.88 +/- 8.99
Rh incompatibility	7	1.7	17.91 +/- 0.86
Pre-lacteal feeding received	7	1.7	14.3 +/- 0.14
Maternal DM	13	3.2	15.89 +/- 1.38
Delayed initiation of feeding	255	62.3	20.38 +/- 7.88
G6PD deficiency	16	8.5	21.11 +/- 11.16
Sepsis	22	9.3	23.79 +/- 10.5

DISCUSSION

The present study identified term neonates with normal birth weight, ABO incompatibility, improper breastfeeding practices, G-6-PD deficiency, positive family history of neonatal jaundice in older sibling and maternal diabetes mellitus as etiological factors associated with significantly high initial TSB. **ABO incompatibility was associated with a statistically significant number of cases of neonatal jaundice developing within 24 hours of life**.

The mean initial TSB in the study ranged between 19.49 mg/dl to 19.96 mg/gl. But it did not show any significant association with any tribe, even though **neonates born to Khasi parents had a statistically significant higher number of cases in the initial TSB ranges of 10-14.9 mg/dl, 15-19.9 mg/dl and 20-24.9 mg/dl.**

Out of total 409 neonates studied, 188 were males and 221 were females. The study showed a **higher mean initial TSB among female neonates (mean TSB: 20.69mg/dl; SD: 8.28mg/dl) compared to male neonates (mean TSB: 18.37 mg/dl; SD: 3.49 mg/dl)** which was statistically significant. But this gender predilection is not seen when the initial TSB is between 15-19.9 mg/dl, which accounted for 57.8% of study population. In this group almost equal numbers of cases were found among both genders (males-28.9%; females-28.6%). This is similar to the findings of Rithanya & Sheela,(2019)[2], where 55% of female neonates were found to have jaundice. This is of particular relevance in our study as Meghalaya is a state which has a matrilineal tradition amongst the local tribes and hence female neonates are better cared for and hence brought to medical attention faster. This is in stark contrast to the significant male preponderance as established by Sahoo et al(2016)[3] in Andhra Pradesh and Lalita Bahl et al (1994)[4] in Shimla and Carolyn et al (2006)[5].

11% (44/409) of neonates studied were born preterm where as 89% (365/409) were term neonates. **Term neonates showed a statistically significant higher mean initial TSB compared to preterm neonates** in the study. This is in contrast to the findings of Ali et al in Rajasthan (2016)[6], where 51% of neonates with hyperbilirubinemia were preterm. Bhutani et al (2013) in their study also found out that prematurity was a significant risk factor for hyperbilirubinemia and is known to be a basis for increased biologic vulnerability to risk of bilirubin induced neurotoxicity.

20% (81/409) of all neonates studied were of low birth weight while the rest (80%; 328/409) were 2500 g or above at birth. The study showed a statistically significant **higher mean initial TSB value among babies born with birth weight 2500 g and above (mean TSB: 20.31 mg/dl; SD:6.87 mg/dl) compared to those with a birth weight below 2500 g (mean TSB: 16.83 mg/dl; SD:4.58 mg/dl)**. It also showed a statistically significant higher number of cases among those with a birth weight of 2500 g or above when the initial TSB is 15-19.9 mg/dl.(p-value: 0.0039). Low birth weight was identified as a significant risk factor for the development of jaundice, but 80% of

neonates included in the present study belong to the weight band of 2500 g and above, which explains the finding. This is similar to the study done by Rithanya and Sheela in 2019[2]. No significant difference of onset of jaundice or level of mean TSB was noted on the basis of weight in studies by Jamir et al (2016)[7] and Ali et al (2015)[6].

7% (26/409) of neonates studied developed jaundice within 24 hours of life. Among those neonates 76.9% had ABO incompatibility. 68% of infants developed jaundice between 24-72 hours. This is similar to the findings of Ashish Kalraiya et al (2018)[8], where 86.6% of neonates developed jaundice between 24-72 hours. Ali et al (2015)(6) also stated that 58% of infants developed jaundice within 24-72 hours, with 9.6% developing jaundice within 24 hours and the most common cause was thought to be pathological.

45% (184/409) of all neonates studied were born by normal delivery, 46% (190/409) were by LSCS and remaining 9% (35/409) by instrumental delivery. No statistically significant correlation could be established between mode of delivery and mean initial TSB. Neonates born by normal vaginal delivery showed a statistically significant number of cases among those presented with initial TSB of 10 - 14.9 mg/dl whereas neonates born by LSCS showed a statistically significant higher number of cases among those presented within initial TSB of 15 - 19.9 mg/dl. No significant difference was noted in any of the studies reviewed based on the mode of delivery.

19% (79/409) of all neonates studied had ABO incompatibility. **ABO incompatibility was associated with a statistically significant higher mean initial TSB value**. This was similar to the findings of Ashish Kalraiya (2018)(8) and Ali et al (2015)[6].

2% (7/409) of all cases studied had Rh incompatibility. Present study did not reveal any statistically significant relationship between mean initial TSB value and Rh incompatibility. This was similar to the findings put forward by Rithanya and Sheela (2019)[2].

9% (38/409) of neonates studied had an older sibling with neonatal jaundice. **Neonates with positive family history of neonatal jaundice in sibling have a statistically significant higher mean initial TSB**. No contemporary study on neonatal jaundice has evaluated the same.

Only 3% (13/409) of all neonates enrolled in the study were born to mothers with diabetes mellitus. This is similar to the findings of Sahoo et al[3] and Ashish Kalraiya et al (2018)[8]. Present study showed that **10.7% of neonates with initial TSB 10-14.9 mg/dl were born to mothers with diabetes mellitus** which was statistically significant. Hence it was concluded that maternal diabetes was a significant etiological factor.

9% (16/409) of all cases had G6PD deficiency. Neonates with G6PD deficiency had a higher mean initial TSB, but the result was not statistically significant. 16.7% of neonates with initial TSB 40 mg/dl and above had G6PD deficiency, which was statistically significant. Hence it was concluded that **G6PD deficiency is associated with more severe neonatal jaundice**. But it was significantly lower than Anil Narang et al (1997)[9] and Jamir et al (2016)[7].

5% (22/409) of all neonates had proven sepsis. **Neonates with proven sepsis showed a statistically significant higher mean initial TSB.** Ali et al (2015)[6] and Rithanya et al (2019)[2] showed a similar incidence.

Table III. Comparison Of Etiological Factors With Other Similar Studies

Factors (in %)	Present study (2020)	Ali et al (2015)	Ashish Kalraiya et al (2018)	Jamir et al (2016)	Sahoo et al (2016)	Anil Narang et al (1997)	Rithanya et al (2019)	Lalita Bahl et a (1994)
Idiopathic	58.9	10.4	42.24	60.7		57.8	66.21	11.4
Prematurity	10.8			8.7	7.54		16.21	
LBW	19.8							
Maternal DM	3.2		3.2	0.2	3.8			
Sepsis	9.3	6	33.86	5.3	2.8	7.4	6.75	10.5
G6PD defeciency	8.5	0.8		12		17.7		
Delayed initiation of feeding	62.3				48		5.40	
ABO incompatibility	19	24.4	13.36	1.3	16	6.1	2.70	
Rh incompatibility	1.7	13.6	5.27	2	4.8	2.9	1.35	1.9

5% (22/409) of all cases received both phototherapy and double volume exchange transfusion. The mean initial TSB value for neonates who received both interventions was markedly higher than those neonates who received only phototherapy. Hence, **the higher the initial TSB more the possibility of requirement of double volume exchange transfusion.** This was similar to the findings of Jamir et al (2016)[7].

KEY MESSAGES

What Is Already Known?

There are various etiological factors responsible for development of neonatal jaundice including **prematurity, low birth weight, ABO incompatibility, Rh incompatibility, maternal diabetes mellitus, delayed initiation of feeding, G6PD deficiency and sepsis**.

What this study adds?

Neonates with positive family history of neonatal jaundice in sibling have significantly higher levels of total serum bilirubin.

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