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Original Research Article

Comparison of etiological factors of full term neonates with severe and moderate hyperbilirubinemia: a tertiary hospital based study in Eastern region of India

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ABSTRACT

Background: In approximately 60% of term infant and 80% 0f preterm infant developed hyperbilirubinemia in the first week of life. Different etiological factors are responsible for it. This study focuses on comparison of etiological factors of severe and moderate hyperbilirubinemia in full term neonates.
Methods: This is a tertiary hospital based descriptive survey research.80 full term neonates in each group with severe and moderate hyperbilirubinemia were selected by convenience sampling to compare the etiological factors of severe and moderate hyperbilirubinemia.
Results: Neonates with ABO incompatibility, cephalhematoma, G6PD deficiency, Rh incompatibility and polycythemia in both groups had higher mean total serum bilirubin (TSB) level. Neonates with sepsis in both the groups and idiopathic cases of moderate group showed lower mean TSB levels. Higher mean TSB level was seen in idiopathic cases of severe group. There was no neonate of breast-milk jaundice in the severe group but 2.50% of them belonged to the moderate group. There was significant association between severe and moderate bilirubin level and the post-natal age of neonate.
Conclusions: Mean total serum bilirubin level values were higher in cephalhematoma, G6PD deficiency, Rh incompatibility, ABO incompatibility, polycythemia, sepsis and in idiopathic cases in the severe group as well as in moderate group. Total serum bilirubin tends to be higher in the age group of 1-5 days. Awareness and etiology specific prevention is essential to control the damage due to hyperbilirubinemia.

Keywords: Etiological factors, Full term neonates, Hyperbilirubinemia

INTRODUCTION

In approximately 60% of term infant and 80% 0f preterm infant developed hyperbilirubinemia in the first week of life.[1] In most of the cases neonatal hyperbilirubinemia is seen among the preterm neonates and is a benign problem. It is also well established that high level of unconjugated bilirubin can cause neurological impairment even in full-term neonates. A recent study was done in the tribal communities of Meghalaya, showed that total serum bilirubin was higher among the term neonates, birth weight 2500gm or above, female sex and ABO incompatibility.[1-2] The etiology of hyperbilirubinemia is easily affected by environment and other relative factors.[2]

Therefore, the analysis of the etiology of neonates with severe and moderate hyperbilirubinemia in eastern India is of great significance to reduce the incidence of hyperbilirubinemia and its serious complications in this region.

The objective of the present study was to compare the etiological factors responsible for severe and moderate hyperbilirubinemia in full term neonates in eastern zone of India.

METHODS

Research approach and design

This study was a tertiary hospital based descriptive survey research.

Study location, duration and population

Study was conducted in the Sick Neonatal Care Unit of Dr. B.C. Roy P.G.I.P.S in Kolkata which is one of the largest tertiary care pediatric hospital in Eastern India. Data were collected between December 2000 to March 2022. All full-term neonates with severe and moderate hyperbilirubinemia were included as study population.

Sample size, sampling technique and criteria for sample selection

Non probability convenience sampling technique was adopted to select the 80 full term neonates in each group with severe and moderate hyperbilirubinemia admitted in the sick new born care unit according to inclusion and exclusion criteria after obtaining informed consent from the parents or legal guardians of the neonates (Figure 1).

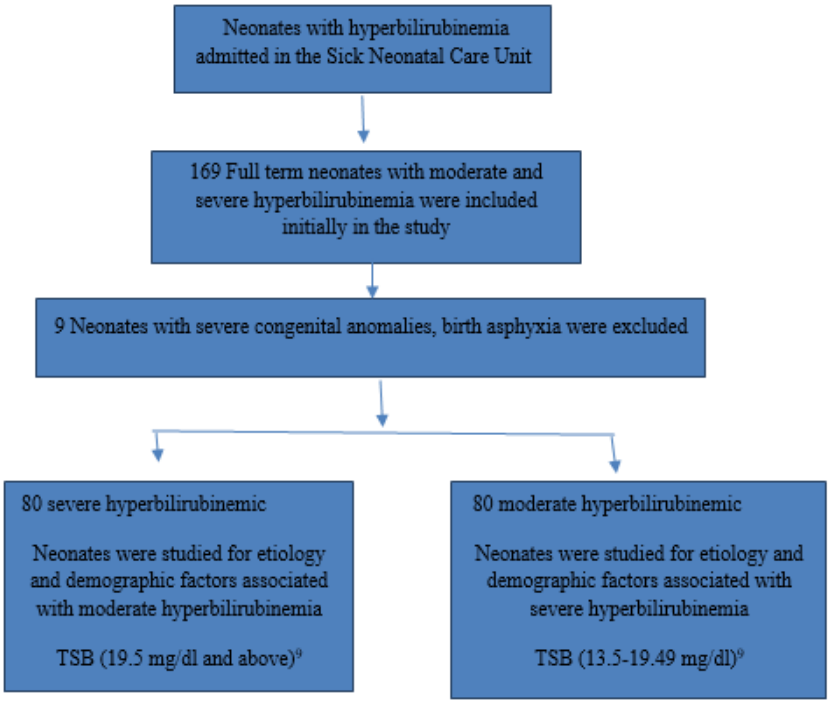

Figure 1: Flow diagram of cases in the present study.

Variables

Age of the neonate, gestational age, gender, birth weight, and religion, education of the father and mother, socioeconomic status and the etiological factors were the measurable variables.

Data collection tools and technique

The data were collected after approval from institutional ethics committee in a pretested proforma. Demographic tools and etiological factors were self-structured. Data sources were history, blood for total serum bilirubin, complete blood count, DCT, reticulocyte count, mother and baby's blood grouping. G6PD Level, RH typing. All the ethical principles of research were followed though out the data collection process. Strobe checklist guideline for observational study was followed for preparation of the manuscript. Standard Kuppuswami scale was used to categorize the parent's socioeconomic status.[7-8]

Statistical methods

Descriptive statistics were used to find the frequency, percentage, range, mean, median, standard deviations and normally distributed data of all the variables of the study and for analytical statistics chai square test of association was calculated. The statistical tools used to compute the data was MS Excel 07 and IBM SPSS-N-23.

RESULTS

Demographic characteristics of the study participants

73.75% of the neonates with severe and 60% with moderate hyperbilirubinemia were in the age group of 1-5 days.85% of the neonates with severe hyperbilirubinemia and 81.25% with moderate hyperbilirubinemia had gestational age between 37-39 weeks. 67.50% and 76.25% of neonates with severe and moderate hyperbilirubinemia respectively were having birth weight more than 2500gm. 53.75% in severe group and 61.25% in the moderate group were male.52.50% in the severe group and 53.75% in moderate group belonged to Hindu religion. 60% of the fathers in the severe group and 47.50% of the fathers from the moderate group were educated to the secondary level. 62.50% of mothers from the severe group and 60% from the moderate group were educated to the secondary level. 61.25% of parents in the severe group and 67.50% of parents in the moderate group belonged to lower middle class. No family belonging to upper class was found to be included in the study belonged to upper class (Table 1).

Comparison of gestational age, postnatal age, birth weight and TSB level of neonates

In the severe group the mean TSB level was 25.17mg/dl with a range between 39.9-19.96 mg/dl, and the median was 24.2. In the moderate group the mean TSB level was 16.67 mg/dl with a range between 19.4-13.9 mg/dl and the median was 16.8. So, data obtained were normally distributed.

In the severe group the mean birth weight was 2.69 kg with a range between 3.7 -1.6 kg and the median was 2.7. In the moderate group the mean birth weight was 2.66 with a range between 4-1.67 kg and the median was 2.67kg (Table 2).

Table 1: Frequency and percentage distribution showing demographic characteristics of neonates.

Demographic characteristics	Severe hyperbilirubinemia		Moderate hyperbilirubinemia	
	Frequency	**Percentage**	**Frequency**	**Percentage**
Age (in days)				
1-5	59	73.75	48	60
5-10	19	23.75	18	22.50
10-15	1	1.25	6	7.50
>15	1	1.25	8	10
Gestational age (in week)				
37-39	68	85	65	81.25
39-42	12	15	15	18.75
Gender				
Male	43	53.75	49	61.25
Female	37	46.25	31	38.75
Birth weight (in gms)				
<2500	26	32.50	19	23.75
≥2500	54	67.50	61	76.25
Religion				
Hindu	42	52.50	43	53.75
Muslim	38	47.50	37	46.25
Socio economic status				
Lower	5	6.25	4	5.00
Upper lower	19	23.75	14	17.50
Lower middle	49	61.25	54	67.50
Upper middle	7	8.75	8	10
Upper	nil	-	nil	-
Educational qualification of father				
Primary	20	25	19	23.75
Secondary	48	60	38	47.50
Higher secondary	6	7.50	16	20.00
Graduate and above	6	7.50	7	8.75
Educational qualification of mother				
Primary	17	21.25	17	21.25
Secondary	50	62.50	48	60.00
Higher secondary	10	12.50	10	12.50
Graduate and above	3	3.75	5	6.25

Table 2: Comparison of gestational age, postnatal age, birth weight and TSB level of neonates.

Variables	Severe hyperbilirubinemia						Moderate hyperbilirubinemia					
	Range	Mean	Median	SD	Q1	Q3	Range	Mean	Median	SD	Q1	Q3
TSB level	39.9-19.96	25.17	24.2	4.61	21	28	19.4-13.9	38.26	38	1.21	37	38
Post-natal age	17-1	4.42	4	2.76	2	6	21-1	5.92	5	4.15	3	5
Birth weight	3.7-1.6	2.69	2.7	0.46	2.4	3	4-1.67	2.66	2.67	0.42	2.5	2.67
Gestational age	42-37	38.2	38	1.14	37	39	42-37	38.26	38	1.21	37	38

Different etiological factors and their incidence in the development of neonatal hyperbilirubinemia

No cause (idiopathic) was found in 16.25% of severe and 13.75% of moderate hyperbilirubinemia. Among the known causes, 48.75% in the severe group and 36.25% in the moderate group were attributed to ABO incompatibility. 16.25% in severe group and 13.75% in moderate group had G6PD deficiency. 11.25% in severe group and 13.75% in moderate group had polycythemia as the causative factor. 2.50% in each group had cephalhematoma. Rh incompatibility was the causative factor in 2.50% in severe group and 3.75% in moderate group. 2.50% had sepsis in severe group whereas 13.75% had sepsis in moderate group. There was no case of breast-milk jaundice in severe group but 2.50% cases in the moderate group had breast-milk jaundice (Table 3).

Table 3: Different etiological factors and their incidence of neonatal hyperbilirubinemia.

	Severe hyperbilirubinemia			Moderate hyperbilirubinemia		
Etiological factors	**Fr**	**%**	**Mean±SD**	**Fr**	**%**	**Mean±SD**
Sepsis	2	2.50	20.56±0.21	11	13.75	16.81±1.54
ABO incompatibility	39	48.75	26.68±2.36	29	36.25	16.96±1.12
Breast milk jaundice	Nil	-	-	2	2.50	16.20±0.21
Cephalhematoma	2	2.50	29.36±1.21	2	2.50	17.02±0.29
G6PD deficiency	13	16.25	26.84±3.21	11	13.75	17.08±0.94
Idiopathic	13	16.25	25.36±2.25	11	13.75	15.49±1.03
Polycythaemia	9	11.25	23.94±4.26	11	13.75	17.03±1.51
Rh incompatibility	2	2.50	26.75±2.29	3	3.75	17.60±0.96

Major causes of moderate and severe hyperbilirubinemia

ABO incompatibility (48.75% In severe group and 36.25% In moderate group), G6PD deficiency (16.25%in severe group and 13.75% in moderate group), polycythaemia (11.25% in the severe group and 13.75% in the moderate group) and sepsis (2,50% in severe group and13.75% in moderate group) are found to be the major causes of moderate and severe hyperbilirubinemia. Idiopathic cases (16.25% in severe group and 13,75% in moderate group) constituted another major cause (Table 3).

Causes of hyperbilirubinemia and mean TSB values

Mean TSB values were higher in cephalhematoma, G6PD deficiency, Rh incompatibility, ABO incompatibility, polycythemia, sepsis and in idiopathic cases in the severe group as well as in moderate group (Table 3).

Association of severe hyperbilirubinemia with etiology and demographic factors

There was no association of severe hyperbilirubinemia with etiology of jaundice, birth weight, gestational age, sex, religion, socioeconomic status and education of the parents of the neonates. The association of severe hyperbilirubinemia was found only with the age (1-5 days) of the neonate (p=0.01).

DISCUSSION

ABO incompatibility (48.75% in severe group and 36.25% in moderate group), G6PD 8 (16.25%in severe group and 13.75% in moderate group), polycythaemia (11.25% in the severe group and 13.75% in the moderate group) and sepsis (2.50% in severe group and 13.75% in moderate group) are found to be the major causes of moderate and severe hyperbilirubinemia. Idiopathic cases (16.25% in severe group and 13.75% in moderate group) constituted another major cause. Considering the mean serum bilirubin level, this result was supported by Jia-Xin Xu et al, Mohan et al, Kalraiya et al considering the mean serum bilirubin level.[1-3]

The present study showed that mean total serum bilirubin tends to be higher with the etiology of ABO incompatibility, G6PD deficiency, polycythemia, sepsis and idiopathic cases. Higher mean TSB Levels are also found with the etiology of G6PD deficiency, Rh, ABO incompatibility and in idiopathic cases in the study done by Mohan et al.[1]

The commonest cause of hyperbilirubinemia was ABO incompatibility and this was supported by the study of Kalraiya et al and Xu et al.[3,2]

The association of severe hyperbilirubinemia was found in the neonates of 1-5 days. This study was supported by Mohan et al.[1]

There was no association of severe hyperbilirubinemia with etiology of jaundice, birth weight, gestational age, sex. This is not supported by study of Rithanya et al, Sahoo et al in Andhra Pradesh and Bhal et al.[4-6]

This study adds that cephalhematoma and polycythemia are also the contributing factors of jaundice in both the group whereas breast feeding jaundice is only seen in moderate hyperbilirubinemia group.

Limitations

During inclusion of subject's randomization was not done. It is a single center study.

CONCLUSION

Hemolytic disease like ABO incompatibility followed by G6PD deficiency and idiopathic causes are the main causes for the full term neonates in Eastern India. Hyperbilirubinemia can cause hearing loss, motor and intellectual development disorders, and even death. This can cause heavy burden for the family as well as nation. Awareness among the health care delivery members as well as among the parents is important. Specific prevention and treatment according to the etiology may reduce the ill effect of hyperbilirubinemia.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Annexure-I: Strobe checklist.

	Item No.	Recommendations	Page no.
Title and abstract	1	*(a)* Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) *Cohort study*-Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*-Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*-Give the eligibility criteria, and the sources and methods of selection of participants (*b*) *Cohort study*-For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*-For matched studies, give matching criteria and the number of controls per case	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4
Bias	9	Describe any efforts to address potential sources of bias	-
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	
Statistical methods	12	*(a)* Describe all statistical methods, including those used to control for confounding (*b*) Describe any methods used to examine subgroups and interactions (*c*) Explain how missing data were addressed (*d*) *Cohort study*-If applicable, explain how loss to follow-up was addressed *Case-control study*-If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*-If applicable, describe analytical methods taking account of sampling strategy (*e*) Describe any sensitivity analyses	4
Participants	13*	(a) Report numbers of individuals at each stage of study-eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage Consider use of a flow diagram	4 13
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) *Cohort study*-Summarise follow-up time (eg, average and total amount)	5,10
Outcome data	15*	*Cohort study*-Report numbers of outcome events or summary measures over time	5-6

Continued.

	Item No.	Recommendations	Page no.
		Case-control study-Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study*-Report numbers of outcome events or summary measures	
Main results	16	*(a)* Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included *(b)* Report category boundaries when continuous variables were categorized *(c)* (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	5-6
Other analyses	17	Report other analyses done-eg analyses of subgroups and interactions, and sensitivity analyses	-
Discussion			
Key results	18	Summarise key results with reference to study objectives	7
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	7
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7
Generalisability	21	Discuss the generalisability (external validity) of the study results	
Other Information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	8