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Original Research Article

The study of association of fetal and maternal factors in the occurrence of hyperbilirubinemia in early neonatal period

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ABSTRACT

Background: Hyperbilirubinemia in neonates is considered to be one of the common phenomena which generally occurs during the first week of life and usually leads to NICU admission in both term and preterm new-born babies. It is also regarded as one of the most common causes which leads to neonatal morbidity and mortality.
Methods: A total of 100 neonates along with their mothers were enrolled in the study from time period between 2018 to March 2019. Newborns were assessed daily for the jaundice and serum bilirubin levels were done. Various fetal-maternal factors included in proforma were. analysed to find out the association of feto-maternal factors in the occurrence of significant neonatal hyperbilirubinemia. Two groups, group A <15.7 mg/dl and group B>=15.7 mg/dl were taken. For data analysis chi square test is applied and p-value is calculated.
Results: Statistically significant association between total serum bilirubin with neonatal factors like birth weight ($p<0.014$), maturity ($p<0.011$), period of gestation ($p<0.003$), and heart rate abnormality ($p<0.005$) and maternal factors like age in years ($p<0.05$), oral contraceptive pills use ($p<0.005$), and anti-epileptics use ($p<0.034$) were found to be linked to neonatal hyperbilirubinemia.
Conclusions: Neonatal jaundice should be considered as the main policy in all health care settings of the country. Therefore, identification of factors affecting the incidence of jaundice can be effective in preventing susceptible predisposing factors in new-borns and high-risk mothers.

Keywords: Aternal factors, Hyperbilirubinemia, Neonates

INTRODUCTION

Hyperbilirubinemia in neonates is considered to be one of the common phenomena which generally occurs during the first week of life and usually leads to NICU admission in both term and preterm newborn babies.[1-3] Based on the present incidence, about "sixty percent" of the term newborn and "eighty percent" of premature babies have clinical symptoms, including yellowish coloration of the skin, mucous membrane and sclera, caused by increased serum bilirubin levels.[4,5]

Jaundice when appears on the first day of life is always considered as pathologic, therefore, it is imperative to find its causes. Early jaundice mainly occurs due to increased hemolysis of the red blood cells and internal hemorrhage (cephalhematoma, liver or spleen hematoma) or infection. Furthermore, jaundice is also considered to be pathologic when it persists even after two weeks.

Various predisposing factors that are responsible in the occurrence of this disease are gestational diabetes mellitus, race, lower gestational age, polycythemia, male sex, cephalhematoma, medications, Trisomy 21, weight loss, breastfeeding, delayed passage of meconium and family history of jaundice in previous siblings.[6-10] The other common cause of jaundice can also be "ABO incompatibility" while Rh incompatibility and mode of

delivery can be among the other probable factors. Furthermore, congenital infections like Cytomegalovirus, rubella, toxoplasmosis, Syphilis, and maternal age more than 25 years are some of the other factors which may contribute.[11]

An inappropriate balance between bilirubin production and its conjugation is the main mechanism which leads to neonatal hyperbilirubinemia, which further leads to an increase in serum bilirubin levels. It can also occur due to the immature hepatic development and rapid breakdown of red blood cells.[12-15]

Even though icterus is a nonthreatening condition, but daily examination and clinical assessment of all the newborns is very beneficial and essential in preventing them from developing severe jaundice further leading to "acute bilirubin encephalopathy".[16] Bilirubin accumulation in the brain may results in brain injury which can be temporary or permanent. Even though, Kernicterus is usually uncommon event but regarded as a grave complication of jaundice. Therefore, it is of paramount importance to diagnose jaundice early.[17,18]

Physiological or nonpathological jaundice results due to insufficient uptake, transport and conjugation of serum bilirubin in the hepatocytes of newborn. Several Other factors including absence of intestinal bacteria, diminished or decrease in gastrointestinal motility and deferred passage of "bilirubin rich meconium", which converts bilirubin into urobilinogen also contributes in causing jaundice by increasing "enterohepatic circulation".[19,20] Delay in maternal breastfeeding initiation and nursing care problems result in maternal milk insufficiency and increases the chances of neonatal hyperbilirubinemia.[21]

Phototherapy, exchange transfusion, IV immunoglobulins and antiepileptics like phenobarbitone are the various treatment modalities available in the management of jaundice.

METHODS

Hospital based "cross sectional observational" study was conducted in the department of pediatrics in TMMC and RC, Moradabad from July 2018 - 2019.

Inclusion criteria

- All the preterm/term/postterm neonates delivered in TMMC and RC, who have developed clinically significant jaundice according to Krammer Zone Stage 5 and Hour-specific bilirubin nomogram.

Exclusion criteria

- Neonates in whom informed written consent not given by the attendants.
- Neonates who left hospital against medical advice.

All the neonates fulfilling the inclusion criteria were examined daily from birth until 7 days of life for evidence of clinical jaundice

Babies who were found icteric uptill sole (according to Krammer zone staging), the investigations like Total Serum Bilirubin, Direct serum bilirubin, Indirect Serum Bilirubin and baby blood group were send in order to assess the severity and cause of jaundice.

Reports were compared with HOUR-SPECIFIC BILIRUBIN NOMOGRAM.

Babies in whom initial T.S.B level is at or above the phototherapy range were enrolled after taking informed written consent from mother/father/legally acceptable caregiver.

Details of demographic data, antepartum/intrapartum events were taken from mother and medical records as per the proforma.

Babies in whom initial T.S.B levels did not fall in the range of pathological jaundice are followed up for worsening jaundice and were enrolled later on un till 7 day of life during their hospital stay

Various fetal-maternal factors observed in proforma are analysed to find out the association of feto-maternal factors in the occurrence of significant neonatal hyperbilirubinemia.

RESULTS

A total of 100 neonates along with their mothers were included in the study. In the present study, 86% of the mothers were in the age group between 20-30 years, 59% of them were multiparas, 18% of them had history of hypertension (antenatal complication), around 23% of them had history of thyroid disorders, 8% of them had history of gestational diabetes, about 41% were anemic, only 4% of them had antepartum hemorrhage.

Majority (63%) of them underwent delivery under spinal anaesthesia, 9% of them underwent oxytocin induced delivery and most (37%) of them had bad obstetrical history (Table 1).

The data presented in (Table 2) reveal that 57% of the neonates were male babies, around 57% were belongs to birth weight of 1.5-2.5 Kgs, majority (55%) of them had a maturity of SGA, around 55% of them had >37 weeks of period of gestation, most (46%) of them were first order babies, only 9% of them had meconium stained amniotic fluid delivery, about 5% of them had heart rate abnormality, only 8% had lower APGAR score, majority (64%) born through LSCS, and most (73%) of them had

exclusive breast feeding and around 41% of the neonates had blood group incompatibility.

Table 1: Frequency and percentage distribution of sample characteristics (maternal factors) (n=100).

Demographic variables		N	%
Age in years	20-30	86	86.0
	>30	14	14.0
Parity	Primi	41	41.0
	Multi	59	59.0
History of hypertension (antenatal complication)	Yes	18	18.0
	No	82	82.0
History of thyroid disorder (antenatal complication)	Yes	23	23.0
	No	77	77.0
History of gestational diabetes (antenatal complication)	Yes	8	8.0
	No	92	92.0
Anemic (antenatal complication)	Yes	41	41.0
	No	59	59.0
Antepartum hemorrhage (antenatal complication)	Yes	4	4.0
	No	96	96.0
Type of delivery		57	28.5
Spontaneous		28	28.0
Oxytocin induced		9	9.0
Spinal anesthesia		63	63.0
Bad obstetrical history		28	14.0
Yes		37	37
No		63	63

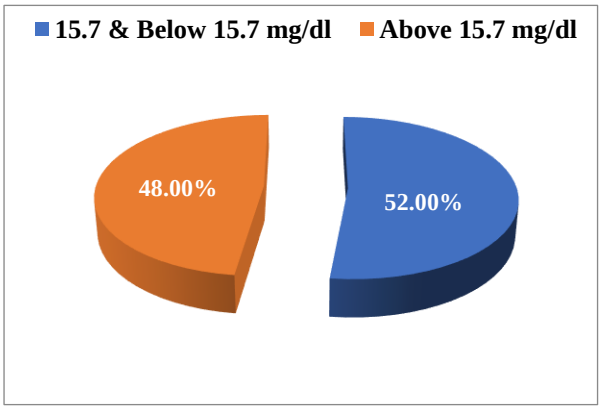

Figure 1: Distribution of neonates based on category of total serum bilirubin value in mg/dl.

Pie chart showing frequency and percentage distribution of the neonates based on category of total serum bilirubin value in mg/dl (N=100) (Figure 1). The data presented in Figure 4 revealed that 52% of the neonates have total serum bilirubin value 15.7 and below 15.7 mg/dl and 48% of them have total serum bilirubin value above 15.7 mg/dl.

The data presented in the (Table 3) depicts that there is a statistically significant association between total serum bilirubin with maternal factors like age in years ($p<0.05$), oral contraceptive pills use ($p<0.005$), and anti- epileptics use ($p<0.034$).

Table 2: Frequency and percentage distribution of sample characteristics (Neonatal factors) (N=100).

Demographic variables		N	%
Gender of baby	Male	57	57.0
	Female	43	43.0
Birth weight	> 2.5 kgs	37	37.0
	1.5-2.5 kgs	57	57.0
	1-1.4 kgs	4	4.0
	< 1 kgs	2	2.0
Maturity	SGA	55	55.0
	AGA	43	43.0
	LGA	2	2.0
Period of gestation	> 37 wks	55	55.0
	37-40 wks	45	45.0
Birth order	First	46	46.0
	Second	30	30.0
	Third and higher	24	24.0
Meconium stained amniotic fluid delivery	Yes	9	9.0
	No	91	91.0
Heart rate abnormality (<60)	Yes	5	5.0
	No	95	95.0
Low APGAR score (<6)	Yes	8	8.0
	No	92	92.0
Mode of delivery	NVD	36	36.0
	LSCS	64	64.0
Type of feeding	Exclusive breast feeding	73	73.0
	Exclusive top/formulated feeding	5	5.0
	Breast feeding with occasional top/formulated feeding	22	22.0
Blood group incompatibility	Yes	41	41.0
	No	59	59.0

The data presented in the (Table 4) depicts that there is a statistically significant association between total serum bilirubin with neonatal factors like birth weight ($p<0.014$), maturity ($p<0.011$), period of gestation ($p<0.003$), and heart rate abnormality ($p<0.005$).

DISCUSSION

The study was carried for a period of 12 months with an aim to study the association between neonatal hyperbilirubinemia and fetal-maternal factors, which will help in understanding multiple risk factors responsible in the development of hyperbilirubinemia and taking measures to prevent health consequences associated with hyperbilirubinemia among neonates. The observations made in this study are discussed here.

Table 3: Association between categories of total serum bilirubin with selected maternal factors (N=100).

Maternal factors		Total serum bilirubin		X^2	Df	p value
		15.7 and below 15.7 mg/dl	Above 15.7 mg/dl			
Age in years	20-30	48	38	3.580	1	0.05*
	>30	4	10			
Parity	Primi	25	16	2.243	1	0.134
	Multi	27	32			
History of hypertension	Yes	9	9	0.035	1	0.851
	No	43	39			
History of thyroid disorder	Yes	13	10	0.245[a]	1	0.621
	No	39	38			
History of gestational diabetes	Yes	4	4	0.014[a]	1	0.906
	No	48	44			
Anemic	Yes	24	17	1.190[a]	1	0.275
	No	28	31			
Antepartum hemorrhage	Yes	2	2	0.007[a]	1	0.935
	No	50	46			
Type of delivery	Spontaneous	19	9	4.562	2	0.102
	Oxytocin induced	3	6			
	Spinal anesthesia	30	33			
Bad obstetrical history	Yes	15	22	3.090	1	0.079
	No	37	26			
Oral contraceptive pill use	Yes	2	11	8.026	1	0.005*
	No	50	37			
Anti-epileptics use	Yes	0	4	4.514	1	0.034*
	No	52	44			
*p<0.05 (level of significance)						

Table 4: Association between categories of total serum bilirubin with selected neonatal factors (N=100).

Neonatal factors		Total serum bilirubin		X^2	Df	p value
		15.7 and below 15. mg/dl	Above 15.7 mg/dl			
Gender of baby	Male	31	26	0.302	1	0.582
	Female	21	22			
Birth weight	> 2.5 kgs	13	13	10.548	3	0.014*
	1.5-2.5 kgs	24	24			
	1-1.4 kgs	33	33			
	< 1 kgs	24	24			
Maturity	SGA	36	36	9.039	2	0.011*
	AGA	19	19			
	LGA	15	15			
Period of gestation	> 37 wks	36	36	8.864	1	0.003*
	37-40 wks	19	19			
Birth order	First	29	29	5.112	2	0.078
	Second	17	17			
	Third and higher	12	12			
Meconium stained amniotic fluid delivery	Yes	7	7	2.633	1	0.105
	No	2	2			
Heart rate abnormality (<60)	Yes	5	5	4.858	1	0.005*
	No	0	0			
Low APGAR score (<6)	Yes	6	6	1.843	1	0.272
	No	2	2			
Mode of delivery	NVD	21	21	0.904	1	0.342
	LSCS	15	15			
Type of feeding	Exclusive breast feeding	36	37	1.838	2	0.399
	Exclusive top/formulated feeding	4	1			
	Breast feeding with occasional top/formulated feeding	12	10			
Blood group incompatibility	Yes	22	22	0.077	1	0.782
	No	19	19			

*p<0.05 (level of significance)

Distribution of sample characteristics (maternal factors)

In the present study, 86% of the mothers were in the age group between 20-30 years, 59% of them were multiparas, 18% of them had history of hypertension (antenatal complication), around 23% of them had history of thyroid disorders, 8% of them had history of gestational diabetes, about 41% were anemic, only 4% of them had antepartum hemorrhage. Majority (63%) of them underwent delivery under spinal anaesthesia, 9% of them underwent oxytocin induced delivery and most (37%) of them had bad obstetrical history.

The study conducted by (Taneja, Pande, Kumar, and Agarkhedkar) supported the findings of the current study. The study was conducted among 100 mothers. The study findings revealed that, 73% of the mothers were in the age group of <30 years, 49% of them were multiparas, 8% of them had history of gestational diabetes, 17% of the mother had preeclampsia and 59% of them underwent oxytocin induced delivery.[22]

The study conducted by (Tavakolizadeh, Izadi, Seirafi, Khedmat, and Mojtahedi) supported the findings of the current study. The study was conducted among 200 mothers.

The study findings revealed that, the mean age of mothers was 28 years, 70.5% of them were multiparas, around 89.1% of mothers underwent oxytocin induced delivery and 48% of the mother had history of abortion.[23]

Distribution of sample characteristics (neonatal factors)

In the present study, 57% of the neonates were male babies, around 57% had birth weight of 1.5-2.5 Kgs and around 37% were >2.5 kgs. Majority (55%) of them were SGA. Around 55% of them were >37 weeks of period of gestation. Most (46%) of them were first order babies of which only 9% of them had meconium stained amniotic fluid, about 5% of them had heart rate abnormality, 92% of neonates had APGAR more than 6, majority (64%) of the neonates were born through LSCS and most (73%) of them had exclusive breast feeding and around 41% of the neonates had blood group incompatibility.

The study conducted by Pankajakshy, supported the findings of the current study. The results revealed that 56% of them were male babies, 16.4% of the babies had Rh incompatibility, 8.2% of the mothers had history of antepartum hemorrhage, 1.4% of them were anemic, 37% of the neonates were born through LSCS.[24]

The study conducted by Brits et al, supported the findings of the current study. The study was conducted among 96 others and their infants. The findings revealed that the mean age of the mother was 26.5 years and the mean birth weight of the neonates was 3.15 kgs and mean gestational age was 38.5 weeks.[25]

Distribution of neonates based on category of T.S.B. (total serum bilirubin) value in mg/dl

In the present study, 52% of the neonates had T.S.B. (total serum bilirubin) value below 15.7 and 48% of them had T.S.B. (total serum bilirubin) value above 15.7 miligram per decilitre.

The study conducted by (Tavakolizadeh, Izadi, Seirafi, Khedmat, and Mojtahedi) supported the findings of the current study. The study revealed that 81.5% of the neonates had total serum bilirubin below 15.7 mg/dl and 18.5% of them had T.S.B. (total serum bilirubin) value above 15.7 miligram per decilitre.[23]

The study conducted by Pankajakshy, 2017 supported the findings of the current study which revealed that 29.2% of neonates did not develop neonatal jaundice and 70.8% of neonates developed neonatal jaundice.[24]

Association between categories of (T.S.B.) total serum bilirubin with selected maternal factors

In the present study, there is a statistically significant association between total serum bilirubin with maternal factors like age in years probability of less than 0.05, oral contraceptive pills use probability of less than 0.005, and anti-epileptic use probability of less than 0.034 and there is no statistically significant association between total serum bilirubin with maternal factors like parity, history of hypertension, anemia, history of thyroid disorder, history of gestational diabetes, antepartum hemorrhage and type of delivery probability of more than 0.05.

The study conducted by Pankajakshy, contradicted and supported the findings of current study. The findings revealed that there is a statistically significant association between serum bilirubin with history of hypertension ($p<0.001$), history of gestational diabetes ($p<0.001$), type of delivery ($p<0.001$) and there is no statistically significant association between serum bilirubin with maternal factors like parity, antepartum hemorrhage ($p>0.05$).[24]

Similarly, the study conducted by (Taneja, Pande, Kumar, and Agarkhedkar) contradicted and supported the findings of this study. The findings revealed that there is no statistically significant association between serum bilirubin with maternal factors, maternal age ($p>0.05$) and there is no statistically significant association between serum bilirubin with maternal factors like parity and history of gestational diabetes ($p>0.05$).[22]

Association between categories of total serum bilirubin with selected neonatal factors

In the present study, there is a statistically significant association between total serum bilirubin with neonatal factors like birth weight ($p<0.014$), maturity ($p<0.011$), period of gestation ($p<0.003$), and heart rate abnormality

(p<0.005) and there is no statistically significant association between total serum bilirubin with gender of baby, birth order, meconium stained amniotic fluid, APGAR score, mode of delivery, type of feeding and blood group incompatibility (p>0.05).

The study conducted by (Mirghafourvand, Seyedi, Jannat Dost, Mohammad-Alizadeh-Charandabi, and Asghari Jafarabadi) supported some of the variables of this study. The study results revealed that there is a statistically significant association between total serum bilirubin with neonatal factors like period of gestation, age, type of feeding (p<0.001) and there is no statistically significant association between total serum bilirubin with neonatal factors like blood group incompatibility (p>0.05).[26]

The study conducted by (Oyapero et al) does not supported few of the findings of the current study. The study results revealed that there is no statistically significant association between total serum bilirubin with gender of baby, birth weight, gestational age, mode of delivery (p>0.05).[27]

CONCLUSION

This study concluded that early recognition of various maternal and fetal factors is beneficial and favorable in preventing the babies from severe jaundice. Concerning about the consequences of irreversible complications due to hyperbilirubinemia and the prevention of these complications, the present study was intended to investigate the several predisposing (maternal and neonatal) risk factors in the occurrence of jaundice in newborn babies delivered in TMMCRC, Moradabad.

The study proved that neonatal variables such as low birth weight babies weighing between 1.5-2.5 kgs, SGA, term newborns, neonates with heart rate abnormality, low apgar score were more commonly developed jaundice. Jaundice was also seen in babies with blood group incompatibility including both ABO and Rh incompatibility. Maternal variables like maternal age of between 20-30yrs, use of oral contraceptives and antiepileptics shows positive correlation with incidence of jaundice in neonates.

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