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Neonatal Hyperbilirubinemia Associated With Oxytocin Labour Augmentation

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Abstract:
Introduction*: Neonatal Hyperbilirubinemia is a common manifestation among the newborns. Most of the neonates (50% of full term and 80% of preterm) develop it on account of increased production of the bilirubin among other reasons. There are many studies suggesting that administering oxytocin to induce labour caused neonatal hyperbilirubinemia.*
Objective*: To compare the incidence of hyperbilirubinemia in neonates born to mothers with and without oxytocin augmentation during labour.*
Materials and Methods: *100 Patients were taken for this study. All the Women were admitted in the labour room with spontaneous onset of labour, in latent or active phase of 1st stage of labour at Chittaranjan Seva Sadan carrying pregnancy with period of gestation 38 weeks and above. The patients were divided into two groups.50 women fulfilling all inclusion and exclusion criteria who had oxytocin administered were considered for the study group and 50 women with same criteria without oxytocin administration were considered as control group. Total bilirubin levels were measured on day 1 by collecting 10ml of cord blood at delivery and on day 3 and 5 by heel prick using spectrophotometry. Data was analysed in MS excel sheet. Statistical analysis was done through unpaired one tailed 't' test.*
Results: *Average total bilirubin was 4.99 on day 1, 8.9 on day 3, and 5.75 on day 5 in the study group and 3.68 on day 1, 5.68 on day 3, and 3.74 on day 5 for the control group. 15 babies were admitted in NICU with a mean stay of 3.5 days where 11 babies received phototherapy in the study group compared to admission of 4 babies with a mean stay of 2.75 days with 4 babies receiving phototherapy in control group.*
Conclusion: *The findings in this study show that oxytocin administration during labour for augmentation results in increased total bilirubin levels in the neonate, increased NICU admissions and mean stay along with phototherapy. Since all the common causes of neonatal hyperbilirubinemia in an otherwise normal pregnancy were ruled out, the results may be attributed primarily to oxytocin administration.*

Keywords: ***Hyperbilirubinemia, Oxytocin, phototherapy***

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I. Introduction:

Neonatal Hyperbilirubinemia is a common manifestation among the newborns. Most of the neonates (50% of full term and 80% of preterm) develop it on account of increased production of the bilirubin(less lifespan of the RBC and high haemoglobin), decreased hepatic uptake of bilirubin in plasma, defective bilirubin concentration, defective bilirubin excretion, increased enterohepatic circulation. It is generally mild and appears after 2-3 days and peaks after 4-5 days of birth in term neonates and generally less than 12-15mg%. It is a bit deeper and appears earlier in case of preterm infants but never occurs before 24 hours. There may be certain conditions where hyperbilirubinemia may be exaggerated, like cephalhematoma, Intra ventricular haemorrhage, hypothyroidism, hypoxia, congenital heart diseases, delayed passage of meconium, congenital infections, polycythemia and certain drugs.[1]

Oxytocin is a hormone produced endogenously in the supraoptic and paraventricular nucleus of the hypothalamus and stored in the posterior pituitary and released in the blood circulation. Synthetic oxytocin can be administered from outside to enhance the action of endogenous oxytocin. It predominantly affects the uterine

smooth muscles and causes contraction of the uterine musculature. Its action is physiological. In small doses oxytocin has vasodilatory properties and might cause transient hypotension and tachycardia. But in high concentrations, due to activation of vasopressin receptors, it has weak antidiuretic property and pressor activity. In case of delayed progress of labour due to inadequate uterine contractions, synthetic oxytocin may be supplemented from outside to aid the uterine contraction and subsequent vaginal delivery.[2]

There are many factors which can lead to development of Hyperbilirubinemia in a neonate like blood group incompatibility, gestational age, preeclampsia, certain drugs used by mother, abnormal deliveries and oxytocin administration.[3,4,5,6.]

The neonatal hyperbilirubinemia practice guidelines published in 2004 by the American Academy of Paediatrics (AAP) expresses the paediatric community's concern regarding bilirubin-induced neurological pathology.[7] Serum bilirubin levels at birth - normally 1.8-2.8mg/dl. Between the 3rd and 4th day the bilirubin levels in mature infants increases to 5-10mg/dl. It is clinically manifested with bilirubin level of more than 5 mg/dl and is harmless. But in some cases may lead to neurotoxicity in severe condition, therefore early detection and treatment of neonatal hyperbilirubinemia is crucial in the prevention of bilirubin induced encephalopathy.[8,9]

Many theories have been proposed to explain hyperbilirubinemia in neonates caused due to oxytocin administration to mother. Most plausible explanation for this is the possibility that administering oxytocin stimulates uterine contractions with redistribution of the blood between placenta and the fetus.[10] More specifically increased red cell mass of the infant would result in more bilirubin production from degradation of these RBCs.[11-14]Other minor fascinating reasons may be probable effect of oxytocin on RBC directly causing premature removal from the circulation, stimulation of haeme oxygenase activity and increased heme breakdown, inhibition of glucoronyl transferase,[15] interference with normal hepatic maturation process.[16]Though the validity of these reasons is under question, they may be considered for studies.

Though medical education and research is pushing its limits, study on administering oxytocin effects on neonate needs to be vast and the effects need to be segregated and the proper pathophysiology needs to be established with reproducible results. Oxytocin is the most commonly used drug in obstetric practice, and is on the WHO list of essential medicines. Neonatal hyperbilirubinemia may have adverse effects later on in the life.

II. Objectives:

1) To compare the incidence of hyperbilirubinemia in neonates born to mothers with and without oxytocin augmentation during labour.

2) To study other neonatal outcome parameters like Apgar scores, NICU admission and stay, need for phototherapy.

III. Materials And Methods:

Place of Study: After getting institutional Ethics committee approval, this study has been conducted in the department of Obstetrics and Gynaecology of ChittaranjanSevaSadan college of Obstetrics, Gynaecology and Child Health, Kolkata.

Type of study: Prospective comparative observational study

Strength of the study: 150 women (75 women in control group and 75 women in study group) were included after proper informed consent. As the labour progressed, some women in both groups were dropped due to appearance of various exclusion criteria (25 in study group and 22 in control group, we excluded 3 more cases from control group for equal distribution). S0, 100 women, 50 in each group were finally included in the study.

Duration of the Study: 9 months (from March 2019 to December 2019)

Inclusion and Exclusion criteria:

Primigravida mothers with normal BMI, with uncomplicated low risk term pregnancy (≥38 weeks) with spontaneous onset of labour needing augmentation of labour delivered vaginally (Normal Vaginal Delivery) were included in the study.

Pregnant women with Rh Negative pregnancy, GDM /overt diabetes, APH, evidence of Placental insufficiency, FGR, Oligohydramnios, Polyhydramnios, Hypo/Hyperthyroidism, on any medications other than Iron and Folate supplementation along with intrapartum features of evidence of fetal distress, meconium stained liquor and instrumental vaginal delivery/ caesarean section modes of delivery were excluded from the study. Also babies born with cord around the neck, congenital anomalies/infections, evidence of pathological jaundice, polycythemia, cephalhaematoma, birth weight less than 2500 grams, Apgar score less than 6 were excluded from the study as well.

Some women (25 in each group) were excluded after recruitment.

Sample design: Women admitted in the labour room with spontaneous onset of labour, in latent or active phase of 1st stage of labour at Chittaranjan Seva Sadan carrying pregnancy with period of gestation 38 weeks and

above.50 women fulfilling all inclusion and exclusion criteria were considered for the study. Similarly 50 women with same criteria were considered as control group.

Method of data collection:

Preliminary data like demographic information, antenatal history, clinical findings of each visit and investigation reports of all women were collected from Antenatal card.

Date and indication of admission to hospital were noted.

Findings of intrapartum FHR monitoring by CTG or stethoscope were recorded and partogram was maintained.

After delivery, perinatal outcomes were studied in detail and recorded. Total bilirubin levels were measured on day 1 by collecting 10ml of cord blood at delivery and on day 3 and 5 by heel prick.[17] Bilirubin was calculated by spectrophotometry. Any maternal complication was also noted.

Parameters and Procedures:

A. Maternal

1. Maternal demographic and obstetric data: Age, Parity, Gestational age
2. Labour events: FHR tracing by CTG, Partogram, Colour of liquor, Oxytocin administration.
3. Postpartum – any complications like PPH, mortality.

B. Baby

Apgar score at 5 minutes, Birth weight ,Features of birth asphyxia, Total bilirubin levels (Day 1,3,5), Admission to NICU ,Number of days stay in NICU and Phototherapy details.

Study Tools:

Case Record Form, Antenatal OPD Ticket, CTG machine and CTG paper: BPL cardiotocography machine, Partogram, Sphygmomanometer, Weighing machine, Measuring tape.

Study Procedure:

It was a prospective comparative observational study. After approval from the Ethics Committee of the Institution, Informed written consents were taken from all women recruited for and willing to participate in this study. Women considered for this study were primigravida carrying pregnancy with period of gestation 38 weeks and above.

Women admitted in labour room with spontaneous onset of labour in either latent or active phase of first stage of labour. Admission Cardiotocography was done in all cases. Partograph was plotted in all the cases and progression of labour was followed up in all the cases. Internal examination was performed every 4 hours in case of spontaneous rupture of membranes and 2 hourly in case of artificial rupture of membranes. Women in whom meconium stained liquor was noted were excluded from the study. Ringer Lactate was used for intrapartum fluid administration. Cases without satisfactory progress of the labour due to inadequate uterine contractions were administered oxytocin to augment labour. Protocol used was a low dose oxytocin labour augmentation protocol starting with a dose of 2 milli international units of synthetic oxytocin. No. of uterine contractions, duration of the uterine contraction and intensity of the uterine contractions, maternal pulse, fetal heart rate were noted. Dose of oxytocin was slowly stepped up in case of inadequacy of uterine contractions. Final dose of oxytocin used and the duration of the augmentation was noted.

Table 1:

Starting dose	Drip rate	Obsevation time	Fetal Heart rate	Maternal Vitals	No. and intensity of uterine contractions	Remarks
2 milli units	16 drops/min	30 minutes				
4 milli units	16 drops/min	15 minutes				
8 milli units	32 drops/min	Maximum dose given				

The above given chart was maintained to check for the maternal and fetal parameters during labour.

All labor events including intrapartum FHR monitoring by intermittent auscultation by stethoscope or continuous electronic fetal monitoring was done and persistent fetal bradycardia, when observed, was noted.

Labour was followed up until the delivery and cases with normal vaginal delivery without any instrumentation were included.

Cases, where babies were born with cord around the neck , cephalhematoma, features of birth asphyxia, congenital anomalies, low birth weight were excluded from the study to reduce the chances of results being because of the above said reasons.

All the newborns were attended by a neonatologist and all the details were duly noted.

After delivery maternal outcomes were noted

Perinatal outcomes like birth weight, Apgar score, NICU admissions, indication for admission, No. of days of admission were noted. Total bilirubin in the neonates on day 1, 3 and 5 were noted.

50 women were considered in the control group with similar inclusion and exclusion criteria where labour was not augmented with oxytocin. All the above mentioned parameters were noted in the babies born to these mothers and compared to the results of the women in the study group.

IV. Results And Discussion

Table2: Maternal Demographic and Obstetric Variables:

This table shows the maternal age, BMI and gestational age distribution.

Variables		Study group(Oxytocin administered) n=50	Control n=50
Age	<20 YEARS	31	19
	21- 25 YEARS	19	31
BMI	18.5-25	50	50
Gest Age	38-39^{+6} WEEKS	35	45
	>40 WEEKS	15	5

Fig 1:

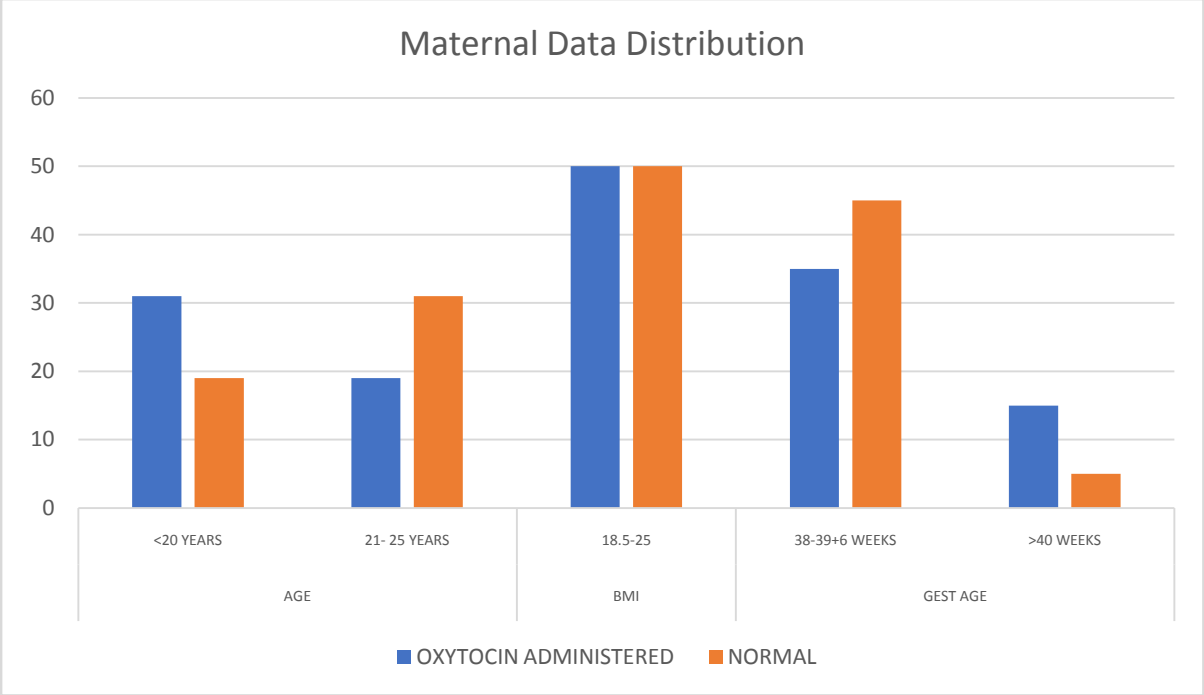


Table3: Birth weight

BIRTH WEIGHT (IN GMS)	STUDY GROUP(OXYTOCIN ADMINISTERED) n=50	CONTROL N=50
2500-2750	20	19
2750-3000	22	18
3000 and above	8	8

Table4: Neonatal OutcomeVariables Distribution:

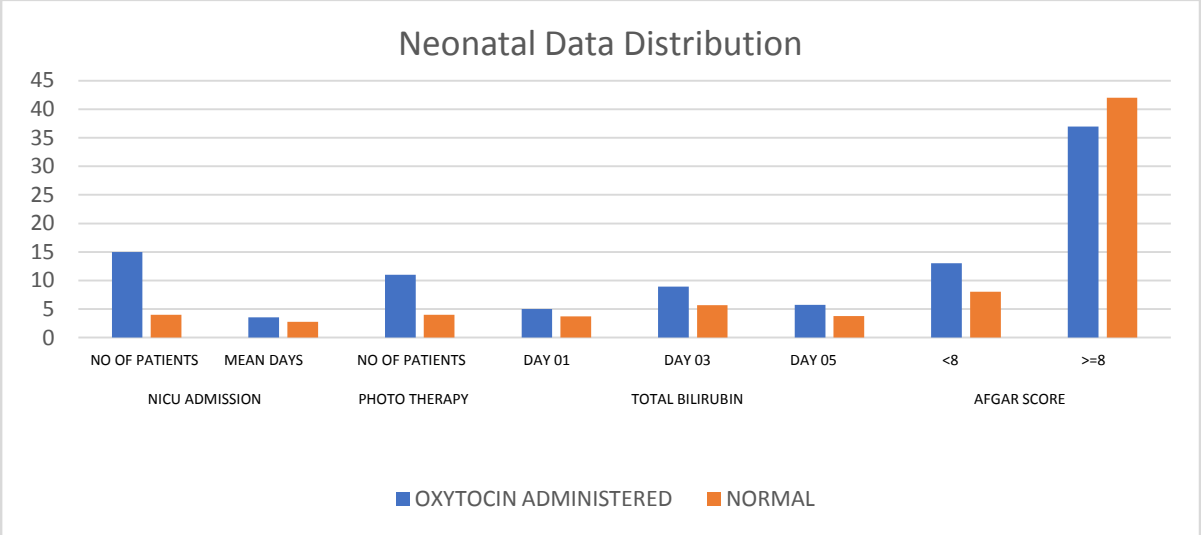
This table shows Apgar scores, NICU admissions, No. of days of stay and Mean bilirubin levels in both study and control group.

Variables		Study group (Oxytocin Administered)n=50	Control group. N=50	Mean Difference	p-Value
Nicu Admission	No Of Patients	15	4		
	Mean Days	3.53±1.47	2.75±0.5	0.7	<0.05*
Phototherapy Given	No Of Patients	11	4		
Total Bilirubin	Day 1	4.99±1.20	3.68±0.95	1.31	p<0.05*
	Day 3	8.90±3.62	5.68±2.96	3.22	p<0.05*
	Day 5	5.75±1.71	3.74±1.57	2.01	p<0.05*
Apgar Score	6-8	13	8		

	>8	37	42		

(Statistically significant *)

Fig 2:



Oxytocin has been an integral and important part of managing labour in our country since a long time now. Risks like transient intra uterine fetal compromise, birth asphyxia and increased operative interventions are well studied and documented. Uncommon conditions that may be associated with oxytocin administration in the mother during labour is hyperbilirubinemia in the neonates. Though this hyperbilirubinemia is well within the physiological limits, there is a theoretical risk and a few studies suggesting that the oxytocin administered do cause it and it has been verified in our study as well with increased mean bilirubin levels, NICU admissions and mean stay, increased rates of need for phototherapy in women where oxytocin was used for augmentation of labour.

This is a prospective observational comparative study and women between 18-25 years were considered in the study with most women aged 19 years. In total 100 women were considered in the study and they were divided equally into 2 groups, 50 women were considered in the study group where labour was augmented with Oxytocin and 50 women were considered in the control group where labour was not augmented with Oxytocin. In both groups most women had a BMI of 21.

32 women had a gestation age of 39 weeks, 13 women had a gestation age of 38 weeks, and only 5 women had a gestation age of more than 40 in the control group. Similarly, 21 women had a gestation age of 39 weeks, 14 women had a gestation of 38 weeks, and 15 women had a gestation age of more than 40 in the study group.

In the study group 20 cases had birth weight between 2500-2750 gm, 22 cases had birth weight between 2750-3000 gm, and 8 cases had birth weight above 3000 gm. In the control group, 19 cases had birth weight between 2500-2750 gm, 18 cases had birth weight 2750-3000 gm, 13 cases had birth weight above 3000 gm.

Average total bilirubin was 3.68 on day 1, 5.68 on day 3, and 3.74 on day 5 for the control group. For the study group, average total bilirubin was 4.99 on day 1, 8.9 on day 3, and 5.75 on day 5.The results show a significant increase in the total bilirubin levels in the oxytocin induced compared to control group on all three days($p<0.05$). These results are comparable to the results in the study by Patil S et al,[17]Singhi et al.[18]

In the study group, 13 cases had an Apgar score 6-8, and 37 cases had an Apgar score greater than 8. In the control group, 8 cases had an Apgar score 6- 8, and 42 cases had an Apgar score greater than 8.

15 cases were admitted to NICU in the study group, of which 11 babies received phototherapy. 4 cases were admitted to NICU in the control group, and all of them received phototherapy. Mean stay in NICU was 3.5 days in study group against 2.75 days in control group, and the difference is statistically significant.

V. Conclusion

The findings in our study show that oxytocin administration during labour for augmentation results in increased total bilirubin levels in the neonates. Since oxytocin is the most commonly used drug in the obstetric practice for quite some time now and neonatal hyperbilirubinemia is associated with adverse effects later in life,

we suggest extreme caution when administering oxytocin for augmentation of labour, to give best possible perinatal outcome.

CONFLICT OF INTEREST

There is no conflict of interest in this study.

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