A prospective observational study to evaluate the association of various maternal risk factors with increasing incidence of term neonatal jaundice

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ABSTRAK

Latar Belakang*: Di wilayah kami, sebagian besar ibu dipulangkan pada hari ke-3 pascakelahiran. Namun selama beberapa tahun terakhir, jumlah pasien yang dirawat di NICU juga meningkat sehingga memperpanjang masa tinggal ibu di rumah sakit sehingga menyebabkan peningkatan infeksi yang didapat di rumah sakit pada ibu dan bayinya. Penelitian ini dikembangkan dalam konteks ini.*
Tujuan*: Penelitian ini dilakukan dengan tujuan untuk mengetahui kejadian penyakit kuning neonatal pada neonatus cukup bulan dan peran berbagai faktor ibu yang bertanggung jawab atas hiperbilirubinemia fisiologis berlebihan pada neonatus cukup bulan.*
Metode:*. Dengan menggunakan grafik fototerapi berbasis usia kehamilan NICE, penelitian ini menganalisis serum bilirubin bayi baru lahir cukup bulan pada hari ke-2 kehidupan mereka. Total 155 ibu antenatal diambil untuk penelitian. Hubungan antara faktor risiko ibu dan penyakit kuning neonatal serta perbandingan faktor risiko pada bayi baru lahir cukup bulan, cukup bulan, dan terlambat dinilai menggunakan uji chi-square atau uji eksak Fisher.*
Hasil: *Insiden penyakit kuning neonatal pada penelitian ini adalah 58,1%. Usia, BMI, pertambahan berat badan ibu tidak mempunyai hubungan bermakna dengan penyakit kuning neonatal. Ketidakcocokan golongan darah memiliki korelasi positif (P=0,001) Usia kehamilan pada saat persalinan menentukan outcome neonatal. (P=0,001). Seiring bertambahnya usia kehamilan, outcome neonatal akan lebih baik. Kejadian hiperbilirubinemia lebih banyak pada minggu ke 37 -38 jika dibandingkan pada minggu ke 39. Penyakit penyerta ibu, perubahan volume cairan ketuban, cara persalinan tidak memiliki signifikansi statistik. ketika faktor bayi baru lahir dianggap sebagai berat lahir, masalah pertumbuhan jenis kelamin, golongan darah tidak memiliki signifikansi statistik sedangkan dehidrasi terbukti signifikan (P=0,001). cairan ketuban bernoda mekonium [P-0,034] ditemukan berhubungan dengan perkembangan penyakit kuning neonatal.*
Kesimpulan: *Prevalensi penyakit kuning lebih tinggi pada penelitian ini. Ketidakcocokan golongan darah ibu dan janin, usia kehamilan saat melahirkan, cairan ketuban berlumuran mekonium, dehidrasi neonatal ditemukan berhubungan dengan perkembangan penyakit kuning neonatal.*

KATA KUNCI : *penyakit kuning neonatal; faktor risiko ibu; fototerapi; ketidakcocokan golongan darah; penyakit penyerta*

ABSTRACT

Background: *In our setting majority of the mothers were discharged on postnatal day 3.but over the past few years the NICU admissions also increased prolonging the hospital stay of mothers leading to increase in the hospital acquired infections for both mother and baby. This study was developed in this context.*

Objectives: *The present study was performed with the purpose of establishing the incidence of neonatal jaundice in term neonates and the role of the various maternal factors being responsible for exaggerated physiological hyperbilirubinemia in term neonates.*

Methods: *Using the NICE gestational age-based phototherapy chart, this study analysed serum bilirubin of the term newborns on their day 2 of life. Total 155 antenatal mothers were taken for study. Associations between maternal risk factors and neonatal jaundice and comparing risk factors in early-term, term, and late-term newborns were assessed using chi-squared or Fisher's exact tests*

Results: *Incidence of neonatal jaundice is 58.1% in this study. Age, BMI, weight gain of the mother had no significant correlation with neonatal jaundice. Blood group incompatibility had a positive corelation (P=.001) Gestational age at the time of delivery determines the neonatal outcome. (P=.001). As gestation advances the neonatal outcomes are better. Hyperbilirubinemia incidence more at 37 -38 weeks when compared to 39 weeks. Maternal comorbidities, amniotic fluid volume changes, mode of delivery didn't have statistical significance. when new-born factors are considered birth weight, gender growth problems, blood group has no statistical significance whereas dehydration proved to be significant (P=.001). meconium-stained amniotic fluid[P-0.034] were found to be associated with the development of neonatal jaundice.*

Conclusions: *The prevalence of jaundice is higher in this study. maternal and foetal blood group incompatibility, gestational age at delivery, meconium-stained amniotic fluid, neonatal dehydration was found to be associated with the development of neonatal jaundice.*

INTRODUCTION

Jaundice, is a symptom or sign of a disease process, characterized by the yellow-orange discoloration of the skin and sclera due to excessive bilirubin deposition in the skin and mucous membranes. it is a physiological condition, not a disease itself. Bilirubin is formed when the haem component of RBCs cells is broken down to biliverdin in the spleen and then change into unconjugated bilirubin. As unconjugated bilirubin is not water soluble, it is transferred from the spleen to the liver via the bloodstream, bound to the plasma protein albumin. In the liver it becomes conjugated bilirubin, then gets secreted into the gallbladder. In the gut, bilirubin is metabolized to other gall pigments and finally excreted in the feces(1).

The neonatal jaundice is described as the imbalance between bilirubin production and conjugation, which can result in increased bilirubin levels. This imbalance is due to the immature liver of the neonate and the rapid breakdown of red blood cells, which may be multifactorial. At bilirubin levels of between 85 µmol/L and 120 µmol/L, neonatal jaundice can be diagnosed (2). The NICE guideline takes into consideration the infants' age and neonatal jaundice (3) .

Neonatal jaundice is influenced by so many external factors .in one study different variables studied are gestational age, birth weight, maternal infections and other illnesses during pregnancy, and premature

rupture of membranes as complications during labor and the mode of delivery (4). The prevalence of neonatal jaundice is 60% globally with almost 70 % incidence in our study setting.In our current context, there has been a recent increase in NICU admissions due to hyperbilirubinemia. Upon reviewing the existing studies on the risk factors for neonatal jaundice, it has become evident that maternal risk factors contribute to the incidence of neonatal jaundice.
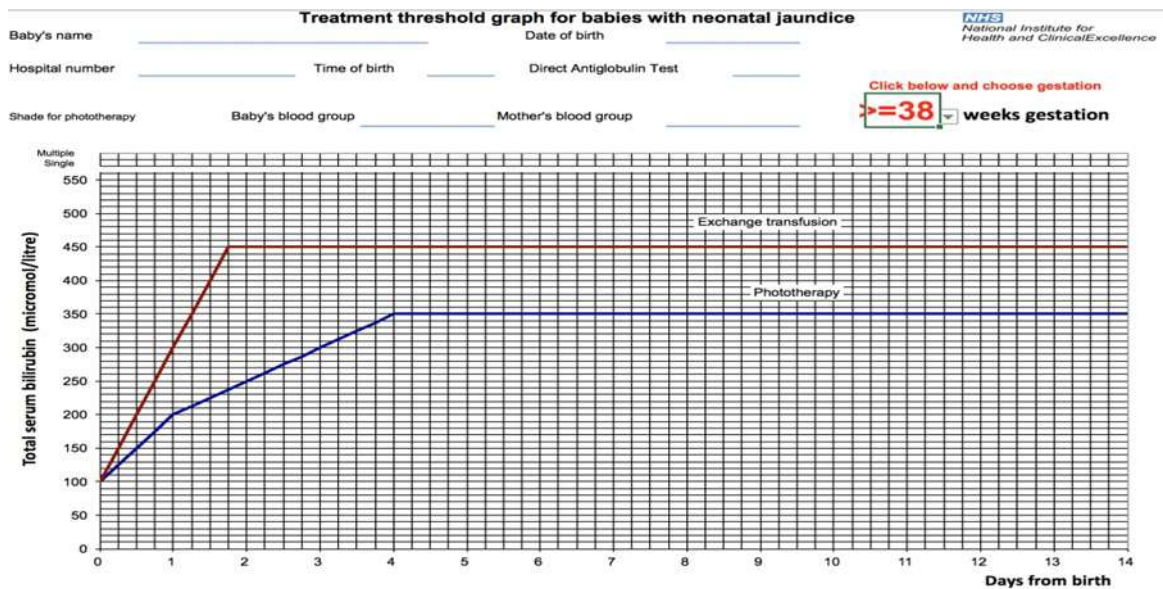

Figure 1: Nice chart

Measurements of maternal age, weight, BMI, pregnancies, delivery type, oxytocin induction, Premature rupture of Membranes {PROM}, RR, and HR were taken in a study. Maternal-foetal ABO blood group incompatibility, in which the mother has blood group O, and the newborn has either blood group A or B, which occurs in 15-20% of all pregnancies (5). Haemolysis due to ABO incompatibility is minimal, but severe cases of Kernicterus is reported too. Maternal weight gain above the recommendations for their pre pregnancy weight is associated with an increased risk of the adverse obstetric outcomes like macrosomia, neonatal hyperbilirubinemia and neonatal hypoglycaemia (6).

Neonatal jaundice can cause electrolyte imbalance, bilirubin induced neurologic dysfunction, encephalopathy, kernicterus.

Maternal education level should have an impact on neonatal jaundice. History of a previous offspring with jaundice affect the knowledge of the mothers on hyperbilirubinemia (7).The incidence of maternal and foetal injuries is more with instrumental deliveries. vacuum extraction can cause various scalp injuries leading to extraction of blood in turn increases bilirubin load on the neonatal liver, leading to the development of hyperbilirubinemia (8).

The common maternal comorbidities for neonatal jaundice were preeclampsia, hypertension, diabetes mellitus, vaginal bleeding, type of delivery, labour injuries, home deliveries, skin ecchymosis, and cephalohematoma, cultural beliefs like use of

traditional supplements, breast problems, and decrease in breastfeeding (9,10).

Despite advancements in obstetric practices, it is crucial to investigate the reasons behind the rising prevalence of neonatal jaundice. In our setting most of the newborns have neonatal jaundice, so the postnatal hospital stay is prolonged. In order to prevent the morbidity associated with neonatal jaundice, emphasis must be given in the preventive strategy. The ideal preventive method found to be useful is the frequent breastfeeding knowledge about the feeding practices following baby friendly hospital initiatives. mothers are counselled through the antenatal classes in the antenatal period, giving more emphasis in the third trimester. Therefore, the objective of my research is to identify the maternal risk factors, explore methods of prevention or modification, and subsequently reduce neonatal morbidity in our specific setting. This study aims to examine various risk factors, both maternal and fetal, that impact term neonatal jaundice.

MATERIALS AND METHODS

This study is a cross-sectional study done in a tertiary care centre, Jubilee mission medical college Thrissur over a period of 1 year from 2021 to 2022. This included all singleton mothers whose babies had hyperbilirubinemia after taking informed consent. The accepted sample size minimum comes to 140. Sample size is based on the proportion of 55.2% observed in an earlier publication [1] with 95% confidence level and 15% relative allowable error minimum sample size comes to 140. All women eligible for the study as per inclusion and exclusion criteria will be enrolled.

Hypothesis: whether maternal risk factors have a role in the development of neonatal jaundice?

Primary Outcome: incidence of neonatal hyperbilirubinemia for which serum bilirubin on day 2 is measured and plotted as per nice guidelines chart.

Inclusion criteria

All Full-Term babies {neonates born after 37 completed weeks of gestation} with serum bilirubin more than threshold level in NICE gestation wise phototherapy chart. Healthy babies not on any medication. Mothers 18 years and older with singleton pregnancy, and mothers who gave informed consent.

Exclusion criteria

Preterm babies/low birth weight babies, post-term (after 42 weeks) babies, babies with major illness. After informed consent, patient details including Obstetric & delivery details and neonatal morbidity details were collected from labor room and Neonatal Intensive Care Units. The obstetric population was taken as women who delivered at term (37 weeks to 42 weeks) in our setting. The risk severity assessment uses hour-specific Total Bilirubin values and the presence or absence of additional risk factors (including gestational age).

This approach of assessing risk severity is consistent with the practice guidelines developed by the American Academy of Paediatrics (AAP) and the United Kingdom's National Institute for Health and Clinical Excellence (NICE guidelines for neonatal jaundice.

Regarding the incidence of hyper-

bilirubinemia in term neonates' results were summarised by frequencies and percentages (categorical variables) and means, standard deviations, or percentiles (numerical variables, based on data distribution). Associations between maternal risk factors and neonatal jaundice and comparing risk factors in early-term, term, and late-term newborns were assessed using chi-squared or Fisher's exact tests.

RESULTS AND DISCUSSION
RESULTS

A Total of 155 booked antenatal mothers who met the inclusion criteria were taken up for the study. All Mothers were singletons who were 37 weeks or more.

The Incidence of neonatal jaundice is 58.1% in this study. The age distribution of participants ranges from 19 years to 40 years. (mean -26.69 SD-4,395). The majority of patients were of younger age. 42% were below 25 years, 40% between 26-30 years, 18 % above 30 years. There is no association found between maternal age and neonatal jaundice in my study. Even though incidence seems to be high in the 25-30 yrs. no statistical association was found.

lood group and neonatal jaundice

The prevalence of negative blood groups was 9% only. 43.9 % O positives, 47% other positive groups like A+/B+/AB+. The negative blood group has a higher risk of Neonatal Jaundice. Maternal blood group was statistically found to be significant in the development of neonatal jaundice. Negative blood groups have higher association with neonatal jaundice in this study. Among O positive blood group 67.6% of mothers had babies with neonatal jaundice.

Table 1. Association of maternal blood group and neonatal jaundice

Blood groups	Frequency	Phototherapy		
		No	Yes	Total
Negative	14	2 (14.3%)	12 (85.7%)	14 (100%)
O Positive	68	22 (32.4%)	46 (67.6%)	68 (100%)
Other Positives [A+/B+/Ab+]	73	41 (56.2%)	32 (43.8%)	73 (100%)
		P Value	DF	Significance
		13.03	2	0.001

Table 2. Distribution of gestational age and association with neonatal jaundice

Gestational age	Frequency	Phototherapy		
		No	Yes	Total
37 Weeks	44	8 (18.2%)	36 (81.8%)	44(100%)
38 Weeks	79	39 (49.4%)	40 (50.6%)	79(100%)
39 Weeks	30	16(53.3%)	14(46.7%)	30(100%)
40 Weeks	2	2(100%)	0	2(100%)
		P Value	DF	Significance
		14.68	2	0.001

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Figure 2. Association of maternal comorbidities with neonatal jaundice

Gestational age at time of delivery

The majority of mothers were induced at 37-38 weeks of Gestational age. In the study 44 participants were induced at 37 weeks, 79 at 38 weeks,30 at 39 weeks, 2 at 40 weeks. The risk of Neonatal Jaundice is higher at 38 weeks.

In the GDM group, 11.6% of individuals experienced hyperbilirubinemia, with a p-value of 0.431. Similarly, in the HTN group, the incidence of hyperbilirubinemia was 3.2%, with a p-value of 0.312. In the covid group, 8.4% of individuals had hyperbilirubinemia, with a p-value of 0.363. Additionally, in the hypothyroid group, the incidence of hyperbilirubinemia was 9.4%, with a p-value of 0.521. However, none of these findings were deemed statistically significant.

The presence of meconium-stained amniotic fluid has been identified as a significant risk factor for Neonatal Jaundice, with a P value of 0.034. out of 155 participants only 6 has meconium-stained liquor.

Table 4. Labour induction frequencies

Labour induction	Frequency	Percent
Spontaneous	25	16.1
PGE1/PGE2	101	65.2
C sections	29	18.7
	Df	Significance
P value	1	0.658
.837a		

On the other hand, there is no statistically significant association between labour induction and analgesia and the occurrence of Neonatal Jaundice.16.1% had spontaneous onest of labour, 65.2% were medically induced with either PGE1 [misoprostol] or PGE2 {dinoprostone}, 18.7% were delivered by caesarean. Whatever be the induction method it has no significant association with NNJ. (P=0.658).

Figure 3. Labour analgesia and neonatal jaundice

Majority (63.9%) doesn't prefer Labour analgesia.56 participants opted for some mode of analgesia (either Entonox/epidural or iv analgesics) but no statistical significance (P=0.283) with Neonatal Jaundice.

Fetal Factors

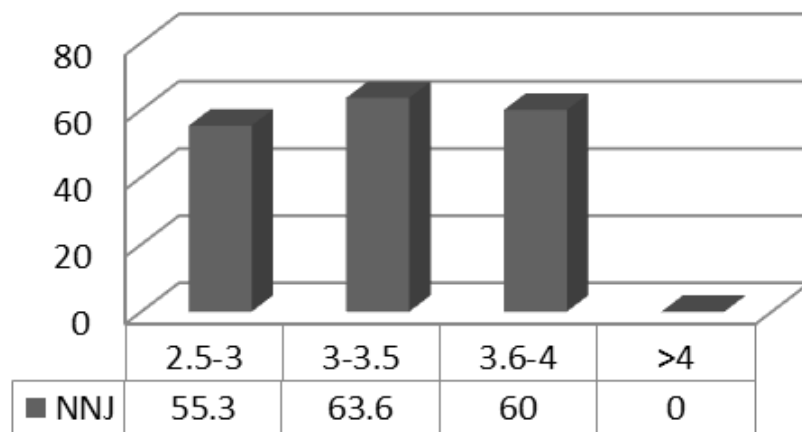Fetal factors, such as gender (p value-0.941), birth weight (p-0.497), blood group (p-0.477), growth parameters (p-0.139), and neonatal problems (p-0.103), exhibited no statistical significance. Majority of babies were females, incidence of jaundice is found higher in females.
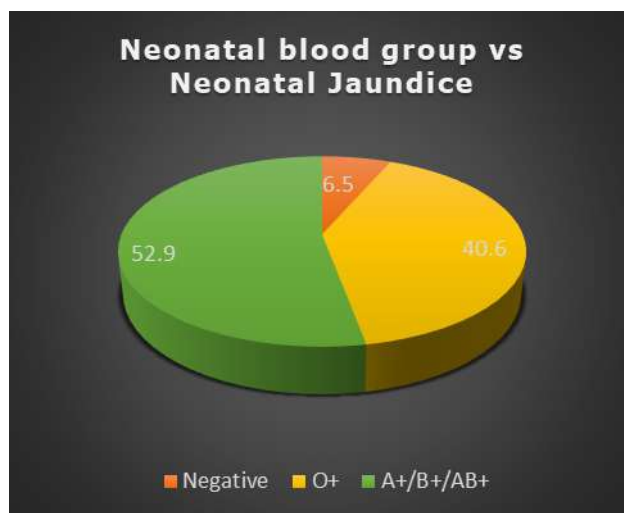
55.3% developed jaundice in 2.5-3 kg weight group, 63.6% developed in the 3-3.5 kg weight, 60% developed in the 3.6- 4 kg group. Neonatal jaundice mostly observed in 3-3.5 birth weight group, but no statistical significance with NNJ. (P=0.497).

Table 5. Baby gender and phototherapy

Baby gender	Frequency	Percent
Female	84	54.2
Male	71	45.8
Total	155	100
P value	DF	Significance
.005a	1	0.941

Figure 4. Birth weight and neonatal jaundice

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Figure 5. Neonatal blood group and neonatal jaundice

Table 6. Growth patterns and neonatal jaundice

SGA/FGR/LGA	Frequency	Percent	Phototherapy
No	144	92.9	59.7
Yes	11	7.1	36.4
Total	155	100	
P value	Df	Significance	
2.290a	1	0.13	

6.5 % were negative groups, 40.6% were O+ groups, 52.9% were A+/B+/AB+ groups. No statistical association found between new-born blood group and Neonatal Jaundice. 92.9% babies were adequate for growth, 7.1% were either fetal growth restricted /large for gestation.

Table 7. Neonatal Dehydration and Neonatal Jaundice

Neonatal dehydration	Frequency	Percent
No	142	91.6
Yes	13	8.4
Total	155	100
P value	Df	Significance
10.248a	1	0.001

A total of 8.4% of infants (13 babies) exhibited signs of dehydration. Factors contributing to this condition include insufficient feeding, inadequate suckling, improper feeding techniques, and a lack of awareness among mothers regarding the importance of feeding every two hour.

DISCUSSION

The dilemma in neonatal jaundice and its sequelae and advances in the management field has done wonders over the decades. The majority of jaundice cases run a benign course, is reassuring whereas a few of patients exhibit a severe form of

jaundice. It is essential to emphasize that the phototherapy has significantly enhanced the clinical burden associated with jaundice, thereby diminishing its impact on affected individuals.

The current study found no statistically significant correlation between the mother's age, body mass index (BMI), and weight gain and neonatal jaundice (11). The correlation between neonatal jaundice and maternal blood group were 85.7 % in negative blood groups, ABO incompatibility particularly between O blood group mother and non–O blood group neonate is frequently observed as a cause of hyperbilirubinemia in neonate, necessitating the use of phototherapy (12). It is important to note that incompatibility also arises between other blood groups.[13] In a prospective study conducted in Iran primary cause of neonatal jaundice was found to be physiological followed by ABO incompatibility (14). The majority of patients had blood group B, while the predominant blood group among the mothers was O, as observed in this study(15).

The present study did not establish a correlation between maternal risk factors, particularly comorbidities, and the occurrence of hyperbilirubinemia in infants. Specifically, 12% of mothers with gestational diabetes mellitus, 80% with hypertensive disorders, 50% with hypothyroidism, and 46% with COVID-19 infection were found to have infants with hyperbilirubinemia, but no statistically significant association was demonstrated.According to a recent study conducted by Thiru Moorthi the analysis of maternal-related risk factors revealed that 58% of women fell between 26-35 years, 44% were overweight, 53% of women were primigravidas, Furthermore, it was observed that 52% of mothers underwent a C-Section delivery, which correlated with the occurrence of neonatal jaundice (16).

The causal factor of neonatal outcomes is the gestational age at the time of delivery. For the purposes of this study, only neonates born at term (i.e. gestational age >37 weeks) were included, and further subdivided into early term, term, and late term categories. The incidence of neonatal jaundice was found to be highest among early term neonates (37-38 weeks), and a positive correlation was observed between gestational age and neonatal jaundice (P=.001) (17).

According to a study conducted by Joshua and his team, term neonates were stratified into low-risk and high-risk based on various factors including maternal blood type, maternal age, gestational age at delivery, estimated birth weight, parity, CBC at admission, and maternal blood pressure at admission (18).

This study utilised data-driven machine learning and statistical methods models based on maternal and neonatal data for risk stratification for neonatal jaundice. In mothers with Rh negative blood type, cord bilirubin plays a crucial role. The diagnostic accuracy based on cord bilirubin cut-off of 2.5–3 mg/dl in term neonates predicting the need for phototherapy (19)

The significance of dehydration as a contributing factor to neonatal jaundice has been established. Given that infants rely solely on breast milk for the first six months of life, it is imperative that mothers receive appropriate counselling to ensure its effective implementation. The findings of this study

indicate that all infants exhibiting signs of dehydration required phototherapy, with a statistically significant p-value of 0.001(20).

According to a study conducted in Dubai, the adherence to breastfeeding policies under the Baby-Friendly Hospital Initiative (BFHI) is rigorously observed (21). The signs of sufficient nourishment are as follows: the infant exhibits a consistent weight gain following the initial two weeks of life. They exhibit a state of good health during their wakeful periods and experience peaceful sleep approximately two hours after a satisfactory feeding. Moreover, it is expected that babies will urinate a minimum of six to eight times during the daytime and twice during the nighttime within a 24-hour period. In my centre BFHI were strictly followed.

The Baby-friendly Hospital Initiative is the propaganda of the WHO/UNICEF. It has Ten Steps to Successful Breastfeeding to see through the needs of infants and families in all levels of neonatal care(22).Considering neonatal factors prematurity is the foremost contributor (23). However, my study solely focuses on term babies. The neonatal birth weight, gender, blood group, growth restrictions and macrosomia didn't exhibit any correlation with neonatal jaundice. Nonetheless, a study conducted in 2014 revealed a correlation between birth weight and neonatal jaundice, particularly in low-birth-weight infants (24).

It has been observed that neonates may develop jaundice regardless of the mode of delivery. There appears to be no discernible difference in the incidence of jaundice between vaginal and abdominal deliveries. However, it has been noted that instrumental deliveries may result in a slight increase in neonatal jaundice due to blood collection resulting from cephalhematoma or foetal injuries. A study conducted in Bhutan has revealed that neonates delivered via caesarean section were 92% less likely to develop jaundice when compared to those born vaginally (25,26).

Strength and limitations

This study was conducted at a tertiary center, allowing for easy sample selection. All subjects willingly participated, and the study followed a prospective design using validated phototherapy guidelines. Thorough assessments were conducted on all subjects in a prospective manner. However, there were certain limitations to our study. We only followed up with the subjects during their hospital stay, so any long-term effects were not recorded. Additionally, as an observational study, there is an inherent bias towards those who required interventions to prevent adverse outcomes outside of the study. Furthermore, since term pregnancies were included, many of the subjects were considered low risk. The assessment of high-risk factors was not thoroughly conducted, as seen in other studies.

CONCLUSION AND RECOMMENDATION

The present study conducted an assessment and analysis of maternal and foetal factors in the development of neonatal jaundice. A total 155 antenatal mothers were taken up for the study. Only term pregnancies were included. Incidence of neonatal jaundice is 58.1%. in this study. Blood group incompatibility (P-0.001), gestational age at delivery[P-0.001], meconium-stained

amniotic fluid(P-0.034), neonatal dehydration(P-0.001) were found to be associated with the development of neonatal jaundice.

Among blood groups, negative groups have stronger association probably due to Rh incompatibility. The risk of Neonatal Jaundice is found to be higher at 38 weeks of gestation in this study. The presence of meconium-stained amniotic fluid has been identified as a significant risk factor for Neonatal Jaundice, with a P value of 0.034.some factors are not statistically found significant in this study even though they are proven in various studies such as maternal comorbidities, mode of induction and analgesia and fetal factors, such as gender (p value-0.941), birth weight (p-0.497), blood group (p-0.477), growth parameters (p-0.139), and neonatal problems (p-0.103).

Enlightening mothers about the risk factors causing neonatal jaundice via antenatal classes, counselling on importance of breast feeding and its techniques. Timely referral of high-risk cases and careful monitoring, timed termination of pregnancy is crucial in neonatal morbidity. Neonates should be followed from the day of delivery till day of discharge and on every timed vaccination visits.

The findings suggest that adequate control of comorbidities, monitoring of foetal growth, provision of antenatal classes on high-risk areas, emphasis on delivery at 39 weeks except in high-risk cases, rooming-in, exclusive breast-feeding practices, implementation of BFHI, proper breast-feeding techniques, daily examination of neonate, and estimation of bilirubin before discharge and follow-up are crucial in the prevention and management of neonatal jaundice. It is recommended that every antenatal mother should receive individualised management, regardless of low or high risk. The current state of neonatal jaundice is the result of decades of development, and further research in this field is necessary

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