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Clinical profile of pathological jaundice among neonates admitted in the National Referral Hospital, Bhutan

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ABSTRACT

Introduction: Neonatal jaundice is a common condition. There are various maternal and neonatal clinical characteristics that have been described regarding pathological jaundice. We aimed to describe the clinical profile of pathological jaundice and to estimate its prevalence among newborns admitted at the National Referral Hospital of Bhutan. **Methods:** A descriptive study design was used to study cases of pathological jaundice admitted at the Gyalsuen Jetsun Pema Neonatal Intensive Care Unit (NICU) of the National Referral Hospital of Bhutan, for a period of 1 year from 7th November 2018 to 6th November 2019. Data was collected using a predesigned case proforma, entered and analyzed in EpiData after obtaining ethical clearance from the Research Ethics Board of Health, Bhutan. Descriptive analysis was done for the socio-economic characteristics. Chi square test was used to find the significant association between categorical variables at 5% significant level. **Results:** ABO blood group incompatibility and neonates less than one week of age were found to be most common clinical profile. The neonates born to primiparous mothers were 1.45 times (95% CI 1.07 – 2.00) more likely to suffer from excessive weight loss compared with multiparous mothers and it this association was highly significant (*p*-value of 0.016). Facility based prevalence of pathological neonatal jaundice was 63.66%. The median age on admission was 4 days. **Conclusions:** ABO incompatibility, neonates less than one week of age, primiparous mothers with feeding issues should be closely followed or screened for pathological jaundice especially during the first one week of life. The prevalence of pathological jaundice was observed to be high in our setting.

Keywords: Blood group incompatibility; Feeding issues; Pathological jaundice; Prevalence; weight loss.

INTRODUCTION

Neonatal jaundice is a very common condition worldwide occurring in up to 60% of term and 80% of preterm newborns¹. It is one of the main reasons for neonatal admissions and morbidity especially during the first week of life.

Jaundice in newborns can be physiological or pathological. Jaundice attributable to physiological immaturity of neonates to handle increased bilirubin production is termed as physiological jaundice². The elevated bilirubin in newborns is due to the immature hepatic metabolism of bilirubin, the increased red blood cell turnover, and the shorter lifespan of red blood cells.

Pathological jaundice is defined as any newborns requiring either phototherapy or exchange transfusion for the

treatment of jaundice². Severe neonatal jaundice is defined as any pathological jaundice whose Total Serum Bilirubin (TSB) level falls above the exchange transfusion range³. The TSB level depends upon the age and gestation age of the baby.

Neonatal jaundice may not be a major cause of mortality but is still an important cause of morbidity especially in developing countries. Severe neonatal jaundice can lead to serious and irreversible neurodevelopment consequences if not treated timely.

Studies around the world have described various clinical profile and incidence of severe neonatal jaundice. The incidence of severe neonatal jaundice was found to be highest in low to middle income countries like in Southeast Asian region. The lowest incidence was found in more developed regions^{3,4}. In 2016, neonatal death due to neonatal jaundice was ranked seventh globally among all causes of neonatal deaths⁴.

There are many known maternal and neonatal risk factors that cause pathological jaundice^{1,2}. Neonatal factor includes neonates in their first week of life, prematurity, low birth weight, male child, inadequate feeding or excessive weight loss, ABO and Rh incompatibility, birth asphyxia, cephalohematoma,

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sepsis and previous siblings with jaundice requiring treatment. Maternal factors like primiparity, maternal age, prolonged labour, use of oxytocin, and maternal co morbidities are also known to cause jaundice. Apgar score was used to assess the condition of the baby soon after birth at 1 and 5 minutes.

Since no study has been conducted on neonatal jaundice in our setting this research was designed to study the clinical profiles of pathological jaundice. This study provides a baseline data on clinical profile and prevalence of pathological jaundice in the National Referral Hospital.

METHODS

After obtaining ethical clearance from the Research Ethics Board of Health, Ministry of Health, Bhutan vide letter number Ref. No. REBH/Approval/2018/060 dated 2nd October 2018, a descriptive study conducted at the Gyaltsuen Jetsun Pema Neonatal Intensive Care Unit (NICU) of Jigme Dorji Wangchuck National Referral Hospital (JDWNRH) from 7th November 2018 to 6th November, 2019. JDWNRH serves as the National Referral hospital in Bhutan and NICU includes the critical care unit with 14 beds and the nursery unit with 23 beds.

There were 2493 neonates admitted in the NICU of which 1587 had pathological jaundice. Of 1587 neonates with pathological jaundice, 407 neonates were recruited for the study using systematic random sampling. as shown in the Figure below.

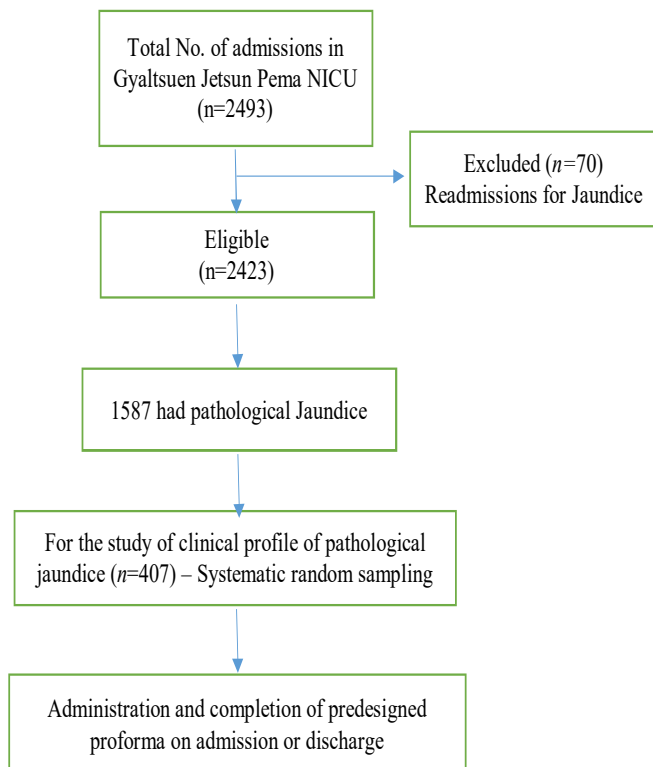


Figure 1. Flowchart of patient recruitment and data collection

Data collection was done using a self-developed case proforma after reviewing the existing literature which was pilot tested and validated by the experts in the field. Demographic details, clinical history, examination and investigation findings were collected using the proforma and from the Maternal and Child Health handbook. Neonatal characteristics included were age, sex, gestation age, birth weight, ABO and Rh incompatibility, sepsis, cephalohematoma, excessive weight loss and feeding issues. Maternal characteristics included were age and parity of mothers, use of oxytocin for labour, prolonged labour and comorbidities like Gestational Diabetes Mellitus (GDM), gestational hypertension and thyroid disorders.

Data collected was entered on a password protected computer while the hard copies of the proforma were stored in a secured location. No personal identifiers of the informants were used. Data were checked for completeness and double entered into Epidata version 3.1 to eliminate errors in data entry. Data management, processing and analysis were done using Epidata Analysis version V2.2.2.183.

Variables were coded and descriptive analysis were performed. Demographic and clinical characteristics were given in frequencies with their percentages. Median was calculated to determine the age on presentation of neonates with jaundice. Graphical methods and tables were also used to summarize the descriptive statistics. Fisher exact test was used to assess the association between parity and excessive weight loss.

Prevalence of pathological jaundice was calculated by dividing the total number of neonates with pathological jaundice by the total number of neonates admitted in NICU of JDWNRH during the one year study period.

RESULTS

During the study period, 2493 neonates were admitted at the Gyaltsuen Jetsun Pema NICU, JDWNRH. Out of the total admissions, 344 were admitted in critical care unit and the remaining 2149 neonates in the nursery unit. Of the total admissions, 1587 (63.66%) babies had pathological jaundice.

Neonatal Characteristics

Clinical presentation

In our study, of 407 neonates recruited, 86.98% of them had icterus till lower legs/arms and palms and soles.

On admission, 30 (7.37%) neonates had fever, 145 (35.63 %) had feeding issues, 5 (1.23%) had cephalohematoma and none had features of neurological dysfunction.

From 407 babies, 360 (88.45%) were born at term and 47 (11.55 %) were born preterm. Out of these neonates, 354 babies (85.01%) had birth weight of more than 2500 grams and 10 (2.46%) had very low birth weight of less than 1500 grams. The study found that 78% of the neonates developed jaundice within their first week of life. The median age on the diagnosis of jaundice was 4 days.

Table 1. Birth characteristics of neonates with pathological jaundice admitted in NICU* of JDWNRH† from 2018 - 2019 (n=407)

Birth characteristics	n (%)
Type of birth	
Term birth	360 (88.45)
Preterm birth	47 (11.55)
Sex	
Male	246 (60.44)
Female	161 (39.56)
Birth weight (in grams)	
≤ 1500	10 (2.46)
1501 – 2499	51 (12.53)
2500 – 3999	334 (82.06)
≥ 4000	12 (2.95)
Apgar at 5 minutes	
Less than 7	2 (0.49)
7 or more	405 (99.51)

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Table 2. Clinical characteristics of neonates with pathological jaundice admitted in NICU*, JDWNRH†, 2018-2019 (n=407)

Clinical characteristics	n (%)
ABO‡ or Rh§ incompatibility	
ABO‡ incompatibility	90 (22.11)
Rh§ incompatibility	0 (0.00)
No ABO‡/Rh§ incompatibility	317 (77.89)
Excessive weight loss¶	
Yes	122 (29.97)
No	285 (70.03)
Feeding issues	
Yes	145 (35.63)
No	262 (64.37)
Neonatal sepsis	
Yes	24 (5.90)
No	383(94.10)
Cephalhematoma	
Yes	5 (1.23)
No	402 (98.77)

*Neonatal Intensive Care Unit, †Jigme Dorji Wangchuck National Referral Hospital, ‡Blood Group, §Rhesus factor, ¶Excessive weight loss - Loss of 10% or more of birth weight

Ninety (22.11%) neonates had ABO incompatibility. None had Rh incompatibility nor isoimmune hemolytic disease. One hundred forty five (35.63%) newborns had feeding issues like inadequate breast milk production, poor feeding technique, etc. Excessive weight loss was observed in 122 (29.98%) neonates.

Sixty-one (31.44%) neonates of the 194 multiparous mothers had a history of previous siblings or family history of neonatal jaundice requiring treatment. However, out of these neonates, 16 had ABO incompatibility, 15 had feeding issues and 13 were male babies.

There were 23 cases of severe pathological jaundice but none required exchange transfusion. Neonates with ABO incompatibility¹³ and feeding issues⁷ were found to be the most common clinical profile.

Table 3. Association between parity and excessive weight loss in neonates with pathological jaundice in NICU*, JDWNRH†, 2018-2019 (n=407)

Parity	Number of neonates with excessive weight loss (n=122)	Number of neonates with no excessive weight loss (n=285)	95% CI‡	p-value
Primi§	75	138	1.45	0.016
Multi¶	47	147	(1.07-2.00)	

*Neonatal Intensive Care Unit, †Jigme Dorji Wangchuck National Referral Hospital, ‡Confidence Interval, §Primiparous, ¶Multiparous

Maternal Characteristics

Among the 407 mothers included, 317 (77.88%) mothers were between 21 and 34 years of age, 31 (7.62%) were teenagers and remaining 59 (14.50%) were 35 years of age and above.

Two hundred and thirteen (52.33%) mothers were primiparous and the remaining 194(47.67%) mothers were multiparous. In our study, 40% of primiparous mothers had some sort of feeding issues among which 35% of their neonates had excessive weight loss. Among the multiparous mothers, 30% of them had feeding issues and 25% newborns had excessive weight loss. The neonates born to primiparous mothers were 1.45 times (95% CI 1.07 – 2.00) more likely to suffer from excessive weight loss compared with multiparous mothers and it this association was highly significant (p-value of 0.016)

Table 4. Demographic and clinical characteristics of mothers of neonates with pathological jaundice admitted at NICU*, JDWNRH†, 2018-2019 (n=407)

Variables	n	(%)
Age (in years)		
≤ 20	31	7.62
21-34	317	77.88
≥35	59	14.50
Parity		
Primiparous	213	52.33
Multiparous	194	47.67
Gestation age (in weeks)		
<37	47	11.55
≥37	360	88.45
Oxytocin induction		
Yes	109	26.78
No	298	73.22
Prolonged labour		
Yes	13	3.19
No	394	96.81
Gestational Hypertension		
Yes	17	4.18
No	390	95.82
Gestational Diabetes Mellitus		
Yes	5	1.23
No	402	98.77

*Neonatal Intensive Care Unit,†Jigme Dorji Wangchuck National Referral Hospital

DISCUSSION

Neonatal characteristics

The majority of newborns (78%) in our study were less than 7 days of age at the time of diagnosis of pathological jaundice. Our study finding was consistent to the observation made by a similar study carried out in Ethiopia showing 90% of neonates developed jaundice within their first week of life⁵. This may be because, physiologically, neonatal jaundice peaks between three to seven days of age.

The current study found that more than half of the babies with pathological jaundice were males (60.44%). Similar findings were also reported in India⁶. In our study, huge percentage of neonates were term and had normal birth weight. Most of the neonates enrolled in our study were admitted in the nursery unit (phototherapy unit) primarily for the treatment of jaundice which

includes mostly term and healthy neonates. The remaining small percentage were from the NICU which principally manages pre term babies. This corroborates the findings made in India and Nigeria reporting 81 to 92% and 83.12% respectively of term neonates to have pathological jaundice^{7,8}.

ABO incompatibility was found in 22.11% of neonates but none had Rh incompatibility in this study. A retrospective study conducted in the central regional referral hospital, Bhutan, in 2018, found that O and A blood group were more common blood groups⁸. In the same study only 0.15% of them were found to be Rhesus D negative. Thus, there is a higher chance of ABO incompatibility between the mothers and their newborns in our setting. We did not find any case of Rh incompatibility in our study. The higher prevalence of Rh incompatibility in different studies could be due to the geographical distribution of ABO and Rh grouping.

Twenty-four neonates (5.90%) with pathological jaundice had sepsis. As most of our admissions were from the nursery unit where most of the neonates were term and healthy, the number with co-existing sepsis was low. Other studies showed similar findings as well^{2,7,9}.

Maternal characteristics

A significant association was found between primiparous mothers and excessive weight loss. Excessive weight loss in our neonates born to primiparous mothers could have caused more breastfeeding jaundice or exaggerated physiological jaundice due to increased enterohepatic circulation. Neonates of primiparous mothers with excessive weight loss could be due to in experienced or little knowledge on good positioning and attachment on breast feeding or could be due to unawareness on feeding adequacy. Aiswarya et al found that 72.72 % mothers were primiparous in India¹⁰. Similarly, a study by Scrafford et al found significant association between primiparity and neonatal jaundice¹¹.

Large number (77.88%) of mothers in our study were between 21 and 34 years of age. The higher proportions could be because most of these mothers were in the most reproductive age period between 20 and 30 years. This could also be due to the good family planning interventions inculcated in our health system.

Our study showed an association between primiparous mothers and excessive weight loss in neonates compared with multiparous mothers which was highly significant (p-value of 0.016). A systematic review and meta-analysis by Seyedi et al found that the use of oxytocin increased the serum bilirubin level on the 2nd day of life⁹. Brits et al found that the use of oxytocin was not associated with a higher incidence of neonatal jaundice¹². This was because majority of the babies included in the study were born via Caesarean section for various indications. However, statistically significant number of neonates developed

pathological jaundice after inducing/augmenting labor than those born spontaneously in another study¹³.

In our study we observed high prevalence (63.66%) of pathological jaundice among neonates admitted at the national referral hospital. This may be because of the large number of deliveries being conducted at the national referral hospital as it caters services to huge portion of Bhutanese population. A similar prevalence (67%) of pathological jaundice was observed in a study done in Kerala¹⁰. On the contrary two other studies found out lower prevalence (19% and 22%) of pathological jaundice^{2,14}. This disparity in findings could be due to difference in the study center where they have included exclusively neonates from the Critical care unit, whereas we included neonates from both nursery unit and NICU. It could also be due to the difference in size of the neonatal population used for the calculation of prevalence.

CONCLUSIONS

The most common clinical profile of neonates with pathological jaundice observed in our study were ABO incompatibility, primiparous mothers with feeding issues and neonates less than one week of age. Significant association was found between primiparity and excessive weight loss. The prevalence of pathological jaundice was found to be 63.66% in our setting.

RECOMMENDATIONS

The primary health workers involved with mothers and neonates should be made aware of the development of pathological jaundice in neonates and their clinical features leading to severity. Hence during the immediate and subsequent post-natal visits, neonates particularly born to primiparous mothers with feeding issues and excessive weight loss, O positive mothers with possible ABO incompatibility and neonates less than one week of age should be assessed for jaundice.

A larger, well-designed study could determine associated risk factors and the burden of pathological neonatal jaundice in Bhutan.

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AUTHORS CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

KD: Concept, design, data collection and analysis, manuscript writing and review.

TL: Concept, design, manuscript writing and review

MLM: Concept, design, manuscript writing and review

P: Concept, design, manuscript writing and review

Author agree to be accountable for all respects of the work in ensuring that questions related to the accuracy and integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

None

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