Neonatal Hyperbilirubinemia: A Retrospective Study

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ABSTRACT

Background: Neonatal Hyperbilirubinemia is a common problem encountered in neonates and often requires admission and treatment. Almost 60% of the term babies and 80% of the preterm babies develop jaundice. East Asians have higher baseline neonatal bilirubin levels than whites and are predisposed to the development of severe neonatal hyperbilirubinemia.

Objectives: To determine the important prognostic factors in Neonatal Hyperbilirubinemia and to correlate variables with severity of presentation.

Material and Methods: A retrospective study was conducted in the Paediatrics Unit 3 of Civil Hospital Karachi from June to November 2017 on admitted patients below one month of age with clinically diagnosed jaundice. Total and indirect serum bilirubin levels, and data of gender, age, birth weight, blood group incompatibility, and breast feeding were obtained.

Results: Of 255 cases, 80% were resolved. Phototherapy was the most common method of treatment (in 91.8% of cases). Males slightly outnumbered females (1.39:1). 6.3% of jaundiced neonates died; 3.5% developed kernicterus before death. Low birth weight was observed in 50.2% of cases while preterm gestation was seen in 39.2% of cases.

Conclusion: Important prognostic factors for Hyperbilirubinemia were presence of kernicterus, anemia, age group of the infant, severity of hyperbilirubinemia and the therapy provided.

Keywords: Neonatal hyperbilirubinemia; Preterm; Kernicterus; Low Birth Weight

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INTRODUCTION

The great burden imposed by neonatal hyperbilirubinemia is exemplified by the fact that globally; about 60% of the term babies and 80% of the preterm babies develop jaundice¹. Neonatal jaundice also happens to be the most common cause of neonatal hospital readmission². The trends of neonatal hyperbilirubinemia vary between developing and developed countries with research still underway to pinpoint the causes of such disparities^{3, 4, 5}. Neonatal hyperbilirubinemia has a plethora of causes, both pathological and physiological⁶. While the physiological causes include breast-feeding and high cell turnover in relation to clearance of bilirubin, the pathological causes are divided into three categories: increased bilirubin load, decreased bilirubin conjugation, and impaired bilirubin excretion⁷. The most cases of neonatal jaundice are idiopathic and environmental and inherited factors can affect so they depend on race, genetic polymorphisms; inherited and acquired defects e.g. spherocytosis, Gilbert's syndrome, Najjar 1 and 2.⁸ Pakistan is a resource-constrained nation which makes effective screening and early treatment paramount in managing a public health issue. However, very little research has been done on this particular issue despite the fact that 27.6%

infants in Pakistan develop jaundice every year⁹ and we've relied almost exclusively on foreign literature. Even though East Asians have higher baseline neonatal bilirubin levels than whites and are predisposed to the development of severe neonatal hyperbilirubinemia.¹⁰

Our primary goal is to isolate important prognostic factors in the management of hyperbilirubinemia while our secondary objective is to search for factors affecting the severity of presentation in these patients. We hope our findings will allow us to improve current management guidelines.

MATERIAL AND METHODS

It was a retrospective cross sectional study, conducted during the period of June 2017 and November 2017. Patients aged below one month clinically diagnosed with jaundice and admitted in paediatric unit 3 of civil hospital were selected. Patients who were hospitalized for other reasons and then later developed jaundice, or those with comorbidities were excluded from the study. After taking permission from Head of Department, we looked at patients' records and filled out our proforma to collect data on gender, age, birth weight, blood group incompatibility, and breast feeding. Sampling technique was Non-probability purposive. The sample size in this study was 255 and was calculated using openepi.com based on the findings of Tikmani SS et al. in 2010¹¹. We used SPSS 16.0 for frequencies and distributions. We ran Chi-square for qualitative variables and student T tests to look for quantitative variables and significant relationships. P-values under 0.05 were taken as significant.

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RESULTS

Table 1 compares the characteristics of infants that developed kernicterus with those who did not develop kernicterus. Both groups are comparable with respect to sex, however, a relationship between the birth weight and kernicterus was found with a higher incidence of kernicterus in infants with low birth weight ($p=0.004$). Preterm infants were also seen to be more likely to develop kernicterus; 18 preterm infants developed kernicterus compared to only 4 term infants ($p=0.0000$).

During the 6-month study period, 255 cases were reviewed. Of these jaundiced neonates, having an average age of 4.79 ± 1.20 days, 7(2.7%) were very low birth weight ($<1.5\text{kg}$), 129(50.2%) were low birth weight ($<2.5\text{kg}$) and 100 (39.2%) were preterm (<37 weeks). The male-to-female ratio was 1.39:1 and the mean age of appearance of jaundice was 2.48 ± 1.32 days. Phototherapy was

the most common treatment, used in 234 (91.8%) cases, while 21 (8.2%) were only given supportive treatment. 204 (80%) cases were resolved, 5 (2%) were referred, 30 (11.8%) left against medical advice and 16 (6.3%) died, 9 of which had developed kernicterus before death. Only 41 (16%) infants had anemia out of which 6 expired. Out of the remaining 214 infants that did not have anemia 10 expired. This shows that infants that presented with anemia had a poorer prognosis. A statistically significant relationship was also found between age and the outcome; the infants in Age Group 3(9days and above) had the worst prognosis with 3 out of 10 infant being deceased (30%). The majority of the infants were of Age Group 2 (4-9 days) which had no deaths; however, Age Group 1 (0-4) had a death rate of 10.7%.

Table 1. Total no of cases analysed are 255(n=255)

	kernicterus	Anemia	Birth Weight	Therapy
TOTAL NO OF cases (n=255)	YES=22(8.6%) NO=233(91.4%)	Yes=41(16.1%) NO=214(83.9%)	VLBW=7(2.7%) LBW=129(50.6%) NBW=119(46.7%)	Supportive=21(8.2%) Phototherapy=234(91.8%)

Table 2. Features of resolved and deceased cases

	kernicterus	Anemia	Birth Weight	Therapy
Resolved cases (n=205)	10(4.9%)	35(17.1%)	VLBW=6(2.9%) LBW=103(50.2%) NBW=96(46%)	Supportive=13(6.3%) Phototherapy=192(93.7%)
Deceased cases(n=17)	9(52.9%)	6(35.3%)	VLBW=1(5.9%) LBW=8(47.1%) NBW=8(47.1%)	Supportive=1(5.9%) Phototherapy=16(94%)

DISCUSSION

Pakistan is among those top 10 countries which have largest number of neonatal deaths worldwide and among the top 15 causes of this mortality, one important is bilirubin induced mortality.^{12, 13} Although other cause of neonatal mortality are more prevalent like birth asphyxia, intrapartum complication but one can't deny the contribution of neonatal jaundice for increasing mortality.¹² After birth 3 to 6 days are critical for NNJ as serum bilirubin level peaks during this period.¹⁴

If it is detected, monitored and managed timely then mortality can be reduced but in resource limited countries timely diagnosis as well as management is compromised as most mothers either don't pay attention because of lack of awareness and if they get access to health facilities the management is hampered by financial factors of the several variables tested, our research focused on variables that have prognostic significance. The variables in question are the presence of kernicterus, anemia along with the severity of hyperbilirubinemia, the age group of the patient, and the modality of treatment employed. Among those who developed kernicterus only 10(4.9%) cases survived while 9(52.9%) patients with kernicterus failed to survive in spite of giving phototherapy.

Kernicterus is well known complication of jaundice in which indirect bilirubin level rises to much to get access to brain by crossing blood brain barrier hence badly effecting the prognosis. Kernicterus is a well-known complication of neonatal hyperbilirubinemia. Its adverse effect on outcome was also a prominent finding in the work of Hameed NN et al. carried out in Iraq¹⁵. Kernicterus is directly related to level of indirect hyperbilirubinemia so it is of no surprise that severity of hyperbilirubinemia also effect prognosis indirectly by unswervingly effecting development of kernicterus shown by other studies as well the severity of hyperbilirubinemia is also a well-recognized prognostic factor as proven by several studies including one conducted by Kuzniewicz MW et al. in 2009¹⁶. Phototherapy is a well-known treatment modality for managing Neonatal jaundice. Its use in developed countries like USA is increasing considering it a safe modality in treating jaundice in neonatal group. In our study phototherapy is given to 91.8% cases out of which 192(82.1%) were resolved and 9.4% had kernicterus. Out of

17 cases which failed to survive 16 were given phototherapy but shows no improvement so effect of phototherapy alone can't improve survival other modalities like severity of hyperbilirubinemia, anemia, and birth weight have strong impact on outcome of disease. In addition, the relationship between treatment modality and outcome is not only intuitive, but well established in literature¹⁷. We find that there is a dearth of literature on the effects of thrombocytopenia, leukopenia, and anemia on outcomes in cases of neonatal hyperbilirubinemia even though their prognostic utility in other scenarios have been thoroughly researched^{18,19}. Our secondary findings include the severity of presentation of neonatal hyperbilirubinemia being closely related to birth weight and gestational age. This finding ties in well with what several other authors have found^{20,21}.

CONCLUSION

This study concluded many factors affect the outcome of neonates with hyperbilirubinemia. These include the presence or absence of kernicterus, anemia, the type of therapy provided, the birth weight of the infant and the severity of hyperbilirubinemia. Moreover, it was also found that the birth weight and gestational age of the infant influenced the severity of presentation.

RECOMMENDATIONS

Based on our findings, we would like to recommend updates to the current management guidelines where the aforementioned prognostic factors are given paramount importance in deciding whether we treat as opposed to waiting for spontaneous resolution, how closely/regularly we monitor the patient, which patients need hospital admission, and which factors should be tackled by policy changes to affect positive change on a larger scale.

LIMITATIONS

Although this study was carefully prepared, we are aware of its limitations. First of all, this study is conducted on a small sample size. Secondly, Civil Hospital Karachi sees patients mostly from the lower socioeconomic group. For more accuracy, the study should also involve patients who did not require admission and those who were admitted in other Paediatrics Units of Civil Hospital Karachi, along with patients in other hospitals of Karachi. Thirdly, about 12 percent of patients could not reach their potential outcome as they Left against

Medical Advice (LAMA). Lastly, due to a lack of facilities or finances for further investigations such as Coomb's test, and serum levels of G6PD and Alkaline Phosphatase, the causes of Jaundice were not explored and hence could not be included in this study.

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