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**ORIGINAL ARTICLE**

# Prevalence and Factors Associated with Significant Rebound Hyperbilirubinemia after Phototherapy Among Neonates: A Cross Sectional Survey

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## ABSTRACT

**Objective:** The study was conducted to determine the frequency of post-phototherapy rebound hyperbilirubinemia in neonates.
**Background:** Serum total bilirubin is rapidly reduced in newborn hyperbilirubinemia following intensive phototherapy. With this approach, there is a worry that the bilirubin level frequently rises slightly after stopping phototherapy, a condition called as rebound hyperbilirubinemia. In preterm newborns, those receiving phototherapy for fewer than 72 hours, and those whose Coombs test is positive, post-phototherapy rebound hyperbilirubinemia occurs most frequently.
**Materials and Methods**: A cross sectional survey was conducted in postnatal wards, NICU, Neonatal step down unit, and Pediatric wards at the Agha Khan University Hospital, Karachi, Pakistan from July to December 2016. Using a consecutive sampling method, 178 neonates were included in the study. Data included basic demographic information, along with the gestational age, gender, mode of delivery, and details of phototherapy. Besides, frequency, percentages and descriptive statistics, we employed Chi square test of association considering p-value ≤0.05 as significant.
**Results:** There were 50.6% male and 49.4% female neonates. Total 15.7% neonates were found with rebound hyperbilirubinemiaMean age was 66.21±53.92 hours. Mean length of stay in hospital was 3.14±2.08 days. Mean phototherapy duration was 37.90±6.52 hrs.
Practical implication: this study is done to check for rebound hyperbilirubinemia in neonates after phototherapy.
**Conclusion:** Our study found 15.7% neonates with rebound hyperbilirubinemia and was also found significant with age at admission, birth weight, and hospital stay length.
**Keywords:** Post-Phototherapy, Rebound Hyperbilirubinemia, Neonates, prevalance

## INTRODUCTION

As shown by cases of kernicterus in apparently healthy term and near-term neonates, neonatal hyperbilirubinemia is still a public health problem[1]. In the first week of life, hyperbilirubinemia affects around 60% of term and 80% of preterm newborns[2]. Although most newborns do not need active treatment, severe jaundice can induce encephalopathy, which can lead to disability or even death. The most common treatment for newborn jaundice is phototherapy. Pharmacological therapy and exchange transfusion are the two other treatments for hyperbilirubinemia. Since phototherapy was introduced, the requirement for exchange transfusions has dramatically decreased[1]. Serum total bilirubin (STB) in newborn hyperbilirubinemia is swiftly brought below the therapeutic threshold by intensive phototherapy[3]. Rebound hyperbilirubinemia, which is often an elevation of little more than 1 to 2 mg per dl, is a worry with this method since it frequently happens that the bilirubin level rises slightly after stopping phototherapy[4]. Despite the American Academy of Pediatrics' advice that infants not be kept in hospitals for the determination of repeated bilirubin levels after discontinuing phototherapy, this concern has led some doctors to recheck serum bilirubin levels after removing newborn infants from phototherapy[5].

After quitting phototherapy, underlying changes in bilirubin production and excretion could nonetheless continue and result in bilirubin rebound. Numerous observational studies have already addressed the necessity to evaluate the bilirubin rebound after quitting phototherapy. These investigations, which included neonates born at term or preterm gestation, as well as those who had or hadn't a positive direct Coombs test, came to the conclusion that considerable bilirubin rebound is uncommon and that it is thus unnecessary to evaluate it[3]. Particularly when the Coombs test is positive, in preterm newborns, and in those who had phototherapy for fewer than 72 hours, post-phototherapy rebound hyperbilirubinemia develops[2].

In a study by Kaplan et al., the incidence of severe rebound bilirubin was found to be 13.3% (30/226); a considerable portion of neonates (26/31) who rebounded had had phototherapy for less than 72 hours. They restarted phototherapy at pre-determined bilirubin levels of >256 mol/l (15 mg/dl), and their choice to do so was impacted by the existence of risk variables for hyperbilirubinemia. They found that neonates treated during the first 72 hours of birth, those with Direct Coombs test positive, and newborns under 37 weeks of gestation were more likely to experience a large post-phototherapy rebound[6].

Having bilirubin rebound levels measured in newborns following extensive phototherapy is intended to become routine practice. The group of newborns at high risk will be identified and treated sooner thanks to this method of universal screening for rebound bilirubin levels, which will also assist to lower the incidence of severe hyperbilirubinemia and bilirubin encephalopathy.

We feel that sample size in our study is too low and need very long term followup to see the proper results and to relate for this study we feel this research gap.

## MATERIALS AND METHODS

We conducted a cross sectional survey study in Postnatal wards, NICU, Neonatal step down unit, and Pediatric ward at the Agha Khan University Hospital, Karachi, Pakistan from July 2016 to December 2016. Using a consecutive sampling method, 178 neonates were included in the study. Neonates with gestational age more than 34 weeks and receiving phototherapy for at least 12 hours were included in the study. However, neonates with gestational age less than 34 weeks or receiving exchange transfusion at the bedside were excluded from the study.

Data was analyzed using SPSS version 20. We camculated frequency and percentages for qualitative variables and mean& SD for quantitative variables. To evaluate the association among variables we used the post stratification chi square test was applied by taking P-value ≤0.05 as significant.

## RESULTS

Out of 178 neonates, 15.7% neonates were found with rebound hyperbilirubinemia. Figure I

The mean age of the admitted neonates was 66.21±53.92 hours, mean gestational age of neonates was 36.03±1.01 weeks, mean birth weight was 2.27±052 Kg , mean length of stay was 3.14±2.08 days, mean duration of phototherapy was 37.9±6.52 hours. Table I

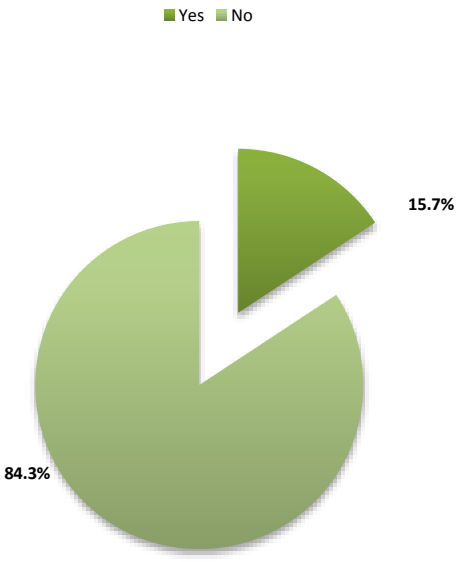


Figure 1: Rebound Hyperbilirubinemia

Table 1: Descriptive Statistics in the Study

| Statistic | Mean | SD |
|---|---|---|
| Age (Hours) | 66.21 | 53.22 |
| Gestational Age( Weeks) | 36.03 | 1.01 |
| Birth Weight (Kg) | 2.27 | 0.52 |
| Length of Hospital Stay (Days) | 3.14 | 2.08 |
| Duration of Phototherapy (Hours) | 37.9 | 6.52 |

There were 50.6% were male and 49.4% were females, 47.8% neonates were aged more than 48 hours, rest were younger than 24 hours, 35.4% were aged between 24 hours to 48 hours, and 28.6% neonates were low birth weight. Table II

The Chi square test of association showed significant association of rebound hyperbilirubinemia with age at admission (p=0.000), birth weight (p=0.005) and hospital stay length (p=0.006). However, no significant association was found with gender (p=0.634) and mode of delivery (p=0.885). Table III

Table 2: Frequency Distribution of Variables in the Study

| Variable | | No. | Percentage |
|---|---|---|---|
| Age | <24 Hours | 30 | 16.9 |
| | 24-48Hours | 63 | 35.4 |
| | > 48 Hours | 85 | 47.8 |
| Gender | Male | 90 | 50.6 |
| | Female | 88 | 49.4 |
| Birth Weight | < 2.5Kg | 51 | 28.6 |
| | ≥ 2.5Kg | 127 | 71.2 |
| Rebound Hyperbilirubinemia | Yes | 28 | 15.7 |
| | No | 150 | 84.3 |
| Maternal Hypertension | Yes | 32 | 18 |
| | No | 146 | 82 |
| Mode of Delivery | SVD | 40 | 22.5 |
| | LSCS | 138 | 77.5 |

Table 3: Chi Square Association of Rebound Hyperbilirubinemia with Various Factors

| Variables | | Rebound Hyperbilirubinemia | | | P-Value |
|---|---|---|---|---|---|
| | | Yes | No | Total | |
| Gender | Male | 13 (46.4) | 77 (51.3) | 90 (50.6) | 0.634** |
| | Female | 15 (53.6) | 73 (48.7) | 88 (49.4) | |
| | | | | | |
| Birth Weight | ≤2.5 kg | 26 (92.2) | 100 (66.7) | 126 (70.8) | 0.005* |
| | >2.5 kg | 2 (7.1) | 50 (33.3) | 52 (29.2) | |
| | | | | | |
| Length of Hospital Stay | ≤1 day | 3 (10.7) | 34 (22.7) | 37 (20.8) | 0.006* |
| | 2-3 days | 10 (35.7) | 80 (53.3) | 90 (50.6) | |
| | >3 days | 15 (53.6) | 36 (24) | 51(28.7 | |
| | | | | | |
| Mode of Delivery | SVD | 6 (21.4) | 34 (22.7) | 40 (22.5) | 0.885** |
| | LSCS | 22 (78.6) | 116 (77.3) | 138 (77.5) | |
| | | | | | |
| Age at the time of Admission | <24 hrs | 17(60.7) | 13 (8.7) | 30(16.9) | 0.000* |
| | 24-48 hrs | 10 (35.7) | 53 (35.3) | 63(35.4) | |
| | >48 hrs | 1(3.6 | 84(56) | 85(47.8) | |

## DISCUSSION

Uncertainty exists over the bilirubin levels' natural course once phototherapy has ended. The idea behind managing neonatal hyperbilirubinemia is to keep bilirubin levels below those that might be "neurotoxic" to the nervous system. The blood-brain barrier's development, postnatal age, the pace at which serum bilirubin rises, the quantity of serum albumin, the presence of hemolysis, and concomitant conditions can all affect how much bilirubin is neurotoxic. Further research is needed to determine if untreated rebound bilirubin might reach harmful levels in the late neonatal era[3].

Post-phototherapy rebound has only been carefully explored in a small number of research[7-12].The mean bilirubin levels at the time of rebound testing were significantly lower than at the time of phototherapy discontinuation, according to a study that pooled term, premature, and low birth weight neonates. However, the study did not provide information on the peak rebound bilirubin concentrations. Only the first serum bilirubin measurement made within 30 hours of phototherapy was taken into account in their analysis, and significant rebound was not defined by predetermined criteria[8,10].

When term newborns with non-haemolytichyperbilirubinemia reached their natural peak, Lazar and colleagues[8] monitored the blood bilirubin levels. The peak in the top range of rebound bilirubin was 267 mmol/l. Neonatals with hemolytic disorders cannot be inferred from the findings, nevertheless. Although there were no established standards for repeat phototherapy, Maisels and Kringutilised a repeat phototherapy event as an indicator of bilirubin rebound. Compared to just 0.7% of those readmitted for main phototherapy, secondary phototherapy was started in 8.2% of those who had early treatment during their hospitalisation for childbirth[9].

Although top limits of the rebound were not disclosed, Al-Saedi120 observed newborns for 8.3 (5.3) hours after phototherapy and documented reduction in mean post-phototherapy bilirubin concentrations. Although 5.1% of these newborns received recurrent phototherapy, Erdeve and colleagues[11] observed that bilirubin concentrations did not significantly rise in 375 neonates who were monitored for up to 12 hours after phototherapy was stopped. However, neither the top bound of the rebound range nor the prerequisites for further phototherapy were specified in that study. One 36-week-old newborn was treated with phototherapy again for a rebound bilirubin level of 17.0 mg/dl in Del Vecchio et al's study of 48 neonates[12].

In infants with 2000 g birth weights who received prophylactic phototherapy, Brown and colleagues[13] found only slight increases in serum bilirubin concentrations; however, in infants with 2000 g birth weights who received phototherapy only if

they actually experienced hyperbilirubinaemia, STB values continued to decline after phototherapy was stopped. Tan and colleagues discovered that, even if predetermined criteria were not defined, only 7.89 out of every 1000 newborns required retreatment with phototherapy[14].

Although these early results show that the use of these nomograms reduces the number of newborns exposed to the possible risks of phototherapy, long-term follow-up is required to make sure that mild neurologic toxic effects do not worsen. Knowledge of neurotoxic bilirubin levels was a key factor in establishing the criteria for phototherapy; however, prospective analysis will be required to confirm their safety.

**Limitation of the Study:** Because of the limited sample size and urban setting of the study, it is possible that the findings cannot be applied to bigger populations.The present study's primary drawbacks are its single-center experience and nonrandomized study methodology.

## CONCLUSION

The idea behind managing neonatal hyperbilirubinemia is to keep bilirubin levels below the range where it turns neurotoxic. Therefore, a rebound bilirubin level must be obtained in high-risk neonates (born at less than 35 weeks gestation or birthweight <2000 gm or onset of phototherapy within 60 h of age) 18-24 h after stopping phototherapy.

**Conflict of Interest:** Authors declared no any conflict of interest in this study

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**Author's Contribution:** XY and XY collected the data, XY and XY analyzed the data, XY and XY drafted the manuscript and XY critically analyzed the draft.

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