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Rebound hyperbilirubinemia in a sample of newborns with jaundice

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Abstract

Background and objectives: Neonatal jaundice represents a prevalent public health problem in Erbil city. Rebound jaundice after termination of phototherapy is common and related to many factors, so the aim of the study is to estimate the prevalence of rebound jaundice among neonates after termination of phototherapy and identifying any associated factors. **Method:** A cross sectional study was conducted in Neonatal Care Unit of Raparin Teaching Hospital in Erbil during the period from 1st of September, 2018 to 28th of February, 2019 on sample of 100 neonates with jaundice. The selected neonates were followed for up to 72 hours after discharge from hospital. Total serum bilirubin levels of neonates were measured at admission, on discharge and within 72 hours of phototherapy termination. **Results:** The rebound jaundice was present in 20% of neonates after stopping the phototherapy. Those were significantly related to certain socioeconomic and clinical data like (male gender, prematurity, low birth weight, Glucose-6-phosphate dehydrogenase deficiency, higher total serum bilirubin at admission, lower total serum bilirubin at discharge, low hemoglobin, high reticulocyte counts and shorter phototherapy duration). **Conclusions:** The prevalence of rebound jaundice after termination of phototherapy was high. So follow up is mandatory within 72 hours of phototherapy termination.

Key words: Neonates, Phototherapy, Rebound jaundice.

Introduction

Hyperbilirubinaemia is a prevalent clinical problem that is shown in about 60% of neonates within their earlier life. The rebound hyperbilirubinaemia is the possible result of shorter period or insufficient phototherapy, especially when infants are preterm and have a positive Coombs test[1]. Specific definition or cutoff values for rebound hyperbilirubinemia are variable with different guidelines. According to American Academy of Pediatrics (AAP), discharge of jaundiced neonates should not be done and phototherapy should be ceased only after total serum bilirubin (TSB) level of less than 13 mg/dL[2]. While National Institute for Health and Care Excellence in United Kingdom recommends discontinuation of phototherapy after declining of TSB by 3 mg/dL below treatment threshold[3]. In Erbil city, the neonatal jaundice represents the most common cause of neonatal admission to neonatal care unit[4].

Earlier discharge of neonates with hyperbilirubinemia is regarded as the main risk factor for rebound hyperbilirubinemia which lead to the need of another phototherapy and re-admission to hospital[5]. In Iraq, it was found that increase body surface area of neonates with shorter duration of phototherapy is the main risk factor for rebound hyperbilirubinemia[6]. Some mechanisms of hyperbilirubinemia continue even after discontinuation of phototherapy, which lead to rise in serum bilirubin and contributing to rebound hyperbilirubinemia[7]. Most authors refer to measurement of TSB 24 hours after discharge from hospital and define the rebound as a TSB level at phototherapy termination[8, 9] while others define it depending on treatment threshold at the time of rebound[10]. Risks related to rebound hyperbilirubinemia are mostly bilirubin toxicity which might be complicated by encephalopathy, re-admission to hospital causing a burden on national health system with cost and high bed occupancy rates and recurrent phototherapy associated with risks of phototherapy toxicity like dehydration, frequent bowel motion and erythematous rash, although they are rare[2,3,11]. Higher proportion of admitted neonates with jaundice to hospitals and different definitions of bilirubin levels at discharge, in addition to increased prevalence of re-admitted neonates for phototherapy in Kurdistan argued us to conduct this study which aimed to measure the prevalence of rebound jaundice after termination of phototherapy and identifying

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associated factors.

Patients and methods

A cross sectional study was conducted at Neonatal Care Unit (NCU) of Raparin Teaching Hospital in Erbil during the period from 1st of September, 2018 to 28th of February, 2019. All neonates presented to NCU with jaundice were the study population. Neonates of age less than 2 weeks with jaundice regardless of gestational age and birth weight were the inclusion criteria. History of asphyxia, major congenital anomalies, sepsis and direct hyperbilirubinemia were the exclusion criteria. The sample size was 100 neonates with jaundice who were included in the study after eligibility to inclusion and exclusion criteria. The ethical part of this study included parental oral informed consent, maintenance of neonatal management under supervision of researchers and taking approval from the Research Ethics Committee of Kurdistan Board for Medical Specialties. All these ethical considerations were done according to Helsinki Declaration.

The data of neonates were collected directly from the parents and filled in a prepared questionnaire including general characteristics of neonates (age, gender, gestational age, birth weight, onset of jaundice, previous history of neonatal jaundice and mode of delivery) and bilirubin characteristics (causes of hyperbilirubinemia, hemolytic causes of hyperbilirubinemia, TSB level at admission, at discharge and within 72 hours of phototherapy termination). The phototherapy was commenced according to AAP guideline2. The phototherapy was done lying on supine position and under monitoring of resident doctors with supervision of pediatrician. The TSB was measured within 72 hours of phototherapy cessation and rebound jaundice was defined as a rise of TSB to treatment threshold according to AAP phototherapy threshold level[5]. The collected data were analyzed statistically by SPSS software version 22. Chi-square test, Fischer's exact test and Independent sample t-test were applied for analyzing the data as suitable. Level of significance (p-value) was regarded statistically significant if it was 0.05 or less.

Results

A total of 100 neonates with jaundice were included in this study with mean age (5.7±2.2 SD) days, predominant age group was 4-7 days (51%), while those above 7 days and those ≤3 days accounted for 34% and 15% consecutively. Females were more than males (51% vs. 49%) and the mean gestational age was (36.2±1.9 SD) weeks, 51% of them were preterm and 49% were term babies. The birth weight was less than 2.5 Kg in 29% and ≥ 2.5 Kg in 71% of them. The onset of jaundice was mainly during the first 3-5 days (55%) of neonatal life while (45%) in the first 2 days. Previous history of neonatal jaundice among siblings was reported in (18%), however, jaundice was unnoticed in (82%) of them. Most of them were product of C/S (61%) rather than normal vaginal delivery (39%). No significant differences were observed between neonates with no rebound and those with rebound jaundice regarding age, onset of jaundice, previous history of siblings with NNJ and mode of delivery. Male gender was significantly associated with rebound jaundice as was premature neonates and low birth weight, Table 1.

Table (1): General characteristics distribution according to rebound jaundice.

Variable	No rebound	Rebound	p-value
	No. (%)	No. (%)	
Age of neonates			0.07
2-3 days	15 (18.7)	0 (0)	
4-7 days	30 (37.5)	11 (55.0)	
>7 days	25 (31.3)	9 (45.0)	
Gender			0.004
Male	33 (41.2)	16 (80.0)	
Female	47 (56.8)	4 (20.0)	
GA			0.03
Preterm	36 (45.0)	15 (75.0)	
Term	44 (55.0)	5 (25.0)	
Birth weight			<0.001
<2.5 Kg	13 (21.2)	16 (80.0)	
≥2.5 Kg	67 (78.8)	4 (20.0)	
Onset of jaundice			0.4
1^{st}-2^{nd} days	34 (42.5)	11 (55.0)	
3^{rd}-5^{th} days	46 (57.5)	9 (45.0)	
Previous history of sibling NNJ			0.9
Positive	14 (17.5)	4 (20.0)	
Negative	66 (82.5)	16 (80.0)	
Mode of delivery			0.4
Normal vaginal delivery	16 (20.0)	2 (10.0)	
Cesarean section	64 (80.0)	18 (90.0)	

The main causes of hyperbilirubinemia were physiological (36%), prematurity (33%) and hemolytic (31%). The hemolytic diseases were commonly ABO blood groups incompatibility (41.9%), RH incompatibility (38.7%) and deficit G6PD (19.4%). Mean TSB at admission was (18.5±2.8SD) mg/dl, at discharge was (10±1.3SD) mg/dl and within 72 hours follow up was (12.1±2.5SD) mg/dl. The rebound jaundice within 72 hours follow up was observed in 20% of jaundiced neonates with a mean of (12.1±2.5SD) mg/dl, Table 2.

Table (2): Causes of hyperbilirubinemia and bilirubin levels of children.

Variable	No. (%)
Causes of hyperbilirubinemia	
Physiological	36 (36.0)
Prematurity	33 (33.0)
Hemolytic	31 (31.0)
Hemolytic causes of hyperbilirubinemia	
RH incompatibility	12 (38.7)
ABO incompatibility	13 (41.9)
G6PD deficiency	6 (19.4)
TSB at admission	mean±SD (18.5±2.8 mg/dl)
TSB at discharge	mean±SD (10±1.3 mg/dl)
TSB during follow up	mean±SD (12.1±2.5 mg/dl)
Rebound jaundice	
No rebound	80 (80.0)
Rebound	20 (20.0)
Total	**100 (100.0)**

A highly significant association was observed between neonatal G6PD deficiency and rebound jaundice, Table 3.

Table (3):: Rebound hyperbilirubinemia versus non-rebound in association with the etiology.

Variable	No rebound	Rebound	p-value
	No. (%)	No. (%)	
Causes of hyperbilirubinemia			<0.001
Physiological	36 (45.0)	0 (0)	
Prematurity	18 (22.5)	15 (75.0)	
Hemolytic	26 (32.5)	5 (25.0)	
Hemolytic causes of hyperbilirubinemia			<0.001
RH incompatibility	12 (46.2)	0 (0)	
ABO incompatibility	13 (50.0)	0 (0)	
G6PD deficiency	1 (3.8)	5 (100.0)	

Table 4 showed that mean TSB at admission was significantly higher and at discharge lower for neonates with rebound jaundice. The mean hemoglobin level was significantly lower and mean reticulocyte count was higher among neonates with rebound jaundice. The mean duration of phototherapy for neonates with rebound jaundice was (30.2±9.2SD) hours which was significantly shorter than (34.5±12.3SD) hours of no rebound jaundice.

Table (4): Profile means distribution according to rebound jaundice.

Variable	No rebound	Rebound	p-value
	Mean (SD)	Mean (SD)	
TSB at admission (mg/dl)	17 (1.8)	20.1 (2.8)	<0.001
TSB at discharge (mg/dl)	10.3 (1.6)	9.6 (0.8)	0.008
Hb (g/dl)	16.6 (2.3)	15.2 (3)	0.01
Reticulocyte count (%)	3.8 (1.3)	4.5 (1.3)	0.01
Duration of phototherapy (hrs)	34.5 (12.3)	30.2 (9.2)	0.05

Discussion

The phototherapy is the best treatment of indirect hyperbilirubinemia for neonates from its first use in 1950s[12]. Body surface area exposed and wavelength intensity of light are the main factors affecting effectiveness of phototherapy. Rebound jaundice was detected after earlier stopping the phototherapy[13].This study showed that rebound jaundice was present in 20% of jaundiced neonates after termination of phototherapy. This prevalence is higher than results of previous Iraqi study which showed that rebound jaundice was detected in 15% of jaundiced neonates after intensive phototherapy and in 5% of jaundiced neonates after conventional phototherapy[6]. Our study prevalence is also higher than rebound jaundice prevalence of 4.6% reported by Chang et al[5]. A study carried out by Niknafs et al7 found that prevalence of neonatal re-admission to neonatal care unit was 11.3%. This high prevalence of rebound jaundice in current study might be attributed to increase in neonatal admission to the single Pediatric hospital in Erbil city study; due to rise in population especially after displacement and migration of hundreds of thousands of population to Erbil city, which increase the bed occupancy rates in neonatal care units and argued the Pediatricians to early discharge of jaundiced neonates. However, present study prevalence of 20% is lower than prevalence of rebound jaundice in post-phototherapy of 24.9% detected by Elhawary et al[14].

Our study revealed that male gender was significantly related to rebound jaundice. This finding is inconsistent with results of Berkwitt et al15 which reported that there was no significant effect of gender on rebound hyperbilirubinemia. This inconsistency might be due to relation of male gender in our study with other common risk factors related to rebound jaundice (like G6PD deficiency). In current study, preterm and low birth weight neonates were significantly associated with rebound jaundice. Similarly, recent study by Valinjkar et al who found that the main risk factors for rebound jaundice after shorter phototherapy duration were prematurity and low birth weight[16]. Our study showed that prematurity was the major cause of hyperbilirubinemia and the main significant cause of rebound jaundice ($p<0.001$). This finding is consistent with many literatures like Maisels et al[11], Bansal et al[17] and Facchini et al[18]. Our study also showed a highly significant association between neonatal G6PD deficiency and rebound jaundice. Similarly; Soni et al[19] found that G6PD deficiency was one of the predominant risk factors for development of rebound jaundice. In our study, means of TSB at admission for neonates with rebound were significantly higher than those with no rebound. This finding coincides with results of previous Woodgate`s study[20]. Inversely, mean TSB at discharge was significantly lower for neonates with rebound, indicating that rapid decline of TSB might be related to rebound jaundice. This finding is in agreement with results of Maisels et al[11] which reported that intensive phototherapy leads to rapid decline in TSB and higher risk for rebound jaundice. Our study showed a significantly poor hematological status of neonates with rebound (low Hb and high reticulocyte count). This finding is consistent with results of Yuradakök study[21]. The main interesting finding in our study was the shorter duration of phototherapy significant link to rebound jaundice that is similar to findings of different studies such as Berkwitt et al[15] and Sharba[6].

Conclusions

Prevalence of rebound jaundice among neonates after termination of phototherapy is high. The common associated factors are male gender, prematurity, low birth weight, G6PD deficiency, rapid decline in TSB and shorter duration of phototherapy. Strong recommendation is to follow up neonates within 72 hours of phototherapy cessation.

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