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Original Article

Review of hospitalized newborns due to indirect hyperbilirubinemia: A retrospective, observational study

Murat Cansever[1], Ahmet Ozdemir[2]

[1]Erciyes University Faculty of Medicine, Department of Pediatric Allergy and Immunology, Kayseri, Turkey
[2]Kayseri Training and Research Hospital, Department of Pediatric Neonatology, Kayseri, Turkey

Abstract

Aim: The aim of our study to identify characteristics of patients admitted to our hospital due to indirect hyperbilirubinemia and to determine risk factors for indirect hyperbilirubinemia.

Material and Methods: The study included 130 patients (gestational age≥36 weeks) who admitted to newborn clinic with the diagnosis of indirect hyperbilirubinemia. In all patients, risk factors, peripheral venous serum samples, complete blood count and biochemical parameters before and after phototherapy were assessed. The phototherapy and exchange transfusion decisions were made according to total serum bilirubin (TSB) levels proposed by Turkish Neonatology Association.

Result: In patients included, mean gestational age was 38.54±0.95 weeks (range: 36-41) while mean birth weight was 3241.53±414.60 g (range: 2020-4400). Of the patients, 71 (54.6%) were boys. Time of presentation was 3.56±1.2 days while total bilirubin level was 21.31±3.83 mg/dL. No underlying cause was detected in 71 patients while there was dehydration in 30 (23.0%), ABO incompatibility in 41 (31.5%) and Rh incompatibility in 20 patients (15.3%). Mean phototherapy duration was 69.78±20.36 hours (range: 48-120). Seven patients received intravenous immunoglobulin (IVIG) therapy. Of these, there was Rh incompatibility in 4 patients and ABO incompatibility in 3 patients. Overall, 6 patients underwent exchange transfusion. In 3 patients, exchange transfusion was required despite IVIG therapy. The hemoglobin, MCV and total bilirubin levels were 15.89±2.92 g/dL, 105.51±6.59 fL and 21.31±3.83 mg/dL before therapy whereas 14.07±2.90 g/dL, 101.41±8.15 fL and 11.33±2.18 mg/dl after therapy, respectively.

Conclusion: Based on our results, the most common cause of hyperbilirubinemia is idiopathic jaundice ((most probably physiological jaundice or breast milk jaundice) in newborns; followed by ABO incompatibility.

Keywords: Phototherapy; Indirect Hyperbilirubinemia; Exchange Transfusion; Risk Factors; Newborn.

INTRODUCTION

Non-pathological jaundice arises from common neonatal alterations in bilirubin metabolism, resulting in increased bilirubin production, decreased bilirubin clearance and elevated enterohepatic circulation (1) Although it is physiological, hyperbilirubinemia and jaundice is a natural process that should be monitored in newborns (2). Although it is possible to prevent morbidity and mortality by early diagnosis and timely management, indirect hyperbilirubinemia remains to be an important issue among neonatal emergencies (3).

In this study, it was aimed to reveal clinical findings and laboratory characteristics by reviewing data from patients admitted to neonatal unit with indirect hyperbilirubinemia and to identify risk factors for indirect hyperbilirubinemia.

MATERIAL and METHODS

In this study, we retrospectively reviewed data from 130 patients (gestational age≥36 weeks) with diagnosis of indirect hyperbilirubinemiawho admitted to Neonatal Clinic of Kayseri Teaching and Research Hospital for phototherapy and/or exchange transfusion. The study included infants born at obstetrics clinic and diagnosed as hyperbilirubinemia during follow-up in neonatal care unit, infants diagnosed as jaundice during outpatient follow-up, those referred to our hospital with hyperbilirubinemia, and those diagnosed as jaundice in pediatric emergency department. The patients with gestational age<36 weeks and those admitted for reasons other than hyperbilirubinemia were excluded. In all patients, data were collected by using predefined form, "Follow-up Sheet for Jaundice in Infants". Five infants were excluded

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Corresponding Author: Murat Cansever, Erciyes University Faculty of Medicine, Department of Pediatric Allergy and Immunology, Kayseri, Turkey, **E-mail:** mcansever66@hotmail.com

from analysis due to incomplete data. Gestational age was determined according to first day of last menstrual period and/or obstetrical sonography measurements. New Ballard scoring was used to control newborns within first 24 hours of life. In all newborns admitted to neonatal unit with hyperbilirubinemia, venous blood samples were drawn to biochemical test tubes and total and direct bilirubin levels were studied in biochemistry laboratory. Decision making process for phototherapy and exchange transfusion was performed according to total serum bilirubin (TSB) level proposed by American Academy of Pediatrics (AAP). Data were analyzed by SPSS for Windows version 22.0 (Statistical Packages for Social Sciences; SPSS Inc., Chicago, IL). All parents or caregivers gave written informed consent at admission.

RESULTS

During one-year study period, 130 patients with hyperbilirubinemia were admitted to our hospital including 59 girls (45.4%) and 71 boys (54.6%). The mean gestational age was 38.54±0.95 weeks. It was found that mean time to presentation was 3.56±1.12 days. Mean birth weight was 3,214.53±414.60 g in the study population. Mean TSB level was 21.31±3.83 mg/dL at presentation (Table 1).

There was Rh incompatibility in 20 patients (15.3%), ABO incompatibility in 41 patients (31.5%), and both Rh and ABO incompatibility in2 patients (1.5%). Nu underlying cause was detected in 71 patients (54.6%) (Table 2). Table 2 also presents mean bilirubin levels of the patients.

Table 3 presents data at admission and discharge in the study population.

Table 1. Demographic characteristics of patients admitted for indirect hyperbilirubinemia

Gestational age* (hafta)	38.54±0.95 (36-41)
Age at presentation* (day)	3.56±1.12 (1-6)
Birth weight *(gram)	3241.53±414.60 (2020-4400)
Gender	
Female n, %	59 (45.4)
Male n, %	71 (54.6)
Total bilirubin level* (mg/dL)	21.31±3.83 (8.7-34.2)

Table 2. Distribution of cases according to blood type incompatibility, mean length of stay and bilirubin level at admission

Blood type incompatibility	Number of patients		Mean bilirubin level (mg/dL)	Mean bilirubin level (mg/dL)
	n	%		
Rh incompatibility	20	15.3	20.94±4.85	70.80±18.21
ABO incompatibility	41	31.5	21.93±4.30	72.00±22.76
ABO plus Rh incompatibility	2	1.5	18.46±3.95	66.32±17.45
No blood type incompatibility	71	54.6	20.98±4.56	70.72±19.86

Table 3. Hematological and biochemical parameters before and after treatment

	N	Minimum	Maximum	Mean	Standarddeviation
Hemoglobin (g/dL)	130	8.90	22.50	15.89	2.92
MCV	130	84.60	126.00	105.51	6.59
MCHC	130	30.50	39.30	33.83	1.43
Reticulocyte (%)	130	0.10	16.60	5.63	3.72
RDW	130	12.40	23.80	15.72	2.14
TSB at admission (mg/dL)	130	8.7	34.2	21.31	3.83
TSB at discharge (mg/dL)	130	5.40	14.20	11.12	1.90
Duration of phototherapy (hour)	130	48	120	69.78	20.36

MCV: Mean corpuscular volume, MCHC: Mean corpuscular hemoglobin concentration, RDW: Red cell distribution width

DISCUSSION

The amplification of mechanisms resulting in pathological conditions such as increased bilirubin production, decreased bilirubin clearance and elevated enterohepatic circulation willlead hyperbilirubinemia. The identification of underlying reason for indirect hyperbilirubinemia is helpful in the prediction whether therapeutic interventions will be prevent severe hyperbilirubinemia (1). Indirect bilirubin level exceeds 13 mg/dl in 6-7% of healthy term infants and bilirubin level>15 mg/dL is found in 3% of these term infants. In indirect hyperbilirubinemia, risk factors include prematurity, positive family history for indirect hyperbilirubinemia, history of maternal diabetes mellitus, race, male gender, agents such as vitamin K3 or novobiocin, altitude, polycythemia, trisomy 21, subcutaneous bleeding, cephalohematoma, oxytocin induction, breastfeeding, dehydration or weight loss due to caloric deficiency (4) In previous studies, it was found that bilirubin levels were higher in infants born via normal spontaneous vaginal delivery than those born via cesarean section and that jaundice prevalence was higher in infants with vacuum-

assistance during delivery (5,6). In our study, total bilirubin level at admission was found to be significantly higher in infants born via normal spontaneous vaginal delivery than those born via cesarean section (p=0.04).

The finding of marked decreased in indirect bilirubin levels following phototherapy favors the fact that phototherapy is an effective treatment modality in indirect bilirubinemia. In our study, age at presentation was comparable to those reported in the literature (7,8).

In our study, there was ABO incompatibility in 31.5%, Rh incompatibility in 15.3% and ABO plus RH incompatibility in 1.5% of the patients. There was ABO blood type incompatibility in 28%, Rh blood type incompatibility in 4.9% and and both ABO and Rh blood type incompatibility in 3.5% of patients. In a study from Turkey, Bolat et al. found ABO incompatibility in 29.2% of infants admitted to hospital due to indirect bilirubinemia for phototherapy while ABOincompatibilitywas reported in 28% of patients in another study [9,10]. In addition, ABO incompatibilityrate was reported as 21% by Kahveci et al., 21.9% by Yiğit et al., and 19.3% by Kılıç et al. (11-13). In our study, 3 patients (7.3%) with ABO incompatibility required exchange transfusion. In various studies from Turkey, need for exchange transfusion rate ranged from 3.4% to 20.4% The Rh incompatibility alone was detected in 20 patients while it was found in combination with ABO incompatibility in 2 patients in our study. This finding is attributed to higher antenatal care rate, resulting in higher rates of anti-D immunoglobulin administration among our patients. The lower rate of Rh incompatibility, an important risk factor, when compared to previous years is attributed to contemporary perinatology studies. The ABO incompatibility still appears as an important risk factor; early diagnosis and accurate management results in favorable outcomes. These findings emphasize the value of preventive healthcare services.

It has been reported that TSB level can exceed physiological limits with no underlying cause in 10% of healthy, term newborns (14-16). In our study, no etiological factor was detected in 71 patients (54.6%). It was though that 30 cases (42.2%) could be delayed breast milk jaundice based on age at presentation while 41 cases (57.8%) were considered as exaggerated physiological jaundice.

In previous studies, it was reported that indirect hyperbilirubinemia is more prevalent among boys (17,18). In our study, TSB level was 21.16±3.68 mg/dL in boys and 21.48±4.03 mg/dL in girls with no significant difference although jaundice was more common among boys (p>0.05).

CONCLUSION

In conclusion, indirect hyperbilirubinemia remains to be an important issue despite contemporary methods and treatment modalities. In current technology, it is thought that indirect hyperbilirubinemia can be prevented by appropriate approach without permanent neurological sequel regardless of underlying etiological factors. Thus, establishing a protocol in neonatal units for management of indirect hyperbilirubinemia will decrease hyperbilirubinemia incidence. In addition, undesired complications such as kernicterus can be prevented by regular follow-up during first week of life and providing education to parents. Blood typing at antenatal period, providing counseling to parents about neonatal jaundice are simple, inexpensive measures which are highly effective.

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Murat Cansever ORCID: 0000-0002-0187-3810
Ahmet Ozdemir ORCID: 0000-0002-7572-069X

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