



Evaluation of Neonates Hospitalized with Indirect Hyperbilirubinaemia

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ABSTRACT

Objective: Neonatal jaundice is a common problem and is the most common cause of hospitalization. We aimed to determine the characteristics and etiological factors of late preterm and term newborns hospitalized due to indirect hyperbilirubinemia.

Methods: Late preterm and term newborns hospitalized between January 1,2009 and December 31,2014 with a diagnosis of indirect hyperbilirubinemia were included. Demographic and clinical characteristics, duration, and patterns of treatment were obtained retrospectively. Etiological factors were determined.

Result: Late preterm and term infants with indirect hyperbilirubinemia were included (n=412). 54.6% of the patients were male, 40.8 % were first babies, the mean gestational age was 38.3±1.1 weeks, and the mean birth weight was 3031±520 grams. 84.5 % were exclusively breastfed. The time of presentation was 4.6 ±2.6 days, and the serum total bilirubin level was 18.6 ±4.7 mg/dl. ABO incompatibility was found in 29 %, dehydration in 10.7 %, and Rh incompatibility in 7.1% of the patients. The mean duration of hospitalization was 3.1 ±2.2 days, and the mean duration of phototherapy was 44.8±22.8 hours. 16 patients received intravenous immunoglobulin. An exchange transfusion was performed in 14 patients. In the group with a serum total bilirubin level of ≥ 20 mg/dl, male gender and normal spontaneous vaginal delivery were statistically significantly higher than the group with a serum total bilirubin level below 20 mg/dl (p = 0.02 for both).

Conclusion: Indirect hyperbilirubinaemia, which is common in the neonatal period, should be recognized early and is a treatable condition. We should promptly identify and treat the cause before complications arise.

Keywords: Etiological factors, indirect hyperbilirubinemia, newborn

İndirekt Hiperbilirubinemi Tanısı ile Hospitalize Edilmiş Yenidoğanların Değerlendirilmesi

Araştırma Makalesi

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ÖZET

Amaç: Sarılık yenidoğan döneminde sık karşılaşılan sorundur ve hastane yatışlarının en sık nedenidir. Bu çalışmada, indirekt hiperbilirubinemi nedeni ile hospitalize edilen geç preterm ve term yenidoğanların özelliklerini ortaya koymak ve etiyolojik faktörlerini belirlemek amaçlanmıştır.

Yöntem: İndirekt hiperbilirubinemi tanısı ile 1 Ocak 2009-31 Aralık 2014 tarihleri arasında hastaneye yatırılan geç preterm ve term yenidoğanlar çalışmaya alındı. Hastaların demografik ve klinik özellikleri, tedavi süreleri ve şekilleri retrospektif hasta dosyalarından elde edildi. Etiyolojik faktörler belirlendi.

Bulgular: 1 Ocak 2009-31 Aralık 2014 tarihleri arasında hastanemiz yenidoğan yoğun bakım ünitesinde takip edilmiş 4831 hastanın 412'si dahil edilme kriterlerini karşılayan indirekt hiperbilirubinemili geç preterm ve term bebeklerdi. Hastaların %54,6'sı erkek, %40,8'i ilk bebek, doğum haftası ortalama 38,3±1,1 ve doğum ağırlığı 3031±520 gram olarak saptandı. Vakaların %84,5'i yalnızca anne sütü alıyordu. Başvuru zamanı 4,6±2,6 gün ve serum total bilirubin düzeyi 18,6±4,7 mg/dl idi. Hastaların %29'unda ABO uyumsuzluğu, %10,7'sinde dehidratasyon ve %7,1'inde Rh uyumsuzluğu vardı. Ortalama yatış süresi 3,1±2,2 gün ve fototerapi süresi 44,8±22,8 saat olarak bulundu. 16 hastaya intravenöz immünglobülin verilmişti. 14 hastaya kan değişimi yapılmıştı. Serum total bilirubin düzeyi ≥20 mg/dl olan grupta erkek cinsiyet ve normal spontan vajinal yol ile doğan bebek serum total bilirubin düzeyi 20 mg/dl'nin altında olan gruptan istatistiksel olarak anlamlı yüksek saptandı (her ikisi için p=0,02).

Sonuç: Yenidoğan döneminin sık görülen indirekt hiperbilirubinemi erken fark edilmesi gereken ve tedavi edilebilir bir durumdur. Nedeni hızlıca saptanmalı ve komplikasyon gelişmeden tedavi edilmelidir.

Anahtar Kelimeler: Etiyolojik faktörler, indirekt hiperbilirubinemi, yenidoğan

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Introduction

The most prevalent reason for hospitalization during the first week after birth is jaundice, which affects 60 % of full-term newborns and 80 % of preterm infants. Numerous factors, including gestational age, birth weight, race, geographic location, genetic background and concomitant illnesses, might affect the intensity and duration of jaundice in neonates. The chance of having excessive bilirubin levels rises in tandem with the number of risk factors. Serum total bilirubin (STB) levels above 17 mg/dL after the 72nd hour is significant in late preterm and term newborns; levels above 20 mg/dL are critical; levels above 25 mg/dL are excessive; and levels above 30 mg/dL are classified as dangerous hyperbilirubinemia.^{1,2} The American Academy of Pediatrics (AAP) suggests that, in order to lower hospital admissions and the risk of kernicterus associated with indirect hyperbilirubinemia, every healthcare facility identify risk factors prior to discharge and establish a protocol for detecting and monitoring the rate of bilirubin increase.² The goals are to stop bilirubin levels from rising too high, reduce the chance of brain injury, and end kernicterus instances. In the process of developing an indirect hyperbilirubinemia monitoring protocol in our hospital, this study intends to assess and compare the etiologies, bilirubin levels, and demographic, clinical, and laboratory characteristics of late preterm and term infants diagnosed with indirect hyperbilirubinemia who are admitted to our neonatal unit.

Materials and Methods

This retrospective analysis comprised 412 late preterm and term neonates who were observed in our neonatal intensive care unit from January 1, 2009, to December 31, 2014, for indirect hyperbilirubinemia. Those with congenital cardiac disease, metabolic disorders, chromosomal abnormalities, and sepsis monitoring were not included in the sample, nor were babies delivered before 37 weeks or beyond 40 weeks. Only infants born between 37 and 40 weeks who were diagnosed with indirect hyperbilirubinemia were included. This study collected the following information from patient files and hospital systems: gender, gestational age, time of hospital admission, weight at birth, feeding technique, mode and location of delivery, birth order, day the baby was brought to the hospital, length of hospital stay and the day the family noticed jaundice. comprehensive blood count, serum total bilirubin, direct bilirubin levels, C-reactive protein (CRP), venous hematocrit and reticulocyte values, maternal and neonatal blood groups, presence of reducing substances in urine, thyroid-stimulating hormone level, pyruvate kinase and glucose-6-phosphate dehydrogenase (G6PD) levels, and direct Coombs test results were among the laboratory data collected. Patient records also contained details regarding the therapies that the patients received, including the length of phototherapy, intravenous immunoglobulin (IVIG), and exchange transfusion.

Statistical Analysis

The SPSS (Statistical Package for Social Sciences) for Windows 15.0 application was used to undertake the statistical analysis of the results. Descriptive statistical analysis was used to assess the demographic features. The comparison of qualitative and quantitative data was done using descriptive

statistical techniques (mean, standard deviation, median, minimum, and maximum), as well as Student's t-test, Chi-square test, and Fisher's exact test. The significance level was set at $p < 0.05$.

Ethical Approval: The Cumhuriyet University Ethics Committee granted its approval for the study (Decision No. 04/07, Date: 2015).

Result

Among the 4,831 patients monitored in our hospital's neonatal intensive care unit from January 1, 2009 to December 31, 2014; 412 were late preterm and term infants diagnosed with indirect hyperbilirubinemia. Of these patients, 81 (19.7 %) were referred from other facilities, and 331 (80.3 %) were born in our hospital. Forty-eight percent of the patients were first-born males, making up 54.6 % of the patient population. The mother's age ranged from 16 to 44 years on average, and 62.9 % of the babies were born naturally through spontaneous vaginal delivery (NSVD). The average birth weight was 3,034 +/- 529 grams, and the average gestational age was 38.3 +/- 1.1 weeks. Eighty-four percent of the babies were nursed exclusively. Within the first week, 75% of the patients were admitted to the hospital; admissions took place on days 1 through 16 days (on average, the 4th day). Table 1 provides a summary of the patients' indirect hyperbilirubinemia causes. The average period of phototherapy for the patients was 48 hours, and their average serum total bilirubin (STB) level was 18.6 mg/dL. Sixty-four (15.5 %) of our patients had a direct Coombs test that was positive. Intravenous immunoglobulin (IVIG) treatment was administered to sixteen patients who had significant hyperbilirubinemia (>20 mg/dL) as a result of blood group incompatibility and STB levels at the exchange transfusion threshold. With mean STB levels of 32.8 +/- 14 (26-47) mg/dL, a total of 14 patients underwent exchange transfusion; three of these patients underwent exchange transfusion after IVIG treatment. Eighty percent of the newborns receiving exchange transfusions were delivered naturally by vaginal delivery (NSVD), and the average time of the transfusions was between 2.9 and 1.2 days. Six of these babies were incompatible with ABO, five were incompatible with Rh, and three were incompatible with both ABO and Rh (Table 2). Both male newborns and those born via normal spontaneous vaginal delivery (NSVD) were substantially more likely to be in the severe hyperbilirubinemia group ($p=0.02$) when the patients were split into two groups based on their STB values (<20 mg/dl ve ≥ 20 mg/dl). In the group with severe hyperbilirubinemia, there were statistically significantly more patients with G6PD deficits and urinary tract infections ($p = 0.07$ for both). Patients with STB 20 mg/dL had substantially lower hematocrit levels than those with STB <20 mg/dL ($p = 0.04$). Severe hyperbilirubinemia was present in 33.6 % of individuals with ABO incompatibility and 14.1% of individuals with Rh incompatibility. Regarding additional risk variables including dehydration, feeding technique, Rh incompatibility, and ABO incompatibility, no significant differences were seen between the groups (Table 3). Out of the 412 patients that underwent phototherapy, 12% had diarrhea, 15% had skin rashes, and 2 had necrotizing enterocolitis sepsis after receiving an exchange transfusion. During the transfusion, a patient's bradycardia and apnea were noted as causes of death.

Table 1. Identifiable causes of indirect hyperbilirubinaemia in patients

Etiological factors	n (%)
ABO mismatch	122 (29.6)
Dehydration	45 (10.9)
Rh incompatibility	30 (7.2)
Urinary tract infection	12 (2.9)
G6PD deficiency	12 (2.9)
Hypothyroidism	5 (1.2)
Cephal haematoma	4 (0.9)
Surrenal haematoma	4 (0.9)
Polycythemia	4 (0.9)
ABO+Rh incompatibility	3 (0.7)
Hereditary spherocytosis	2 (0.4)
Galactosemia	2 (0.4)
Unidentified cause	167 (40.5)

G6PD: glucose 6 phosphate dehydrogenase

Table 2. Some laboratory results and treatment methods of the patients

Total serum bilirubin (mg/dl)	18.6 (8-47)
Direct bilirubin (mg/dl)	0.6 (0.1-8)
Haematocrit (%)	49.8 (23-72)
Leucocytes (n)	11170 (3400-47000)
Reticulocyte (%)	1 (0-18)
Duration of phototherapy (hours)	48 (12-168)
Blood exchange n (%)	14 (3.4%)
IVIG treatment n (%)	16 (3.9%)

Values were given as mean (minimum-maximum) and n (%).

IVIG: intravenous immunoglobulin

Table 3. Comparison of the groups with and without severe hyperbilirubinaemia in terms of demographic, clinical and laboratory data

n(%)	STB<20 mg/dl (n=284)	STB≥20 mg/dl (n=128)	p
Gender			
Female	166 (58.5)	59 (46.1)	0.02*
Male	118 (41.5)	69 (53.9)	
Mode of delivery			
Normal	168 (59.2)	91 (71.1)	0.02*
Sectio	116 (40.8)	37 (28.9)	
Gestational age	38.28±1.3	38.2±1.1	0.72
Dehydration	31 (10.9)	12 (9.4)	0.63
Diet			
Breast milk	236 (83.1)	112 (87.5)	0.51
Formula milk	7 (2.5)	2 (1.6)	
Mix tipe milk	41 (14.4)	14 (10.9)	
Hematocrit	50.6±8.6	47.9±8.7	0.04*
Leukocyte count	10595±4750	12626±5449	0.053
ABO incompatibility	79 (27.9)	43 (33.6)	0.23
Rhincompatibility	25 (8.8)	18 (14.1)	0.11
Urinary infection	4 (1.4)	8 (6.2)	0.07
G6PD defisity	4 (1.4)	8 (6.2)	0.07
D.combs positive	41 (14.4)	23 (18)	0.36

*p<0.05, STB:serum total bilirubin, G6PD: glukoz 6 fosfat dehidrogenaz

Discussion

Talk about one of the most prevalent conditions in the newborn stage is jaundice. It affects 60 % of full-term babies, and 5–10 % of these instances necessitate hospital care. Male gender, breastfeeding, being the first child, early discharge of the mother and child after delivery, and pathological weight loss are risk factors for developing jaundice that requires medical attention.³⁻⁶ Studies show that jaundice exhibits regional, ethnic, and cultural variances, and that each nation must establish its own guidelines for treating jaundice.⁴ In wealthy nations, mother-child pairs' postpartum hospital stays have gotten shorter, especially in the last ten years. But as a result, infants with indirect hyperbilirubinemia are being readmitted at a significantly higher rate after being discharged.^{6, 7} Neonatal jaundice is known to affect male infants more frequently than female neonates, with a male-to-female ratio of 1 to 1.5.^{2,8} In a similar vein, male newborns accounted for 54.6 % of the cases in our study. First-born parents' inexperience with baby care and feeding, along with the delayed increase in breast milk supply following the first birth, are the likely causes of the greater frequency of newborn jaundice in these children.^{1,9} Bülbül et al., however, discovered that having a first child did not increase the risk.¹⁰ Although 40.8 % of the newborns in our study were the first in their families, there was no evidence linking this to an increased risk of high bilirubin levels. As opposed to cesarean sections, the American Academy of Pediatrics (AAP) states that having a normal spontaneous vaginal delivery (NSVD) increases the risk of high bilirubin levels.² While Phuapradit et al. could not detect a link between the technique of delivery and jaundice,¹³ other research^{11,12} corroborate the AAP data. According to our research, babies delivered via NSVD had statistically considerably higher STB values than babies delivered by cesarean surgery. G6PD deficiency, subgroup incompatibility, and ABO and Rh incompatibility are the most frequent hemolytic causes of indirect hyperbilirubinemia.^{14,15} ABO incompatibility was found in 11.1% and Rh incompatibility in 7.4% of patients with indirect hyperbilirubinemia, according to Kâini et al.¹⁶ Indirect hyperbilirubinemia was seen in 21.3% of ABO incompatibility cases, according to Sarici et al.¹⁷ ABO incompatibility affected 29% of our patient population, while Rh incompatibility affected 7.2%. Of them, six individuals had ABO incompatibility and five had Rh incompatibility; significant hemolysis was seen in both groups. This suggests that blood group screening should be done on patients who have indirect hyperbilirubinemia. The most prevalent erythrocyte enzyme deficit in the world, G6PD deficiency is linked to kernicterus and indirect hyperbilirubinemia.^{18,19} G6PD deficiency was found to be 2.8% in our study. It is well known that infants who are solely breastfed are more likely to develop jaundice. According to the Schneider study, 2% of breastfed newborns and 0.3% of formula-fed infants had severe jaundice, while 14% of breastfed infants and 4% of formula-fed infants had mild jaundice.²⁰ Hyperbilirubinemia was

found in 28% of term newborns who were fed solely breast milk, according to Bhat et al.²¹ We found no evidence of a substantial relationship between dietary status and bilirubin levels in our investigation. For certain cases, the etiology of indirect hyperbilirubinemia remains unknown despite the identification of numerous factors. In Canadian research, 64% of 258 individuals with severe hyperbilirubinemia had no known etiology.²² Urinary tract infection (UTI) and congenital hypothyroidism have been found to have rates of 4%, 7.5%, and 1.2–3.9%, respectively, among other etiologic causes in neonates with jaundice.^{23–25} As etiologic variables, we discovered hypothyroidism in 5% of the patients and UTI in 2.8 % of them. With evolving technology, phototherapy has been applied more broadly and more successfully in the treatment of infant jaundice.^{4,26} From the time of their admission to the clinic, all of the patients in our study received phototherapy. If the STB level is more than 25 mg/dl in healthy term neonates, exchange transfusion is advised.^{10,27} According to reports in the literature, newborns who received exchange transfusions had STB levels ranging from 26 to 38 mg/dl.^{7,10} The most frequent reason for infants receiving exchange transfusions has been determined to be ABO incompatibility.^{10,28–30} ABO incompatibility was revealed to be the most common reason in 3.4 % of our patients (mean STB levels of 31.1 mg/dl), who underwent exchange transfusion.

Conclusion

In summary, indirect hyperbilirubinemia is a significant and prevalent illness that affects newborns. A thorough investigation of the underlying reason is necessary. In order to stop difficulties from developing, it's also critical to identify patients as soon as possible and start the proper treatment. Not one acknowledgement.

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