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Assessments at week 2 and 3 in Term Newborns Diagnoses with Prolonged Jaundice

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Abstract

Introduction: Jaundice is one of the most common problems at neonatal period and seen in 60-70% of all newborns at first days of life. Prolonged jaundice is defined as hyperbilirubinemia persisting at the end of week 2 in term newborns.

In this study, we reviewed term newborns diagnosed with prolonged jaundice. It was aimed to demonstrate delaying laboratory evaluations for a week in infants with favorable clinical presentation can prevent unnecessary tests in majority of newborns.

Materials and Methods: The study included full-term newborns who presented after day 14 of life and diagnosed with prolonged jaundice at neonatology outpatient clinic of Health Sciences University, Keçiören Teaching and Research Hospital in 2016. Overall, 336 infants with prolonged jaundice were screened. The infants with congenital anomaly, those with findings of sepsis or severe infection, those with history of intrauterine infection, those with history of acholic stool and those with no available data were excluded. In 180 patients included, clinical evaluations, bilirubin levels and advanced test results were assessed at baseline and weekly follow-up.

Findings: Of the infants included, 51.7% were boys while 48.3% were girls. The most common blood type was A Rh (+). There was ABO incompatibility alone in 24 infants (14.2%), Rh incompatibility alone in 6 infants (3.5%) and ABO plus Rh incompatibility in 3 infants (1.2%). In 130 infants, total bilirubin was studied on both week 2 and 3. At week 3, total bilirubin value was ≥10 mg/dl in only 36 infants (27.7%) while it was decreased below 10 mg/dL in 94 infants (72.3%). Urinary tract infection (UTI) was detected in 7 of 38 infants with available tests at week 2. Two of 6 infants with UTI had other clinical signs of UTI. Mean total bilirubin value was 17.9 mg/dL in 5 infants. A significant correlation was found between UTI and vomiting, breastfeeding and feeding pattern ($p<0.05$). Congenital hypothyroidism was detected in 6 of 38 infants with available tests at week 2. It was seen that 2 infants had suspected congenital hypothyroidism in neonatal heel prick test and underwent further evaluations while mean total bilirubin value was 17.5 mg/dL at week 2 in remaining 4 infants. Given the vast majority of cases are breast milk jaundice, a novel cut-off value was defined for total bilirubin measurement at week 2 to distinguish the cases in which total bilirubin decreases below 10 mg/dL at week 3.

Conclusion: Although several disorders that may lead prolonged jaundice at neonatal period have been identified, it is well-known that prolonged jaundice can be seen without any pathological condition in majority of infants fed by breast milk. Delaying laboratory evaluations recommended at week for prolonged jaundice is an approach that may prevent unnecessary testing in most infants.

Keywords: Prolonged jaundice, total bilirubin, newborn

Introduction

Jaundice is one of the most common problems at neonatal period, which is seen in 60% of full-term infants and 80% of preterm infants [1]. In newborns, higher number of red blood cells and shorter lifespan of red blood cells are major reasons for increased bilirubin production. Jaundice develops in most newborns as a results of these physiological alterations [2]. In full-term infants, prolonged jaundice is defined as hyperbilirubinemia lasting more than 14 days of life. Majority of prolonged jaundice cases are breast milk jaundice [3]. The diagnostic workshop for etiology include many blood and urine tests. However, there is no consensus on the priority and value of laboratory tests employed in the evaluation for prolonged jaundice. Congenital hypothyroidism is a rare endocrine disorder. It is a serious but treatable cause of prolonged indirect hyperbilirubinemia (IHB). In congenital hyperthyroidism, early diagnosis and timely treatment are highly important for normal development of intelligence. It is included in the neonatal screening program in Turkey. It was reported that development of intelligence is normal when diagnosed and treated within first 4 weeks of life. In addition, prolonged jaundice may be due to urinary tract infection in newborns [4].

In this study, we reviewed term newborns diagnosed with prolonged jaundice. It was aimed to demonstrate delaying laboratory evaluations for a week in infants with favorable clinical presentation can prevent unnecessary tests in majority of newborns.

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Material and Method

This study was approved by Ethics Committee of Health Sciences University, Keçiören Teaching and Research Hospital (approval#12.04.2017/1394). In the study, we reviewed the files of full-term newborns who presented and diagnosed with prolonged jaundice at neonatology outpatient clinic of Health Sciences University, Keçiören Teaching and Research Hospital. The infants with total bilirubin ≥10 mg/dL were considered as prolonged jaundice. We extracted data regarding history, systemic examination and laboratory evaluations from electronic records of 336 infants who were diagnosed as prolonged jaundice between 01.01.2016 ad 31.12.2016. We excluded 81 infants with gestational age of 37 weeks and 75 infants with no available data. In addition, we intended to exclude infants with congenital anomaly, findings of sepsis or severe infection, history of intrauterine infection or history of acholic stool; however, no infant with such clinical conditions were detected.

In 180 patients included, day of presentation, clinical assessments at presentation and during weekly follow-up, bilirubin levels and results of further examinations for etiology were assessed. For each infant included, research data sheet was completed. In all patients, we recorded data regarding age, mode of delivery, birth weight, feeding and vomiting status, maternal age, gravidity, blood types of mother and baby, history of traumatic delivery, feeding characteristics, smelly urine, treatments given for jaundice, ethnicity, weight gain, height, head circumference, presence of cephalic hematoma or ecchymosis, and total bilirubin measurements during weekly follow-up. In 84 infants underwent evaluations for etiology of hyperbilirubinemia, blood type and results of direct Coombs (DC) test, complete blood count, reticulocyte count, urinalysis, urine culture test, thyroid function tests, G6PD and urine glucose chromatography were extracted. Urinary tract infection was diagnosed by ≥ leukocyte per field in urine microscopy and single microorganism growth (>105 CFU/mL) in urine sample collected in a sterile manner. TSH was studied by Abbott Architect I200R immunoassay analyzer using chemiluminescence method. The patients with TSH>10 µIU/ml who were prescribed thyroid hormone replacement were deemed as congenital hypothyroidism. Throughout study period, transcutaneous bilirubin measurements were performed using JM103 Drager jaundice meter which was set to display average of 3 measurements. In all infants evaluated, total bilirubin and direct bilirubin values from venous samples were studied using Abbott Architect I200R immunoassay analyzer at central laboratory. Complete blood count and reticulocyte count were performed using Cell Dyn 3700 hematology analyzer.

Statistical analysis

All statistical analysis were performed using IBM SPSS version 23.0. Descriptive statistics are presented as count and percent for categorical variables whereas standard deviation, median, and minimum-maximum for continuous variables. The categorical variables were analyzed using Chi-square test. The normal distribution was tested continuous variables and the differences between groups were analyzed using Mann-Whitney U test. ROC analysis was performed too identify a novel cut-off point for total bilirubin measurement in the diagnosis of prolonged jaundice. A p value≤0.05 was considered as statistically significant.

Findings

The study included 180 full-term newborns diagnosed with prolonged jaundice. Mean birth weight was 3260±385.9 g while mean birth height was 49.7±1.9 cm. Mean maternal age was 27.5±5.4 years ranging from 17 to 42 years. Mean age at presentation was 18.2±4.2 days ranging from 14 to 39 days.

Of the infants included, 51.7% were boys while 48.3% were girls. When mode of delivery was assessed, it was found that 57.2% of infants were born via normal spontaneous vaginal delivery while 38.3% was first pregnancy. When blood types were assessed, it was found that the most common blood type A Rh (+) in both mothers and infants while there was ABO incompatibility alone in 24 infants (14.2%), Rh incompatibility alone in 6 infants (3.5%) and ABO plus Rh incompatibility in 3 infants (1.2%). None of the infants had history of traumatic delivery. Table 1 presents demographic characteristics.

It was found that there was poor feeding in 4 infants (2.2%), vomiting in 8 infants (4.4%), failure to gain weight in 13 (7.2%) and foul odor in urine in 1 infant (0.6%). It was seen that 27 of infants (15%) underwent phototherapy.

When distribution of total bilirubin values were assessed, there were 159 infants with total bilirubin≥10 mg/dL in week 2 (day 14-20). The first presentation to hospital was at week 3 or later in remaining 21 infants. OF these, first total bilirubin measurement was performed at week 3 in 13 infants and at week 4 in 8 infants.

In 130 infants, total bilirubin was studied on both week 2 and 3. At week 3, total bilirubin value was ≥10 mg/dl in only 36 infants (27.7%) while it was decreased below 10 mg/dL in 94 infants (72.3%). This result was important since the study aimed to assess whether laboratory tests can be delayed one week by assessing full-term newborns with prolonged jaundice at weeks 2 and 3.

Table 2 presents that there was no significant differences in parameters evaluated between infants with total bilirubin <10 mg/dL and those with total bilirubin >10 mg/dL at week 3 or later (Chi-square test, p>0.05).

Table 1: Presents demographic characteristics

Birth weight (g)	3260.3 ±385.9		3210	(2350-4285)
Maternal age (years)	27.5 ±5.4			27 (17-42)
Age at presentation (days)	18.2 ±4.2			17 (14-39)
Height (cm)	49.75 ±1.9			50 (45-57)
Head circumference (cm)	35.9 ±1.5			36 (33-47)
		n		
Gender	Female	87		48.3
	Malle	93		51.7
Mode of delivery	NSVD	103		57.2
	C/S	77		42.8
Pregnancy order	First pregnancy	69		38.3
	Subsequent pregnancy	111		61.7
Maternal blood type	A+	71		41.5
	A-	3		1.8
	B+	32		18.7
	B-	1		.6
	0+	43		25.1
	0-	8		4.7
	AB+	11		6.4
	AB-	2		1.2
Infant blood type	A+	83		48.3
	A-	4		2.3
	B+	25		14.5
	B-	4		2.3
	0+	40		23.3
	0-	4		2.3
	AB+	10		5.8
	AB-	2		1.2
Incompatibility	Yok	136		80.5
	AB0	24		14.2
	Rh	6		3.5
	ABO+Rh	3		1.2
Ethnicity	Turkey	173		96.1
	Foreign national	7		3.9

Table 2: Comparison of some clinical findings between infants with total bilirubin<10 mg/dL and >10 mg/dL at week 3 or later

		Tbil>10		Tbil<10		
		Count (n)	*Percent (%)*	*Count (n)*	*Percent (%)*	*p value*
Gender	Female	49	52.1	21	42.9	0.293
	Male	45	47.9	28	57.1	
Mode of delivery	SVD	53	56.4	30	61.2	0.578
	C/S	41	43.6	19	38.8	
Feeding	Good	94	100.0	48	98.0	0.343
	Poor	0	0.0	1	2w.0	
Vomiting	No	91	96.8	48	98.0	0.576
	Yes	3	3.2	1	2.0	
Pregnancy	First pregnancy	35	37.2	18	36.7	0.953
order	Subsequent pregnancy	59	62.8	31	63.3	
Incompatibility	No	67	77.0	41	87.2	0.170
	AB0	18	20.7	4	8.5	
	Rh	2	2.3	2	4.3	
Feeding pattern	Breast milk	70	74.5	41	83.7	0.339
	Formula	1	1.1	1	2.0	
	Mixed	23	24.5	7	14.3	
Drugs used	None	26	27.7	14	28.6	0.908
	Vitamin D	68	72.3	35	71.4	
Smell in urine	No	94	100.0	49	100.0	-
	Foul odor	0	0.0	0	0.0	
Weight gain	No	5	5.3	6	12.2	0.140
	Yes	89	94.7	43	87.8	
Phototherapy	No	78	83.0	43	87.8	0.452
	Yes	16	17.0	6	12.2	
Ethinicity	Turkey	88	93.6	48	98.0	0.240
	Foreing national	6	6.4	1	2.0	

Table 3 presents some continuous variables and differences between groups. The continuous variables showed skewed distribution in Kolmogorov-Smirnov test; thus, descriptive statistics are presented as median and minimum-maximum. The groups were compared using Mann Whitney U test. No significant difference was found in parameters evaluated between groups ($p>0.05$).

Table 3: Comparison of some descriptive characteristics between infants with total bilirubin<10 mg/dL and >10 mg/dL at week 3 or later

		Tbil<10		Tbil>10	
	Mean ±Standard deviation	Median (Min-Max.)	Mean. ±Standard deviation	Median (Min-Max)	p value
Birth weight (g)	3275.0 ± 389.1	3265 (2400-4285)	3242.7 ± 369.8	3200 (2470 - 4000)	0.743
Maternal age	27.3 ± 5.6	27 (17 - 40)	27.4 ± 5.4	27 (19 - 42)	0.917
Height (cm)	49.7 ± 1.7	50 (46 - 57)	49.8 ± 1.9	50 (46 - 57)	0.887
Head circumference (cm)	35.9 ± 1.2	36 (33 - 40)	35.8 ± 2.0	36 (33 - 47)	0.456

The prolonged jaundice was diagnosed at the end of week 2 in 88.3% whereas at the end of week 3 in 7.2% and at the end week 4 in 4.4% of infants. In all infants diagnosed on days 21-27 and 28-34, laboratory evaluations were started within same week; however, of the infants diagnosed on days 14-20, laboratory evaluations were started within same week in 23.9% (n=38), on days 21-28 in 11.3% (n=18) and on days 28-35 in 4.4% (n=7).

In our study, it was found that total bilirubin decreased below 10 mg/dL in 94 of 159 infants diagnosed at week 2 while it was above 10 mg/dL in 36 infants. When timing of laboratory evaluations was assessed, it was found that total bilirubin was above 10 mg/dL in 5 of 96 infants without any laboratory evaluation while in 12 of 38 infants who underwent laboratory evaluations at week 2, 17 of 18 infants who underwent laboratory evaluations at week 3 and 2 of 7 infants who underwent laboratory evaluations at week 4.

Regardless of time of diagnosis, feeding was considered as good in all infants who underwent no laboratory evaluation. In 3 infants with vomiting, no laboratory test was performed as they had good feeding and adequate weight gain. UTI was detected in 7 of 38 infants who underwent laboratory evaluations at week 2, 5 of 31 infants who underwent laboratory evaluations at week 3 and 3 of 15 infants who underwent laboratory evaluations at week 4. It was found that there was vomiting in 3 and poor feeding in 2 infants who underwent laboratory evaluations at week 2; all of which were diagnosed with UTI. It was found that there was failure to gain weight in 6 infants who underwent laboratory evaluations at week; UTI was detected in one while congenital hypothyroidism in one of these infants. It was found that there was failure to gain weight in 3 infants who underwent laboratory evaluations at week 3, all of which were diagnosed with UTI. Again, it was found that there was poor feeding in 2 and vomiting in another 2 infants who underwent laboratory evaluations at week 4, all of which were diagnosed with UTI.

It was found that TSH was 5-10 µIU/mL in 1 and >10 µIU/mL in 6 of 38 infants who underwent laboratory evaluations at week 2 while it was >10 µIU/mL in 1 of 31 infants who underwent laboratory evaluations at week 3. It was found that hemoglobin was 15.22 g/dL in infants who underwent laboratory evaluations at week 2 whereas 14.63 g/dL in infants who underwent laboratory evaluations at week 3 and 12.43 g/dL in infants who underwent laboratory evaluations at week 4. Mean reticulocyte count was higher in 15 infants who underwent laboratory evaluations at week 4 when compared to infants who underwent laboratory evaluations earlier. DC test was found to be negative in all infants. Again, urine glucose chromatography and G6PD level were found to be normal in all infants.

In 6 infants with TSH>10 µIU/mL in , mean T4 was 0.85 ng/dL while mean hemoglobin was 16.33 g/dL and mean reticulocyte count was 0.73. In these infants, mean total bilirubin was 14.6 mg/dL (range: 10.0 -19.9 mg/dL) at week 2. It was seen that 2 infants (total bilirubin: 10 mg/dL and 13 mg/dL, respectively) had suspected congenital hypothyroidism in neonatal heel prick test and underwent further evaluations. In remaining 4 infants, mean total bilirubin was 17.5 mg/dL (Range: 16.4-19.9 mg/dL).

In one infant with total bilirubin of 12 mg/dL, control tests were performed as TSH was 5.6 µIU/ml. In the control tests, it was found that TSH decreased below 5.0 µIU/ml; thus, congenital hypothyroidism was excluded.

It was found vomiting was present in 35.7% of infants diagnosed with UTI while no vomiting was observed in infants without UTI. Again, it was found that feeding was good in all infants without UTI, the rate was 71.4% in infants with UTI. When feeding pattern was assessed, it was seen that formula feeding or combined feeding was more common in infants diagnosed with UTI when compared to those without UTI. No significant correlation was detected between UTI and hemoglobin values (Mann Whitney U: 396.500; p=0.452).

Of 38 infants who underwent laboratory evaluations at week, no UTI was detected in 28 while UTI was detected in 7. Mean total bilirubin was 14.3 mg/dL in infants with UTI while it was 16.5 mg/dL in infants without UTI but the difference did not reach statistical significance (p>0.05).

These results provide important data since in our study, it was aimed to reduce test burden, costs and parental anxiety by delaying laboratory evaluations one week in infants without risk factor. In addition, establishing a novel cut-off value will help to distinguish cases with normal laboratory evaluations in which total bilirubin value decrease below 10 mg/dL since majority of the cases have breast milk jaundice.

ROC analysis was performed to determine a novel cut-off value for total bilirubin measurements at week 2. It was aimed to discriminate infants with prolonged jaundice at week 3 more effectively at week 2.

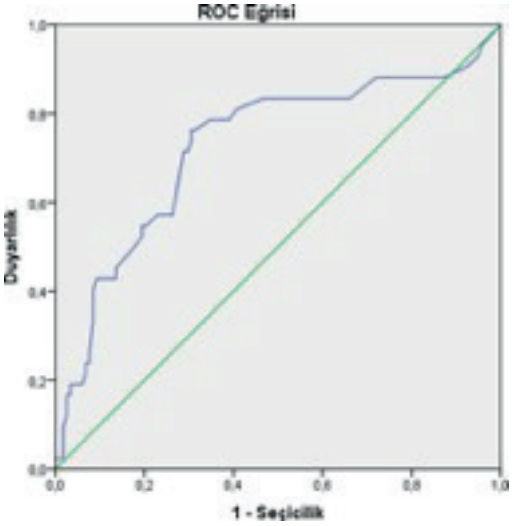

Figure 1: ROC analysis of total bilirubin level on days 14-20. The area under curve (AUC) was estimated as 0.725; the sensitivity and discriminative value were estimated as 0.76 and 0.70, respectively. Diagnostic value was found to be significant for bilirubin (p<0.05).

Discussion

Jaundice is one of the most common problems at neonatal period, which is seen in 60% of full-term infants and 80% of preterm infants [1]. It affect 2-15% of all infants and 40% of breastfed infants [4]. Vast majority of prolonged jaundice are breast milk jaundice. However, the question "Are infants undergoing substantial tests" have been brought in mind in recent years since laboratory evaluations recommended for etiologic evaluation of prolonged jaundice include many blood tests and urinalysis [3].

In this study, we reviewed full-term neonatal infants and aimed to demonstrate delaying laboratory evaluations for a week in infants with favorable clinical presentation can prevent unnecessary tests in majority of newborns.

The finding that, of 130 infants with total bilirubin measurement at both week 2 and 3, total bilirubin value was ≥10 mg/dl in only 36 infants (27.7%) while it was decreased below 10 mg/dL in 94 infants (72.3%) at week 3 is highly supportive for our hypothesis. In a prospective study including 183 full-term infants with prolonged jaundice, Tyrell et al. assessed the infants on day 14 and 21 and found that laboratory evaluations were normal in 79 infants (43.2%) at week 2 and that no infant had jaundice at week 3 [5]. In a study including 154 infants with prolonged jaundice, Hannam et al. found no pathology in 145 infants (95%) [6]. Authors concluded that number of tests can be safely minimized in infants with prolonged jaundice by a comprehensive clinical assessment. However, no further comprehensive study has been performed. In a study including 154 infants with prolonged jaundice, Cetinkaya et al. found that all laboratory evaluations were normal in 81 infants (%53), indicating prolonged jaundice due to breast milk. Authors found that mean bilirubin value was lower in the group with breast milk-associated prolonged jaundice when compared to other groups (due to UTI, hemolytic causes, hypothyroidism) [7].

In a study, Koc et al. evaluated 94 infants with prolonged jaundice. No etiology was detected in 55 infants (56.7%) and total bilirubin value returned normal during follow-up [8]. In a study by Tekinalp et al., breast milk jaundice was identified as the cause of prolonged jaundice in 76.8% of cases [9]. In our study, of 180 infants with prolonged jaundice, UTI was detected in 15 (8.3%) and hypothyroidism in 7 (3.9 while no etiology was detected in 158 infants (87%) and prolonged jaundice was attributed to breast milk jaundice.

In our study, we reviewed 180 infants with prolonged jaundice including 87 girls (48.3%) and 93 boys (51.7%). Male: female ratio was found as 1.1. Several authors have reported that male gender is a risk factor for IHB [10.11]. In the prospective study by Cetinkaya et al., male: female ratio was found as 1.4 in 154 infants with prolonged jaundice [7]. Our results are in agreement with literature.

When age at presentation was assessed, it was found that 88% of infants were diagnosed on days 14-20. This emphasizes the importance of the assessment for prolonged jaundice at week 2. When the infants were assessed by birth weight, mean birth weight was 3260 ±385.9 g (range: 2350-4285 g). Since only infants with gestational age ≥37 weeks, there was no infant with low birth weight. However, Osborn and Frisberg suggested a close association between low birth weight and jaundice [12, 13]. In our study, ABO incompatibility was detected in 14.2% while Rh incompatibility in 3.5%. ABO incompatibility was found in 13.4% by Cetinkaya et al. and 19% by Tuygun et al. [7, 14]. In our study, total rate of Rh incompatibility was detected as 4.7% including 3.5% of cases with Rh incompatibility alone and 1.2% of cases in combination with ABO incompatibility. This rate was reported as 3.8% by Cetinkaya et al. and 3.9% by Tuygun et al. [7, 14]. Our results are consistent with literature.

Congenital hypothyroidism is a rare endocrine disorder (1:3000-1:4000). It is a serious but treatable cause of prolonged indirect hyperbilirubinemia (IHB). In congenital hyperthyroidism, early diagnosis and timely treatment are highly important for normal development of intelligence [1].

In our study, congenital hypothyroidism was detected in 7 infants; 6 of which was diagnosed at week 2. Of the infants diagnosed at week 2, 2 had suspected screening in neonatal heel prick test. It is striking that remaining 4 infants had high total bilirubin levels ranging from 16.4 to 19.9 mg/dL in the assessment at week 2. In their study, Araz et al. evaluated 80 infants with total bilirubin level >5 mg/dL for congenital hypothyroidism and found hypothyroidism in 5 infants (6.3%) [15]. In a study by Siklar et al. hypothyroidism was detected in 6 (5%) of 110 infants with prolonged jaundice [16]. Our results are in agreement with literature.

In congenital hypothyroidism, early diagnosis and timely

treatment are highly important for normal development of intelligence. It was reported that development of intelligence is normal when diagnosed and treated within first 4 weeks of life. In Turkey, congenital hypothyroidism was added to National Screening Program in 2006, allowing early diagnosis in infants. Although prolonged jaundice is an important clue alarming the clinicians for early diagnosis of congenital hypothyroidism, total bilirubin level was significantly higher in infants diagnosed with congenital hypothyroidism in our study. Given that, we think that delaying laboratory evaluation for one week will not lead delay diagnosis in infants with good clinical presentation.

In newborns, prolonged jaundice can develop due to urinary tract infection. Failure to gain weight, irregular body temperature, difficulties in feeding, irritability, vomiting, abdominal distention and foul odor in urine are alarming for UTI [17].

In a study, Tuygun et al. assessed 231 full-term infant with prolonged jaundice and found UTI in 17 infants (7.4%). It was found that there were one or more clinical signs of UTI (fever, vomiting, irritability, anemia etc.) 11 infants with UTI [14]. Littlewood reviewed 66 infants with UTI for jaundice and noted that other clinical signs of UTI were present in all cases with jaundice [18].

In our study, UTI was detected in 15 (8.3%) of 180 infants diagnosed with prolonged jaundice. When 7 infants diagnosed at week 2 were assessed, the presence of failure to gain weight and vomiting in two infants with total bilirubin of 12 mg/dL was alarming for UTI. The presence of vomiting, poor feeding and formula feeding or mixed feeding pattern showed significant difference between infants with and without UTI. It was found that mean total bilirubin was 15.5 mg/dl in 4 infants without any symptom other than jaundice. In a study including 121 infants with prolonged jaundice, Okten et al. found that all infants with UTI were in the group with total bilirubin level of 12 mg/dL [19]. All findings suggest that infants with UTI can be selected among infants diagnosed with prolonged jaundice at week 2 by a detailed clinical assessment including questioning UTI symptoms, weight gain and total bilirubin measurement; proposing an appropriate approach to prevent performing laboratory evaluations in all infants with prolonged jaundice.

In a prospective study including 121 infants with prolonged jaundice, Okten et al. assigned infants into two groups: infants with total bilirubin<12 mg/dL and those with total bilirubin>12 mg/dL. A potential cause of jaundice was detected in 79% of infants with total bilirubin>12 mg/dL and in 32% of infants with total bilirubin<12 mg/dL, indicating a significant difference. It was shown that there was prematurity and/or low birth weight in 45%, ABO incompatibility in 30%, Rh incompatibility in 3.7%, and subgroup incompatibility in 22% of the infants with low total bilirubin level. In this group, no infant was diagnosed with UTI, congenital hypothyroidism or sepsis. No etiology was detected in 67.1% of infants and jaundice was attributed to breast milk [19]. The findings reported by Okten et al. support reliability of cut-off value determined in our study.

In our study, it was found that infants with total bilirubin >15 mg/dL who were diagnosed with prolonged jaundice at week 2 can have UTI and hypothyroidism; thus, laboratory evaluations can be performed at week 2 by questioning in details regarding UTI and hypothyroidism. Although several disorders that may lead prolonged jaundice at neonatal period have been identified, it is well-known that prolonged jaundice can be seen without any pathological condition in majority of infants fed by breast milk [20]. It was found that total bilirubin was >12.65 mg/dL at week 2 in infants in which total bilirubin level persisted above 10 mg/dL at week 3. It may be an appropriate approach to perform laboratory evaluations for prolonged jaundice in infants with total bilirubin>12.65 mg/dL.

In conclusion, Although several disorders that may lead prolonged jaundice at neonatal period have been identified, it is well-known that prolonged jaundice can be seen without any pathological condition in majority of infants fed by breast milk. In newborns, prolonged jaundice can be due to a severe underlying etiology including urinary tract infection, congenital hypothyroidism or biliary atresia; however, this approach does not delay diagnosis or treatment. Delaying laboratory evaluations recommended at week for prolonged jaundice in infants considered as well clinically is an approach that may prevent unnecessary testing in most infants.

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