

# Urinary Tract Infection in Term Neonates with Prolonged Jaundice

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**Introduction:** The aim of this study was to evaluate the frequency of urinary tract infection (UTI) in neonates with prolonged jaundice.

**Materials and Methods:** Newborn infants with jaundice lasted more than 2 weeks were included in this study. Patients who had other signs or symptoms were excluded. Workup of prolonged hyperbilirubinemia was performed, including direct Coomb's test, blood group of the neonate and the mother, complete blood count, blood smear, glucose-6-phosphate dehydrogenase (G6PD), reticulocyte count, serum level of bilirubin (unconjugated and conjugated), thyroid function tests (serum thyroxine [T4] and thyroid-stimulating hormone), urinalysis, and suprapubic urine culture. Pediatric nephrologists carried out further investigation including kidney function tests, renal ultrasonography, voiding cystourethrography, and Technetium Tc 99m dimercaptosuccinic acid renal scintigraphy for patients with a positive urine culture for microorganisms.

**Results:** Of 100 neonates who were evaluated, 43 were boys and 57 were girls. All of the neonates were breastfed. Six suffered from UTI (4 boys and 2 girls). Reflux was detected on voiding cystourethrography in 1 and cortical defect in the kidney on renal scan in 2 boys.

**Conclusion:** In our region, with a high rate of breastfeeding, UTI remains as an important cause of prolonged jaundice. Despite the high rate of urogenital system abnormality accompanied by neonatal UTI, there was not a significant difference between the signs and symptoms of jaundice in patients with and without UTI. Performing urine cultures should be considered as a routine procedure in the evaluation of every infant with prolonged jaundice.

*Keywords: neonatal jaundice, urinary tract infection, newborn infant, breast feeding*

*Urol J. 2007;4:91-4.  
www.uj.unrc.ir*

## INTRODUCTION

Renal scarring, hypertension, and even kidney failure can be prevented by early diagnosis and treatment of urinary tract infection (UTI).<sup>(1)</sup> Symptoms and signs of UTI in infants are nonspecific and hyperbilirubinemia is commonly the main clinical feature at presentation that may be the only manifestation of UTI.<sup>(2)</sup>

Prolonged jaundice is more common in breastfed infants than artificially-

fed infants. Studies performed in developed countries focusing on nonbreastfed infants have suggested that prolonged jaundice should aggressively be investigated in artificially-fed infants.<sup>(3)</sup> The majority of researchers have considered Asian ethnicity as a risk factor and showed that the peak serum levels of bilirubin in full-term Asian and American-Indian neonates were twice more than that in white and black populations.<sup>(4)</sup> All of the mentioned causes may distract physicians from diagnosing

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Received February 2007  
Accepted May 2007

UTI as an important cause of prolonged jaundice. Complete clinical assessment is needed in all cases of prolonged jaundice; however, the indications and extent of investigation remain unclear.<sup>(5)</sup> This study was conducted to evaluate the frequency of UTI and to determine the importance of performing UTI workup in neonates with prolonged jaundice in an area with a high rate of breastfeeding.

## MATERIALS AND METHODS

We conducted this cross-sectional descriptive study from April 2005 to March 2006 on 107 newborn infants older than 2 weeks with visible yellow skin or eye color who were otherwise clinically well. They had been admitted to the newborn nursery of Imam Hospital for evaluation of prolonged jaundice. The Research Council of Urmia University of Medical Sciences approved the study design and written informed consent was obtained from the infants' parents. Demographic and clinical features including age, weight, sex, gestational age, status of feeding, and postnatal events were recorded. Premature neonates, those previously treated for jaundice, and those with uncooperative parents were excluded.

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Workup of prolonged hyperbilirubinemia was performed, including direct Coomb's test, blood group of the infant and the mother, complete blood count, blood smear, glucose-6-phosphate dehydrogenase (G6PD), reticulocyte count, serum level of bilirubin (unconjugated and conjugated), thyroid function tests (serum thyroxine [T4] and thyroid-stimulating hormone), urinalysis, and suprapubic urine culture. Pediatric nephrologists carried out further investigation including kidney function tests, renal ultrasonography, voiding cystourethrography (VCUG), and Technetium Tc 99m dimercaptosuccinic acid (<sup>99m</sup>Tc-DMSA) renal

scintigraphy in the patients with a positive urine culture for microorganisms. Prolonged jaundice was defined as jaundice lasting for more than 14 days in full-term infants. The cause of jaundice was diagnosed in each case and proper treatment and follow-up were performed. The collected Data were analyzed and presented in 2 conditions: first, in all patients, and second, in 2 groups according to the diagnosis of UTI. Data were analyzed with the SPSS software (Statistical Package for the Social Sciences, version 10.5, SPSS Inc, Chicago, Ill, USA) using the chi-square test and Mann-Whitney *U* test, as appropriate. Results of quantitative variables were presented as mean  $\pm$  standard deviation and 95% confidence interval.

## RESULTS

Seven neonates were excluded due to the unwillingness of their parents to continue the study. A total of 43 boys and 57 girls were studied (Table). All male infants were uncircumcised. According to the records of the family members, jaundice had been started during the first week of life. Test results revealed that none of the infants had direct hyperbilirubinemia; also, it was shown that breastfeeding, fetomaternal incompatibility in Rh and blood group, and congenital hypothyroidism were of the most important causes of hyperbilirubinemia. Six patients suffered from UTI, 4 of whom were boys. The isolated microorganisms were *Escherichia coli* in 3 patients, *Klebsiella pneumoniae* in 2, and *Protens* in 1.

The mean age at admission was  $23.0 \pm 5.9$  days and  $27.3 \pm 10.8$  days in the patients with and without UTI, respectively ( $P = .52$ ). The mean body weight was  $3.80 \pm 0.46$  kg and  $3.93 \pm 0.67$  kg, respectively ( $P = .33$ ). The mean serum level of total bilirubin was  $10.36 \pm 1.60$  mg/dL and  $10.37 \pm 1.95$  mg/dL in the patients with and without UTI, respectively ( $P = .99$ ; Table). Kidney function tests were within

Clinical and Demographic Data of Neonates With Prolonged Jaundice at Admission\*

Factors	All Patients	Patients With UTI	Patients Without UTI
Sex			
Male	57	4	41
Female	43	2	53
Mean age, d	$27.1 \pm 10.6$ (24.97 to 29.19)	$23.0 \pm 5.9$ (16.80 to 29.10)	$27.3 \pm 10.8$ (25.10 to 29.50)
Mean serum bilirubin, mg/dL	$10.37 \pm 1.90$ (9.92 to 10.49)	$10.36 \pm 1.60$ (9.25 to 11.48)	$10.37 \pm 1.95$ (9.97 to 10.77)
Mean body weight, kg	$3.92 \pm 0.66$ (3.70 to 4.05)	$3.80 \pm 0.46$ (3.30 to 4.29)	$3.93 \pm 0.67$ (3.79 to 4.07)

\*Values in parentheses are percents for sex proportions and 95% confidence interval for means.

reference ranges in all of the patients. In the neonates with UTI, bilateral reduced absorption of isotope was detected in renal parenchyma of 1 boy on the  $^{99m}\text{Tc}$ -DSMA scan. Unilateral reflux of grade 3 to 4 was confirmed in another boy by the VCUG.

## DISCUSSION

In the present study, UTI was detected in 6% of the jaundiced infants. Isolated microorganisms in this study included *Escherichia coli*, *Klebsiella pneumoniae*, and *Proteus mirabilis* that are among the common causes of UTI in neonatal period. The rate of UTI in our series is in accordance with the results of a study by Garcia and Nager.<sup>(6)</sup> Also, similar to our results, Falcao and colleagues reported that *Escherichia coli* was the most common isolated microorganism in newborns' UTI.<sup>(7)</sup> The incidence of neonatal UTI varies from 0.1% to 1% in the general population of healthy newborns,<sup>(8)</sup> while it was 6 times higher in this study. To our best knowledge, this is the first research in this region with a high rate of neonatal breastfeeding. Also, it should be noted that previous studies have confirmed the protective effect of newborn circumcision against UTI during infancy.<sup>(9)</sup> In our series, circumcised infant were not included and the high rate of jaundice might be interpretable by this situation, too.

A study in Tehran revealed that jaundice was due to breastfeeding and congenital hypothyroidism in 76.6% and 10% of the cases, respectively, and these two were the main causes of hyperbilirubinemia followed by TORCH infections, G6PD deficiency, and cephalohematoma.<sup>(10)</sup> In agreement with our results, in a study by Hannam and colleagues, 2 out of 9 patients were found to have UTI; therefore, they recommended urine culture for investigation of prolonged jaundice.<sup>(11)</sup> In another study, it was revealed that of 127 infants with prolonged jaundice, 125 were breastfed.<sup>(12)</sup> It is suggested that the incidence of prolonged jaundice in full-term breastfed infants is higher (9.2% at 28 days).<sup>(3)</sup> It is well known that the incidence of UTI in boys is higher than in girls within the first year of the life.<sup>(13,14)</sup> Four out of 6 patients diagnosed with UTI in this study were males. Age, weight, and serum total bilirubin level of patients with and without UTI were not different. In this study, all newborns were breastfed similar to another study conducted in Iran.<sup>(15)</sup>

It is shown that newborn infants with UTI present with unconjugated hyperbilirubinemia in the early stages but conjugated hyperbilirubinemia after 6 week.<sup>(16)</sup> Although Garcia and Nager reported that patients with an elevated conjugated bilirubin fraction were more likely to have UTI,<sup>(6)</sup> none of our patients had an increased direct bilirubin level.

Although performing renal ultrasonography, VCUG, and  $^{99m}\text{Tc}$ -DMSA scan are recommended after the first UTI, controversies continue about complications and results of these tests.<sup>(17)</sup> In this study, ultrasonography did not show any significant pathologic finding in UTI cases. The results of  $^{99m}\text{Tc}$ -DSMA scan were abnormal in 1 male infant with UTI and VCUG revealed grade 3 to 4 reflux in another male case. It has been proved that the presence of vesicoureteral reflux is significantly related to younger age at the time of UTI presentation.<sup>(12)</sup> In contrast to these results, a search conducted in Turkey revealed a high rate of abnormality in the urogenital system of newborn infants with UTI.<sup>(18)</sup>

## CONCLUSION

In our region, with a high rate of breastfeeding, UTI remains as an important cause of prolonged jaundice. Despite the high rate of urogenital system abnormality accompanied by neonatal UTI, there was not a significant difference between the signs and symptoms of jaundice in patients with and without UTI. Performing urine cultures should be considered as a routine test in the evaluation of every infant with prolonged jaundice.

## ACKNOWLEDGEMENT

The authors would like to thank Drs Davoud Omrani, Amir Heydari, and Zahra Yekta and members of the Research Council of Urmia University of Medical Sciences for supporting this study.

## CONFLICT OF INTEREST

None declared.

## FINANCIAL SUPPORT

This study was approved and financially supported by the Research Council of Urmia University of Medical Sciences.

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## EDITORIAL COMMENT

I read this article with interest and would like to thank the authors for their excellent study. The cause-and-effect relation of UTI and jaundice is still a matter of debate. We can also speculate that UTI might be a concurrent disease along with jaundice in newborn infants. A meta-analysis of the studies published on infants with UTI showed that 12% of 255 neonates with UTI had jaundice, which is a very small proportion.<sup>(1)</sup>

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## REPLY BY AUTHOR

We acknowledge the comment by Dr Asgari and the fact that the cause-and-effect between UTI and jaundice is not clear yet. As we mentioned in the Introduction of this paper, symptoms and signs of UTI in infants are nonspecific and hyperbilirubinemia (without its common etiologies) is usually the only manifestation when UTI is diagnosed. Such a concurrent development of UTI and jaundice of unknown cause has been reported in many studies (references 1, 6, and 16) and we believe that our result shows a relation, though not clearly.

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