

Evaluation of Urinary Tract Infection in Newborns with Jaundice in South of Iran

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Abstract

Background: Neonatal jaundice is clinically presented in 60% of full-term newborns. About 8% of newborns with jaundice have urinary tract infection (UTI) without any other clinical signs in favor of UTI. In present study we evaluated clinical and paraclinical data that help to rapid and early diagnosis of UTI in apparently healthy newborns with jaundice.

Methods: From February to August 2006, 51 apparently healthy full-term newborns with jaundice and UTI who had been admitted for management of jaundice in Motahary hospital, Jahrom (south of Iran), were studied and compared with 56 neonates with jaundice but without UTI. All the neonates had not any other symptoms such as fever or lethargy. At the time of admission, total and direct bilirubin, Coombs' test, mother and neonate blood group, urinalysis and urine culture were requested.

Results: There was no significant difference of gestational age, birth weight, age of admission, age at the time of starting jaundice, and total serum bilirubin between the two groups. There was significant difference of direct bilirubin level, mean of decrease serum bilirubin after 24 hours, gender, and blood groups. Male gender with mean decrease of bilirubin less than 2.2 mg/dl after 24 hours phototherapy and direct bilirubin more than 1.6 mg/dl, during the first two weeks of neonatal period has about 7 times more risk for UTI. The presence of those three above mentioned factors had only 30% sensitivity and more than 94% specificity for suspicious of UTI in asymptomatic neonates with jaundice.

Conclusion: Jaundice may be the only presenting sign of UTI in newborns, so according to high specificity for the presence of three below factors simultaneously, it seems better to evaluate newborns for UTI if they have high level of direct bilirubin (more than 1.6 mg/dl), slow decrease in serum bilirubin level with phototherapy (less than 2.2mg/dl/day) especially in male newborn with blood group B.

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Keywords • Jaundice • newborn • urinary tract infection

Introduction

Neonatal jaundice is clinically presented in 60% of full-term newborns.¹ About 8% of newborns with jaundice have urinary tract infection (UTI).²⁻⁶ The American Academy of Pediatrics (AAP) has published guidelines outlining

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the management of healthy newborns with hyperbilirubinemia, which includes the evaluation of; maternal ABO and Rh typing, direct Coombs' test, blood and Rh (D) typing of infants' cord blood, and a total serum bilirubin level.¹ In normal healthy neonates with jaundice who have not any other findings, urinalysis and urine culture were not recommended. Urinary tract infection in neonate may be presented with non-specific signs and symptoms such as lethargy, poor feeding, and fever.⁷ Jaundice may be the first sign of UTI in asymptomatic infants before other signs and symptoms become evident.² Therefore, some studies recommended that laboratory evaluations for UTI should be included as part of the evaluation in asymptomatic infants with jaundice.²

The purpose of the present study was to evaluate the clinical and paraclinical parameters in asymptomatic infants with jaundice that can predict UTI and the need for urinalysis and urine culture.

Patients and Methods

Study participants

In a prospective study, from February to August 2006, 51 apparently healthy full-term newborns with jaundice and UTI who had been admitted for management of jaundice in Motahary hospital, Jahrom (south of Iran), were studied and compared with 56 neonates with jaundice but without UTI. Clinical jaundice was defined as any yellow or green-yellow discoloration of the skin, mucous membranes, or sclera. Patients were excluded if they had fever by history, documented fever ($T > 38^{\circ}\text{C}$), vomiting, diarrhea, poor feeding, tachypnea (more than 55 breaths/min), lethargy or irritability. All of the participants were examined by a pediatrician to rule out sepsis or other infections. Infants who had factors that could intensify the hyperbilirubinemia such as hemolysis, and hematoma were excluded from the study.

Demographic information including perinatal, and intrapartum events, such as gestational age, birth weight, maternal infections, pregnancy complications, prolonged rupture of membranes, mode of delivery, history of UTI in mother, and maternal fever were collected. Other historical factors included the onset of jaundice and progression of jaundice as reported by parents, and whether the infant was breastfed or formula-fed.

Clinical Procedures

All study participants had a urine sample obtained by urine bag at the time of admission. In the laboratory, a standard urinalysis was performed using Multistix 10 (Uriyab,

bakhtarshimi, Iran), and urine specimens were centrifuged at 2000 revolutions per minute for 5 minutes, resuspended and stained. The microscopic examination under high-power field (HPF) for pyuria, reported as leukocytes per HPF and bacteriuria. All urine specimens were sent for standard quantitative culture and considered positive if a single pathogen ≥ 100000 colony-forming/ml units was isolated. In our center mothers refuse for urine sampling by suprapubic and catheterization, so, in positive cases, a second urine culture was requested to decrease the possibility of contamination. The patients with both two positive urine cultures were considered as infected. In addition, a serum bilirubin level (total and direct), maternal and neonatal blood group Coombs' test, G6PD level, and reticulocyte count were examined for all the study participants. Serum bilirubin level rechecked 24 hours after phototherapy. Duration of phototherapy was recorded. We prescribed appropriate antibiotics for neonates with UTI. We also requested renal sonography for all of them.

The data were validated and analyzed using SPSS software version 11.5. Descriptive data were reported as mean \pm standard deviation. The associations between categorical variables were analyzed using the Fisher exact test or the χ^2 test, and continuous variables were analyzed using Student *t* test. Statistical significance was defined as a *P* value $< .05$. Confidence intervals (CIs) were also calculated.

Results

Fifty one neonates with jaundice and UTI were compared with 56 neonates with jaundice but without UTI. Mean gestational age of all neonates were 39.6 weeks (range: 37-40) and mean birth weight was 3.038 kg (range: 2.1 – 4.2). Fifty five percent of neonates were male. Mean age at the time of admission and onset of jaundice were 5.9 ± 3.3 days and 3.18 ± 0.88 respectively. About 75.7% of the mothers had normal vaginal delivery. All of neonates were breast fed. Table 1 shows the demographic characteristics of the two groups with and without UTI.

The most common organism in neonates with UTI was *E coli* (53.7%) followed by *Klebsiella* (29.9%) and *enterobacter* (16.4%). There was not significant association between type of organism with blood group and total and direct bilirubin.

There was no significant difference between the two groups in respect of gestational age, birth weight, type of delivery and age at the onset of jaundice, but there was significant difference in sex distribution between the two groups. Male gender was more in group with UTI than the group without UTI (64.7% v 35.3 % $P = 0.002$).

Table 1: Comparison of characteristics of neonates with and without UTI

	Without UTI (n= 56)	With UTI (n = 51)	P value
Gestational age (weeks)	39.6±0.73	39.5 ±0.8	0.28
Weight (gram)	3097 ±417	3018±481	0.44
Percent of male	35.3	46.7	0.007*
Percent of cesarean section	17.9	31.4	0.08
Onset of jaundice (day)	3.1 ±0.83	3.2±1	0.61
Age of admission	5.7±2.4	5.9±2.3	0.65
Total bilirubin (mg/dl)	17.3±1.72	17±1.95	0.52
Direct bilirubin level (mg/dl)	1.4±.52	1.7±.62	0.03*
Mean of decrease in bilirubin/ 24hrs	2.1±1.65	1.5±1.75	0.04*
Mean duration of phototherapy	4.01±1.35	4.7±2.28	0.04*

The most common blood group in all neonates was O+ (39.5%) followed by B+ (26.3%). There was significant difference between type of blood group in neonate with UTI and those without UTI. Blood group type B was more common in neonates with UTI than those without UTI (41.2% v 25% = 0.03).

The mean bilirubin concentration at the time of admission was 17.05 ± 1.8 mg/dl. Table 1 shows comparison between serum level of total and direct bilirubin, and mean decrement in serum bilirubin level after 24 hours phototherapy in both groups. There was no significant difference in total serum level at the time of admission, but there was statistically significant difference in direct bilirubin. The neonates with UTI had more level of direct bilirubin than those neonates without UTI (1.7± 0.62 v 1.4 ± 0.52 mg/dl, P = 0.03). Based on cut off value 1.6 mg/dl, there was significant association between serum direct bilirubin more than 1.6 mg/dl and UTI. The prevalence of UTI was more in neonates with direct bilirubin more than 1.6 mg/dl (54.7% v 45.3%, P= 0.021, Odds ratio = 2.16).

Mean of decrease in serum total bilirubin after 24 hours phototherapy was less in neonates with UTI than neonates without UTI (1.5 ± 1.75 v 2.1 ± 1.65, P= 0.04). The most significant cut-off value for mean of decrease bilirubin vis-à-vis UTI was 2.2. There UTI was more prevalent in group with lower mean of decrease serum bilirubin (51.1% v 48.5%, P=0.002, Odds ratio = 2.8). According to lower rate of response to phototherapy, the neonates with UTI needed longer duration of phototherapy (4.7± 2.28 v 4.01 ± 1.35 days, P= 0.04).

Logistic regression model for four variable; sex, blood group, serum direct bilirubin, and

mean of decrease in total bilirubin showed significant difference between the two groups (P = 0.02). All the variables except blood group had correlation with the incidence of UTI. Table 2 shows the significance of the presence of two or three factors to increase the risk of UTI. If a neonate with jaundice has three variables included male gender, mean of decrease bilirubin less than 2.2 mg/dl after 24 hours phototherapy and direct bilirubin more than 1.6 mg/dl, he/she has about 7 times more risk for UTI. Although presence of these three factors had about only 30% sensitivity, it has more than 94% specificity for suspicious of UTI in asymptomatic neonates with jaundice.

Discussion

Jaundice may be the first presentation of UTI in neonates.² Chavalitdhamrong et al, in a small series of 69 asymptomatic neonates with unexplained jaundice, found evidence of UTI in 2 infants.⁸ In the study of Francisco the prevalence of UTI in asymptomatic neonates with jaundice was 7.5% and the most common organism was E coli.²

Bilgen and his coworkers in Turkey studied 102 asymptomatic neonates in whom UTI was diagnosed in eight (8%) cases.⁹ Of those eight patients, only four (50%) had pyuria. He recommended urine culture should be considered in the bilirubin work-up of infants older than three days of age with an unknown etiology. Fang also concluded that high grade fever and pyuria are unreliable criteria for screening of UTI in young infants presenting with prolonged jaundice. Urine cultures should be obtained in such patients to determine whether UTI is present.¹⁰ In the present study

Table2: The significance of presence of three variables as risk factors for UTI in asymptomatic neonates with jaundice.

	With UTI (%)	Without UTI (%)	P value	Odds ratio	95% Confidence Interval
Male + decrease bilirubin < 2.2 mg/dl/day	69.4	30.6	0.01	3.93	1.67- 9.27
Male + direct bilirubin > 1.6 mg/dl	77.3	22.7	0.01	5.31	1.78 – 15.8
Male+ decrease bilirubin < 2.2 mg/dl/day + direct bilirubin > 1.6 mg/dl	82.4	17.6	0.01	6.93	1.86 – 25.9

all neonates with jaundice and UTI were afebrile and asymptomatic.

Although many studies showed more prevalence of UTI in jaundice after the first week, the mean age of our neonates was 5.9 \pm 3.3 days. But no significant difference between the two groups was detected. In the study done by Ghaemi et al, UTI was found in 5.8% of infants with late onset jaundice. They suggested that evaluation for UTI should be considered as a screening test in all cases of late onset neonatal jaundice,¹¹ but late onset jaundice was not significant value for suspicion of UTI in the present study.

There was no significant difference in total serum bilirubin between the two groups at the time of admission, but significant difference was detected in direct bilirubin and mean of decrease in serum bilirubin level. Infants with UTI may present with unconjugated hyperbilirubinemia in the early stage. After 6 weeks, it is always conjugated hyperbilirubinemia.¹²

The hyperbilirubinemia associated with UTI can be unconjugated and related to hemolysis caused by E coli and other Gram-negative organisms or it can be conjugated secondary to cholestasis.¹³⁻¹⁵ The mechanism by which UTI causes cholestasis is not clear, but possible mechanisms include microcirculatory changes in the liver, direct effects from bacterial products, and/or from endotoxin-induced mediators.¹⁶⁻¹⁷ It is postulated that even mild hemolysis can overload the immature liver conjugating mechanism, leading to an increase in serum bilirubin levels. Laboratory data indicated that hemolysis was an important factor in the pathogenesis of jaundice in UTI.¹⁸ Urinary tract infection with enterohemorrhagic E coli has caused hemolytic-uremic syndrome.¹⁹ In present study, the neonates with UTI had more level of serum direct bilirubin.

Urinary tract infection was more common in male neonates and also in neonates with blood group B+. This finding was similar to other studies.¹³

Conclusion

Although jaundice may be the first presenting sign of UTI, urine culture has not been recommended as routine work up in neonates with jaundice. We studied multiple co factors in neonates with jaundice and UTI. If a neonate has two or more of the following conditions, UTI must be considered and it is advised to perform urine culture: 1-High level of direct bilirubin (more than 1.6 mg/dl), 2- Slow decrease in level of bilirubin with phototherapy, 3- Male gender especially with blood group B. The presence of three factors had more than 94% specificity for suspicious of UTI in asymptomatic neonates

with jaundice. Based on literature review, this is the first study of multiple variables regarding UTI in neonates with jaundice.

References

- 1 American Academy of Pediatrics, Provisional Committee for Quality Improvement and Subcommittee on Hyperbilirubinemia. Practice parameter: management of hyperbilirubinemia in the healthy term newborn. *Pediatrics* 1994; 94: 558-62.
- 2 Garcia FJ, Nager AL. Jaundice as an Early Diagnostic Sign of Urinary Tract Infection in Infancy. *Pediatrics* 2002; 109: 846-51.
- 3 Abbott GD. Neonatal bacteriuria: a prospective study of 1460 infants. *Br Med J* 1972; 1: 267-9.
- 4 Edelman CM Jr, Ogwo JE, Fine BP, Martinez AB. The prevalence of bacteriuria in full-term and premature newborn infants. *J Pediatr* 1973; 82: 125-32.
- 5 Drew JH, Acton CM. Radiological findings in newborn infants with urinary infection. *Arch Dis Child* 1976; 51: 628-30.
- 6 Wettergren B, Jodal U, Jonasson G. Epidemiology of bacteriuria during the first year of life. *Acta Paediatr Scand* 1985; 74: 925-33.
- 7 Littlewood JM. Sixty-six infants with urinary tract infection in first month of life. *Arch Dis Child* 1972; 47: 218-26.
- 8 Chavalitdhamrong PO, Escobedo MB, Barton LL, et al. Hyperbilirubinaemia and bacterial infection in the newborn. A prospective study. *Arch Dis Child* 1975; 50: 652-4.
- 9 Bilgen H, Ozek E, Unver T, et al. Urinary tract infection and hyperbilirubinemia. *Turk J Pediatr* 2006; 48: 51-5.
- 10 Fang SB, Lee HC, Yeung CY, Tsai JD. Urinary tract infections in young infants with prolonged jaundice. *Acta Paediatr Taiwan* 2005; 46: 356-60.
- 11 Lee HC, Fang SB, Yeung CY, Tsai JD. Urinary tract infections in infants: comparison between those with conjugated vs unconjugated hyperbilirubinaemia. *Ann Trop Paediatr* 2005; 25: 277-82.
- 12 Ghaemi S, Fesharaki RJ, Kelishadi R. Late onset jaundice and urinary tract infection in neonates. *Indian J Pediatr* 2007; 74: 139-41.
- 13 Seeler RA. Hemolysis due to gram-negative urinary tract infection. *Birth Defects Orig Artic Ser* 1977; 13: 425-31.
- 14 Bernstein J, Brown AK. Sepsis and jaundice in early infancy. *Pediatrics* 1962; 29: 873-82.
- 15 Sieniawska M, Wróblewska-Kaluzewska M, Nalecz A, et al. Hyperbilirubinemia in infants with urinary tract infection. *Pol Med*

- Sci Hist Bull* 1976; 15: 79-81.
- 16 Roelofsen H, van der Veere CN, Ottenhoff R, et al. Decreased bilirubin transport in the perfused liver of endotoxemic rats. *Gastroenterology* .1994; 107: 1075-84.
 - 17 Roelofsen H, Shoemaker B, Bakker C, et al. Impaired hepatocanalicular organic anion transport in endotoxemic rats. *Am J Physiol* 1995; 269: G427-34.
 - 18 Bezanilla JL, Vallo A, Soriano JR. Urinary tract infections presenting with jaundice. *An Esp Pediatr* 1975; 8: 79-84.
 - 19 Starr M, Bennett-Wood V, Bigham AK, et al. Hemolytic-uremic syndrome following urinary tract infection with enterohemorrhagic *Escherichia coli*: case report and review. *Clin Infect Dis* 1998; 27: 310-5.