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Original Article

Unexpected Neonatal Jaundice as an Early Diagnostic sign of Urinary Tract Infection

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Abstract

Background: Determination of contributing factors for jaundice would result in better programming for prevention. This study was performed to determine the prevalence rate of Urinary Tract Infection (UTI) among neonates with jaundice admitted in Arash Hospital from October 2013 to October 2014.

Methods: In this descriptive cross-sectional study, term neonates with non-hemolytic jaundice admitted in Arash Hospital from October 2013 to October 2014 were evaluated for UTI by urine culture and the data were recorded by checklist using medical documents.

Results: A total of 436 term infants were enrolled in the study. Mean age at the time of admission was 6.03±3.355 days with age range of 3-18 days including 291(0.66%) males and 145(0.33%) females. Urine culture was positive in 32 neonates (7.3%).

The most common germs were Klebsiella in 37.5%, *Escherichia coli (E. coli)* in 21.9%, *Staphylococcus* in 9.4%, *Pseudomonas* in 3.1%, *Enterococcus* in 15.6%, *Enterobacter* in 9.4%, and Group B *Streptococcus (GBS)* in 3.1%.

Conclusion: Urine culture should be a part of routine clinical evaluation for all icteric neonates at the age of 5-6 days or more who have no risk factors to exclude the possibility of coincidental UTI.

Keywords: Urinary tract infection, Neonate, Jaundice

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Introduction

Jaundice is a common and important neonatal disorder which if not treated may result in subsequences such as kernicterus. Hence, diagnosis, screening and determination of the etiology and treatment would result in better prognosis. Jaundice is seen in 60% of term and 80% of preterm neonates in their first week of life (1-5). The idiopathic hyperbilirubinemia may be related to sepsis or Urinary Tract Infection (UTI) especially in neonates with prolonged jaundice (2,3,6). UTI is present in 0.7 to 1.4% of asymptomatic term neonates, about 5 to 11% of febrile newborns, 6.5% of neonates with hyperbilirubinemia and 55% of them have structural abnormalities in urinary tract system (7). The symptoms of UTI range from asymptomatic to unspecific (nausea, vomiting, fever, jaundice, and poor-feeding) and sometimes severe ones. Thus, jaundice may be the first symptom of UTI (2,3,6-10). Despite some studies about association between bacterial infections with hyperbilirubinemia, the American Academy of Pediatrics does not recommend routine assessment for these infections (11). The aim of this study was to determine the prevalence of UTI in hospitalized term neonates diagnosed with asymptomatic unconjugated hyperbilirubinemia.

Materials and Methods

Study design and population

In this descriptive-comparative cross-sectional study, all healthy term newborns (gestational age≥37 weeks) with jaundice admitted in Arash Hospital from October 2013 to October 2014 were evaluated for UTI by urine culture. Written consent was obtained from parents before enrollment. This study was approved by medical ethics committee of TUMS in accordance with the Declaration of Helsinki.

Participants

The chief complaint of subjects was yellow to green color change in skin, sclera, and conjunctiva. The inclusion criteria were age less than four weeks for term infants and hyperbilirubinemia according to a curve representing the bilirubin level trends in neonates at particular age determining eligibility for hospital admission. The cases older than 28 days, those with icterus on the first day of life, hemolytic jaundice, and symptoms other than jaundice were excluded. The early hyperbilirubinemia was defined after 24 hours of life up to 2 weeks and the prolonged or delayed hyperbilirubinemia was defined after 2 weeks in term neonates. Management of hyperbilirubinemia was performed largely based on American Academy of Pediatrics (AAP) guidelines (11) and serum bilirubin was measured using the spectrophotometric method with the selectra-2 autoanalyzer.

Data collection

Demographic data including sex, gestational age, age of onset, duration of jaundice, and weight were recorded by checklist using medical documents. The urine bag was used for urine sampling and in positive cases (after signing the informed consent form), the suprapubic sample was obtained. In cases with two failures or in cases with contraindication to suprapubic sampling, nelaton catheter was used and the results of urinalysis and urine culture were recorded. The leukocyte count in high power field and the bacteria count were recorded. The positive samples were more than 104 colonies in catheter urine sample or more than 1 colony in suprapubic urine sample. The type of microorganism in positive cultures was determined.

Data analysis

Data analysis was performed by SPSS software, version 13.0 (Statistical Package for the Social Sciences; Chicago, USA). A P value of<0.05 was indicated as significant.

Results

A total of 436 term infants were enrolled in the study. The mean±standard deviation (SD) for gestational age at birth was 38.3±0.4 weeks; mean age at the time of admission was 6.03±3.355 days with age range of 3-18 days including 291(0.66%) males and 145 (0.33%) females.

The urine culture was positive in 32 cases (7.3%) for which the male/female ratio was 17/15. The majority of neonates had early onset hyperbilirubinemia (93.7%). All except three neonates (9.4%) had normal birth weight. The frequency distribution of age and bilirubin level is demonstrated in table 1. Frequency distribution of microorganisms is shown in table 2. There was abnormal ultrasound result in one case. The blood culture result was negative in all cases. The

Voiding Cystourethrogram (VCUG) was not done in patients.

Table 1. Frequency distribution of age and bilirubin level

	Age (Day)	Total bilirubin	Direct bilirubin
Mean	6.03	18.303	0.513
Median	6.00	18.150	0.500
Standard deviation	3.355	3.9077	0.1845

Table 2. Frequency distribution of micro-organisms

Microorganisms	Frequency	Percentage
Klebsiella	12	37.5
E. coli	7	21.9
Staph	3	9.4
Pseudomonas	1	3.1
Enterococcus	5	15.6
Enterobacter	3	9.4
GroupB Streptococcus (GBS)	1	3.1
Total	32	100.0

Discussion

Determination of contributing factors for jaundice would result in better programming for prevention. This study was performed to determine the prevalence rate of urinary tract infection among neonates with asymptomatic unconjugated hyperbilirubinemia.

In this study, the urine culture was positive in 32 neonates (7.3%) and it was similar to the previous studies (2,3,8,9,12-14). Unlike other studies, Nickavar *et al* (15) showed a significantly higher prevalence (42.1%). The most common germs were *Klebsiella* in 37.5 % and *Escherichia coli (E. coli)* in 21.9%. These findings were similar to the results of Shahian *et al* (2) and Omar *et al* (3). In a study conducted by Özcan *et al* (9), causative agents were *Klebsiella* in 30.76% and *Enterococcus* in 26.92% respectively, and *E. coli* was the fourth cause, while in other studies (6,7,12,15-17), *E. coli* was the most common pathogen. The study by Bilgen *et al* showed that the most common germ was *Enterobacter* (14).

In this study, the average hospitalization age of neonates with hyperbilirubinemia was 6.03±3.355 days (begins after the third day and continues to seventh day of birth); therefore, the most common kind of hyperbilirubinemia in our study was early onset hyperbilirubinemia (93.7%). These findings were consistent with some previous studies (2,3,6,12,15) that reported average age of hospitalization to be less than 2 weeks and mostly in the first week of life. In Bilgen *et al*'s study (14), the mean age of icterus onset was five days, and work-up was recommended for idiopathic neonatal jaundice after one week. In the study of Pashapour *et al* (13), the mean age of admission was 16.8-29.1 days and this was similar to our study. The prevalence of UTI in male icteric neonates (53.1%) in our study was more than females and other studies (3,6,7,12-15,18) reported nearly similar prevalence but in the study of Shahian *et al* and a study conducted by Özcan *et al*, the prevalence in males was significantly higher (87 and 88.5%, respectively) (2,9). In the present study, 90.6% of icteric neonates with UTI had a birth weight in normal range (2500-4000) and 100% of them were full-term neonates. None of icteric neonates with UTI had positive blood culture. These findings were in line with previous studies (2,3,6,7,12-15).

In the present study, the urinary tract ultrasound result was abnormal only in one case (3.1%) and VCUG was not done. As early VCUG performance is usually accompanied with false positive results indicating the presence of Vesicoureteral Reflux (VUR), so based on our hospital protocol, VCUG will be done after neonatal periods. This value was consistent with Omar *et al*'s (4%) (3) findings but the study of Shahian *et al* (2), Ghaemi *et al* (6), Pashapour *et al* (13), and Bilgen *et al* (14) showed higher prevalence of urinary tract abnormalities and this difference may be due to smaller sample size. In the study conducted by Nickavar *et al* (15),

37.5% of newborns had abnormalities in renal ultrasound. They also assessed cystography which was not used in our study. Xinias *et al* (7) reported that VUR was found in 16.66% of icteric neonates with UTI and renal scintigraphy showed renal cortex changes in 46.7% of them. Thus, hyperbilirubinemia is related to pathological findings in the renal cortex. Other studies (19-24) indicated relatively similar results. As there is a decreasing cortical function in kidneys during neonatal periods, renal scintigraphy was not considered for our newborns with UTI.

For all icteric neonates without any risk factors at the age of 5-6 days or more, according to the obtained results, it may be concluded that urinary tract infection is nearly seen in one out of fourteen

admitted neonates with jaundice and is generally due to *Klebsiella* and *E. coli*.

Hence, regarding the importance of this issue, the prevalence rate of UTI in all neonates with jaundice should be calculated considering icterus duration. The limitations of the current study were the lack of ability to assess the role of circumcision in decreasing the prevalence of UTI and also lack of follow up of our newborns by ultrasound and VCUG for evaluation of prevalence of structural disorders in the urinary tract system.

Conclusion

Urine culture should be a part of routine clinical evaluation for all icteric neonates at the age of 5-6 days or more who have no risk factors to exclude the possibility of coincidental UTI. However, it is recommended to perform cohort studies in multicenter hospitals with larger sample size to achieve more reliable results.

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Conflict of Interest

All the authors declare that they have no conflict of interest.

References

1. Namasivayam A, Waldemar A. Jaundice and Hyperbilirubinemia in the newborn. In: Behrman RE, Kliegman RM, Jenson HB, eds. Nelson Textbook of Pediatrics. Philadelphia, PA: Elsevier/W.B. Saunders Co.; 2015.p. 871-80.

2. Shahian M, Rashtian P, Kalani M. Unexplained neonatal jaundice as an early diagnostic sign of urinary tract infection. Int J Infect Dis 2012;16(7):487-90.

3. Omar C, Hamza S, Bassem AM, Mariam R. Urinary tract infection and indirect hyperbilirubinemia in newborns. N Am J Med Sci 2011;3(12):544-7.

4. Porter ML, Dennis BL. Hyperbilirubinemia in the term newborn. Am Fam Physician 2002;65(4):599-606.

5. Ullah S, Rahman K, Hedayati M. Hyperbilirubinemia in neonates: Types, causes, clinical examinations, preventive measures and treatments: A narrative review article. Iran J Public Health 2016;45(5):558-68.

6. Ghaemi S, Fesharaki RJ, Kelishadi R. Late onset jaundice and urinary tract infection in neonates. Indian J Pediatr 2007;74(2):139-41.

7. Xinias I, Demertzidou V, Mavroudi A, Kollios K, Kardaras P, Papachristou F, et al. Bilirubin levels predict renal cortical changes in jaundiced neonates with urinary tract infection. World J Pediatr 2009;5(1):42-5.

8. Bahat Ozdogan E, Mutlu M, Camlar SA, Bayramoglu G, Kader S, Aslan Y. Urinary tract infections in neonates with unexplained pathological indirect hyperbilirubinemia: Prevalence and significance. Pediatr Neonatol 2018;59(3):305-9.

9. Özcan M, Sarici SÜ, Yurdugül Y, Akpinar M, Altun D, Özcan B, et al. Association between early idiopathic neonatal jaundice and urinary tract infections. Clin Med Insights Pediatr 2017;11:1179556517701118.

10. Lee SJ. Urinary tract infection. In: Behrman RE, Kliegman RM, Jenson HB, eds. Nelson Textbook of Pediatrics. Philadelphia, PA: Elsevier/W.B. Saunders Co.; 2015.p. 2556-62.

11. American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics 2004;114(1):297-316.

12. Zarkesh M, Assl AS, Ramtinfar S, Shakiba M. Incidence of hyperbilirubinemia and urinary tract infection (UTI) in asymptomatic term neonates under two weeks of age. Iran J Neonatol 2015;6(3):45-8.

13. Pashapour N, Nikibahksh AA, Golmohammadlou S. Urinary tract infection in term neonates with prolonged jaundice. Urol J 2007;4:91-4.

14. Bilgen H, Özek E, Ünver T, Biyikli N, Alpay H, Cebeci D. Urinary tract infection and hyperbilirubinemia. Turk J Pediatr 2006;48(1):51-5.

15. Nickavar A, Khosravi N, Doaei M. Early prediction of urinary tract infection in neonates with hyperbilirubinemia. J Ren Inj Prev 2015;4(3):92-5.

16. Tola HH, Ranjbaran M, Omani-Samani R, Sadeghi M. Prevalence of UTI among Iranian infants with prolonged jaundice, and its main causes: A systematic review and meta-analysis study. J Pediatr Urol 2018;14(2):108-15.

17. Hannam S, McDonnell M, Rennie JM. Investigation of prolonged neonatal jaundice. Acta Paediatr 2000;89(6):694-7.

18. Firoozi H, Seidan Anbi S, Mousavi S, Farshidi F, Rezai M. Prevalence of urinary tract infection in neonates with hyperbilirubinemia. J Mazandaran Univ Med Sci 2019;28(169):91-7.

19. Mohanna MA Bin, Raja'a YA. Frequency and treatment of urinary tract infection in children subjected to urine culture, in Sana'a, Yemen. J Ayub Med Coll Abbottabad 2005;17(2):20-2.

20. Nasher MA, Nasher TM, Gunaid AA. Etiologies of the urinary tract infections in a Yemeni city. Saudi Med J 2001;22(7):599-602.

21. Wu CY, Chiu PC, Hsieh KS, Chiu CL, Shih CH, Chiou YH. Childhood urinary tract infection: a clinical analysis of 597 cases - PubMed. Acta Pediatr Taiwanica 2004;45(6):328-33.

22. Vachvanichsanong P. Urinary tract infection: One lingering effect of childhood kidney diseases - review of the literature. J Nephrol 2007;20(1):21-8.

23. Chandra M. Reflux nephropathy, urinary tract infection, and voiding disorders. Curr Opin Pediatr 1995;7(2):164-70.

24. White B. Diagnosis and treatment of urinary tract infections in children. Am Fam Physician 2011;83(4):409-15.