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Original Article

# Prevalence of urinary tract infection in 2-8-week-old infants with jaundice

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## Abstract

***Background*** Urinary tract infections (UTI) in infants may manifest in various ways and often appear without symptoms. Previous studies have reported that jaundice has been observed in infants aged less than 8 weeks with UTIs. However, a prospective study on the prevalence of UTI in infants with jaundice aged 2-8 weeks is warranted in order to improve diagnosing capability and provide prompt treatment.

***Objective*** To investigate the prevalence and profiles of UTI in infants with jaundice aged 2-8 weeks.

***Methods*** This cross-sectional study was carried out in June-December 2011 in infants with jaundice aged 2-8 weeks. Subjects were patients from the Department of Child Health, Cipto Mangunkusumo Hospital (CMS), as well as the Pediatric Polyclinics of Budi Kemuliaan and Thamrin Hospitals. All subjects underwent total, direct and indirect bilirubin examinations, urinalyses and urine cultures.

***Results*** Of the 110 subjects recruited, the prevalence of UTI was 18.2%. More boys than girls had UTIs (13 boys, 7 girls). The microorganisms found in subjects with UTIs were *Escherichia coli* (10/20), *Klebsiella pneumoniae* (8/20), and *Enterobacter aerogenes* (2/20). Indirect hyperbilirubinemia was found in 5/20 subjects. There were more subjects with UTIs in the non-exclusively breastfed (8/20) and non-breastfed (8/20) groups than in the exclusively breastfed group (4/20), the full term gestational age (GA) group (17/20) than the preterm GA group (3/20), and the normal birth weight group (15/20) than the low birth weight group (5/20). The median age of jaundice onset was 3.5 days (range 1-40 days), and the median duration of jaundice was 13.5 days (range 3-56 days).

***Conclusion*** The prevalence of UTI in infants aged 2-8 weeks with jaundice was 18.2%. More boys than girls had UTIs. The most common infecting microorganism found in our subjects was *Escherichia coli*. In daily medical practice, infants with prolonged jaundice of more than 2 weeks should be tested by urinalysis and urine cultures for the presence of UTIs. **[Paediatr Indones. 2012;52:304-8]**.

***Keywords***: *jaundice, UTI, infants, hyperbilirubinemia*

Urinary tract infection (UTI) is a morbidity-causing disease in infants, occuring in both developed and developing countries. UTI prevalence has been estimated to be 0.1-1% in term neonates and 7-9% in infants.[1-3] Urinary tract infection in neonates should be managed promptly in order to avoid permanent kidney damage which may lead to hypertension and terminal kidney failure.[2-3] Physiological jaundice occurs in almost 60% of term infants and will self-resolve without treatment. Nevertheless, in some cases, jaundice may persist for more than 2 weeks.[4] In infants with prolonged jaundice but no other symptoms, it is difficult to differentiate if the jaundice is caused by a UTI or breastmilk, leading to undetected UTIs. Previous studies stated

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that jaundice is the only clinical manifestation of UTIs in neonates.[5-9] Garcia *et al.* reported that UTIs occurred in 7.5% of 160 infants with jaundice aged less than 8 weeks and who had no other symptoms.[5] Chen *et al*. and Omar *et al*. also reported similar results in 2011.[6,7]

There have been few prospective studies on UTI prevalence in infants aged 2-8 weeks with jaundice in Indonesia. Therefore, we aimed to find out the UTI prevalence among infants aged 2-8 weeks with jaundice to increase awareness of this clinical manifestation of UTIs.

## Methods

This cross-sectional study was conducted in the Department of Child Health at CMH, as well as the Pediatric Polyclinics at Budi Kemuliaan and Thamrin Hospitals in June-December 2011. Subjects were infants aged 2-8 weeks with jaundice. All subjects' parents provided informed consent. We excluded patients with signs and symptoms of sepsis, history of antibiotic treatment, currently under antibiotic treatment, or had pale stool. The required sample size was calculated to be 107 subjects. This study was approved by the Ethics Committee of the University of Indonesia Faculty of Medicine.

All eligible subjects underwent total, direct and indirect bilirubin examinations, urinalyses and urine cultures. Urine specimens were collected with sterile technique using a urine collector after the genitalia and external urethral orifice were thoroughly cleaned with 0.9% NaCl solution and dried with sterile gauze. Urine collectors were changed every 30 minutes until adequate urine volume was collected. Urine specimens were then transferred to sterile containers, then delivered to the Microbiology Laboratory within 2 hours or stored at 4°C in the CMH Microbiology Laboratory for culturing.

We also collected 3mL of blood specimens for total, direct, and indirect bilirubin examinations. Blood specimens were drawn and examined by laboratory staff in each hospital, while urine cultures were performed only in the CMH Microbiology Laboratory. Parents were informed of all test results and subjects with proven UTIs were treated with appropiate antibiotics, based on the culture and sensitivity findings.

Data was analyzed with the SPSS 17.0 program.

## Results

During the study period, there were 127 infants with jaundice identified in the three hospitals. Seventeen infants were excluded, leaving 110 subjects for this study. We found the prevalence of UTIs in infants aged 2-8 weeks with jaundice was 18.2%, according to positive urine cultures. The most common microorganisms

**Table 1.** Characteristics of subjects

| Characteristics | Frequency | | |
|---|---|---|---|
| | UTI n=20 | Without UTI n=90 | Total n=110 |
| Sex, n (%) | | | |
| Boys | 13 | 48 (53.3) | 61 (55.4) |
| Girls | 7 | 42 (46.7) | 49 (44.5) |
| Breastfeeding, n (%) | | | |
| Exclusive | 4 | 62 (68.8) | 66 (60.0) |
| Non-exclusive | 8 | 17 (18.8) | 25 (22.7) |
| Not breastfed | 8 | 11 (12.2) | 19 (17.2) |
| Birth weight, n (%) | | | |
| ≥2500 grams | 15 | 80 (88.8) | 95 (86.4) |
| <2500 grams | 5 | 10 (11.1) | 15 (13.6) |
| Gestational age, n (%) | | | |
| Full term | 17 | 83 (92.2) | 100 (90.9) |
| Preterm | 3 | 7 (7.7) | 10 (9.0) |
| Amniotic membrane rupture >24 hours, n (%) | 1 | 3 (3.3) | 4 (3.6) |
| Untreated maternal leukorrhoea, n (%) | 2 | 6 (6.6) | 8 (7.3) |
| Untreated maternal UTI, n (%) | 0 | 3 (3.3) | 3 (2.7) |
| Normal delivery | 14 | 61 (67.8) | 75 (68.2) |

found in urine cultures were *Escherichia coli* (10/20), *Klebsiella pneumoniae* (8/20), and *Enterobacter aerogenes* (2/20). Among 20 infants with UTI, 13 infants were boys. The incidence of UTI was higher in boys (21.3%) than in girls (14.4%) (**Table 1**). In subjects with UTIs, 17/20 were term infants, 15/20 had normal birthweight, 8/20 infants were non-exclusively breastfed and 8/20 were in the non-breastfed group. One subject in the UTI group, the mother had a premature membrane rupture of more than 24 hours, putting this newborn at higher risk. In addition, the risk factor of untreated maternal leukorrhoea was found in 2 infants with UTI (**Table 1**).

(19/20), gentamicin (17/20), ceftazidime (15/20), and ceftriaxone (14/20). Oral antibiotics with better sensitivities were cefuroxime (15/20), cefixime (14/20), cephalexin (13/20), and cotrimoxazole (12/20).

## Discussion

Urine samples can be collected by various methods, such as suprapubic aspiration, catheterization, clean catch urine, and urine collectors.[10] We chose the urine collector method because it is non-invasive and easy to perform, although it is known to have high false

**Table 2.** Cholestasis and unconjugated hyperbilirubinemia in subjects with and without UTIs

| Variable | UTI n=20 | Without UTI n=90 |
|---|---|---|
| Cholestasis, n (%) | 4 | 4 (4.4) |
| Unconjugated hyperbilirubinemia, n (%) | 16 | 86 (95.5) |

**Table 3.** Urinalysis profiles of jaundice infants aged 2-8 weeks

| Urinalysis | Frequency | |
|---|---|---|
| | UTI (n=20) | Without UTI (n=90) |
| Leukocyturia, n | 13 | 6 |
| Hematuria, n | 2 | 0 |
| Leukocyte esterase (+), n | 10 | 6 |
| Nitrite (+), n | 3 | 0 |
| Bacteriuria, n | 2 | 0 |
| Leukocyte esterase (+) and nitrite (+), n | 3 | 0 |
| Leukocyte esterase (+), nitrite (+), and leukocyturia, n | 2 | 0 |

In the UTI group, the median age of jaundice onset was 3.5 days (range 1-40 days) and median duration of jaundice was 13.5 days (range 3-56 days), while in the non-UTI group, the median age of jaundice onset was 3.0 days (range 1-40 days) and median duration of jaundice was 12.0 days (range 1-49 days). In the UTI group, 4 subjects had cholestasis and 16 had unconjugated hyperbilirubinemia (**Table 2**).

In the UTI group, leukocyturia was found in 13/20 subjects with positive leukocyte esterase in most cases (10/20). Bacteriuria was found in 2/20 cases, and positive nitrite was found in only 3/20 cases (**Table 3**). In our study, the microorganisms grown were most commonly sensitive to parenteral antibiotics of meropeneme (20/20), amikacin (18/20), imipenem

positive rates.[11] Schroerder *et al*. suggested collecting urine specimens twice if using the urine collector method.[12] However, due to parental consent and cost considerations, we collected urine specimens only once for each patient. Schroerder *et al*. also stated that bacterial contamination of the urine can be avoided if a sterile urine specimen is collected and interpreted carefully. Several factors should be considered when determining the urine collection method, such as patients' ages and parental consent.[12]

A limitation of our study was that we did not have a control group of healthy infants without jaundice as a comparison, since jaundice in infants with UTIs could be a coincidence or have a cause other than a UTI. Chen *et al*. suggested using a group of healthy infants without jaundice as a comparison to

determine if jaundice was the primary manifestation of UTI and not coincidental.[6]

In our study, we limited subjects to the age range of 2-8 weeks since babies are usually checked by health workers in primary health care settings during that age period.[13] In addition, those with prolonged jaundice for more than 2 weeks were chosen in order to exclude physiological jaundice. We found the UTI prevalence to be greater than that of a study by Garcia *et al*.,[5] possibly due to our collecting urine only once for each patient. Li *et al*. had a 36.8% false positive rate using urine collectors, but that decreased to 12.6% on a second examination.[14]

Most subjects (60%) from both groups were exclusively breastfed. Of the positive urine culture patients, 8/20 infants were non-exclusively breastfed and 8/20 infants were not breastfed. Similary, Ghaemi *et al.* and Pashapour *et al.* found more positive urine cultures results in infants who did not receive breast milk.[15,16] Breast milk contains immunological factors useful for preventing infection, such as secretory immunoglobulin A (sIgA) which is found in colostrum at 3-4 days post-delivery. Secretory IgA protects infants from infections caused by pathogens (bacteria, viruses, parasites, and fungi) in the gastrointestinal and respiratory tracts. Anti-infective factors in breast milk also protect babies from infections caused by *Escherichia coli, Klebsiella pneumoniae, Salmonella, Shigella* species, *Streptococcus pneumoniae*, etc.[17,18]

In our study, the age of jaundice onset and jaundice duration were not different between UTI group and non-UTI group. These findings were similar with the study of Omat *et al*.[7] as well as the study of Bilgen *et al*.[19]

Unconjugated hyperbilirubinemia is associated with hemolytic disorders, metabolic and endocrine disorders, and infections. UTI-related unconjugated hyperbilirubinemia can be caused by hemolysis due to endotoxins produced by *Escherichia coli* and other Gram-negative bacteria. In our UTI group, 4 cases had cholestasis and 16 cases had unconjugated hyperbilirubinemia. Cholestasis was found in cases of jaundice prolonged for more than 3 weeks, in accordance with the theory that liver damage occurs in conditions of prolonged jaundice.[20]

This study shows that in infants aged 2-8 weeks, where the transit time of urine is considered as a short time, but still some infants with UTI had leukocyte esterase and nitrite test positive, as well as bacteriuria and pyuria positive in microscopy examination in urinalysis (**Table 3**). Chen *et al*. suggested performing urinalysis and urine culture examinations in infants aged 2-8 weeks with jaundice to establish the diagnosis of UTI.[6]

In conclusion, the prevalence of UTI in infants aged 2-8 weeks with jaundice was 18.2%. The incidence of UTI was higher in boys than in girls. The most common microorganism cultured from our subjects was *Escherichia coli*. Urinalyses for UTI screening and urine cultures should be performed in daily practice for infants with jaundice prolonged for more than 2 weeks. Further research with healthy infants as a control group is needed in order to determine if jaundice is a primary manifestation of UTIs.

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