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Proportion of Urinary Tract Infection in Neonatal Sepsis

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Abstract

Background and Aim: Urinary tract infection (UTI) might be associated with bacteremia and congenital anomalies of the kidney and urinary tract (CAKUT) in neonates, which can lead to renal parenchymal scarring and chronic kidney disease in complicated situations. We aimed to determine the occurrence of UTI in neonatal sepsis.

Methods: A cross-sectional study was conducted on 500 term extramural hospitalized neonates suspected to have infection. They underwent a detailed history, physical examination, and comprehensive sepsis workup. The diagnosis of neonatal UTI was based on a positive urine culture obtained by suprapubic aspiration (SPA).

Results: Out of 500 neonates included in our study (324 boys and 176 girls), blood culture was positive in 84 (36.5%) neonates in the early onset sepsis group (n=230) and in 130 (48.1%) neonates in late onset sepsis group (n=270) ($p < 0.05$). In both early onset sepsis (EOS) and late onset sepsis (LOS) groups, blood culture was found to be positive in a greater proportion of male (41.3%) versus female (29.3%) patients ($p <0.05$). The most common organism isolated from blood and urine culture was Klebsiella followed by E-coli. Urine culture was positive in 34 (6.8%) patients of whom 29 (85%) culture positive cases were from the LOS group ($p <0.05$).

Conclusion: UTI is not uncommon among the hospitalized neonates, and UTI evaluation among septic neonates can prove beneficial for the prevention of long-term sequelae of neonatal UTI.

Keywords: Infection; Neonates; Sepsis; Urine.

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Introduction

Severe bacterial infections are directly responsible for one third of neonatal deaths in developing countries (1). The consequences of neonatal infection extend beyond neonatal mortality, in the form of neurodevelopmental sequelae as well as pulmonary, ophthalmological, and/or renal impairments of various degrees among the survivors (2). Bacterial urinary tract infections (UTIs) in neonates and young children are potentially dangerous, because these might be the forerunners of severe renal disease of childhood. The rate of UTIs among neonates varies between 0.1 and 1%, with higher rates in low birth weight infants (3-6). Relying on this data, most of the neonatal centers do not include UTI workup as part of neonatal sepsis evaluation (7, 8). However, neonatal UTIs can also be part of neonatal sepsis (8), as up to 7% of febrile infants and children have UTIs, and approximately 20% of these UTIs occur in children < 3 months of age (9,10).

The clinical manifestations of UTIs in premature and term neonates are similar, including fever, poor feeding, unsatisfactory weight gain, vomiting, general illness, loose stool, jaundice, and lethargy,

while premature neonates with UTIs may present with respiratory symptoms such as apnea, hypoxia, or tachypnea (11). UTIs in neonates with bacteremia can result in long-term complications like renal parenchymal scarring and chronic kidney disease (12), thus prompting the need for the inclusion of urine culture as part of aggressive neonatal sepsis workup, which otherwise is not included in sepsis evaluation in the first 72 h of life (13).

Methods

A cross-sectional study was conducted from November 2018 to August 2020 (21 Months) after obtaining the ethics committee approval. The study was conducted in the Neonatal Division of Department of Pediatrics G.B. Pant Hospital, a hospital affiliated with Govt Medical College Srinagar and a referral tertiary care hospital for the children of Kashmir valley.

Given an expected occurrence rate of UTI in neonatal sepsis of 5%, the minimum sample size needed to estimate the occurrence rate within an absolute error of 2% at 95% confidence interval was 500. Thus one eligible patient was randomly selected each weekday (all days except Sunday), so that the total number of patients examined and evaluated over a period of 21 months was 500.

All admitted neonates (up to 30 days of life) suspected to have infection or presenting with clinical conditions like hyperthermia, hypothermia, respiratory distress, jaundice, hepatomegaly, lethargy, irritability, refusal of feeds, vomiting, abdominal distension and diarrhea underwent sepsis workup. However, the neonates treated with antibiotics before hospitalization, neonates with syndromic morphology/immune deficiency, those with gross congenital abnormalities involving the genito-urinary tract and anorectal anomalies, preterm neonates, those with antibiotic exposure within 5 days of delivery, and the neonates whose parents were unwilling to give consent were excluded from the study. For the purposes of the study, the data was divided into early and late onset sepsis.

All neonates underwent a detailed relevant history and thorough physical examination along with a comprehensive sepsis evaluation including complete blood count, CRP, urinalysis (UA), blood culture, lumbar puncture, and urine culture (UC). The diagnosis of neonatal UTI was based on a positive urine culture after obtaining >5ml of urine from a well hydrated neonate with the aid of ultrasound through suprapubic aspiration (SPA). All the UA were performed within 30 minutes and urine samples were immediately transferred to the microbiology laboratory. For UA, the specimens were centrifuged at 2000 rpm for 10-12 minutes and were examined microscopically for pyuria reported as the number of leukocytes per high-power field. The presence of 5 or more WBCs/HPF was considered as pyuria. Quantitative urine cultures were performed in the microbiology laboratory, where one mL urine was used to inoculate plates containing peptone based urochrome media incubated at 35-37°C and examined at 24 to 48 hours for colony count and bacterial identification. The growth of a single urinary pathogen at a concentration of at least 100 CFU/mL was defined as a positive urine culture, confirming UTI as a diagnosis (14), and the growth of mixed or nonpathogen organisms was considered contamination. On certain occasions, if there was any delay in the culturing of urine specimens, the samples were stored in the refrigerator until cultured. Informed consent was taken from the parents/legal guardians of the neonates included in the study.

Statistical analysis:

Data was entered in a Microsoft Excel spreadsheet and analyzed using the EpiInfo. Continuous variables are summarized as mean and SD unless not normally distributed. The relationship between two categorical variables was analyzed using Chi Square test. All p values were two sided and p values less than 0.05 were considered statistically significant.

Results

Of 37456 neonates admitted to our neonatal division, 11861 were evaluated for neonatal sepsis during the study period of 21 months (November 2018 to August 2020). Of 11861 neonates, 8945 were term babies and 2916 were preterm. On evaluation, 1735 term neonates had sepsis (suspected and culture proven), of whom 500 were included in our study (324 boys and 176 girls).

The neonates were divided into either the EOS group (age ≤ 72 hours), including 230 (46%) neonates (138 boys and 92 girls) or the LOS group (age > 72 hours) including 270 (54%) neonates (186 boys and 84 girls). Blood culture was positive in 84 (36.5%) neonates in the EOS (n=230) and 130

(48.1%) neonates in the LOS group (n=270) ($p < 0.05$). In both EOS and LOS groups, blood culture was found to be positive in a greater proportion of male (41.3%) versus female (29.3%) patients ($p <0.05$). The organisms isolated from blood and urine cultures along with the frequency of occurrence are shown in Table 1.

Table 1. Organism (s) isolated from blood and urine culture

Organism isolated	Frequency (blood culture)	Frequency (urine culture)
Klebsiella	87 (46.6)	16 (47.06)
E. coli	42(19.6)	16 (47.06)
Enterobacter	26(12.1)	2 (5.88)
CONS	24(11.2)	-
Pseudomonas	17(8.0)	-
Staph aureus	12(5.6)	-
Acinatobacter	6(2.8)	-
Total	214(100.0)	34(100.0)

Klebsiella was the most common organism isolated from blood and urine cultures. Comprehensive analysis of the urine culture positive neonates is shown in Table 2.

Of 500 patients, the urine culture was positive in 34 (6.8%) patients, of whom 29 (85%) were in the LOS group and 5 (15%) wee in the EOS group ($p<0.05$). Among urine culture positive patients, males outnumbered the females (64.7% vs 35.3%).

The organisms isolated from the urine cultures of the patients were Klebsiella and E.Coli in an equal proportion (47.06% each) followed by proteus (5.88%). Of 34 urine culture positive patients, klebsiella and E.coli were isolated both from the urine and blood cultures in 6 and 2 patients, respectively.

Discussion

The rate of UTI was 6.8% among the hospitalized neonates in present study. A study conducted by Morely et al (15) on 207 young infants who presented with fever found that 23.2% (48/207) of the septic neonates had pyuria, of whom 7.2% (15/207) had UTI. In a similar study by Samayam et al (16), 6% of the septic neonates had UTI. Similar results were obtained by Garcia et al (17) who found that the occurrence of UTI was 7.5% in a study population of 160 patients observed.

UTIs affected more boys than girls (64.7% boys, 35.3% girls) in the present study. This male preponderance is similar to earlier studies (18-20). During the early infancy, UTI affects the boys 1.5-5 times more than girls, and is more common in uncircumcised boys (21). It should be noted that none of the boys with UTI were circumcised in the present study. This UTI predominance in uncircumcised male neonates is believed to be related to the preputial colonization of the bacteria. In a the meta-analysis of none published studies conducted by Wiswell et al (22), the incidence rate of UTIs was compared between uncircumcised versus circumcised infant males, and a 12 fold increased risk of UTI was found in boys with foreskin compared to circumcised boys. Although most studies have documented the prepuce–UTI association up to 1 year of age, it has also been reported in premature infants as well as during later childhood and in adults.

Fussell et al (23) concluded that uropathogenic bacteria, particularly P-fimbriated E coli (those associated with pyelonephritis), adhered particularly well to the inner mucosal surface of the foreskin as opposed to the keratinized external surface.

The proportion of males was 60.0% and 68.9% in the EOS and LOS groups, respectively. A similar conclusion was drawn in studies conducted by Bangi et al (24) and Swarnkar et al. (25). The most common organisms isolated from the blood cultures were Klebsiella in 87 (40.6%) and E. coli in 42 (19.6%) followed by Enterococci in 26 (12.1%) neonates. Our findings are in accordance with findings of Blomberg et al (26) and Samayum et al. (16).

According to our observation, gram negative rods like Klebsiella and E. coli organisms were isolated from urine cultures in 16 neonates each, followed by Proteus organism in 2 neonates. Similarly, Samayam et al (16) found that out of 12-urine culture positive neonates, Klebsiella was isolated in 5 cases, E. coli in 4, Pseudomonas in 2, and Candida albicans in 1 case.

However, in studies conducted by Didier et al (27) and Watt et al (28); the most common bacterial etiology for neonatal UTIs was similar to other age groups with Escherichia coli being the most common UTI causative organism.

Table 2. Descriptive analysis of urine culture positive patients

Serial No	Sex	Age	Temp. in Celsius	Serum CRP	TLC	Urine Exam (WBC/HPF)	Bacterial growth in urine
1	Female	4 days	38.7	Positive	15000	70 to 80	Present
2	Female	25 days	39.0	Negative	19000	45 to 50	Present
3	Male	9 days	36.5	Positive	30000	33 to 37	Present
4	Female	23 days	38.8	Negative	17000	12 to 15	Present
5	Female	10 days	35.0	Positive	13000	14 to 18	Present
6	Male	9 days	37.2	Positive	16000	34 to 40	Present
7	Male	5 days	36.5	Positive	21000	25 to 30	Present
8	Male	13 days	39.5	Positive	12000	20 to 25	Present
9	Male	8 days	36.5	Negative	17000	35 to 40	Present
10	Male	8 days	39.0	Positive	12000	15 to 20	Present
11	Male	12 days	36.8	Positive	7000	30 to 35	Present
12	Female	14 days	37.1	Positive	18000	32 to 38	Present
13	Male	46 hours	40.5	Positive	46000	12 to 17	Present
14	Male	17 days	36.9	Positive	12000	15 to 20	Present
15	Male	6 days	36.8	Positive	29000	20 to 25	Present
16	Female	14 hours	36.5	Positive	14000	35 to 40	Present
17	Female	8 days	36.8	Positive	6000	7 to 8	Present
18	Male	11 days	36.5	Positive	13000	15 to 20	Present
19	Male	11 days	39.3	Negative	27000	10 to 13	Present
20	Female	20 days	36.7	Positive	16000	15 to 20	Present
21	Male	36 hours	36.5	Positive	17000	34 to 41	Present
22	Female	42 hours	36.9	Positive	14000	10 to 12	Present
23	Male	15 days	36.8	Positive	19000	12 to 16	Present
24	Male	8 days	36.8	Positive	29000	38 to 40	Present
25	Male	20 days	37.1	Positive	35000	30 to 32	Present
26	Male	13 days	38.6	Negative	12000	18 to 20	Present
27	Male	6 days	36.8	Positive	3000	8 to 10	Present
28	Male	21 days	36.5	Positive	5000	10 to 15	Present
29	Female	24 days	36.5	Positive	21000	15 to 20	Present
30	Female	23 days	34.5	Positive	18000	16 to 20	Present
31	Male	15 days	35.0	Positive	13000	35 to 40	Present
32	Female	28 hours	36.9	Positive	15000	10 to 15	Present
33	Male	16 days	37.1	Positive	20000	15 to 20	Present
34	Male	24 days	36.9	Negative	21000	12 to 17	Present

On sub-analysis, it was found that Klebsiella was isolated from both the blood and urine cultures in 6 neonates and E. coli was isolated from both cultures in 2 patients, indicating that a total of 8 (23.5%) out of 34 urine culture positive patients had the same organism causing UTI and bacteremia exposing the link between blood stream infection and its spread to genitourinary system. Similar results were found by Maherzi M et al (29) where out of 43 patients with positive urine cultures, 6 had the same organism isolated from the blood and urine.

Conclusion

Approximately 7% of neonates with suspected or proven sepsis had concomitant UTI, implying that keeping a high index of suspicion for the concurrent occurrence of UTI among suspected or proven septic neonates may be helpful for early detection

and management of neonatal UTIs and complications thereof to avoid long-term sequelae.

Conflict of Interest

The author declares no conflicts of interest.

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