

Urinary Tract Infection in Neonates with Serious Bacterial Infections Admitted to the University Hospital of the West Indies

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ABSTRACT

Objective: The aim of this study was to describe the epidemiology of urinary tract infection in neonates, with serious bacterial infections, admitted to the University Hospital of the West Indies.

Methods: Admission records of all neonates admitted to the neonatal unit of the University Hospital of the West Indies between January 1995 and December 2000 for sepsis evaluation were reviewed. Infants who had positive bacterial cultures were identified using laboratory records. Those satisfying the criteria for urinary tract infection were selected for detailed analysis. Demographic, clinical and laboratory data were collected using a pre-coded questionnaire. Descriptive analyses were performed.

Results: Fifty-one (38%) of 135 babies with positive bacterial isolates had confirmed urinary tract infection. Male: female ratio was 6:1. Common presenting features included fever (32%), poor feeding (30%) and irritability (22%). The mean white cell count was 14 ± 6.26 . E coli and Klebsiella species were most frequently identified. Factors associated with a diagnosis of urinary tract infection included male gender ($p < 0.001$), age > 48 hours ($p < 0.05$) and a presenting complaint of poor feeding ($p < 0.003$). Imaging studies of the renal tract detected abnormalities in 5 (10.4%) neonates.

Conclusions: Urinary tract infection is an important cause of serious bacterial infection in neonates affecting 1 in 3 babies with proven bacterial infection and may be the first indicator of underlying structural abnormalities. The absence of specific distinguishing clinical features makes it necessary to include urine cultures in the sepsis evaluation of neonates presenting with symptoms suggestive of sepsis.

Infección de las Vías Urinarias en Neonatos Ingresados con Serias Infecciones Bacterianas en el Hospital Universitario de West Indies

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RESUMEN

Objetivo: El propósito de este trabajo fue describir la epidemiología de la infección de las vías urinarias en neonatos con serias infecciones bacterianas, ingresados en el Hospital Universitario de West Indies.

Métodos: Se revisaron las historias clínicas de todos los neonatos ingresados en la Unidad Neonatal del Hospital Universitario de West Indies entre enero de 1995 y diciembre de 2000 para una evaluación de sepsis. Los infantes que presentaron cultivos bacterianos positivos, fueron identificados usando los registros de laboratorio. Aquellos que satisfacían los criterios de infección de las vías urinarias, fueron seleccionados para un análisis detallado. Se compilaron datos demográficos, clínicos y de laboratorio usando un cuestionario pre-codificado. Se llevaron a cabo análisis descriptivos.

Resultados: Cincuenta y uno (38%) de los bebés con aislados bacterianos positivos tuvieron infección confirmada de las vías urinarias. La proporción varón:hembra fue 6:1. Las características comunes que se presentaron, incluyeron fiebre (32%), pobre alimentación (30%) e irritabilidad (22%). El conteo promedio de leucocitos fue 14 ± 6.26 . Las especies identificadas con mayor frecuencia fueron E coli y Klebsiella. Los factores asociados con un diagnóstico de la infección de las vías urinarias incluyeron género masculino ($p < 0.001$), edad > 48 horas ($p < 0.05$) y quejas en cuanto a pobre

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alimentación ($p < 0.003$). Los estudios de imágenes de las vías renales detectaron anomalías en 5 (10.4%) neonatos.

Conclusiones: La infección de las vías urinarias es una causa importante de seria infección bacteriana en neonatos, que afecta a 1 de cada 3 recién nacidos con infección bacteriana demostrada, y puede ser el primer indicador de anomalías estructurales subyacentes. La ausencia de características clínicas distintivas, hace necesario que se incluyan cultivos de orina en la evaluación de la sepsis en neonatos que se presentan con síntomas que sugieren la presencia de sepsis.

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INTRODUCTION

Urinary tract infection is the most common serious bacterial infection found in febrile infants and young children who present without an obvious source of infection (1, 2, 3). These infections account for as many as two-thirds of all culture-positive infections in young infants (3). Prevalence rates for urinary tract infections (UTI) vary with age. Prevalence rates in term newborn infants range from 0.1% to 1% and increase to up to 7–9% in infancy. The preterm neonatal rates have been noted to be higher than that for term neonates and may be as high as 10% with an inverse relation to the birthweight (4, 5). Data from South African studies show prevalence rates for UTI of up to 26% in hospitalized infants and children and 17% in community-based studies (6, 7).

Limited studies are available from developing countries and there are no published data on the epidemiology of this infection in neonates from the Caribbean region (6–8). The vague, non-specific presentation of this disease makes it likely for clinicians to miss the diagnosis unless routine urine cultures are done in the sick infant. Failure to diagnose will result in delay in institution of appropriate therapy and an increase in the already high propensity for scar formation noted in infancy. In appreciation of these challenges, The American Academy of Paediatrics published recommendations for diagnosis, treatment and evaluation of initial UTI in febrile infants and young children. However no recommendations were given for infants below two months of age (9).

The relatively low incidence rates observed in developed countries for the term newborn infants, especially those less than two days old, have caused specialists to question the need to include routine urine cultures in the workup for sepsis in these infants. Tamim *et al* in analyzing the efficacy of urine culture as part of sepsis evaluation in the neonate reported that there was minimal benefit in obtaining cultures from very low birthweight infants in the first 24 hours of life but emphasized that it was important to obtain urine cultures from older patients with signs of sepsis (5).

The few studies from developing countries suggest higher rates of infection in these populations (6–8). Other differences in the epidemiology of this condition may well exist for developing countries making it unwise to adopt recommendations that are based on epidemiological and clinical patterns of this disease in developed countries. There is a need to describe the local and regional patterns of this infection before any consensus recommendations can be

made for investigation and management of UTI in Caribbean neonates. This study seeks to describe the epidemiology of UTI in neonates admitted to the University Hospital of the West Indies (UHWI).

SUBJECTS AND METHODS

Setting: The UHWI is one of the three tertiary level hospitals in the island which offer combined maternal and neonatal care. The neonatal unit is a 30-bed unit and serves primarily the needs of the sick neonate delivered at the UHWI. In addition, the unit accepts a limited number of referrals from other hospitals. The average yearly neonatal admission rate to the unit is 650.

Study population

All neonates admitted to the neonatal unit between January 1, 1995 and December 31, 2000, whose evaluation for sepsis revealed positive bacterial isolates from blood, urine or cerebrospinal fluid, were identified. The sub-group satisfying the criteria for UTI was then selected for detailed review. Urinary tract infection was defined as the growth of a significant number of colonies per ml on agar plated with a sample of urine.

A urine culture was considered to have significant growth of bacteria if

- * Any growth of organisms was obtained from a suprapubic aspirate or
- * $> 10^4$ organisms/ml was obtained from a catheter specimen or
- * $> 10^4$ organisms/ml of a single organism was obtained from a urine bag sample

Samples with multiple organisms were considered to be contaminated if obtained via urine bag collection and were excluded from review.

Information defining age, gender, gestation, birthweight, clinical characteristics, laboratory findings and outcome was extracted from hospital records.

Statistics

Data were analysed using the SPSS statistical programme. Chi-square tests were used to identify factors associated with a diagnosis of UTI.

The UWI/UHWI Ethics Committee granted approval for this study to be conducted.

RESULTS

A total of 135 neonates admitted to the neonatal unit at the UHWI during the study period had confirmed bacterial infections. Of these, 51 (38%) were diagnosed with a UTI. The distribution of culture -positivity amongst neonates admitted to the newborn unit for presumed sepsis is shown in Fig. 1.

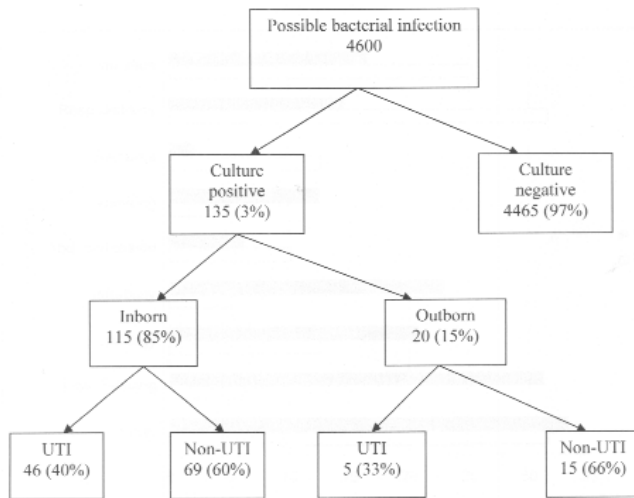


Fig 1: Algorithm showing distribution of UTI cases amongst neonates presenting with features suggestive of sepsis.

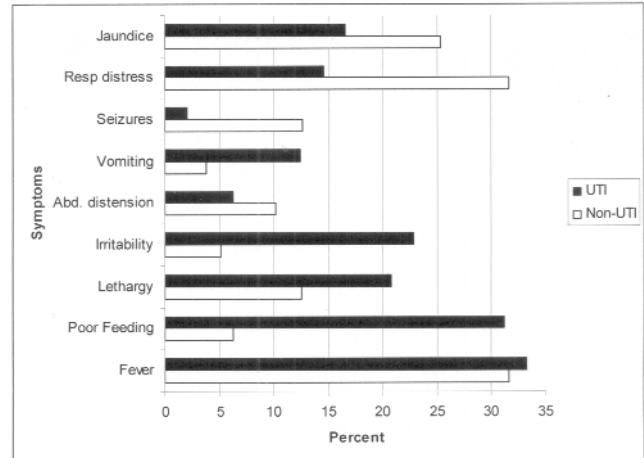
The male: female ratio in neonates diagnosed with UTI was 6:1 as compared with 1.6:1 in those with non-UTI sepsis ($p < 0.001$). The mean birthweight for neonates diagnosed with UTI was 3.03 ± 0.98 kg as compared with a mean birthweight of 2.62 ± 1.08 kg in neonates with non-UTI sepsis ($p = 0.046$).

Thirteen (26%) UTI-diagnosed babies were premature with gestational ages ranging from 27 to 34.5 weeks. The prevalence of UTI in premature babies with proven bacterial infections was 13/46 (28%) as compared with 38/89 (43%) in term babies with proven bacterial infection.

The median age at presentation for neonates with UTI was 4.5 days (0–30) as compared to a median age at presentation for neonates with non-UTI sepsis of 0.5 days (0-27). Twenty-two (43%) neonates with UTI presented in the first 48 hours of life as compared to 51 (61%) neonates with non-UTI sepsis who presented within the first 48 hours of life ($p = 0.042$). Of UTI-diagnosed neonates, premature babies presented earlier at a median age of one day as compared to term babies who presented later at a median age of nine days ($p = 0.037$ Mann-Whitney).

There were no significant differences in presentation between the two groups except that UTI-diagnosed neonates were more likely to present with poor feeding ($p = 0.043$) and irritability ($p = 0.048$) than were non-UTI neonates (Fig. 2).

Overall mean white cell count was $14.56 \pm 10.34 \times 10^9$ /L with no significant differences between UTI and non-UTI babies. Three (6%) neonates with UTI had concurrent docu-



A neonate could have more than one presenting symptom

Fig 2: Presenting symptoms of neonates with and without UTI

mented bacteraemia. The mean white cell count of $15.6 \pm 8.0 \times 10^9$ /L for bacteraemic neonates with UTI was not significantly different from that of $13.9 \pm 5.9 \times 10^9$ /L in non-bacteraemic neonates with UTI ($p = 0.75$).

The main mode of collection was suprapubic aspiration. Urine collection by bag was done in only two cases. *Escherichia coli* and *Klebsiella* species were most frequently identified. Table 1 shows microbial pattern of infection.

Table 1: Frequency of bacterial isolates in Jamaican neonates with UTI

Organism	Frequency (%)
<i>Escherichia coli</i>	16 (31)
<i>Klebsiella sp</i>	15 (29)
<i>Enterobacter sp</i>	8 (16)
<i>Enterococcus</i>	4 (8)
<i>Proteus mirabilis</i>	3 (6)
<i>Acinetobacter sp</i>	2 (4)
<i>Coagulase negative staphylococcus</i>	2 (4)
<i>Pseudomonas aeruginosa</i>	1 (2)

Factors associated with a diagnosis of UTI were male gender ($p < 0.001$), older age > 48 hours ($p < 0.05$) and presenting symptom of poor feeding (0.003).

Forty of 51 neonates had ultrasonographic studies. The prevalence of abnormal findings was 5%. These revealed unilateral renal agenesis with hydronephrotic contralateral kidney in one case and solitary kidney in the other case. Two (4.8%) of 42 neonates had findings of vesico-ureteric reflux disease on micturating cystourethrogram (MCUG). One infant also had associated hydronephrotic changes on ultrasound; the other was documented to have a normal ultrasound. Three of eight renal scans (37.5%) showed abnormalities which included obstructive uropathy in two cases and a non-functioning kidney in the other case.

DISCUSSION

Urinary tract infections are important foci of sepsis in neonates with rates ranging from 0.1% in the term neonate to as high as 25% in the preterm neonate (4, 10). In the newborn unit at the UHWI, only 1.1% of neonates screened for sepsis had documented episodes of UTI but as many as one out of every three babies with bacterial isolates were documented to have positive urine cultures.

Underlying structural or functional abnormalities of the renal tract which are more likely to be present in young children account for the relatively high age-specific incidence. Vesico-ureteric reflux (VUR), a recognized risk factor for UTI has been reported in 18 to 40% of infants investigated after a first episode of UTI (4). There appears to be ethnic differences in prevalence rates of VUR, with lower rates described in persons of African ancestry as compared to Caucasians (11, 12).

In keeping with this observed racial difference, West *et al* reported much lower rates of 10% in a population of Jamaican children undergoing MCUG as part of work-up for UTI, voiding dysfunction or congenital anomalies (13). This however, was a small study and a separate incidence rate was not calculated for children being worked-up solely for UTI. Miller (unpublished data) in a larger study has found an incidence rate of VUR of 16–18% in children undergoing cysto-urethrogram studies as part of the work-up for UTI in the public and private setting in Jamaica respectively. The rate of 4.8% in this study amongst neonates with UTI in whom a voiding cysto-urethrogram was done is lower than that previously reported by West *et al* and that found by Miller. However, this study included only children presenting in the first month of life. Of course, not all infants with reflux disease would necessarily present with a UTI in the neonatal period.

Although it is our institution's current policy to investigate all neonatal cases of UTI with abdominal ultrasound and micturating cystourethrogram, not all the neonates in this study obtained the necessary imaging. The necessity of MCUG studies in the work-up of the Jamaican infant with UTI has been questioned, given documented low rates of VUR by West *et al*. Ultrasonographic abnormalities resulting from reflux while frequent in severe disease may be entirely absent in mild reflux. In the present study, abdominal ultrasonography alone would have missed one case of reflux amongst those investigated, which translates to 2.5% of infants screened with ultrasound alone. Miller (unpublished data) found ultrasound to be sensitive in detecting Grade 4 and 5 VUR but ultrasound did not detect most cases of Grade 3 and all cases of grade 1 and 2 VUR. In that series, 88% of cases with documented VUR on MCUG had normal ultrasonographic study. The consequences of missing infants with underlying VUR or posterior urethral valves, in a country like Jamaica, where there is limited availability of dialysis and renal transplant are far reaching.

The demographic profile of our patients with a high male preponderance and a tendency to present as older neonates does not differ from other reports (2, 4). Symptoms of infection in neonates are generally vague and non-specific. This review supported this experience but found that a history of poor feeding was more likely to be associated with UTI than with other causes of bacterial infection. Gram negative bacilli account for the majority of bacterial infections affecting the urinary tract with *Escherichia coli* recognized as the leading cause in several reports (1, 2, 8). The findings of the present study concur with those reports.

The low rate (6%) of concomitant bacteraemia seems to contradict the teaching that neonatal UTI arises primarily from haematogenous spread (2). The absence of laboratory evidence of haematological responses to serious bacterial infection in most of the study patients with UTI further supports this discrepancy in our setting.

This study highlights the significant contribution that UTI plays in the aetiology of serious bacterial infections in neonates admitted to the UHWI. The absence of useful clinical and laboratory markers that indicate the likelihood of UTI in neonates emphasize the important role of urine cultures in sepsis evaluations as the only reliable means of identifying disease. In addition, the study provides support for continuing the practice of renal tract imaging on all neonates with UTI.

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