Lugira *et al.*
Egyptian Pediatric Association Gazette (2022) 70:2
https://doi.org/10.1186/s43054-021-00088-6

Egyptian Pediatric Association Gazette

RESEARCH Open Access

Prevalence, aetiology, antimicrobial susceptibility testing, and predictors of urinary tract infection among neonates with clinical sepsis: a cross-sectional study

Yasintha S. Lugira[1], Fransisca D. Kimaro[1], Mkhoi L. Mkhoi[2], Samuel G. Mafwenga[3], Angelina A. Joho[4] and James J. Yahaya[5*]

Abstract

Background: Urinary tract infection (UTI) is the most common and life-threatening bacterial infection among neonates. This study aimed to determine the prevalence, aetiology, and susceptible antimicrobial agents among neonates with UTI.

Methods: This was a cross-sectional analytical hospital-based study that included 152 neonates with clinical sepsis who were admitted at Dodoma regional referral hospital from January to June 2020. Bacterial growth of 1×10^3 colony forming units/mL of a single uropathogen was used to define the presence of UTI. Statistical analysis was performed using SPSS version 23.0 and multivariate analysis was used to determine the predicting factors of UTI. $P < 0.05$ was regarded statistically significant.

Results: The prevalence of UTI was 18.4% (28/152). *Klebsiella pneumoniae* 64.3% (18/28) and *Enterobacter* spp. 35.7% (10/28) were the bacterial agents isolated. The bacterial isolates were 90%, and 60% sensitive to ciprofloxacin and amikacin, respectively. Low Apgar score (AOR = 12.76, 95% CI = 4.17–39.06, $p<0.001$), prolonged labour (AOR = 5.36, 95% CI = 1.28–22.52, $p = 0.022$), positive urine nitrite test (AOR = 26.67, 95% CI = 7.75–91.70, $p<0.001$), and positive leucocyte esterase test (AOR = 6.64, 95% CI = 1.47–29.97, $p = 0.014$) were potential predictors of UTI.

Conclusion: The prevalence of UTI confirmed by urine culture among neonates that were included in the present study indicates that this problem is common in the population where the study was conducted. *Klebsiella pneumoniae* and *Enterobacter* spp. were the uropathogens which were isolated. Ciprofloxacin, nitrofurantoin, and amikacin were sensitive to the isolated uropathogens.

Keywords: Urinary tract infection, Antibiotic sensitivity, Clinical sepsis

Background

Urinary tract infection (UTI) is among the primary causes of neonatal sepsis although its rate in newborns is not known. Clinically, UTI is defined as significant bacteriuria irrespective of the site of infection in the urinary tract system [1]. Also, microbiologically, UTI has been defined as the presence of a significant bacteriuria of at least 1000 colony-forming units per millilitre (CFU/mL) of a single uropathogen isolated from the urine sample [2]. The incidence is higher in male neonates and infants in the first 4 months of life and the prevalence changes thereafter [3]. In a study done by Bagga et al. it was found that 1 in 1000 and sometimes 1 in 100 among

*Correspondence: mashimba2009@yahoo.com
[5] Department of Histopathology and Morbid Anatomy, School of Medicine and Dentistry, The University of Dodoma, P. O. Box 395 Dodoma, Tanzania
Full list of author information is available at the end of the article

full-term infants and 1 in 10 premature infants are usually diagnosed with UTI during the first month of life [4].

The prevalence of UTI in neonates with clinical and blood culture-confirmed neonatal sepsis ranges from 7 to 41.3% [5–9]. In Tanzania, the prevalence of UTI among neonates was previously reported to be 11.4% in a study which was conducted in Kilimanjaro [10]. Another study which was conducted in Mwanza reported a prevalence of 20.3% [11]. The prevalence of UTI among febrile infants in the USA has been reported to range from 10.7 to 15.4% [12]. Mohamed et al. reported a prevalence of 6.7% of UTI among neonates in a study which was conducted in Egypt [13].

The clinical presentations are non-specific and the disease's severity ranges from mild to severe. The diagnosis of neonatal UTI can be overlooked because the symptoms are often non-specific and sterile samples may be difficult to obtain. The presentations of UTI in the newborn manifest as systemic symptoms such as persistent jaundice, poor weight gain, irregularity of temperature, lethargic, failure to breast feed, and abdominal distension [1].

The commonest bacteria which cause UTI in newborn and infants are *Escherichia coli* at 90% [12, 13]. Other bacteria include *Klebsiella pneumoniae* and enterococci [14]. These organisms are mainly found in distal part of gastrointestinal tract and colonize the perineal area [15]. Negative microscopic findings for bacteria or dipstick test for nitrite and leukocytes esterase have been found not to rule out the presence UTI [16].

The predictors of UTI in a population of neonates include gestational age, birth weight, chronological age, male sex, exposure to indwelling devices, exposure to enteral feeding, low Apgar score >7 at 5 min, and UTI in index pregnancy [9, 17, 18].

This study was aimed to determine the prevalence of UTI, aetiology, and antibacterial susceptibility patterns among neonates with UTI. In addition, we assessed the predictors of UTI.

Methods

Study design and setting

This was a cross-sectional analytical hospital-based study which included 152 neonates with clinical features of sepsis who were admitted in a neonatal ward during the study period. The study was conducted at Dodoma Regional Referral Hospital (DRRH) which is located in the city of Dodoma from January to June 2020. The paediatric department has two specialized clinics, one of which is a care and treatment clinic (CTC) for paediatric patients who are diagnosed with human immunodeficiency virus (HIV) and the other one is a general paediatric clinic which operates on regular basis. The standard guidelines for treating neonates with UTI in Tanzania [19] are based on the World Health Organization (WHO) guidelines although with some modifications [20].

Study population

The study participants were all neonates aged not more than 28 days who were admitted in the neonatal unit at the department of paediatric. The inclusion criteria for the participants included being admitted in the neonatal unit with a clinical diagnosis of neonatal sepsis during the study period and parents or guardians consenting for their neonates to participate in the study. On the other hand, the exclusion criteria included all neonates who had already received antibiotics 48 h before being recruited in the study and all neonates with obvious urinal genital anomalies. In addition, all neonates who had missing reproductive and child health (RCH) card number 4 during admission, those whose parents or guardians refused to consent, and all neonates whose samples had multiple growths (contamination) were also excluded.

Sample size determination

The sample size was calculated using Leslie Kish formula (1965) and the prevalence of 6.4% of UTI from a study which was previously done in Nigeria by Omoregie et al. [21] was used to obtain the sample size of 152 neonates.

Sampling technique

Convenience sampling method was used to obtain the eligible neonates to be included in the present study. All neonates admitted in the neonatal unit of the department of paediatric at DRRH were screened for eligibility and consecutively selected into the study until the required sample size of 152 participants was obtained.

Data collection procedures

Data were collected prospectively by two trained research assistants using a structured interviewer-administered questionnaire as it was done in the previous study [1]. This was administered to either mother or caregiver of the neonates if the mother of the neonate was absent and it was translated into Swahili local language to make it understandable. The questionnaire comprised of the following sections: sociodemographic characteristics of both neonates and their mothers, maternal history, clinical presentation of the neonates during the course of illness, and laboratory investigations.

The two trained research assistants administered the consent forms and explained first the aim of the study to the parents or guardians of the neonates before collecting the data. The enrolment was done after obtaining informed consent. Mothers or guardians were

interviewed and subjected to full history taking including pre-natal, natal (particularly mode, place, and complications of delivery; birth weight, first cry, and conditions at birth), and post-natal history. Each neonate was examined generally and locally to assess his/her state of consciousness, weight, and vital signs. Abdominal examination (for tenderness, abdominal distention) and neurological examination (eliciting suckling and motor reflexes) were carried out.

Laboratory investigations

Full blood picture (FBP) testing was done using a haematological analyser (CD Cell Dyn Ruby, Singapore). Two millilitres of blood was collected under aseptic technique and was placed in a tube with clot activator; the sample was left for at least 15 min to ensure that it clots. The serum was aspirated and introduced into the disc and placed in the machine. The results of C-reactive protein (CRP) were interpreted such that CRP quantitative assay with $\leq$ 3 mg/dl was considered to be normal whereas high value (>3 mg/dl) implied inflammation.

Proper cleansing of suprapubic region using ethyl alcohol followed by washing with sterile water was carried out, and then, a 5-ml syringe with 22-gauge needle was introduced perpendicularly, one finger breadth above the symphysis pubis under ultrasound guidance. When the needle had just entered the subcutaneous part, a suction force was exerted on introduction. When approximately 2 ml of urine was obtained, the needle was withdrawn and a sterile gauze was applied on the skin. If the first trial failed, a second trial was done within 20–30 min as it was described in the previous study [16].

Urine specimen was collected in two sample containers: one for urinalysis using dipstick method and the second for culture and sensitivity and both were stored in ice pack carrier and carried for processing immediately from the ward where sample collection was done to the laboratory within the same health facility to avoid further growth of organisms in the urine specimen. The samples were carried in closed, sealed, and secure containers for the purpose of safety measures. This procedure was done within 1 h post sample collection. For any circumstance where the sample analysis could not be performed immediately, the sample was refrigerated at temperature between 4 and 8 °C, and the processing was done within 4 h.

Urinalysis was done using urine strip dipstick (Cybowtm, Lot 150318, Dfi Co Ltd, Korea) and analysed for significant proteinuria +, ++, +++, and more than +++ for 30 mg/dl, 100 mg/dl, 300 mg/dl, and >1,000 mg/dl, respectively, and significant haematuria +, ++, +++ in more than 3 RBCs. The presence of nitrite indicated the presence of Gram-negative bacteria which cause UTI and positive leukocyte esterase enzymes indicated the presence of white blood cell in urine which mainly occurs when there is UTI. Participants with either positive nitrite or positive esterase plus one or more findings or both positive nitrite and leukocyte esterase plus one or more findings were considered as probable cases with UTI. Interpretation of the urine dipstick test was based on the manufacturer's instructions of a urine analyser (DIRUI H-100, Changchun, China).

Urine was inoculated and cultured aerobically. After 24–72 h of incubation, followed by doing subculture on sheep blood agar and MacConkey agar using quantitative loop method. The growth of $\geq 1 \times 10^3$ colony-forming unit (CFU) per millilitre ($\geq 1 \times 10^3$ CFU/mL) of a single uropathogen was considered as a positive urine culture whereas multiple growths were considered to have the presence of contamination and the sample was discarded as it was described in the study by Mohamed et al. [13].

Antibiotic sensitivity was determined using Kirby Bauer diffusion method for in vitro drug susceptibility as it was reported by Hudzicki in 2012 [22] for pathogenic bacteria isolates according to clinical laboratory standard institute (CLSI) [23]. For the positive culture sample, sensitivity of isolates of bacteria was done using drug sensitivity plates and incubated at 37 °C for 24 h and inhibition zone >15 mL was considered as positive. The following antibiotics were tested: ampicillin for Gram-positive uropathogens and gentamycin, ceftriaxone, amoxiclav, clindamycin, erythromycin, nitrofurantoin, ciprofloxacin, meropenem, and amikacin for Gram-negative uropathogens.

Quality assurance

All the instruments used were checked for accuracy and zero error. The two research assistants were trained on how to collect data using the questionnaire. In a situation of logistic challenges regarding data collection, the principal investigator was able to convene with the research assistants for clarification. Suprapubic aspiration was done by a medical doctor who was among the investigators (YSL) whereas blood sample collection was done by the research assistants and laboratory procedures were performed by a laboratory technician.

Statistical analysis

Data analysis was done using Statistical Package for Social Sciences (SPSS) (IBM statistic Inc, Chicago) version 20.0. Mean was calculated for continuous data. Association between categorical variables was tested by using the chi-square test. Multivariate regression analysis using Binary logistic regression was performed to determine factors independently associated with UTI in

neonates with clinical sepsis. A two-tailed $p < 0.05$ was considered statistically significant.

Results

Flow chart indicating selection of the study participants included in the study

A total of 1570 paediatric patients were recorded at the department within the study period. Of all the paediatric patients, 31.5% (448/1422) of them were neonates. These neonates were screened based on signs and symptoms of clinical sepsis and at the end, 49.3% (148/300) neonates were excluded due to various reasons including having had received antibiotics within 48 h and refusal of the parents to sign the consent forms. Therefore, a total of 152 neonates with clinical sepsis were recruited in the present study from January to June 2020 (Fig. 1).

Sociodemographic characteristics of neonates and their mothers

Table 1 presents the sociodemographic characteristics of both neonates and their mothers. Majority of the neonates 90.8% (138/152) were of neonatal age less than 7 days and the mean age was 6.2 ± 0.47 days. Most of the neonates 59.9% (91/152) were females. Neonates with low Apgar score were 11.2% (17/152) whereas those with low birth weight were 9.2% (14/152). Other details are presented in Table 1.

Clinical characteristics of the neonates included in the study

Most of the neonates (22.2%) were clinically presenting with failure to breast feed followed by increased breathing rate which was found among 17.3% of all neonates. The rest of the clinical characteristics are as presented in Fig. 2.

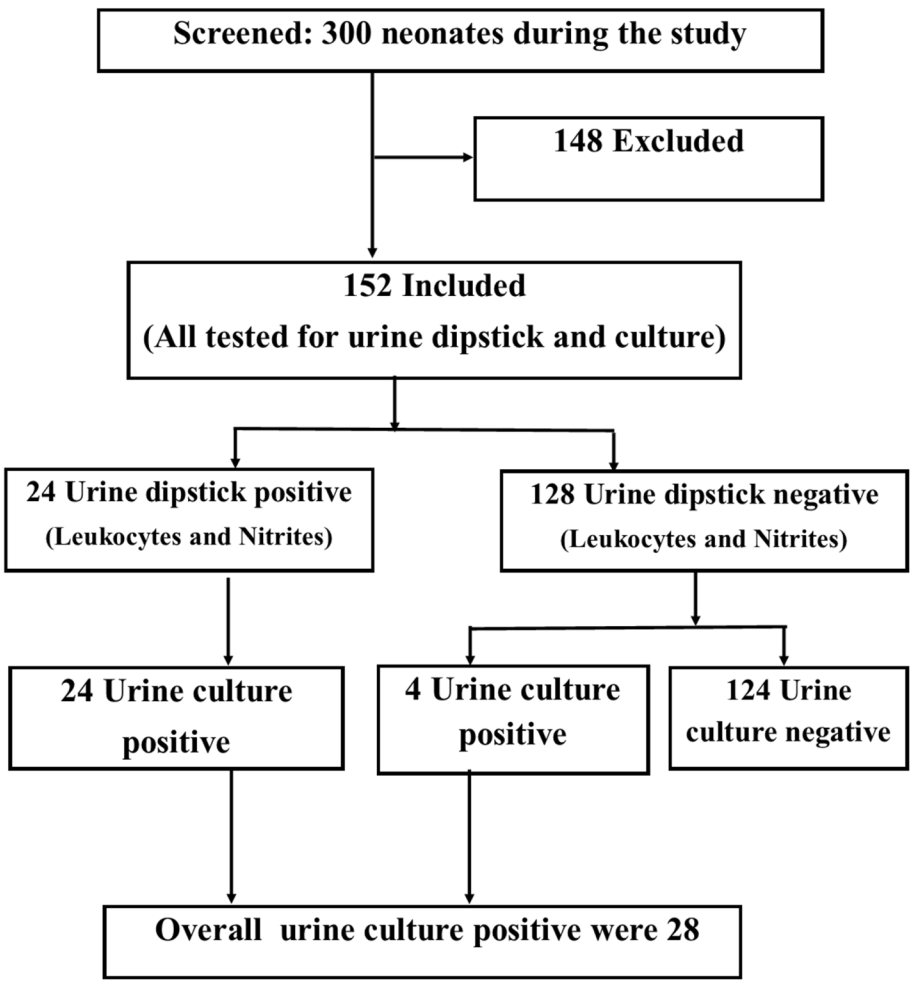

Fig. 1 Flow chart indicating selection of the study participants

Table 1 Demographic and clinical characteristics of neonates and maternal ($N = 152$)

Variable	Frequency (*n*)	Percentage (%)
Age group of the neonates (days)		6.2 ± 0.47
<7	138	90.8
≥7	14	9.2
Sex of the neonates		
Male	61	40.1
Female	91	59.9
Apgar score at 5 min		8.3 ± 0.11
Normal ≥ 7	135	88.8
Low < 7	17	11.2
Neonatal birth weight (kg)		3.7 ± 0.42
Normal ≥ 2.5	138	90.8
Low < 2.5	14	9.2
Maternal age group (years)		22.9 ± 3.14
< 18	16	10.5
18–35	113	74.3
> 35	23	15.2
Maternal education level		
Informal	20	13.2
Primary education	79	52.0
Secondary education	42	27.6
Tertiary education	11	7.2
Maternal occupation		
Self-employed	63	41.4
Employed	29	19.1
Unemployed	60	39.5
Gravidity		2.1 ± 0.68
Primigravida (1)	58	38.2
Multigravida (1–5)	85	55.9
Grandgravida (>5)	9	5.9
Gestational age at booking for ANC services		
First trimester	15	9.9
Second trimester	111	73.0
Third trimester	26	17.1
HIV status		
Positive	5	3.3
Negative	147	96.7
UTI in pregnancy		
Yes	18	11.8
No	134	88.2
Antibiotics for UTI		
Yes	5	27.8
No	13	72.2
PPROM		
Yes	9	5.9
No	143	94.1
Duration of labour (hours)		15.2 ± 0.77
> 18	9	5.9
≤ 18	143	94.1
Mode of delivery		
CS	7	4.6
SVD	145	95.4

PPROM preterm premature rupture of the membranes, *HIV* human immunodeficiency virus, *UTI* urinary tract infection, *CS* caeserean section, *SVD* spontaneous vaginal delivery, *ANC* antenatal clinic

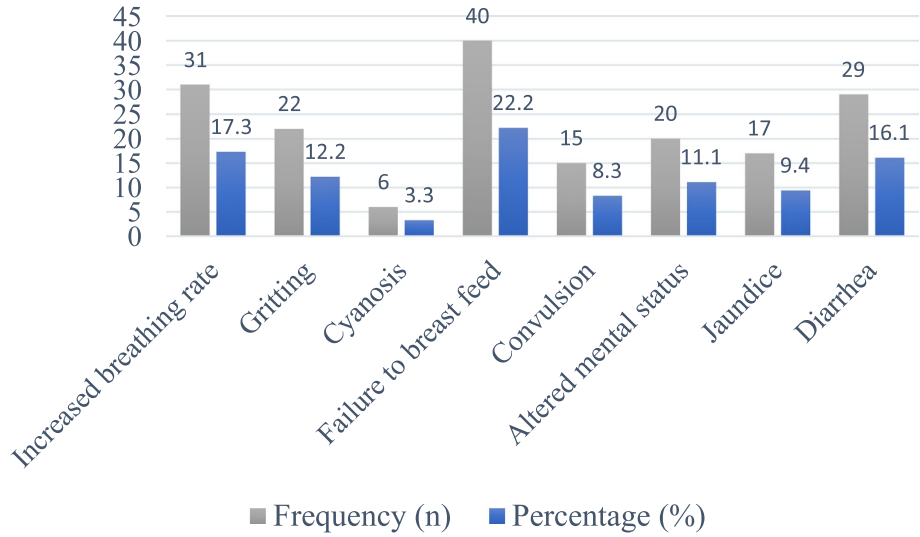

Fig. 2 Clinical characteristics of the study participants

Prevalence and aetiological agents of urinary tract infection among neonates

Neonates who tested positive for dipstick were 15.8% (24/152) and 84.2% (128/152) were dipstick negative. Both neonates who tested positive and negative for urine dipstick test were subjected to urine culture test and it was found that, overall, 18.4% (28/152) neonates had positive urine culture and in 81.6% (124/152) of the neonates their urine culture results were negative. The causative organisms isolated in urine culture among neonates included in this study were *Klebsiella pneumoniae* 64.3% (18/28) followed by *Enterobacter* spp. which consisted of 35.7% (10/28).

Antibiotics sensitivity patterns among neonates with urinary tract infection

In this study, ciprofloxacin, amikacin, nitrofurantoin, and meropenem were sensitive to *Klebsiella pneumoniae* and *Enterobacter* spp. whereas other commonly used drugs such as ampicillin, gentamycin, and ceftriaxone were 100% resistant to the isolated organisms (Table 2).

Predictors of urinary tract infection among neonates

Table 3 presents predictors of UTI among neonates included in the study. After controlling for each independent factor during multivariate analysis, we observed that neonates who had low Apgar score at 5 min were almost 13 times more likely to contract UTI compared to their counterparts who had normal Apgar score at 5 min and the difference was significant (AOR = 12.8, 95% CI = 4.17–39.06, p <0.001). Prolonged labour for more than 18 h had a 5.4-fold increased risk of neonates to contract UTI compared to neonates who were born in less ≤18 h of labour pain and the difference was statistically significant (AOR = 5.4, 95% CI = 1.28–22.52, p = 0.022). Positive nitrite and leukocyte esterase tests in urine of the neonates had 26.7- and 23.7-fold increased risk of UTI compared to negative nitrites and leucocyte esterase and the difference was significant (AOR = 26.7, 95% CI = 7.75–91.70, p<0.00, AOR = 23.7, 95% CI = 7.46–75.05, p <0.001, respectively).

Table 2 Antibiotics sensitivity patterns among neonates with urinary tract infection (N = 152)

Drugs tested	Isolated bacteria	
	***Enterobacter* spp.: *n* (%)**	***Klebsiella pneumoniae*: *n* (%)**
Ciprofloxacin	9 (90.0)	8 (44.4)
Meropenem	4 (10.0)	5 (27.8)
Amikacin	6 (60.0)	5 (27.8)
Gentamycin	0 (0.0)	0 (0.0)
Ampicillin	0 (0.0)	0 (0.0)
Ceftriaxone	0 (0.0)	0 (0.0)
Amoxyclav	2 (20.0)	0 (0.0)
Clindamycin	0 (0.0)	2 (11.1)
Erythromycin	0 (0.0)	1 (5.6)
Nitrofurantoin	3 (30.0)	6 (33.3)

Discussion

UTI is the commonest bacterial infection inflicting mostly the paediatric population with possible adverse effects if it is not treated timely. Establishing the

Table 3 Predictors of urinary tract infection (UTI) among neonates ($N = 152$)

	Univariate analysis		Multivariate analysis	
Variables	**COR (95% CI)**	***p*-value**	**AOR (95% CI)**	***p*-value**
Apgar score (at 5 min)				
Normal	Ref.		Ref.	
Low	2.5 (4.16–38.89)	0.000	12.8 (4.17–39.06)	<0.001
Duration of labour (hours)				
≤18	Ref.		Ref.	
>18	2.1 (2.18–31.38)	0.002	5.4 (1.28–22.52)	0.022
Reflexes				
Normal	Ref.		Ref.	
Abnormal	2.4 (3.41–37.27)	0.000	7.2 (0.03–25.62)	0.08
Nitrites				
Negative	Ref.		Ref.	
Positive	3.2 (7.56–74.73)	0.000	26.7 (7.75–91.70)	<0.001
Leucocyte esterase				
Negative	Ref.		Ref.	
Positive	3.2 (7.93–78.83)	0.000	23.7 (7.46–75.05)	<0.001
WBC count				
Normal	Ref.		Ref.	
High	2.1 (1.80–34.94)	0.006	6.6 (1.47–29.97)	0.014
Lymphocyte count				
Normal range	Ref.		Ref.	
High range	1.8 (1.73–20.10)	0.005	3.7 (1.003–13.48)	0.049

CRP C-reactive protein, *WBC* white blood cell, *COR* crude odds ratio, *AOR* adjusted odds ratio

magnitude of the problem and determining the causative agents as well as knowing the predictors of the risk factors for the infection to occur is very crucial because all help in the clinical management of the neonates particularly in the local context.

The important findings in our study include obtaining the prevalence of UTI among neonates of 18.4% and *Klebsiella pneumoniae* and *Enterobacter* spp. were the only bacterial isolates implicated for causing UTI. Of the panel of antibacterial tested in the study, ampicillin, gentamycin, and ceftriaxone were absolutely resistant to the isolated bacteria; however, interestingly, both isolates were sensitive to ciprofloxacin. Additionally, by far, low Apgar score and positive test for nitrites and leucocytes were the powerful independent predictors of UTI.

The prevalence of UTI among neonates of 18.4% in our study was similar to the prevalence of 18% that was reported in the study done by Nejad et al. in Iran among neonates aged less than 4 weeks as in this study and the mode of urine collection also was the same; they did suprapubic aspiration (Nasrin HN, Mitra H & Farah S, 2010). Similarly, a prevalence of 17% of UTI was reported in a study which was done at California University, USA, among infants aged less than 3 months [7]. These similarities could be explained by the fact that all studies used similar method of collecting urine sample although the study population for the studies compared was different.

The prevalence of UTI found in this study was higher compared to the prevalence of 6%, 6.4%, 7.2%, 12.5%, and 14.5% among neonates which was reported in studies which were done in India, Nigeria, India, Turkey, and Indonesia, respectively [1, 5, 15, 21, 24]. The difference in the prevalence for the different studies compared may be due to the difference in methodology. The variation in inclusion and exclusion criteria, difference in methods of collection of the urine samples, and also study designs might have contributed to the variation in the prevalence of UTI. For example, it has been reported that neonates who are admitted in a neonatal intensive care units (NICU) are more likely to contract the infection because of exposure to hospital acquired infections [8]. Also, the difference in method of sample collection may contribute to the difference in the prevalence of UTI among neonates by for example where the method of sample collection is prone to contamination [25].

Klebsiella pneumoniae has been reported to be the most common cause of UTI among neonates in the literature similar to the finding in the present study [26, 27]. Other studies that were done in Nigeria, Egypt,

India, and Iran reported that *Klebsiella pneumoniae* was the commonest implicated cause of UTI among neonates and it accounted for 28.57% [21], 28% [8], 27% [1], and 31.8% [25]. Also, Msaki et al. reported that 72.3% of the neonates with UTI were positive to *Escherichia coli* followed by *Klebsiella pneumoniae* which consisted of 21.28% [11]. Also, in a study which was done by Gidabayda et al. [10] it was reported that *Escherichia coli* was the most common bacterial isolate (46.2%) followed by *Klebsiella pneumoniae* (30.8%) [28]. Furthermore, studies have reported that *Enterobacter* spp. is another bacterial isolate responsible for causing UTI among neonates, however, not as common as compared to *Klebsiella pneumoniae* [7, 10, 29].

Regarding sensitivity of bacteria to antibiotics in the present study, *Enterobacter* spp. was sensitive to ciprofloxacin, amikacin, and nitrofurantoin. On the other hand, *Klebsiella pneumoniae* was sensitive to ciprofloxacin, amikacin, and nitrofurantoin. In a study which was done in Nigeria among neonates with UTI, it was found that the most common bacterial isolate was *Klebsiella pneumoniae* followed by *Enterobacter* spp. and *Klebsiella pneumoniae* was sensitive by 83.33%, 33.33%, and 33.33% to nitrofurantoin, ciprofloxacin, and gentamicin, respectively [21]. Furthermore, the same study also observed that *Enterobacter* spp. was sensitive by 100% to ciprofloxacin.

In this study, both *Klebsiella pneumoniae* and *Enterobacter* were 100% resistant to ampicillin, ceftriaxone, and gentamicin. This is similar to the findings in a study which was done in Nigeria in which *Klebsiella pneumoniae* was 100% resistant to ampicillin, gentamycin, and co-amoxiclav [21]. Another study which was done in Iran aiming at determining the antimicrobial susceptibility among neonates with UTI found that *Escherichia coli* was resistant to ampicillin, amikacin, and ceftriaxone by 36.6%, 36.6%, and 26.6% whereas *Klebsiella pneumoniae* showed resistance to ampicillin and ceftriaxone by 22.2% and 18.5%, respectively [25]. Furthermore, other studies have also emphasized that, *Klebsiella pneumoniae* has been found to be resistant against ampicillin, cefuroxime, ceftriaxone, and even with multidrug resistance (MDR) [30, 31].

The findings obtained from this study and those in previous studies all indicate that there is a marked increase in antibiotic resistance especially for the first- and second-line antibiotics used for treating UTI among neonates. Self-prescription of common antibiotics in developing countries remains the major contributing factor for antibiotics resistance [32]. Difficulty in performing urine culture according to the stipulated WHO guidelines for management of neonates with UTI paves another way to antimicrobial resistant [33]. Furthermore, it has been reported that low concentrations of drugs in the serum which are mainly due to under dosage or improper frequencies of taking drugs give a room for microbes to modify the binding sites and change structures leading to mutations which in turn cause antimicrobial resistance [34].

Currently in Tanzania, treatment of UTI in neonates and other children aged more than 3 months include nitrofurantoin and amoxiclav [19]. However, due to the lowest sensitivity of only 20% for *Enterococcus* spp. and complete resistance for *Klebsiella pneumoniae* shown in the present study for amoxiclav, this implies that amoxiclav may be replaced by other antibiotics which have shown sensitivity in the management of neonates with UTI.

Although some of the antibiotics are still sensitive to a number of uropathogens in Tanzania, however, according to physicians attending patients with UTI particularly in areas where urine culture testing is not a common practice which prompts empirical use of such antibiotics, there is a possibility of predisposing the patients to developing lung complications for example pulmonary fibrosis [35]. Therefore, measures should always be undertaken in either confirmed or suspected cases of pulmonary fibrosis by taking preventive measures of the exaggerated effects of the complication including stopping of the medication and using methylprednisolone [35].

Neonates with low Apgar score (<7) at 5 min were 13 times more likely to have UTI than neonates who had normal Apgar score (≥7) at 5 min and the association was statistically significant (p <0.001). A similar finding was reported in Eastern Ethiopia in which neonates with low Apgar score (<7) at 5 min were 69 times more likely to have UTI compared to those who had normal Apgar score and the association was statistically significant (AOR = 68.9, 95% CI = 3.63–1308) [36]. Another study which was done in Northwest Ethiopia reported that neonates with low Apgar score (<7) at 5 min were 3 times more likely to contract UTI compared to neonates who had normal Apgar score and it was statistically significant (AOR = 3.2, 95% CI = 1.3–7.7) [37]. This may be explained by the fact that majority of neonates who are born with low Apgar score is mainly due to difficulty in delivery process especially delaying during second stage of labour. Additionally, maternal infections such as malaria and anaemia have been found to increase the chance of neonatal UTI [38].

In this study, neonates who were born among mothers who had prolonged labour (>18 h) for both primigravida and multigravida were 5 times more likely to have UTI than those who were born among mothers without prolonged labour (≤18 h). This is similar to another study which was done in Ethiopia which reported that duration of labour of more than 18 h since rupture of membrane

had 10-fold increased risk of causing UTI compared to normal duration of labour (AOR = 10.4, 95% CI = 2.3–46.5) [37].

It has been reported that prolonged labour is associated with low Apgar score. Also, prolonged labour increases the chance of acquiring ascending infections to mother and neonates [39]. Also, interventions and manoeuvres applied to achieve delivery process predispose ascending infections to the mothers and their newborn (Benson and Mitchell 1958). Therefore, prolonged labour is a predisposing factor of both low Apgar score and UTI among neonates. Therefore, it may explain the fact that there exists a causality relationship for prolonged labour and low Apgar score with UTI in neonates and not just a mere association.

Neonates with positive nitrite and leucocytes esterase tests had 27- and 24-fold increased risk of being diagnosed with UTI, respectively compared to neonates who had negative test for nitrite and leucocytes esterase. In a study done in Brazil, it was observed that the presence of nitrites in the urine had sensitivity of 30.8% (95% CI = 19.9–43.4%) and specificity of 100% (95% CI = 99.2–100%) [2] in the diagnosis of UTI. This shows that the presence of nitrite in urine has higher specificity than sensitivity in the diagnosis of UTI for neonates and even adults. The conversion of nitrates to nitrites in urine is caused by bacterial infections mainly Gram-negative including *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus* spp., and *Enterobacter* spp. [40]. On the other hand, leukocyte esterase is an enzyme which is present in WBC. It is released when WBC undergoes lysis. Therefore, once this enzyme is detected in urine, it indicates the presence of WBC in urine which implicates pyuria. Typically, pyuria implies inflammation in the urinary tract [41]. Although leucocyte esterase has been reported to have higher sensitivity than nitrites test, the specificity of leucocyte esterase is lower than that of nitrites [42].

Other factors that have also been found to increase the chances of neonates to acquire UTI include anorectal malformations and gastrointestinal problems. For example, it has been reported that vesicoureteral reflux develops in approximately 20–47% of children with anorectal malformations [43]. Additionally, the presence of vesicoureteral reflux increases the risk of developing febrile urinary tract infections (UTI), leading to renal scarring and subsequent renal dysfunction [43].

Furthermore, the use of urine dipstick test has been reported to have high false-negative rates which in turn contribute to low sensitivity despite the high specificity [44]. Also, urine microscopy test for patients with UTI particularly neonates has shown higher sensitivity compared to specificity [45].

The limitations of the present study include the following: by the study being cross-sectional, the results cannot be generalizable. Not using random sampling in obtaining the study participants, the study was affected by selection bias. Additionally, by involving hospitalized neonates already with clinical sepsis, it may have influenced our results.

Conclusions

This study reports a relatively significant prevalence of UTI among neonates and it draws attention in the daily management of neonates with UTI in the country. *Klebsiella pneumoniae* and *Enterobacter* spp. should be regarded the most common causative agents of UTI in the locality. Moreover, use of gentamycin, ampicillin, and ceftriaxone in the management of neonatal UTI in the country ought to be revised for the purpose of overcoming resistance. Ciprofloxacin, amikacin, and nitrofurantoin should be deemed as first-line antibiotics for the treatment of UTI in neonates within the country. Also, a step-wise approach to antibiotic management for neonatal sepsis and UTI in the country must be included in the national standard guidelines of treatment so as to continue combating drug resistance for antibiotics in the general population. Additionally, duration of labour, low Apgar score, and positive tests for nitrites and leucocyte esterase were the independent predictors of UTI.

Abbreviations

UTI: Urinary tract infection; CTC: Care and treatment clinic; HIV: Human immunodeficiency virus; WHO: World Health Organization; RCH: Reproductive and child health; EDTA: Ethylenediamine tetraacetic acid; WBC: White blood cell; FBP: Full Blood Picture; CRP: C-reactive protein; CFU: Colony-forming unit; CLSI: Clinical Laboratory Standard Institute.

Acknowledgements

We are grateful to a team of paediatricians of the Dodoma Referral Regional Hospital.

Authors' contributions

All authors participated in the clinical study design and interpretation. YSL and JJY drafted the first version of the manuscript. FDK, YSL, and MLM analysed the data of the study. FDK, YSL, and SGM collected the data of the study and revised a part of the manuscript critically. JJY, FDK, SGM, and MLM reviewed the manuscript critically. All authors read and approved the final manuscript.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

We obtained ethical approval from the Institutional Research Review Committee (IRRC) of the University of Dodoma (Reference: UDOM/DRP/134/VOL VII/021).

Consent for publication

Written informed consent was obtained from the parents or legal guardians of the neonates.

Competing interests

The authors declare that they have no competing interests.

Author details

[1]Department of Paediatrics and Child Health, School of Medicine and Dentistry, The University of Dodoma, Dodoma, Tanzania. [2]Department of Microbiology and Parasitology, School of Medicine and Dentistry, The University of Dodoma, Dodoma, Tanzania. [3]Department of Chemical and Mining Engineering, The University of Dar es salaam, Dar es salaam, Tanzania. [4]Department of Clinical Nursing, School of Nursing and Public Health, The University of Dodoma, Dodoma, Tanzania. [5]Department of Histopathology and Morbid Anatomy, School of Medicine and Dentistry, The University of Dodoma, P. O. Box 395 Dodoma, Tanzania.

Received: 30 August 2021 Accepted: 25 November 2021
Published online: 17 January 2022

References

1. G N, M., S B, S. S. & Paraskawar, P (2014) A study of urinary tract infection in neonatal sepsis. J Evol Med Dent Sci 3:1235–1239
2. Lo DS, Rodrigues L, Koch VHK, Gilio AE (2018) Clinical and laboratory features of urinary tract infections in young infants. J Bras Nefrol 40:66–72
3. Youssef D, Elfateh H, Sedeek R, Seleem S (2012) Epidemiology of urinary tract infection in neonatal intensive care unit: a single center study in Egypt. J Acad Med Sci 2:25
4. Bagga A et al (2003) Bacteriuria and urinary tract infections in malnourished children. Pediatr Nephrol 18:366–370
5. Bahat Ozdogan E et al (2018) Urinary tract infections in neonates with unexplained pathological indirect hyperbilirubinemia: Prevalence and significance. Pediatr Neonatol 59:305–309
6. Ismaili K et al (2011) Febrile urinary tract infections in 0- to 3-month-old infants: a prospective follow-up study. J Pediatr 158:91–94
7. Newman TB et al (2002) Urine testing and urinary tract infections in febrile infants seen in office settings: the pediatric research in office settings' febrile infant study. Arch Pediatr Adolesc Med 156:44–54
8. Kumar S, Shankar B, Arya S, Deb M, Chellani H (2018) Healthcare associated infections in neonatal intensive care unit and its correlation with environmental surveillance. J Infect Public Health 11:275–279
9. Lin DS et al (2000) Urinary tract infection in febrile infants younger than eight weeks of Age. Pediatrics 105:2–7
10. Gidabayda JG et al (2017) Patterns of urinary tract infection amongst children admitted at Kilimanjaro Christian Medical Centre. East African Heal Res J 1:53–61
11. Msaki BP, Mshana SE, Hokororo A, Mazigo HD, Morona D (2012) Prevalence and predictors of urinary tract infection and severe malaria among febrile children attending Makongoro health centre in Mwanza city, North-Western Tanzania. Arch Public Heal 70:1–8
12. Arshad M, Seed PC (2015) UTI in the infant. Clin Perinatol 42:1–16
13. Mohamed W, Algameel A, Bassyouni R, el T Mahmoud A (2020) Prevalence and predictors of urinary tract infection in full-term and preterm neonates. Egypt Pediatr Assoc Gaz 68
14. Masika WG, O'Meara WP, Holland TL, Armstrong J (2017) Contribution of urinary tract infection to the burden of febrile illnesses in young children in rural Kenya. PLoS ONE 12:1–13
15. Samayam P, Chander BR (2012) Study of urinary tract infection and bacteriuria in neonatal sepsis. Indian J Pediatr 79:1033–1036
16. Shaw KN, Gorelick M, McGowan KL, Yakscoe NM, Schwartz JS (1998) Prevalence of urinary tract infection in febrile young children in the emergency department. Pediatrics 102
17. Chan GJ, Lee AC, Baqui AH, Tan J, Black RE (2013) Risk of early-onset neonatal infection with maternal infection or colonization: a global systematic review and meta-analysis. PLoS Med 10
18. Abbaszadeh S, Beiraghdar F (2012) Re: maternal urinary tract infection as a risk factor for neonatal urinary tract infection. Iran J Kidney Dis 6:392–393
19. Health, M. O. F. & Development, C. (2021)Standard Treatment Guidelines and National Essential Medicines List for Standard Treatment Guidelines and National Essential Medicines List for
20. World Health Organization (2005) Urinary tract infections in infants and children in developing countries in the context of IMCI. Discuss Pap Child Heal:1–24
21. Omoregie R, Igbarumah IO, Egbe CA, Ogefere HO (2012) Urinary tract infection among neonates in Benin City, Nigeria. Genomic Med Biomarkers Heal Sci 4:118–121
22. Hudzicki J (2012) Kirby-Bauer disk diffusion susceptibility test protocol. Am Soc Microbiol:1–13
23. CLSI (2019) CLSI - Catalogue 2019 -The Highest Standards for Global Health Care
24. Amelia N, Amir I, Trihono PP (2016) Urinary tract infection among neonatal sepsis of late-onset in Cipto Mangunkusumo Hospital. Paediatr Indones 45:217
25. Gunduz S, Uludağ Altun H (2018) Antibiotic resistance patterns of urinary tract pathogens in Turkish children. Glob Heal Res Policy 3:1–5
26. Ding Y, Wang H, Pu S, Huang S, Niu S (2021) Resistance trends of klebsiella pneumoniae causing urinary tract infections in Chongqing, 2011–2019. Infect Drug Resist 14:475–481
27. Ballén V et al (2021) Antibiotic resistance and virulence profiles of Klebsiella pneumoniae strains isolated from different clinical sources. Front Cell Infect Microbiol 11:1–11
28. Gidabayda J et al (2017) Prevalence, aetiology, and antimicrobial susceptibility patterns of urinary tract infection amongst children admitted at Kilimanjaro Christian Medical Centre, Moshi, Tanzania. East African Heal Res J 1:53–61
29. Taheri PA, Navabi B, Shariat M (2012) Neonatal urinary tract infection: clinical response to empirical therapy versus in vitro susceptibility at Bahrami Children's Hospital- neonatal ward: 2001-2010. Acta Med Iran 50:348–352
30. Fenta A, Dagnew M, Eshetie S, Belachew T (2020) Bacterial profile, antibiotic susceptibility pattern and associated risk factors of urinary tract infection among clinically suspected children attending at Felege-Hiwot comprehensive and specialized hospital, Northwest Ethiopia A prospective study. BMC Infect Dis 20:1–10
31. Samancı S, Çelik M, Köşker M (2020) Antibiotic resistance in childhood urinary tract infections: a single-center experience. Turk Pediatr Ars 55:386–392
32. Chokshi A, Sifri Z, Cennimo D, Horng H (2019) Global contributors to antibiotic resistance. J Global Infect Dis 11:36–42
33. Beahm NP, Nicolle LE, Bursey A, Smyth DJ, Tsuyuki RT (2017) The assessment and management of urinary tract infections in adults: Guidelines for pharmacists. Can Pharm J 150:298–305
34. Fair RJ, Tor Y (2014) Antibiotics and bacterial resistance in the 21st century. Perspect Medicin Chem:25–64. https://doi.org/10.4137/PMC.S14459
35. Mikkelsen LF, Rubak S (2020) Reversible lung fibrosis in a 6-year-old girl after long term nitrofurantoin treatment. BMC Pulm Med 20:1–4
36. Gebremedhin D, Berhe H, Gebrekirstos K (2016) Risk factors for neonatal sepsis in public hospitals of Mekelle City, North Ethiopia, 2015: Unmatched case control study. PLoS ONE 11:1–10
37. Akalu TY et al (2020) Predictors of neonatal sepsis in public referral hospitals, Northwest Ethiopia: A case control study. PLoS One 15:1–12
38. Gilbert NM et al (2013) Urinary tract infection as a preventable cause of pregnancy complications: opportunities, challenges, and a global call to action. Glob Adv Heal Med 2:59–69
39. Bahn SA, Jacobson J, Petersen F (1998) Maternal and neonatal outcome following prolonged labor induction. Obstet Gynecol 92:403–407
40. Christopher M, A. M. L. S. Protesu mirabilis and urinary Infections. Physiol Behav 176:100–106 (2016)

41. Glen P, Hawary A, Prashar A (2016) Sterile pyuria: a practical management guide. Br J Gen Pract 66:e225–e227
42. Bellazreg F et al (2019) Diagnostic value of dipstick test in adult symptomatic urinary tract infections: results of a cross-sectional Tunisian study. Pan Afr Med J 33:1–6
43. Wu, C. et al. Risk factors of vesicoureteral reflux and urinary tract infections in children with imperforate anus. (2021).
44. Lendner I et al (2019) Urine dipstick low sensitivity for UTI diagnosis in febrile infants**. Infect Dis (Auckl) 51(764–771)
45. Leman P (2002) Validity of urinalysis and microscopy for detecting urinary tract infection in the emergency department. Eur J Emerg Med 9:141–147

Publisher's Note