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Incidence and risk factors of urinary tract infection in neonatal sepsis

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Abstract

Background: Neonates with sepsis may have concurrent urinary tract infection (UTI), which may be asymptomatic or have nonspecific symptoms. Failure to diagnose UTI, resulting in a delay of appropriate therapy, has been reported to cause renal scarring, hypertension, and kidney failure among infants. This study aimed to determine the contribution of UTI to neonatal sepsis and to assess different risk factors that could be associated with UTI. This cross-sectional study was conducted at the Neonatal Intensive Care Unit (NICU) of Fayoum University Hospital, Fayoum, Egypt, between March 2018 and January 2019. Neonates of both genders from birth to the 28th day of life with clinical features of either early- or late-onset sepsis (during or after the first 3 days of life, respectively) were enrolled in this study. All neonates were subjected to complete history taking from the parents, full clinical examination, and laboratory investigations including complete blood count, C-reactive protein, blood culture, and urine culture.

Results: The current study included 100 neonates admitted to the NICU with clinical and laboratory features of sepsis. Positive blood culture (proven sepsis) was detected in 60%, and the proportion of positive urine culture (UTI) in the entire study group was 11%. The incidence of UTI was 11.7% in proven sepsis compared to 10% in suspected sepsis, and it was 16.36% in late-onset sepsis (LOS) versus 4.44% in early-onset sepsis (EOS). There was a statistically significant association between poor feeding and feeding intolerance and positive urine culture (UTI). Leukopenia and expert panel criteria score showed high sensitivity (81.80% and 90.90%, respectively) but low specificity for the diagnosis of UTI.

Conclusions: Gram-negative bacteria have been highly suspected in cases of neonatal sepsis. Poor feeding and feeding intolerance have association with positive urine culture. Finally, urine culture for sepsis was recommended especially in the late type.

Keywords: Neonatal sepsis, Urinary tract infection, Expert panel criteria score, Urine culture, Blood culture

1 Background

Urinary tract infection (UTI) is the presence of pathogenic bacteria or a fungus in the urinary tract. Suprapubic aspiration and bladder catheterization have been reported as the only valid methods to obtain a reliable urine culture for a proper diagnosis [1].

Neonates are at high risk of UTI due to the undeveloped immune system. Though fever and poor feeding are the most common findings, the clinical manifestations of neonatal UTI are nonspecific and are similar to those of neonatal sepsis [2]. Neonatal UTI may be secondary to bacteremia; however, it may also start as a primary infection in the urinary tract leading to bacteremia [3].

Neonates with sepsis may have concurrent UTI, which may be asymptomatic or have nonspecific symptoms [4]. The risk of having UTI in neonates who present with sepsis increases with decreasing gestational age, low birth weight, and postnatal age above 72 h after birth. Therefore, urine culture should be done particularly when late-onset sepsis (LOS) is suspected [5].

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The presence of other risk factors for sepsis might make clinicians reluctant to obtain urine cultures during the primary sepsis evaluation, resulting in failure to diagnose UTI and delay of appropriate therapy [6]. Accordingly, long-term complications such as renal scarring, hypertension, and kidney failure might ensue [7].

This study aimed to determine the contribution of UTI to neonatal sepsis and to assess different risk factors that could be associated with UTI.

2 Methods

2.1 Ethical considerations

The study protocol was approved by the Research Ethics Committee, Faculty of Medicine, Fayoum University, Egypt (Approval number: M 305/44; Date: 30–12-2017). We obtained informed consent from the parents of the neonates after informing them about the objectives and procedures of the study. The confidentiality of participants' information and their rights not to participate in the study were respected.

2.2 Study design, setting, and date

This cross-sectional study was conducted at the Neonatal Intensive Care Unit (NICU) of Fayoum University Hospital, Fayoum, Egypt, between March 2018 and January 2019.

2.3 Eligibility criteria

Neonates of both genders from birth to the 28th day of life with clinical features of either early- or late-onset sepsis (during or after the first 3 days of life, respectively) were enrolled in this study. We excluded neonates who received antibiotics before admission to the hospital; therefore, all the enrolled neonates did not experience any antibiotics treatment during or after the first 3 days of life.

Neonates with sepsis were defined using the European expert panel-derived criteria [8]. Patients were required to have at least two clinical plus two laboratory parameters to be included in the study. Neonates with positive blood culture were designated as proven sepsis, while neonates with negative blood culture but with clinical and laboratory findings of sepsis were designated as suspected sepsis.

2.4 Data collection

All neonates were subjected to (a) complete history taking from the parents (prenatal, natal, and postnatal history); (b) thorough clinical examination including assessment of gestational age, measurement of birth weight, and identification of clinical signs of sepsis, such as temperature instability (< 37 or > 38.5 °C), respiratory dysfunction (as apnea, increased oxygen requirement, and signs of respiratory distress), circulatory disturbances (hypotension, tachycardia, shock, and prolonged capillary refill), gastrointestinal dysfunction (abdominal distension, bloody stool, feeding intolerance, hepatomegaly, and jaundice), neurological dysfunction (irritability, hypotonia, and lethargy), hypoglycemia, hyperglycemia, petechiae, or bleeding (with thrombocytopenia or DIC); and (c) laboratory investigations including complete blood count, C-reactive protein, blood culture, and urine culture.

A positive urine culture was defined as isolation of ≥ 10,000 CFU of 1 or 2 organisms from a specimen obtained by urethral catheterization. Candida UTI was diagnosed by the growth of Candida at any colony count. The growth of three or more organisms was considered as contaminated urine. Antibiotic sensitivity was done for positive urine growth. Abdominal ultrasonography was done for neonates with positive urine culture to determine any associated congenital anomalies of kidneys and urinary tract.

Blood culture sets were obtained from patients with bloodstream infections. Aerobic blood culture bottles (BacT/ALERT® culture media PF plus, bioMérieux, France) were forwarded to the Microbiology Unit and incubated in the automated blood culture system BacT/ALERT® 3D (bioMérieux). Negative bottles are automatically resulted and discarded after 5 days of incubation. The performance methods were evaluated for positive blood cultures with monomicrobial bacterial growth. Bottles yielding polymicrobial were excluded.

Blood culture bottles were analyzed after bacT/ALERT®3D system flagged a blood as positive. The bottles were analyzed by Gram staining followed by subculture on an appropriate solid agar medium (aerobic Columbia agar 5% sheep blood, chocolate agar, MacConkey agar, bioMérieux, France) following 18–24-h incubation at 35 °C and 5% CO2 atmosphere. Colonies were used for bacterial identification using biochemical reactions agars and CHROMagar. The colonies were also used for the preparation of the inoculum disk diffusion test (Kirby–Bauer disk diffusion susceptibility test protocol), according to CLSI 2019. Multidrug (MDR) strains are those resistant to at least three classes of antimicrobials [9].

2.5 Statistical analysis

Data were analyzed using the Statistical Package for Social Science software, version 18. Qualitative data were presented as numbers and percentages, and the association between variables was analyzed by chi-square test. Quantitative data included in the study were first tested for normality by the one-sample Kolmogorov–Smirnov test in each study group. Normally distributed data were

presented as mean ± standard error and were compared by the Student's t test. Alternatively, the non-normally distributed data were presented as median and range and were compared by the Mann–Whitney test. Receiver operating characteristic curves were applied to show sensitivity, specificity, positive predictive value, and negative predictive value of different laboratory variables, and the expert panel criteria for diagnosing positive blood and urine cultures. A P value < 0.05 was considered the cutoff value for the statistical significance.

3 Results

The current study included 100 neonates admitted to the NICU with clinical and laboratory features of sepsis. Their median age at admission was 5 days, and the mean birth weight was 2.29 ± 0.82. Males constituted 65%, and 42% were preterm. The highest percent (79%) were born by caesarian section, and 19% had a history of premature rupture of membranes (PROM) (Table 1).

Table 2 shows a mean score of the European expert-derived panel criteria for sepsis of 5.27 ± 1.40. Early-onset sepsis (EOS) represented 45%, while neonates having late-onset sepsis (LOS) were 55%. The most frequent clinical presentation (91%) was combined lethargy, hypotonia, and poor reflexes, followed by respiratory distress (64%), poor feeding (59%), needed mechanical ventilation (51%), feeding intolerance (43%), and temperature instability (37%). Hypotension, convulsions, and bradycardia were less frequent (10%, 5%, and 3%, respectively).

Table 3 describes the laboratory investigations among the study group. The means of total leukocyte count (TLC), platelet count, I/T ratio, C-reactive protein (CRP) levels, and random blood sugar (RBS) levels were 12.30 ± 9, 177.40 ± 138.30, 0.33 ± 0.13, 53.40 ± 32.70, and 155.20 ± 73.50, respectively.

Table 1 Demographic characters among the study group

Variables ($n = 100$)	Mean ± SD	Median/range
Age at admission (days)	7.82 ± 9.40	5/(1–27)
Weight (kg)	2.29 ± 0.82	2.40/(1–4)
	Number (%)	
Gender		
Male	65 (65%)	
Female	35 (35%)	
Gestational age		
Preterm	42 (42%)	
Full-term	58 (58%)	
Mode of delivery		
Vaginal	21 (21%)	
Cesarean section	79 (79%)	
History of premature rupture of membranes		
No	81 (81%)	
Yes	19 (19%)	

SD: standard deviation

Table 2 Frequency of different clinical findings among the study group

Variables	Clinical picture	
	Mean ± SD	Median/range
Expert panel criteria score	5.27 ± 1.40	5/(3–11)
	Number (%)	
Onset of sepsis		
Early	45 (45%)	
Late	55 (55%)	
Clinical presentation		
Lethargy and hypotonic and poor reflex	91 (91%)	
Respiratory distress	64 (64%)	
Poor feeding	59 (59%)	
Need for ventilation	51 (51%)	
Feeding intolerance	43 (43%)	
Temperature instability	37 (37%)	
Apnea	13 (13%)	
Hypotension	10 (10%)	
Bleeding tendency	9 (9%)	
Sclerema	6 (6%)	
Convulsion	5 (5%)	
Cholestatic jaundice	5 (5%)	
Diarrhea	4 (4%)	
Bradycardia	3 (3%)	

SD: standard deviation

Positive blood culture (proven sepsis) was detected in 60%, and the proportion of positive urine culture (UTI) in the entire study group was 11%. Gram-negative bacteria were responsible for most cases of neonatal sepsis (75%), while they were isolated from all urine cultures (100%). Klebsiella spp. was the most common organism isolated from blood cultures (50%) and comprised 66.67% (30/45) of Gram-negative bacteria, while they caused 54.50% of all UTI cases. Candida spp. was isolated from 3 cases of positive blood culture (5%), while they were isolated from three follow-up urine cultures.

The incidence of UTI was 11.70% in proven sepsis compared to 10% in suspected sepsis, and it was 16.36% in LOS versus 4.44% in EOS. Positive urine culture (UTI) was detected in 1 case (3.45%) of early-onset proven sepsis compared to 6 (19.35%) of late-onset proven sepsis, with no significant differences ($p > 0.05$) (Table 4).

Table 5 illustrates a statistically significant association between poor feeding and feeding intolerance and positive urine culture (UTI). The percentages of poor

Table 3 Different investigations among the study group

Variables	Mean ± SD	Median/range	Reference range
TLC ($\times 10^9$ cells/L)	12.30 ± 9	9.30/(2–40)	4–25 at birth 4–30 at 12–24 h 4–20 on day 2 onwards
Platelet count ($\times 10^9$ cells/L)	177.40 ± 138.30	176/(7–978)	150–450
I/T ratio	0.33 ± 0.13	0.30/(0.2–0.8)	< 0.2
CRP (mg/dL)	53.40 ± 32.70	48/(6–192)	< 6
RBS (mg/dL)	155.20 ± 73.50	123/(39–500)	40–180

SD: standard deviation; TLC: total leukocyte count; CRP: C-reactive protein; RBS: random blood sugar

Table 4 Incidence of UTI in different sepsis groups

Variables	Urine culture		*p* value
	Negative (*n* = 89)	**Positive (*n* = 11)**	
	***n* (%)**	***n* (%)**	
Blood culture			
Negative "suspected sepsis" (*n* = 40)	36 (90%)	4 (10%)	0.9
Positive "proven sepsis" (*n* = 60)	53 (88.30%)	7 (11.70%)	
Onset of sepsis			
Early-onset sepsis (*n* = 45)	43 (95.56%)	2 (4.44%)	0.06
Late-onset sepsis (*n* = 55)	46 (83.64%)	9 (16.36%)	
Proven sepsis (*n* = 60)	**Positive urine culture in proven sepsis (*n* = 7)**		
Proven early-onset sepsis (n = 29)	28 (96.55%)	1 (3.45%)	0.055
Proven late-onset sepsis (n = 31)	25 (80.65%)	6 (19.35%)	

feeding were 90% in UTI cases compared to 55.10% in non-UTI ones. The frequency of feeding intolerance was also higher in UTI cases than their counterparts (72.70% versus 39.30%, respectively). Otherwise, there were no statistically significant differences between patients with positive or negative urine culture as regards other clinical presentations. As well, there was no significant difference between both genders regarding the development of positive urine culture ($p = 0.20$). The frequency of positive urine culture was 54.50% in females compared to 45.50% in males.

Table 6 demonstrates the absence of significant associations between the laboratory investigations including TLC, platelet count, I/T ratio, CRP, RBS, and positive urine culture results ($p > 0.05$).

Distribution of the pathogens isolated from the blood cultures according to the onset of sepsis revealed that Gram-negative organisms were predominant in both EOS and LOS (82.70% and 67.70%, respectively). Klebsiella spp. was the commonest pathogen isolated in both EOS (55%) and LOS (45%). Coagulase-negative staphylococci (CoNS) was the main Gram-positive organism isolated in LOS (19.30%). Candida spp. was isolated in 10.4% of EOS and also in two episodes of LOS as follow-up cultures. Regarding urine cultures results, Klebsiella spp. and Enterobacter spp. were isolated (one episode for each) in EOS, whereas Klebsiella spp. was the commonest pathogen isolated from urine cultures of LOS. Follow-up urine cultures revealed growth of Candida spp. in three LOS cases. Matching between blood and urine cultures (the same organism was isolated from the blood and urine cultures) was 20% for Candida spp. and 6.70% for Klebsiella spp., with a total of 26.70% of UTI cases being concordant with blood cultures for the same organism.

Receiver operating characteristic curves revealed that leukopenia, I/T ratio, CRP, platelet count, and RBS showed high sensitivity but all show low specificity for positive blood culture. Further, the sensitivity of leukopenia (86.70%) was much higher than that of leukocytosis (28.30%) as given in Table 7.

Concerning UTI, leukopenia and expert panel criteria score showed high sensitivity (81.80% and 90.90%, respectively) but low specificity for the diagnosis of UTI as demonstrated in Table 8.

Table 5 Clinical presentations as regards urine culture results

Variables	Urine culture				*p* value
	Negative (*n* = 89)		Positive (*n* = 11)		
Males	60	67.40%	5	45.50%	0.20
Females	29	32.60%	6	54.50%	
Expert panel criteria score (Mean ± SE)	5.3	0.14	5.10	0.60	0.60
Clinical presentation					
Poor feeding	49	55.10%	10	90.90%	0.02
Lethargy and hypotonic and poor reflex	82	92.10%	9	81.80%	0.30
Convulsion	4	4.50%	1	9.10%	0.40
Bleeding tendency	8	9%	1	9.10%	0.90
Sclerema	5	5.60%	1	9.10%	0.50
Cholestasis jaundice	5	5.60%	0	0%	1
Diarrhea	4	4.50%	0	0%	1
Hypotension	9	10.10%	1	9.10%	1
Bradycardia	3	3.40%	0	0%	1
Apnea	13	14.60%	0	0%	0.40
Respiratory distress	55	61.80%	9	81.80%	0.30
Temperature instability	31	34.80%	6	54.50%	0.30
Feeding intolerance	35	39.30%	8	72.70%	0.05
Need for ventilation	45	50.50%	6	54.50%	0.80

Table 6 Laboratory investigations in different urine culture results

Variables	Urine culture				*p* value
	Negative (*n* = 89)		Positive (*n* = 11)		
	Mean	SE	Mean	SE	
TLC ($\times 10^9$ cells/L)	12.10	0.90	13.60	3.10	0.60
Platelet count ($\times 10^9$ cells/L)	179.60	14.90	159.80	35.20	0.70
I/T ratio	0.33	0.02	0.37	0.07	0.40
CRP (mg/dL)	54.50	3.80	44.20	8.30	0.30
RBS (mg/dL)	153.20	7	171.30	36.60	0.40

TLC: total leukocyte count; CRP: C-reactive protein; RBS: random blood sugar

4 Discussion

The present study revealed concomitant UTI in neonatal sepsis with an incidence rate of 11%. There was a comparable incidence in both proven and suspected sepsis (11.70% and 10%, respectively). However, the incidence of UTI was higher in LOS (16.36%) than in EOS (4.44%). Furthermore, Gram-negative bacteria were the causative pathogen in all cases, with more than half (54.50%) being caused by Klebsiella spp. The incidence of fungal infection was low where Candida spp. was isolated from three follow-up urine cultures.

Regarding the diagnosis of UTI, poor feeding and feeding intolerance were the clinical manifestations that showed significant association with positive urine culture (UTI). Furthermore, leukopenia and expert panel criteria score showed high sensitivity (81.80% and 90.90%, respectively) but low specificity for the diagnosis of UTI.

In the current study, EOS represented 45%, while LOS was 55%. Early-onset sepsis is caused by infections that occur during the intrapartum period or just before delivery, whereas LOS is due to infections acquired from the environment after the delivery, especially in preterm infants, especially if very low birth weight [10]. A study that included 151 preterm infants with culture-proven neonatal sepsis revealed that LOS (88/151) was more frequent than EOS (23/151). In both types of sepsis, CONS was the most frequent pathogen [11].

Studies related to neonatal sepsis have shown a decrease in EOS cases, especially with Group B Streptococcus, with the improvement in obstetric care and the use of intrapartum antibiotic prophylaxis. Alternatively, they showed an increase in LOS which is related to the increased survival rates and long hospitalization times of premature babies [12].

In the present study, the most frequent clinical manifestations were combined lethargy, hypotonia, and poor reflexes, followed by respiratory distress, poor feeding, the need for mechanical ventilation, feeding intolerance, and temperature instability. In this regard, it has been reported that the clinical manifestations of neonatal sepsis range from subclinical infection to severe focal or systemic disease and they are generally nonspecific [10]. Further, feeding intolerance and apnea have been reported as primary features, along with bradycardia and desaturations. Heart rate variability and hypotension have also been identified as potential indicators [13].

Positive blood culture (proven sepsis) was detected in 60% of the studied infants, while 40% were suspected of sepsis. Blood culture remains the gold standard for the diagnosis of sepsis. The growth of the microorganism in blood culture is diagnostic in the neonatal period; however, the failure to produce it does not exclude the diagnosis. The absence of growth in culture may be related to the insufficient sample, mother's antibiotic use, antibiotic dose applied before sampling, low amount of bacteria in the blood, or short-term bacteremia [14]. It has been reported that automated laboratory methods reveal positive results in 94% of cultures taken before antibiotic treatment within 24 h and 97% were positive within 36 h [15].

In this study, Gram-negative bacteria were responsible for most cases of neonatal sepsis and were predominant

Table 7 Accuracy of laboratory investigations in detecting positive blood cultures among the study group

Variable	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Area under the curve (%)	Cutoff point
TLC						
< 4000	86.70	15	40.50	62.80	43.70	3.95
> 20,000	28.30	90	18.20	23.90	20.30	19.90
Platelet	71.70	42.50	64.40	49.40	58.90	101.50
I/T ratio	87.80	32.10	65.70	62.90	53.70	0.24
CRP	97.60	14.30	63.10	79.90	58.70	16.20
RBS						
< 40	100	0	100	0	50	38
> 180	33.30	77.50	49.70	63.50	59.80	179

TLC: total leukocyte count; CRP: C-reactive protein; RBS: random blood sugar

Table 8 Accuracy of laboratory investigations for diagnosis of UTI

Variable	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy (%)	Cut off point
TLC						
< 4000	81.80	13.50	10.50	85.70	21	3.95
> 20,000	18.20	78.70	9.60	88.60	72	19.90
PLT	44.50	72.60	16.70	91.40	69.50	101.50
I/T ratio	66.70	31.70	10.80	88.50	55	0.25
CRP	66.70	33.30	11	89	37	37.30
RBS						
< 40	100	0	100	0	50	38
> 180	27.30	70.80	10.40	88.70	66	179
Expert panel criteria	90.90	34.80	14.70	96.90	62.10	5.50

TLC: total leukocyte count; CRP: C-reactive protein; RBS: random blood sugar

in both EOS and LOS. Klebsiella spp. was the most common pathogen.

Pathogens that cause sepsis vary according to geographical differences and countries. Group B Streptococcus and Escherichia coli have been reported as the predominant pathogens of neonatal EOS in the USA [16], whereas Gram-negative bacteria like Escherichia coli and CoNS were the leading pathogen in developing countries [17]. Escherichia coli is a Gram-negative bacterium that commonly colonizes human urogenital and enteric tracts. It is considered the second most common pathogen related to EOS onset in term infants and the major determinant of neonatal sepsis in very low birth weight newborns [18]. Furthermore, candidiasis is known as a frequent cause of infection in NICU-admitted patients and is related to high mortality [19]. It is reported to be the third most frequent agent of late-onset neonatal sepsis in babies weighing less than 1500 gm, especially in babies with long-term hospitalization [20]. However, Clancy and Nguyen [21] stated that early diagnosis of blood candida infection is challenging in neonates due to the nonspecific symptoms and the low sensitivity of blood cultures.

Leukopenia, I/T ratio, CRP, platelet count, and RBS showed high sensitivity but all show low specificity for positive blood culture. Further, the sensitivity of leukopenia (86.7%) was much higher than that of leukocytosis (28.3%). This result indicates that leucopenia is a good negative test that could exclude rather than proving the diagnosis of sepsis. In contrast, leucopenia has shown high specificity and positive predictive value but low sensitivity and negative predictive value (good positive test) for detecting EOS as reported by Hassan, Gohil [22]. This difference might be attributed to differences in the blood sampling time, the age of the neonates, or the low sensitivity of this test in the first week of life. Moreover, Hassan, Gohil [22] observed that a combination of any hematological parameter with CRP increases the specificity and positive predictive values

for 94.6% and 96.2%, respectively, for detecting sepsis, and this has been further documented by Sorsa [23].

In the current study, UTI was confirmed in both proven and suspected sepsis. However, the incidence of UTI was higher in LOS than in EOS. Studies of UTI in high-risk neonates are scarce. An earlier study reported a prevalence of neonatal symptomatic bacteriuria of 1.90% and asymptomatic bacteriuria of 0.50% among high-risk neonates [24]. The risk of UTI has been reported to be 13.60–16.40% in term infants presenting with fever or other signs of infection [6], which increases in preterm ones [25]. A more recent study found a high risk (11.30%) of UTI in premature infants who were admitted to the NICU suspected of LOS [1].

Corresponding to our findings, the frequency of UTI based on positive urine cultures in neonates with suspected and proven sepsis was 6%. Further, positive urine cultures were significantly higher in LOS (10.98%) than EOS (1.83%) [4]. Visser and Hall [26] have reported lower values of UTI in EOS (1.60%) and LOS (7.40%).

The discrepancies between different studies as regards the definition of UTI and the characteristics of the studied neonates contribute to the observed difference in neonatal UTI [4].

It has been reported that urine cultures should be a part of aggressive sepsis work in neonates, especially in cases of late-onset sepsis [27]. The use of central arterial or venous lines in these infants, providing a direct source of bacteremia, is such a risk factor and often the cause of bloodstream infections [28]. Alternatively, the low incidence of positive urine cultures in EOS besides their high costs made urine culture not included in their evaluation [5].

Analysis of the causative pathogens of UTI revealed Gram-negative bacteria in all cases (100%), with Klebsiella spp. in more than half of them (54.50%). Candida spp. were isolated from three follow-up urine cultures. Previously, it has been reported that Escherichia coli is the most common bacterial etiology for neonatal UTIs, while Gram-positive organisms are rare [6, 29]. Furthermore, infection with other Gram-negative bacteria as Klebsiella spp. is more common in male infants with vesicoureteral reflux [30]. An earlier study reported a high incidence of candida detection (42%) in hospital-acquired UTI occurring in infants admitted to a neonatal intensive care unit [31].

Matching between blood and urine cultures (the same organism was isolated from the blood and urine cultures) revealed concordance in about one-fourth of cases (26.70% of UTI cases). The concordance was lower (20%) for Candida spp. and much lower (6.70%) for Klebsiella spp.

In the present study, poor feeding and feeding intolerance were the significant clinical features associated with neonatal UTI. This finding agrees with Shrestha, Baral [32] who reported fever and poor feeding as significant manifestations of neonatal UTI. Another study reported that feeding intolerance besides lethargy or irritability and increased numbers of apnea, desaturation, or bradycardia are the most common presenting symptoms [33]. Alternatively, prolonged jaundice has been reported as the most frequent manifestation in a cohort of neonatal UTI [34]. Nevertheless, Foglia and Lorch [35] concluded that all clinical features have limited discriminating power in detecting UTI.

In the current study, the receiver operating characteristics curves showed that leukopenia and expert panel criteria score were good negative diagnostic variables for neonatal UTI. This agrees with Foglia and Lorch [35] who concluded that peripheral white blood cells count and CRP do not discriminate between patients with and without UTI.

In the present study, ultrasonography revealed hydroureter and hydronephrosis in 18% of UTI cases. Congenital anomalies of the urinary tract in association with UTI have been reported by other researchers (ranging from 9.60% to 40%) [1, 36–38]. However, Madhu et al. [39] found normal ultrasonography findings in all UTI cases. Hydronephrosis is the most frequent abnormal finding and has been found in 45% of neonates with UTI [40]. Also, Asghar et al. [41] found hydronephrosis in 12.10%. Bahat Ozdogan et al. [42] reported pelvicaliectasis in 15.60%.

5 Limitations

This study is limited by being cross-sectional where there is no follow-up of the patients' outcomes in both groups with or without UTI.

6 Conclusions

The findings in the present study indicate that UTI could contribute to neonatal sepsis, with much higher possibility of UTI in late-onset than early-onset sepsis. Therefore, urine culture should be included in the sepsis workup, particularly in late-onset types. Furthermore, poor feeding and feeding intolerance are significant risk factors that could be associated with UTI, while leukopenia and expert panel criteria score help only to exclude the diagnosis of UTI.

Abbreviations

CoNS: Coagulase-negative staphylococci; CRP: C-reactive protein; DIC: Disseminated intravascular coagulation; EOS: Early-onset sepsis; LOS: Late-onset sepsis; MDR: Multidrug; PROM: Premature rupture of membranes; RBS: Random blood sugar; TLC: Total leukocyte count.

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Author contributions
All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by AK, FA, and MS. The first draft of the manuscript was written by AA. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study protocol was approved by the Research Ethics Committee, Faculty of Medicine, Fayoum University, Egypt. We obtained informed consents from the parents of the neonates after informing them about the objectives and procedures of the study.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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