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Original Research Article

A PROSPECTIVE OBSERVATIONAL STUDY ON URINARY TRACT INFECTION IN NEONATAL SEPSIS

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Abstract

Background: Urinary tract infection is most frequently occurring conditions in neonates. The clinical presentation of a neonate's urinary tract infection can vary greatly, from a severe illness to milder symptoms including anorexia and difficulty gaining weight. It continues to be difficult to diagnose and treat. Also, it might cause clinical sepsis and bacteraemia. The Objective is to determine the prevalence of UTI among sepsis-suspected hospitalized neonates, considering bacteriuria as an indicator of neonatal UTI. **Materials and Methods:** It is a hospital based prospective observational study, carried out in NICU at Adichunchanagiri Hospital & Research Centre from February 2021 to September 2022 with 125 septic neonates. During the study, the details maternal and obstetric history, and laboratory values were taken in the validated data collection form. **Result:** A total of 125 septic neonates were included in the study where male were dominated with 54.4% (68). Out of 125 septic neonates, 19.2% (24) were pre-term. We observed a 32% (40/125) prevalence of UTI in suspected neonatal sepsis and mortality rate is 17.6% (22). Vaginal examination more than 3 times (27.5% vs 23.5%, OR 1.233) and leucocytosis 7.5% vs 7.1%, OR 1.08) in mother is prone to cause UTI in neonates. The symptoms of neonates such as fever, refusal to feed, convulsions, skin lesions, umbilical discharge are more in sepsis with UTI as odd ratio is >1. A total of 54.4% (68) of the blood samples and 13.6% (17) urine samples shown the growth of pathogens. In blood isolated pathogen were Klebsiella spp. 24% (30), CONS 14.4% (18), E coli 8% (10), and Enterobacter 8% (10). In urine samples isolated pathogens were E coli 4.8% (6), Enterobacter spp. 4% (5), and Klebsiella spp. 4.8% (6). Out of 13 commonly prescribed antibiotics, six were resistant in more than half against E coli, seven are resistant in more than half against Enterobacter spp. and four are resistant in more than half against Klebsiella spp. **Conclusion:** The prevalence of UTI is more in NICU admitted suspected neonatal sepsis. Overall Mortality rate in the study is 17.6% and present of UTI in sepsis will increase the probability of death. UTI is highly prevalent in Pre-term and late onset sepsis. Prolonged rupture of membranes, vaginal examination > 3 times and leucocytosis are the maternal risk factor that can develop UTI in the neonates. Urine culture before prescription is necessary to ensure high patient care and to prevent the antibiotic resistance.

INTRODUCTION

Neonatal sepsis remains one of the leading causes of morbidity and mortality both among term and preterm babies.[1,2] Although advances in neonatal care have better survival and reduced complications in preterm babies, sepsis still contributes significantly to mortality and morbidity among veritably-low-birth- weight (VLBW, <1500 g) infants in Neonatal Intensive Care Units (NICUs).[3,4]

Neonatal sepsis consists of a variety of systemic conditions, including meningitis, pneumonia, rheumatoid arthritis, and urinary tract infections (UTI).Maternal intrapartum fever, UTI, protracted labour, preterm rupture of the membranes (PROM), extended PROM lasting more than 18 hours,

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meconium aspiration, multiple gestations, and chorioamnionitis are all recognised risk factors for neonatal sepsis.[1,5-7] Pregnant women with an UTI have a higher propensity to deliver premature or underweight neonates, who are more susceptible to neonatal sepsis.[8,9]

Urinary tract infection is among the most frequently occurring conditions in neonates. UTI is defined as significant bacteriuria irrespective of the point of infection in the urinary tract.[10] The exact rate of urinary tract infections(UTIs) in babe isn't known, but studies have set up that from about 1 in 1000 to 1 in 100 in full- term babies, and over to 1 in 10 unseasonable babies, will have a UTI during the first month of life.[11] Most newborns & infants present with features of UTI and not asymptomatic bacteriuria. The diagnosis of UTI can be overlooked because the symptoms are often non-specific and the proper samples may be difficult to obtain. UTI in the Neonats are nonspecific.[12] Long-term complications are hypertension and impaired end-stage renal disease, Acute kidney injury Renal scaring and renal insufficiency hypertension in adulthood There are few studies about the inclusion of urine culture as part of aggressive neonatal sepsis workup. Urine cultures are said to be most appropriate when investigating late-onset sepsis.[13]

Hence, The aim of this study was undertaken to determine the prevalence of UTI when sepsis is suspected in hospitalized neonates. In addition, evaluate the risk factors, clinical features in UTI. SIS is being laid on the promotion of strategies to reduce mortality at the community level.[14]

MATERIALS AND METHODS

This is a prospective observational study conducted at Neonatal Intensive Care Unit of Adichunchanagiri Institute of Medical Science (AIMS). Which was tertiary care teaching hospital, situated in rural area of Mandya district, Karnataka,India. A total of 125 newborn infants were included in the study in the period of February 2021 to September 2022.Based on the inclusion and exclusion criteria, neonates were enrolled in the study. Before enrolling in the study, the parents/ guardian provided written consent. The validated data collection form was used to collect detailed maternal and obstetric histories and Venous blood a samples of the neonate were collected in a sterile EDTA tube under sterile conditions, Urine samples by urinary catheterization in aseptic precaution following aseptic precautions and sent to the central laboratory for septic screen, blood and urine culture. A detailed neonatal history pertaining to maternal risk factors gestational age at birth, birth weight, , history of clinical presentations, clinical examination of subjects were documented in the data collection form.

Descriptive statistical tool were used to analyse the data. Cases were divided into early and late sepsis groups. Test of inference (Chi-Square test & student t test) was used for testing the difference of urine culture positivity among neonates with early and late onset sepsis.

Inclusion Criteria

- All babies admitted to NICU.Both term and preterm neonates with clinically suspecting sepsis will be considered.
- Baby weight more than 1kg

Exclusion Criteria

- Gross congenital malformations or significant systemic illness.
- Immunodeficiency disorders.
- Extremely low birth weight babies (less than 1 kg).
- Baby started on antibiotics before admission.
- Life threatening and emergency condition babies
- Mother started on antibiotics before delivery.

RESULTS

Out of 125 suspected sepsis neonate admited in NICU, 54.4% (68) were male and female were 45.6% (57). There were 180.80% (101) of the patients were full-term and 19.20% (24) of the patient were pre-term in study. 84.8% (106) had late onset and 15.20% (19) had early onset neonatal sepsis majority of maternal risk factor among neonatal sepsis were fever within 2 weeks of delivery 97.6% (122) ,followed by vaginal examinations > 3 times 24.8% (31), leucocytosis 7.2% (9), and prolonged rupture of membranes 1.60% (2), Out of 125 neonates , majority of neonate had fever 79.2% (99) followed by refusal to feed 77.6% (97), hurried breathing 66.4% (83), failure to thrive 39.2% (49), excessive crying 37.6% (47), convulsions 15.2% (19), skin lesions 6.4% (8), and umbilical discharge 5.6% (7)the majority of neonate were having jaundice 35.2% (44) followed by irritability 22.4% (28), umbilicus redness 16.8% (21), high pitched cry 15.20% (19), pustules 8.8% (11), icteric 8.8% (11), cyanotic 8.8% (11), umbilicus discharge 8.8% (11), skin pinch 8% (10), Colour pale 8% (10), Open posterior frontanellae 7.2% (9), and Bulged anterior frontanellae 4.8% (6)

Out of 125 patients, 54.4% (68) of the blood samples shown the growth of pathogens.

The majority of isolated pathogen were Klebsiella spp. 24% (30), CONS 14.4% (18), E coli 8% (10), and Enterobacter 8% (10).26.4% (33) of sepsis neonate had decrease urine output

out of 125 urine samples 13.6% (17) shown the growth. E coli isolated in 4.8% (6) of the total sample, Enterobacter spp. 4% (5), and Klebsiella spp. 4.8% (6).32% (40) of the sepsis neonate had urinary tract infection [Table 1].

There was no statistically significant association between the maternal risk and the present of UTI among sepsis (p >0.05). However, prevalent of UTI in the sepsis neonate was more in, Vaginal examination > 3 times and Leucocytosis [Table 2].

There was no statistically significant association between the clinical presentation and the present of

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UTI among sepsis (p >0.05). However, prevalent of UTI in the sepsis neonate was more in, fever, refusal to feed, convulsions, and hurried breath [Table 3].

There was no statistically significant association between urine analysis and the present of UTI among sepsis (p >0.05). However, urine output was decreased and high positive urine culture in the sepsis with UTI neonate [Table 4].

There was no statistically significant association between urine analysis, gender, onset, and gestational with the present of UTI among sepsis (p >0.05) [Table 4].

There was no statistically significant association between USG and the present of UTI among sepsis (p >0.05). In the study, death was much high in sepsis with UTI than sepsis without UTI (OD 2.028) [Table 5].

In the study, gentamicin, piptaz, vancomycin, meropenem, colistin, linezolid, and amikacin were sensitive to at least half of E coli isolated from sepsis neonates with UTI. At least half of the Enterobacter spp. were sensitive to gentamicin, piptaz, vancomycin, meropenem, colistin, and linezolid. At least half of the Klebsiella spp. were sensitive to piptaz, meropenem, colistin, and linezolid [Table 6].

Table 1: Urine culture in sepsis neonates with UTI

Urine culture		Frequency (N=125)	Percentage
No		108	86.40%
Yes	E coli	6	4.80%
	Enterobacter spp.	5	4%
	Klebsiella spp.	6	4.80%

Table 2: Association between maternal risk and present of UTI in sepsis patients

Maternal risk	Sepsis		OR	95% CI		p value
	Without UTI	With UTI		Lower	Upper	
Fever	82 (96.5%)	40 (100%)				0.229
Prolonged rupture of membranes	2 (2.4%)	0				0.328
Vaginal examination > 3 times	20 (23.5%)	11 (27.5%)	1.233	0.524	2.902	0.632
Leucocytosis	6 (7.1%)	3 (7.5%)	1.08	0.222	3.953	0.929

Table 3: Association between clinical presentation and present of UTI in sepsis patients

Clinical presentation	Sepsis		OR	95% CI		p value
	without UTI	with UTI		Lower	Upper	
Fever	67 (78.8%)	32 (80%)	1.075	0.423	2.733	0.88
Refusal to feed	64 (75.3%)	33 (82.5%)	1.547	0.547	0.596	0.367
Failure to thrive	35 (41.2%)	14 (35%)	0.769	0.353	1.678	0.509
Excessive crying	33 (38.8%)	14 (35%)	0.848	0.388	1.856	0.681
Convulsions	12 (14.1%)	7 (17.5%)	1.29	0.466	3.574	0.623
Skin leisons	4 (4.7%)	4 (10%)	2.25	0.533	9.501	0.259
Umbilical discharge	4 (4.7%)	3 (7.5%)	1.642	0.35	7.71	0.526
Hurried breathing	54 (63.5%)	29 (72.5%)	1.513	0.665	3.445	0.322

Table 4: Association between different groups and present of UTI in sepsis patients

Parameters		Sepsis		OR	95% CI		p value
		without UTI	with UTI		Lower	Upper	
Gender	Male	45 (66.18%)	23(33.82%)	1.2	0.390	1.774	0.633
	Female	40(70.18%)	17(29.82%)				
Urine analysis	Output	23 (27.1%)	10 (25%)	1.113	0.471	2.632	0.808
	Culture	8 (9.4%)	7 (17.5%)	2.042	0.294	2.31	0.194
Onset	Early	14 (73.68%)	5 (26.32%)	1.266	0.466	2.63	0.523
	Late	73 (68.87%)	33 (31.13%)				
Gestation	Full-term	72 (71.29%)	29 (28.71%)	2.101	0.844	5.226	0.106
	Pre-term	13 (54.17%)	11 (45.83%)				

Table 5: Association between death and present of UTI in sepsis patients

	Sepsis		OR	95% CI		p value
	without UTI	with UTI		Lower	Upper	
Death	12 (14.1%)	10 (25%)	2.028	0.45	0.68	0.136

Table 6: Sensitive pattern of organisms with regular antibiotics.

Antibiotic	Isolated pathogens (N=17)		
	E coli	Enterobacter spp.	Klebsiella spp.
Ampicillin	17.65% (3)	41.17% (7)	29.41% (5)
Gentamicin	52.9% (9)	58.8% (10)	41.17% (7)
Ofloxacin	23.53% (4)	41.17% (7)	29.41% (5)
Amoxicillin	47.06% (8)	35.29% (6)	29.41% (5)
Cefotaxime	29.41% (5)	29.41% (5)	41.17% (7)
Ceftriaxone	23.53% (4)	29.41% (5)	17.65% (3)

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Piptaz	58.8% (10)	64.7% (11)	58.8% (10)
Vancomycin	64.7% (11)	58.8% (10)	47.06% (8)

DISCUSSION

UTI is a significant clinical issue throughout the newborn stage. As a result, it's critical to diagnose and treat UTIs as soon as feasible.[15] However, since the symptoms are frequently vague and it may be challenging to collect sterile samples, the diagnosis of UTI may go unnoticed.[16]

The study was designed to estimate the prevalence of UTI in suspected neonatal sepsis and the etiological agents causing urinary tract infection. In the study, we observed a 32% (40/125) prevalence of UTI in suspected neonatal sepsis. Contrast to our finding, Woldu MA et al., Tamim et al., Bauer et al., and Ketema E et al., reported lower prevalence of UTI in sepsis (29% vs 25.3% vs 12.2% vs 9% vs 32%).[17-20] There is no statistically significant association between the gender of the neonate with sepsis with or without UTI (p>0.05). However, male patients are 1.2 times more likely to develop UTI than female (33.82% vs 29.82, OR 1.2). Mohseny AB et al., reported similar to our findings.[21] The incidence of UTI is high in the late onset sepsis than early onset sepsis (31.13% vs 26.32%, OR 1.266). It indicates that present of UTI has more probability of developing late onset sepsis. Similarly, pre-term neonates have high prevalence of UTI in septic neonates (45.83% vs 28.71%, OR 2.101). Purniti et al.,22 reported less prevalence of UTI in their study than what we found (17.31% vs 45.83%). All of these insights highlight the need for routine urine culture investigation as part of the assessment and treatment of late-onset sepsis & sepsis in preterm. This is because neonates' UTI symptoms are generally ambiguous, making a diagnosis difficult to make.

In the study we observed the present of maternal risk such as fever 2 weeks prior delivery, prolonged rupture of membranes, vaginal examination > 3 times and leucocytosis. None of the maternal risks are statistically significantly associated with sepsis with or without UTI (p>0.05). However, vaginal examination more than 3 times (27.5% vs 23.5%) and leucocytosis 7.5% vs 7.1%) in mother is prone to cause UTI in neonates (OR >1). Woldu MA et al.[17] reported the higher leucocytosis in mother of septic neonates with UTI. Oumer M et al., reported the same finding in their study.[19] There is no statistically significant association between clinical presentation and the present of UTI among sepsis (p >0.05).

There are no statistically significant differences in the present of abnormal finding in systemic examination among septic with UTI or without UTI (p <0.05). In the systemic examination, we observed, ICR (65% vs 62.4%, OR 1.121), SCR (65% vs 62.4%, OR 1.121), apnoea (10% vs 9.4%, OR 1.069), absent suckling reflex (75% vs 74.1%, OR 1.048) and absent moros reflex (82.5% vs 82.4%, OR 1.01) prevalent more in the septic with UTI patients than without UTI patients. However, hepatomegaly, abdominal distension, and mottling are less prevalent in septic with UTI neonates (OR <1).

Unconjugated bilirubin is statistically significantly associated to septic neonates with UTI (p<0.05). It tends to increase in septic with UTI than septic without UTI (45% vs 25.9%, OR 2.32). Other biochemical test such as conjugated bilirubin, acidotic breathing, ARF, hypoglycaemia and hyperglycaemia are not statistically significant among septic neonates with or without UTI. However, maximum neonates having sepsis with UTI have increase level all the biochemical test.

In the study, 54.4% (68) of total blood samples shows the present of pathogen. It has Klebsiella spp., CONS, E coli and Enterobacter spp. There is no statistically significantly association between blood culture and sepsis with UTI (p>0.212). Similar types of pathogens are detected by Ba-Alwi NA et al., in their study20. However, isolation of pathogen from blood samples among sepsis with UTI is more than those are sepsis without UTI (62.5% vs 50.6%, OR 1.628). From urine sample, 13.6% (17) of samples detected pathogen. E coli, Enterobacter spp. and Klebsiella spp. detected from urine samples. There is no statistically significantly association between urine culture and sepsis with UTI (p>0.194). However, isolation of pathogen among sepsis with UTI is more than those who are sepsis without UTI (17.5% vs 9.4%, OR 2.042). Out of 13 commonly prescribed antibiotics, six were resistant in more than half against E coli, seven are resistant in more than half against Enterobacter spp. and four are resistant in more than half against Klebsiella spp. It highlight the needs of routinely advice urine culture in the late onset sepsis as UTI is highly prevalent ((31.13% vs 26.32%, OR 1.266).

The mortality rate in the study is 17.6% (22). Studies conducted by Ba-Alwi NA et al., Jatsho J et al., Nyenga AM et al., Ogunlesi TA et al., and Kabwe M et al., reported higher mortality rate than our study (45.4% vs 20.5% vs 21% vs 32.2% 43% vs 17.6%) whereas Tumuhamye J et al., reported 15.2% mortality less than our study.[23-26] There is no statistically significant different between the mortality among sepsis with UTI (p>0.05). However, sepsis with UTI neonate is having more mortality than sepsis without UTI (25% vs 14.1%, OR 2.028).

Limitations

The study's limitation is the small number of participants, who may not be representative of all neonates with different types of infections, since a larger population in a multi-center setting could lead to better outcomes.

CONCLUSION

The prevalence of UTI is 32% in NICU admitted suspected neonatal sepsis. Overall Mortality rate in the study is 17.6% and present of UTI in sepsis will

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increase the probability of death by 2.028 times. UTI is highly prevalent in Pre-term and late onset sepsis. Acidotic breathing, increased conjugated bilirubin, and Acute Renal Failure (ARF) seem to be more prevalent in sepsis with UTI. The study identified, prolonged rupture of membranes, vaginal examination > 3 times and leucocytosis are the maternal risk factor that can develop UTI in the neonates. E coli, Enterobacter spp. and Klebsiella spp are three different pathogens present in the urine samples of septic with UTI neonates and all shows partial resistance to commonly prescribed antibiotics. All of these insights highlight the need for routine urine culture investigation as part of the assessment and treatment of late-onset sepsis & sepsis in preterm. This is because neonates' UTI symptoms are generally ambiguous, making a diagnosis difficult to make Implementation of antibiotic stewardship program and routine urine culture before prescription is necessary to prevent the antibiotic resistance.

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