

Frequency of Causative Organism of *Urinary Tract Infection* in Neonate Presenting with Sepsis

MASOOD MAZHAR¹, IQBAL AHMAD², ASIF KARIM³

ABSTRACT

Background: Morbidity and mortality both among term and preterm infants is mostly related to neonatal sepsis. Although survival improved and complications reduced in preterm infants due advances in treatment, but sepsis still has major impact on mortality and morbidity in Neonatal care Units. Urinary tract infection (UTI) in neonatal age occurs with neonatal sepsis. Bacteremia may be cause or the effect of UTI. Hypertension and CRF are the complications of Progressive renal damage in early childhood. The clinical manifestations of UTI in the neonatal period may vary and are nonspecific, as well as the sepsis itself.

Aim: To determine the frequency of causative organism of Urinary tract infection in neonate presenting with sepsis

Setting: This study was carried out in the Department of Pediatric Medicine of B. V. Hospital, Bahawalpur in period of six months.

Methods: A total of 251 infants of both gender with UTI and sepsis were included in the study. Preterm newborns and infants with contraindication for bladder catheterization were excluded. We collect under aseptic techniques and obtained from all the patients by bladder catheterization. Samples were properly sent to the laboratory for microscopic analysis and culture/sensitivity, where different medias like Pyocyanin, nutrient agar and TSA (Trypticae soy agar) were used. Data for causative organism was collected and noted.

Results: Age range in this study was from 0-28 days. Mean age of infants were 19.004 ± 5.64 days, mean duration of complain was 29.027 ± 7.72 hours and mean weight was 3.117 ± 0.37 Kg. Majority of the infants were from 16-28 days (74.9%) of age. Male infants were 78.5%. Pseudomonas was seen in 6.4% patients. E.coli was seen in 39.8% patients. Klebsiella was seen in 36.7% patients.

Conclusion: My study concluded that urine culture, analysis, and Gram-stain should be performed in routine work of all patients of neonatal septicemia, especially in males, for early detection and prompt treatment of neonatal UTI.

Keywords: Sepsis, Urinary tract infection, Pseudomonas, E.coli, Klebsiella

INTRODUCTION

According to Health Organization (WHO) reported in 2006 that almost 4 million die within the first four weeks of life,¹ out of these 99% occur in developing countries (approximately half following difficult deliveries at home) against 1% in developed countries.² 30-40% of all these deaths are due to neonatal infections³.

Morbidity and mortality both among term and preterm infants is mostly due to neonatal sepsis⁴. In spite of advances in neonatal care sepsis still contributes significantly to mortality and morbidity in Neonatal Care Units^{5,6}.

The clinical presentation of neonatal sepsis is generally nonspecific⁷. These include fever or

hypothermia, respiratory distress including cyanosis and apnea, feeding difficulties, lethargy or irritability, hypotonia, seizures, poor perfusion, bleeding, abdominal distention, visceromegaly, jaundice etc^{8,9}. Sometimes may present with respiratory difficulties that may be due to acidosis, pneumonia or meconium aspiration¹⁰.

In one report 1% prevalence of fever in term newborns with 10% of the febrile ($\geq 37.8^\circ\text{C}$ rectal or core body temperature) infants having culture-proven sepsis¹¹. Term newborns most likely to react to a bacterial infection in the form of fever while preterm newborns react with hypothermia due difficulty with temperature control especially in the first 2 days^{12,13}.

In infant and children urinary tract infection is a common infection¹⁴. Urinary tract infection (UTI) often associated with neonatal sepsis in neonates. The prevalence of UTI among late-onset sepsis neonates in developed countries varies from 7.4 to 25.3%, with higher rates in preterm infants^{15,16}. Hypertension and CRF are the complications of Progressive renal

¹Assistant Professor Paediatric, Ibn e Siena Hospital Multan

²Assistant Professor Paediatrics, Shahida Islam Medical, College Lodhran

³Paediatrician, THQ Hospital, Lodhran

Correspondence to Dr. Masood Mazhar Email: masoodmazhar112@gmail.com Cell: 0333 6126612

damage in early childhood.¹⁷ The clinical manifestations of UTI in the neonatal period may vary and are nonspecific, as well as the sepsis itself^{14,18}.

Amelia N has found in one study that frequency of *Pseudomonas* is 6.4%, *Staphylococcus* 6.4% and *Klebsiella* was 2.1% in neonate presented with sepsis¹⁹.

Omar C and others has noted in one study that frequency of *Pseudomonas* was 6.25%, *E. coli* 37.5% and *Klebsiella* was 46.87% in neonate presented with sepsis.²⁰

A midstream urine sample is the preferred way of collecting urine sample in toilet-trained children; other ways are by catheter or by suprapubic aspirate. UTI is unlikely if the urinalysis is completely normal. Antibiotic treatment for seven to 10 days is recommended for febrile UTI. Oral antibiotics may be offered as initial treatment when the child is not seriously ill and is likely to receive and tolerate every dose.

Moreover it is important to recognize whether there is pyelonephritis in a neonate who shows clinical signs of sepsis in order to provide appropriate treatment. So we like to determine the frequency of causative organism of *Urinary tract infection* in neonate presenting with sepsis in our general population and to modify the treatment plan accordingly. This study will help us in designing more effective management of sick neonates on community basis.

MATERIAL AND METHODS:

This study was conducted in the Department of Pediatric Medicine, B V Hospital, Bahawalpur. **Sample Size:** Sample size was according to the given formula:

$$n = \frac{z^2 pq}{d^2}$$

Expected least prevalence of *Pseudomonas* = 6.25%²⁰ where q=1-p, d= 3% with 95% Confidence level n= 251

Non-probability consecutive sampling technique was used.

Inclusion criteria: Infants age 0-28 days present with UTI and sepsis as per operational definitions with at least 48 hours duration.

Exclusion criteria:

- Premature newborns(less than37 weeks)
- Contraindication for bladder catheterization (thrombocytopenia (<50000 ml)on laboratory test)

Data collection procedure: Patients fulfilling the inclusion criteria from indoor department of pediatric medicine of BVH, Bahawalpur were included in the study after permission from ethical committee of

research department. Age, gender and weight of all patients were taken. Informed consent was taken from parents with full confidentiality with proper counselling about risk free for patient taking part in the study.

Urine was collected in a sterile way and obtained from all the patients by bladder catheterization. All samples were properly sent to the laboratory for examination.

Data for causative organism was collected according to operational definitions and noted on especially designed proforma.

Data analysis: Data was analyzed by using SPSS version 16. Different variables like age groups, gender and detected organisms were computed. Chi-square test was used and p ≤0.05 was statistically significant.

RESULTS

In this study age of patients vary from 0-28 days. Mean age of infants were 19.004± 5.64 days, mean duration of complain was 29.027± 7.72 hours and mean weight was 3.117±0.37 Kg as shown in Table-I. Majority of the infants were from 16-28 days (74.9%) of age as shown in Table–II. Male infants were 78.5% as shown in Table-III. *Pseudomonas* was positive in 6.4% patients as shown in Table-IV. *E.coli* was positive in 39.8% patients as shown in Table-V. *Klebsiella* was seen in 36.7% patients as shown in Table-VI.

Table I: Mean±SD of patients according to age, duration of complain and weight. (n=251)

| Demographics | Mean±SD |
|------------------------------|--------------|
| Age (days) | 19.004± 5.64 |
| Duration of complain (hours) | 29.027± 7.72 |
| Weight (Kg) | 3.117±0.37 |

Table II: Frequency and %age of Age

| Age (days) | n | %age |
|------------|-----|------|
| 0-15 | 63 | 25.1 |
| 16-28 | 188 | 74.9 |

Table- III: Frequency and %age of Gender

| Gender | n | %age |
|--------|-----|------|
| Male | 197 | 78.5 |
| Female | 54 | 21.5 |

Table- IV: Frequency and %age of *Pseudomonas*

| <i>Pseudomonas</i> | n | %age |
|--------------------|-----|------|
| Yes | 16 | 6.4 |
| No | 235 | 93.6 |

Table- V: Frequency and %age of *E.coli*

| <i>E. coli</i> | n | %age |
|----------------|-----|------|
| Yes | 100 | 39.8 |
| No | 151 | 60.2 |

Table- VI: Frequency and %age of Klebsiella

| Klebsiella | n | %age |
|------------|-----|------|
| Yes | 92 | 36.7 |
| No | 159 | 63.3 |
| Total | 251 | 100 |

Table- VII: Pseudomonas with respect to age groups

| Age group (days) | Pseudomonas | |
|------------------|-------------|------------|
| | Yes | No |
| 0-15 | 4(6.3%) | 59(93.7%) |
| 16-28 | 12(6.4%) | 176(93.6%) |
| Total | 16(6.4%) | 235(93.6%) |

P value=0.992

Table- VIII: Pseudomonas with respect to gender

| Gender | Pseudomonas | |
|--------|-------------|------------|
| | Yes | No |
| Male | 12(6.1%) | 185(93.9%) |
| Female | 4(7.4%) | 50(92.6%) |
| Total | 16(6.4%) | 235(93.6%) |

P value=0.726

Table- IX: Pseudomonas with respect to duration of sepsis

| Duration of sepsis (hours) | Pseudomonas | |
|----------------------------|-------------|------------|
| | Yes | No |
| 1-24 | 5(7.9%) | 58(92.1%) |
| 25-48 | 11(5.9%) | 177(94.1%) |
| Total | 16(6.4%) | 235(93.6%) |

P value=0.558

Table- X: Pseudomonas with respect to weight

| Weight (Kg) | Pseudomonas | |
|-------------|-------------|------------|
| | Yes | No |
| 2.5-3 | 8(5%) | 152(95%) |
| >3 | 8(8.8%) | 83(91.2%) |
| Total | 16(6.4%) | 235(93.6%) |

P value=0.237

Table- XI: E-coli with respect to age groups

| Age groups (days) | E coli | |
|-------------------|------------|------------|
| | Yes | No |
| 0-15 | 21(33.3%) | 42(66.7%) |
| 16-28 | 79(42%) | 109(58%) |
| Total | 100(39.8%) | 151(60.2%) |

P value=0.223

Table- XII: E-coli with respect to gender

| Gender | E coli | |
|--------|------------|------------|
| | Yes | No |
| Male | 77(39.1%) | 120(60.9%) |
| Female | 23(42.6%) | 31(57.4%) |
| Total | 100(39.8%) | 151(60.2%) |

P value=0.641

Table-XIII: E-coli with respect to duration of sepsis

| Duration of sepsis (hours) | E coli | |
|----------------------------|-----------|------------|
| | Yes | No |
| 1-24 | 22(34.9%) | 41(65.1%) |
| 25-48 | 78(41.5%) | 110(58.5%) |

P value=0.357

Table- XIV: E-coli with respect to weight

| Weight (Kg) | E coli | |
|-------------|------------|------------|
| | Yes | No |
| 2.5-3 | 72(45%) | 88(55%) |
| >3 | 28(30.8%) | 63(69.2%) |
| Total | 100(39.8%) | 151(60.2%) |

P value=0.027

Table- XV: Klebsiella with respect to age

| Age (days) | Klebsiella | |
|------------|------------|------------|
| | Yes | No |
| 1-15 | 26(41.3%) | 37(58.7%) |
| 16-28 | 66(35.1%) | 122(64.9%) |
| Total | 92(36.7%) | 159(63.3%) |

P value=0.380

Table- XVI: Klebsiella with respect to gender

| Gender | Klebsiella | |
|--------|------------|------------|
| | Yes | No |
| Male | 75(38.1%) | 122(61.9%) |
| Female | 17(31.5%) | 37(68.5%) |
| Total | 92(36.7%) | 159(63.3%) |

P value=0.373

Table- XVII: Klebsiella with respect to duration of sepsis

| Duration of sepsis (hours) | Klebsiella | |
|----------------------------|------------|------------|
| | Yes | No |
| 1-24 | 26(41.3%) | 37(58.7%) |
| 25-48 | 66(35.1%) | 122(64.9%) |
| Total | 92(36.7%) | 159(63.3%) |

P value=0.380

Table- XVIII: Klebsiella with respect to weight

| Weight (Kg) | Klebsiella | |
|-------------|------------|------------|
| | Yes | No |
| 2.5-3 | 55(34.4%) | 105(65.6%) |
| >3 | 37(40.7%) | 54(59.3%) |
| Total | 92(36.7%) | 159(63.3%) |

P value=0.321

DISCUSSION

During the neonatal period, UTI is more prevalent in male than in female infants^{21,22}. This is same as in my study as male infants were 78.5%. That is the reason there are more chances of UTI in young uncircumcised males, increased prevalence of urinary and renal anomalies in males, transient urodynamic dysfunction and vesicoureteral reflux that predominantly affects male infants²¹.

To et al reported a 3.7 fold higher risk of UTI in uncircumcised male infants.²³ Schoen et al reported that the incidence of UTI among uncircumcised male infants was 2.15%, while in circumcised infants it was only 0.22%²⁴

Uncircumcised male are on risk may be due to periurethral bacterial flora²⁵, which is more common in first six months of life, as age increases, chances

of UTI decrease because of retracted skin and improvement in penile hygiene. By the age of 12 months, both periurethral flora excess and the incidence of UTI in uncircumcised males will almost disappear²⁶.

In my study *Pseudomonas* was seen in 6.4% patients, *E. coli* was seen in 39.8% patients and *Klebsiella* was seen in 36.7%. My study results are consistent with Omar C and his associates who found in a study that frequency of *Pseudomonas* was 6.25%, *E. coli* 37.5% and *Klebsiella* was 46.87% in neonate presented with sepsis²⁰.

The microbial pattern of neonatal UTI has changed from that observed in the 1970s compared to that of the 1990s²¹. In 1969, Abbott²⁷ reported that *E. coli* was the most common pathogen causing UTI in neonates in Christchurch, New Zealand. Littlewood et al²⁸ also reported *E. coli* as the most frequent pathogen causing neonatal UTI in Leeds Maternity Hospital. In 1989-1992, Lohr et al²⁹ and Davies et al³⁰ reported that in Charlottesville and Toronto, the most common pathogens of neonatal UTI were coagulase-negative *Staphylococcus*, *Candida* sp. and *Klebsiella* sp. In 2003, Tamim et al reported that *Candida* sp. was the most common microorganism causing UTI among preterm infants with late-onset sepsis, followed by coagulase-negative *Staphylococcus*, *Pseudomonas* sp. and *Klebsiella* sp³¹.

In our study, the microorganisms found in urine cultures were similar to other studies in the last fifteen years. Purniti, in 2002, found *E. coli* as the most common pathogen of neonatal UTI in Sanglah Hospital, Bali. In this study, all subjects who received antibiotics before urine culture were excluded.³² The subjects with prior antibiotics had sterile urine culture. The use of broad spectrum antibiotics may change natural flora in the neonate, increasing the risk of infections by opportunistic microorganisms³³.

Neonatal UTI occurs through hematogenous spread or by ascending microorganisms through the urethral meatus.²¹ In our study, one subject had the same microorganism found in blood and urine cultures (*Klebsiella pneumoniae*), while other six subjects with UTI had different microorganisms in both cultures. Bauer found only six urosepsis from 66 neonatal UTI, suggesting that ascending infection was the more common mechanism in neonatal UTI³⁴.

Late-onset sepsis in the neonatal ward of Cipto Mangunkusumo Hospital were mostly caused by Gram-negative pathogens. Rinawati et al (2002) found the most common bacteria which caused late onset neonatal sepsis in the neonatal ward Cipto Mangunkusumo Hospital were *Enterobacter* sp. and *Klebsiella* sp.

The gold standard in diagnosing UTI is urine culture from appropriate specimens obtained by supra pubic

aspiration or bladder catheterization. The urinalysis cannot substitute urine culture to document the presence of UTI, but it can be valuable for prompt initiation of antibiotics since it provides information more rapidly than does urine culture³⁵.

CONCLUSION

It is concluded that urine culture, analysis and Gram-stain should be performed for septic investigations for neonatal septicemia, especially in males, for early detection and prompt treatment of neonatal UTI.

REFERENCES

1. Chiabi A, Djoupomb M, Mah E, Nguéack S, Mbuagbaw L, Zafack J, et al. The clinical and bacteriological spectrum of neonatal sepsis in a tertiary hospital in Yaounde, Cameroon. *Iran J Pediatr*. 2011 Dec;21(4):441-48.
1. 2.Labie D. Le scandale des quatre millions de morts néonatales chaque année - bilan et actions possibles[internet]. *Médecine/Sciences*; [cited 2015 Mar 6]. Available from: <http://www.hal.inserm.fr/inserm-00103766/fr/>.
3. 3.The WHO Young Infants Study Group. Bacterial etiology of serious bacterial infections in young infants in developing countries: results of a multicenter study. *Pediatr Infect Dis J*. 1999;18:S17-S22.
4. 4.Camacho-Gonzalez A, Spearman PW, Stoll BJ. Neonatal infectious diseases: evaluation of neonatal sepsis. *Pediatr Clin North Am*. 2013;60:367-89.
5. Bizzarro MJ, Raskind C, Baltimore RS, Gallagher PG. Seventy-five years of neonatal sepsis at Yale: 1928-2003. *Pediatrics*. 2005;116:595-602.
6. Hornik CP, Fort P, Clark RH, Watt K, Benjamin DK, Smith PB, et al. Early and late onset sepsis in very-low-birth-weight infants from a large group of neonatal intensive care units. *Early Hum Dev*. 2012;88(Suppl 2):S69-74.
7. Gerdes JS. Diagnosis and management of bacterial infections in the neonate. *Pediatr Clin North Am*. 2004;51:939-59.
8. Bonadio WA, Hennes H, Smith D, Ruffing R, Melzer-Lange M, Lye P, et al. Reliability of observation variables in distinguishing infectious outcome of febrile young infants. *Pediatr Infect Dis J*. 1993;12:111-4.
9. Gerdes JS. Clinicopathologic approach to the diagnosis of neonatal sepsis. *Clin Perinatol*. 1991;18:361-81.
10. 10.Shah BA, Padbury JF. Neonatal sepsis: an old problem with new insights. *Virulence*. 2014;5(1):170-78.
11. 11.Voora S, Srinivasan G, Lilien LD, Yeh TF, Pildes RS. Fever in full-term newborns in the first four days of life. *Pediatrics*. 1982;69:40-4.
12. 12.Weisman LE, Stoll BJ, Cruess DF, Hall RT, Merenstein GB, Hemming VG, et al. Early onset group B streptococcal sepsis: a current assessment. *J Pediatr*. 1992;121:428-33.

13. Hofer N, Müller W, Resch B. Neonates presenting with temperature symptoms: role in the diagnosis of early onset sepsis. *Pediatr Int.* 2012;54:486-90.
14. Klein JO. Bacterial infections of the urinary tract. In: Remington JS, Klein JO, editors. *Infectious disease of the fetus and newborn infant.* 5th ed. Philadelphia: WB Saunders; 2001.p. 1035-46.
15. Visser VE, Hall RT. Urine culture in the evaluation of suspected neonatal sepsis. *J Pediatr.* 1979;94:635-8.
16. Di-Geronimo RJ. Lack of efficacy of the urine culture as part of the initial work-up of suspected neonatal sepsis. *Pediatr Infect Dis J.* 1992;9:764-6.
17. Shaw KN, Gorelick MH. Urinary tract infection in the pediatric patient. *Pediatr Clin N Am.* 1999;46:1111-24.
18. Klein JO, Marcy M. Bacterial sepsis and meningitis. In: Remington JS, Klein JO, editors. *Infectious disease of the fetus and newborn infant.* 5th ed. Philadelphia: WB Saunders; 2001.p. 943-98.
19. Amelia N, Amir I, Trihono PP. Urinary tract infection among neonatal sepsis of late-onset in Cipto Mangunkusumo Hospital. *Paediatrica Indonesiana.* 2005 Sep-Oct;45(9-10):217-22.
20. Omar C, Hamza S, Bassem AM, Mariam R. Urinary tract infection and indirect hyperbilirubinemia in newborns. *N Am J Med Sci.* 2011 Dec;3(12):544-47.
21. Omar C, Hamza S, Bassem AM, Mariam R. Urinary tract infection and indirect hyperbilirubinemia in newborns. *N Am J Med Sci.* 2011 Dec;3(12):544-47.
22. infants: risk factor analysis. *Rev Hosp Clin Fac Med S Paulo.* 2000;55:9-16.
23. Bauer S, Eliakim A Klein JO. Bacterial infections of the urinary tract. In: Remington JS, Klein JO, editors. *Infectious disease of the fetus and newborn infant.* 5th edition. Philadelphia: WB Saunders; 2001. p. 1035-46.
24. Gonzalez R. Urinary tract infection. In: Behrman RE, Kliegman RM, Jenson HB, editors. *Nelson's textbook of pediatrics.* 17th edition. Philadelphia: Saunders; 2004. p. 549.
25. To T, Agha M, Dick PT. Cohort study on circumcision of newborn boys and subsequent risk of urinary tract infection. *Lancet.* 1998;352:1813-16.
26. Schoen EJ, Colby CJ, Ray GT. Newborn circumcision decreases incidence and costs of urinary tract infections during the first year of life. *Pediatrics.* 2000;105:789-93.
27. Wiswell TE. The prepuce, urinary tract infections, and the consequences. *Pediatrics.* 2000;105:860-1.
28. Wiswell TE, Miller GM, Gelston HM. The effect of circumcision status on periurethral bacterial flora during the first year of life. *J Pediatr.* 1988;113:442-6.
29. Abbott GD. Neonatal bacteriuria: A prospective study of 1460 infants. *BMJ.* 1972;1;267-9.
30. Littlewood JM, Kite P, Kite BA. Incidence of neonatal urinary tract infection. *Arch Dis Child* 1969;44:617-9.
31. Lohr JA, Donowitz LG, Sadler JE 3rd. Hospital acquired urinary tract infection. *Pediatrics* 1989;83:193-6.
32. Davies HD, Jones ELF, Sheng RY. Nosocomial urinary tract infections at a pediatric hospital. *Pediatr Infect Dis J.* 1992;11:349-51.
33. Tamim MM, Alesseh H, Aziz H. Analysis of the efficacy of urine culture as part of sepsis evaluation in the premature infant. *Pediatr Infect Dis J.* 2003;22:805-8.
34. Purniti P S. Uji diagnostik beberapa parameter klinis untuk diagnosis ISK pada sepsis neonatorum [thesis]. Denpasar (Bali, Indonesia): Medical School, Udayana Univ.; 2002.
35. Falcao MC, Leone CR, D'Andrea RA, Berardi R, Ono NA, Vaz VAC. Urinary tract infection in full-term newborn, Pomeranz A, Regev R, Litmanovitz I, Arnon S, et al. Urinary tract infection in very low birth weight preterm infants. *Pediatr Infect Dis J.* 2003;22:426-9.