ORIGINAL ARTICLE

Bacterial uropathogens causing late onset sepsis in neonates at a tertiary care hospital.

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ABSTRACT... Objective: To find out different bacterial isolates of urinary tract infection (UTI) in neonates with late onset sepsis (LOS) at a tertiary care hospital. **Study Design:** Cross-sectional study. **Setting:** Department of Pediatrics, Nishtar Hospital Multan. **Period:** August 2020 to February 2021. **Material & Methods:** A total of 176 neonates with LOS and culture positive UTI were enrolled. The urine samples were sent to the institutional laboratory for isolation and identification of the causative agents. Baseline information like age, gender, socioeconomic status, family system and maternal literacy were noted. Once registered, the urine samples were sent to the laboratory of the hospital for isolation and identification of the causative agents. Urine samples were collected within 48 hours of admission. **Results:** Of the 176 neonates, 110 (62.5%) were male while 66 (37.5%) were female. Overall, mean age was 8.64±5.22 days. There were 90 (51.1%) neonates who belonged to rural areas and 86 (48.9%) to urban areas. Poor socioeconomic status was noted in 116 (65.9%) neonates. In terms of maternal literacy, 118 (67.0%) mothers were illiterate. Overall, mean gestational age was 38.59 ± 2.17 weeks. Escherichia coli (E. coli) was the predominant causative organism noted among 146 (83.0%) neonates whereas Klebsiella was seen in 23 (13.1%) while other bacterial isolates were Proteus 2 (1.1%), Pseudomonas aeruginosa 1 (0.6%), Enterobacter aerogenes 1 (0.6%), Enterococcus fecalis 1 (0.6%), Staphylococcus aureus 1 (0.6%) and Group B Streptococcus 1 (0.6%). **Conclusion:** High frequency of Escherichia coli was observed followed by Klebsiella among neonates having urinary tract infection presenting with late onset of sepsis in our study.

Key words: Bacterial Isolates, Sepsis, Urinary Tract Infection.

INTRODUCTION

In 2019, 2.4 million children died during 1st months of their life.[1] In developing countries among neonates, around 50% deaths are estimated to occur within 24-hours of life whereas 75% deaths occur within 1st week of life.[2] Septicemia and prematurity are considered to be the most frequent causes of deaths among neonates.[3,4] In Asian populations, incidence of neonatal sepsis ranges between 7-38/1000 live-births.[5]

Disease spectrum of septicemia may influence due to factors like types of causative pathogen, portal of entry, susceptibility as well as the response of the host.[6] Neonatal sepsis can be categorized as early onset sepsis (EOS) and late onset sepsis (LOS). The EOS is defined as confirmed infection in the blood or cerebrospinal fluid (CSF) among neonates younger than 72 hours of age while LOS is described as onset such as infection after 72 hours to 28 days of life.[7]

The LOS may occur because of vertical, horizontal or nosocomial infections while most frequent manifestations are found to be meningitis (30-40%), bacteremia (40%), septic arthritis (10%) and UTI (15%). Omphalitis and osteomyelitis are some of the rare manifestations of LOS.[8] Among developing parts of the world, gram-negative bacteria are the commonest causative agents of sepsis while in developed countries, group-B Streptococcus are the most frequent etiological agents of neonatal sepsis.[9,10]

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The LOS is mainly caused by Staphylococci agents and E. coli. Some of the most notable risk factors of LOS are low birth-weight, utilization of intravascular catheters, endotracheal intubation, assisted ventilation, surgeries, and contact with colonized person or contaminated equipment.[11,12]

Riaz L et al evaluating neonates having LOS with UTI reported E. coli to be responsible for 84.2% cases while Klebsiella in 13.2 % isolates of UTI with late onset of sepsis.[13] As spectrum of causative agents responsible for LOS because of UTI may change over a period of time across regions and even in hospitals of a country, it is very important to perform periodic surveillance to find out any change in the pattern of causative agents responsible for neonatal sepsis so that prompt treatment can be offered. This study was done to find out different bacterial isolates of UTI in neonates with late onset of sepsis at a tertiary care hospital. The results of this study were thought to help clinicians to ascertain and anticipate causative agents which will ultimately lead to the proper management of these patients contributing to reduction in disease related morbidity and mortality in these neonates.

MATERIAL & METHODS
This cross-sectional study was done at The Department of Pediatrics, Nishtar Hospital Multan, from August 2020 to February 2021. Approval from Institutional Ethical Committee was taken. Written consent was acquired from all study participants.

A sample size of 176 neonates was calculated using formula: $n = z^2pq/d^2$

Where z = 1.96, p = 13.2%[13] (taking Klebseilla least proportion), q=100-p and margin of error as d= 5%

Inclusion criteria was neonates aged 4-28 days of both genders having late onset of sepsis with UTI. Late onset of sepsis was defined in terms of any 2 of followings or more; total leukocyte count < 5000 or > 20000 or absolute neutrophil count < 1000 on complete blood count, temperature instability (>100 ^{0}F or < 96 ^{0}F), raised serum C-Reactive

Protein levels > 6 mg/dl and blood pressure instability. The UTI was labeled as urinalysis showing presence of any 2; positive pus cells, positive leukocyte esterase, positive nitrite with positive urine culture. Any growth observed on urine culture was tested for colony morphology, gram staining and biochemical tests. Exclusion criteria was neonates having open neural tube defects like encephalocele, myelocele and myelomeningocele, or those who had congenital heart disease (assessed clinically). Neonates who were already taking antibiotics in the past 72 hours were also excluded.

Baseline information like age, gender, socioeconomic status, family system and maternal literacy were noted. Once registered, the urine samples were sent to the laboratory of the hospital for isolation and identification of the causative agents. Urine samples were collected within 48 hours of admission. All the relevant information was noted in the study proforma specifically designed for this study.

All the study data was entered and analyzed using SPSS version 26.0. Descriptive statistics was applied to calculate mean and standard deviation for the age. Frequencies and percentage was tabulated for the categorical variables like gender, socioeconomic status, age groups, maternal qualification, residential status and causative agents.

RESULTS
Out of a total of 176 neonates, 110 (62.5%) were male and 66 (37.5%) female. Overall, mean age was 8.64±5.22 days (ranging 4 days to 25 days). There were 90 (51.1%) neonates belonging to rural areas while remaining 86 (48.9%) were from urban areas. Poor socioeconomic status was noted in 116 (65.9%) neonates. In terms of mothers literacy, 118 (67.0%) were illiterate. Overall, mean gestational age was 38.59±2.17 weeks while 32 (18.2%) neonates were born preterm. Table-I is showing characteristics of the neonates involved in the present study.

Characteristics		Number (%)
Gender	Male	110 (62.5%)
	Female	66 (37.5%)
Age (days)	Up to 10 days	143 (81.2%)
	More than 10 days	33 (18.8%)
Residential Status	Rural	90 (51.1%)
	Urban	86 (48.9%)
Socioeconomic status	Poor	116 (65.9%)
	Middle Income	60 (34.1%)
Maternal literacy	Illiterate	118 (67.0%)
	Literate	58 (33.0%)
Preterm		32 (18.2%)
Exclusive Breastfeeding		66 (37.5%)

Table-I. Characteristics of the neonates. (n=176)

It was observed that E. coli was the predominant causative organism noted among 146 (83.0%) neonates whereas Klebsiella was seen in 23 (13.1%) while other bacterial isolates were Proteus 2 (1.1%), Pseudomonas aeruginosa 1 (0.6%), Enterobacter aerogenes 1 (0.6%), Enterococcus fecalis 1 (0.6%), Staphylococcus aureus 1 (0.6%) and Group B Streptococcus 1 (0.6%). as shown in Figure-1.
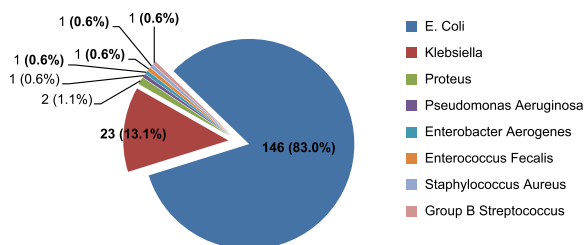

Figure-1. Distribution of causative organisms among study cases. (n=176)

DISCUSSION

Infection is considered to be a major predictor of hospitalization, morbidity and mortality. The incidence of UTI rises postnatal age, ranging between 1- 2% in the 1st 72 hour following birth and it can escalate as much as 25% after 72 hours of life.[14,15]

Our study found that 62.5% neonates were male. A study done by Mohseny AB et al evaluating neonates with LOS because of UTI revealed that 55.5% of the cases were male.[16] A local study done by Ahmed E et al evaluating neonates with sepsis found 57.1% of the study cases to be male which is close to what we noted in the present study.[17] Al-Zwaini et al analyzing cases of neonatal sepsis found higher male predominance as 80% of their neonates were male.[18]

Mean age of our study cases was 8.64±5.22 days. We also noted that 143 (81.3%) neonates were aged less than or equal to 10 days. Ahmed et al in another local study reported overall mean of the neonates with sepsis to be 6.7±4.9 days which is close to our study results.[17] In this study, 51.1% neonates belonged to rural areas while 65.9% were having poor socioeconomic status. Al-Zwaini et al reported 69.1% of neonates with sepsis to be from rural areas which is in compliance with our study results.[18] Overall, mean gestational age was 38.59±2.17 weeks and preterm birth was noted in 18.2% of our study cases. Mathai et al reported mean gestational age to be 38.5±2.2 weeks[19] while Al-Zwaini et al reported 20% cases of neonatal sepsis to be preterm births which is close to what we found.[18] In the present work, E. coli was the predominant causative organism in 83.0% neonates and Klebsiella 13.1%. Madhu et al reported E.coli to be responsible for 53% cases and Klebsiella in 23%[20] while another study reported E.coli to be present in 84.2% and Klebsiella in 13.2% isolates of UTI with LOS.[13]

Our study had some limitations as well. As this was a single center cross-sectional study with a relatively small sample size, further studies involving multiple centers with a large sample size will help confirming the findings of the present study. We were unable to evaluate the sensitivity and resistance patterns of various antibiotics routinely used against causative agents identified in the present study. We also could not evaluate the outcomes among present set of neonates.

CONCLUSION

High frequency of Escherichia coli (E. coli) was observed followed by Klebsiella among neonates having urinary tract infection presenting with late onset of sepsis in our study. Early diagnosis of bacterial pathogens followed by timely management can help reduce burden of related

morbidities and mortalities in these patients which will not only provide psychosocial relief to the suffering families but will also reduce extra hospital care expenditures by healthcare authorities.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

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2	Ateeq Ur Rehman	Literature Review, Data collection.	
3	Afsheen Asghar Khan	Methodology, Data analysis.	
4	Irfan Ali	Literature review, Introduction.	
5	Nasir Iqbal	Data collection, Data analysis.	
6	Muhammad Azam Khan	Discussion, Proof reading.	