



To Assess the Culture Proven Neonatal Sepsis at a Tertiary Care Centre: An Institutional Based Study

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Abstract

Background: *Organisms causing neonatal sepsis vary in different regions and also change with time in the same area. The aim of this study was to evaluate the epidemiology of culture-proven neonatal sepsis.*

Material & Methods: *This was a retrospective descriptive study conducted in the neonatal unit of Gujrat Adani Institute of Medical sciences, Bhuj, Gujrat. It consisted of patients with a positive blood culture during the study period. The clinical data of patients with culture-proven neonatal sepsis were reviewed. Patients with bacteraemia but with no other features suggestive of sepsis or those with organisms considered as contaminants were excluded. Infants who were in the neonatal unit beyond 28 days of life were also excluded from the study.*

Results: *Our study showed that there was no statistically significant differences in the sex, place of birth and mode of delivery between cases of EOS and LOS. There were 213 microorganisms isolated on blood culture of 150 patients with culture proven NNS during the study period. Of the 213 microorganisms, gram negative organisms were the most commonly isolated organisms in cases of culture-proven NNS [105 (49.29%)].*

Conclusion: *We concluded that Gram-negative microorganisms comprised the majority of the neonatal sepsis, with ESBL Klebsiella pneumoniae and A. baumannii being the most prevalent.*

Keywords: *Neonatal sepsis, Gram negative bacteria, Gram positive bacteria, Fungi.*

Introduction

The World Health Organization approximate that there are about 5 million neonatal deaths a year globally.^{1,2} Ninety eight percent of these deaths occur in developing countries.^{1,2} Neonatal sepsis (NNS) is a significant cause of death in developing countries.^{3,4} It is a cause of about 1.6 million deaths per annum in developing countries.¹

Organisms causing sepsis vary significantly between different neonatal units.^{4,5} Even in the same unit, the causes of sepsis changes over time.^{6,7} Furthermore, the antibiotic sensitivity of the organisms changes over time.^{1,4} There has been a worldwide increase in the number of multidrug resistant organisms causing sepsis. Ongoing surveillance of the causes of neonatal sepsis and their antibiotic sensitivity is

paramount.^{1,4} Surveillance data is useful in the design of effective infection control programs and in guiding empiric antibiotic therapy in neonatal sepsis.^{3,8}

Neonates can be regarded as immune compromised individuals.^{9,10} They have a series of defects in their specific and nonspecific immunity, which predisposes them to infection.⁹⁻¹¹ Their immune dysfunction is characterized amongst others by decreased phagocytic activity of white cells, decreased cytokine production and impaired immunoglobulin production. Physical barriers to infections such as the skin are weak and thin, and may be easily interrupted.¹¹

Preterm delivery and low birth weight are well-established risk factors for neonatal sepsis.¹²

Reports from India showed 50-60% of septic babies are premature babies and those with birth weight less than 1500g are more vulnerable.²

A 10 year survey of NNS in a tertiary care neonatal unit in India, showed that in the first 5yrs of the study *Enterobacter aerogenes* was the most common cause of late-onset sepsis whereas *Staphylococcus aureus* became the main organism causing LOS in the later 5 years.⁴ The aim of this study was to evaluate the epidemiology of culture-proven neonatal sepsis.

Material & Methods

This was a retrospective descriptive study conducted in the neonatal unit of Gujrat Adani Institute of Medical sciences, Bhuj, Gujrat. It consisted of patients with a positive blood culture during the study period. The clinical data of patients with culture-proven neonatal sepsis were reviewed. Patients with bacteraemia but with no other features suggestive of sepsis or those with organisms considered as contaminants were excluded. Infants who were in the neonatal unit beyond 28 days of life were also excluded from the study.

Inclusion Criteria

- A neonate was defined as defined as an infant in the first 28 days of life

- Culture-proven sepsis was defined as a pathogenic organism, either bacterial or fungal isolated on blood culture with other clinical and laboratory features consistent with infection.
- Laboratory features of sepsis included an abnormal white cell count, reduced platelet count and/ or a CRP >10. Age appropriate definitions of low or high white cell count and reduced platelets count were used.
- The following organisms were considered to be contaminants:
 1. *Micrococcus species*
 2. *Bacillus species*
 3. *Corynebacterium species*
 4. *Streptococcus viridans*
- Coagulase negative Staphylococcus was considered significant if two blood cultures drawn within 72-hrs of each other grew the same organism or there was a single positive blood culture in association with other laboratory features of sepsis.
- When one significant organism was isolated from the same patient within 7 days, this was considered to be a single episode of sepsis.

Sepsis was categorized into early-onset and late-onset sepsis. Early-onset sepsis was defined as sepsis occurring within 72-hrs of life and LOS as sepsis occurring after 72-hrs of life.

Results

Our study showed that there was no statistically significant differences in the sex, place of birth and mode of delivery between cases of EOS and LOS (table 1).

There were 213 microorganisms isolated on blood culture of 150 patients with culture proven NNS during the study period. Of the 213 microorganisms, gram negative organisms were the most commonly isolated organisms in cases of culture-proven NNS [105 (49.29%)]. Amongst the cases with gram negative organisms, most were due ESBL *Klebsiella pneumoniae* [74 (70.47%)], *Acinobacter baumannii* [18 (17.14%)] and *E.coli*

[10 (9.52%)]. Gram positive organisms constituted 42.25% (90/213) of the organisms isolated. Coagulase negative Staphylococcus [50 (55.55%)] and MRSA [29 (32.22%)] were the most common gram positive organisms isolated.

Yeasts accounted for 8.45% (18/213) of the isolated organisms and the following yeasts were isolated; *C. albicans* [13(72.22%)] and *C.parapsilosis* [5(27.77%)] (table 2).

Table 1: Patient clinical data

| Patient characteristics | | All cases of NNS (N=150) | Early onset sepsis (N=22) | Late onset sepsis (N=128) | P-value |
|-------------------------|---------|--------------------------|---------------------------|---------------------------|---------|
| Sex | Male | 89 (59.33%) | 16 (72.72%) | 73 (57%) | 0.087 |
| | Female | 61 (40.66%) | 6 (27.27%) | 55 (43%) | |
| Place of birth | Inborn | 105 (70%) | 18 (81.81%) | 86 (67.18%) | 0.165 |
| | Outborn | 42 (28%) | 4 (18.18%) | 38 (29.68%) | |
| | Unknown | 3 (2%) | 0 (0%) | 4 (3.12%) | |
| All cause of mortality | | 36 (24%) | 6 (27.27%) | 30 (23.43%) | 0.97 |
| Mode of delivery | NVD | 90 (60%) | 14 (63.63%) | 77 (60.15%) | 0.21 |
| | C/S | 51 (34%) | 7 (31.81%) | 35 (27.34%) | |
| | Unknown | 9 (6%) | 1 (4.54%) | 16 (12.5%) | |

Table 2: Organisms causing NNS

| Organism | No. (Total 213) | Percentage |
|--------------------------------|-----------------|------------|
| Gram positive organism (N=90) | | 42.25% |
| GBS | 2 | 0.938% |
| MRSA | 29 | 13.61% |
| CONS | 50 | 23.47% |
| <i>E. faecalis</i> | 7 | 3.28% |
| <i>E. faecium</i> | 2 | 0.938% |
| Gram negative organism (N=105) | | 49.29% |
| ESBL <i>K. pneumonia</i> | 74 | 34.74% |
| <i>A. Baumannii</i> | 18 | 8.45% |
| <i>E. coli</i> | 10 | 4.69% |
| <i>Pseudomonas aeruginosa</i> | 2 | 0.938% |
| <i>E. cloacae</i> | 1 | 0.469% |
| Fungi (N=18) | | 8.45% |
| <i>C. Albicans</i> | 13 | 6.10% |
| <i>C. Parapsilosis</i> | 5 | 2.34% |

Discussion

The finding of this study confirms that neonatal sepsis is an important cause of morbidity in newborns and that the incidence is on the increase at GAIMS neonatal unit. The incidence of NNS is probably higher than estimated by this study, because patients with clinical or laboratory signs suggestive of sepsis but with negative blood cultures were not included. Although microbial cultures of blood or other sterile body fluids are considered the gold standard in the diagnosis of neonatal sepsis they are subject to low sensitivity.¹³

Similar to the previous studies in the facility the proportion of LOS and EOS remained the same,

with predominance of LOS.^{3,4} Studies by Motara et al and Ballot et al, showed that LOS accounted for 94.3 % and 93.5 % of cases of NNS respectively.^{3, 4} In this study, LOS accounted for 85.33% of cases.⁴ Other studies in both developing and developed countries, also showed that LOS occurred more frequently than EOS.^{14,15} Newborns are considered to be immunocompromised, especially when premature.^{9,10} There are a number of factors which predispose premature and low birth weight infants to infections. The high proportion of gram-negative microorganisms as a cause of neonatal sepsis is similar to findings from surveillance in other developing countries. Similar to other developing

countries gram-negative organisms were predominant in both EOS and LOS.^{1,16} The most common isolate overall was *K. pneumoniae*, followed by CNS, MRSA and *A. baumannii*. The predominance of *K. pneumoniae* in the current study accords with several reports from Nigeria and other developing countries.¹⁶ CNS, a gram-positive was the most common isolate in EOS. CNS have remained an important cause of NNS in the unit accounting for 23.7% of the isolated microorganisms in the current study. This is contrary to reports from other developing countries where CNS are usually amongst the least common organisms.¹⁷ The reason for this might be because isolated CNS is excluded from analysis as it is often considered to be a contaminant.¹⁷ Although CNS is often considered a contaminant, it is a pathogen in neonates, compromised hosts and patients with foreign bodies.⁸ Further evaluations such as a repeat blood culture are required to determine the clinical significance of CNS.^{8,18} The importance of CNS as a cause of NNS has been reported by studies from developed countries and Asian countries.⁸ A one year prospective study in eight neonatal units in Australia, reported that CNS was the most commonly isolated organism.⁸

A study by Ballot et al showed that 70.8% of the isolated *K. pneumoniae* were ESBL producing compared to 70.47% in the current study.⁴ *S. aureus* and *A. baumannii* are two other organisms that are becoming predominant in the unit. The importance of *A. baumannii* as a cause of NNS in the unit was noted by Ballot et al, when this microorganism accounted for 10% of the bacterial isolates compared to the previous study where this organism was not isolated.^{3,4}

This study confirms that sepsis is a significant cause of mortality newborns. Forty-five patients with NNS died before hospital discharge, giving an all-cause mortality of 24%. All-cause mortality for EOS was 27.27% and for LOS was 23.43%. In keeping with findings from other studies, mortality was significantly associated with gram negative sepsis.^{3,4} Other factors associated with

mortality from NNS are delivery outside the GAIMS, vaginal delivery and lack of antenatal care.

Conclusion

We concluded that Gram-negative microorganisms comprised the majority of the neonatal sepsis, with ESBL *Klebsiella pneumoniae* and *A. baumannii* being the most prevalent. CoNS remains an important cause of NNS, and is the most prevalent gram-positive organism isolated.

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