International Journal of Contemporary Pediatrics
*Arora V et al. Int J Contemp Pediatr. 2017 May;4(3):1056-1060*
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20171727

**Original Research Article**

# Meningitis in late onset sepsis

**Vivek Arora*, Lalit Mohan Sharma, Dinesh Jangid, Vijay Choudhary, Ram Prakash Bairwa, Sanjay Singla**

Department of Pediatrics, Rabindranath Tagore Medical college, Udaipur, Rajasthan, India

**Received:** 15 March 2017
**Accepted:** 07 April 2017

***Correspondence:**
Dr. Vivek Arora,
E-mail: vivekarora12udr@gmail.com



## ABSTRACT

**Background:** Neonatal sepsis contributes substantially to neonatal morbidity and mortality and is an ongoing major global public health challenge. In developed countries, this incidence of neonatal meningitis is 0.3 per 1000 live births. In developing countries, the reported incidence of neonatal meningitis is much higher at 0.8-6.1 per 1000 live births, with a mortality of 40-58%. So, this study was undertaken to estimate the incidence of meningitis in late onset sepsis.
**Methods:** This study was conducted in out born NICU of R.N.T. Medical College, Udaipur (Raj.) from November 2016 to February 2017. All neonates between age 7 days to 28 days of life were included in the study. A sepsis screening and blood culture were sent for all neonates. All positive sepsis screen patients were taken for Lumber Puncture. CSF was examined with positive sepsis screen and high clinical suspicion of meningitis. CSF culture was sent for every patient. CT scan was done in patient with proven bacterial meningitis.
**Results:** A total of 90 patients with suspected late onset sepsis were admitted. Most of the neonates were admitted with complain of temperature instability and poor feeding. Meningitis was observed in 55 out of 90 cases (61.11%). Out of 55 patients CSF culture was found positive in 70% cases. Most common organisms were E. coli in 50% cases, *Klebsiella* in 15% and *Enterobactor* in 10%. Mortality was around 45.5% (n=25).
**Conclusions:** Neonatal meningitis is a major disease that results in death and significant mortality and morbidity in neonates.

**Keywords:** Late onset sepsis, Lumber Puncture, Meningitis

## INTRODUCTION

Neonatal sepsis contributes substantially to neonatal morbidity and mortality and is an ongoing major global public health challenge.[1] Neonatal sepsis is divided into early onset sepsis (EOS) and late onset sepsis (LOS). EOS reflects transplacental or ascending infection from maternal genital tract, whereas late onset is associated with nosocomial or community acquired infection. Neonatal meningitis is a major disease that results in significant morbidity worldwide. Of all age groups, neonatal period has the highest incidence of meningitis. In developed countries, this incidence of neonatal meningitis is 0.3 per 1000 live births.[2] In developing countries, the reported incidence of neonatal meningitis is much higher at 0.8-6.1 per 1000 live births, with a mortality of 40-58%.[3]

This is likely an underestimation of true incidence. For infants in the intensive care nursery, 30-50% does not have a Lumber Puncture (LP) performed and when a LP is performed, more than 75% of time it occurs after the initiation of antibiotics, possibly biasing cerebrospinal fluid (CSF) culture results.

True values may actually be higher because of underreporting in regions with limited resources, diagnostic testing and access to health care. So, this study

was undertaken to estimate the incidence of meningitis in late onset sepsis. The objective of the study was to know the incidence of neonatal meningitis in late onset sepsis. Etiological organism in meningitis. Mortality in meningitis. Outcome in meningitis.

## METHODS

This study was conducted in out born nursery of RNT Medical College, Udaipur (Raj.) from November 2016 to February 2017 after taking permission from ethical committee. All neonates between age 7 days to 28 days of life were included in the study. All out born babies referred from various primary health care centre and community health care centre with clinical signs and symptoms of sepsis were included in the study.

Birth weight, Gestational age (GA), day of life, clinical sign and symptoms were recorded on the predesigned proforma. All newborn with suspected neonatal sepsis were included in the study after taking proper consent from the family. A sepsis screening and blood culture were sent immediately.

Sepsis screen included (TLC <5000/mm$^3$, ANC <1800/mm$^3$, CRP >1mg/dl and micro ESR >15mm, IT ratio >0.2). Presence of two of the 5 parameters were taken as positive. All positive sepsis screen patients were taken for Lumber Puncture. CSF was examined with positive sepsis screen and high clinical suspicion of meningitis.

Normal CSF values were taken as 0-30 cells/mm$^3$ PMN 60%. CSF proteins 20-170 mg/dl. CSF glucose less than 2/3 blood sugar or <52 mg/dl. CSF culture was sent for every patient. CT scan was done in patient with proven bacterial meningitis.

## RESULTS

A total of 90 patients with suspected late onset sepsis were admitted in out born nursery of RNT Medical College, Udaipur.

**Table 1: Frequently seen sign and symptoms.**

| Sign/symptoms | % of occurrence |
|---|---|
| Fever/ hypothermia | >50 |
| Poor feeding/lethargy | >50 |
| Vomiting, respiratory distress | 20 |
| Convulsion | 40 |
| Irritability | 32 |
| Full fontanel | 26 |

Most of the neonates were admitted with complain of temperature instability and poor feeding. Around 40% neonates were admitted with convulsion either in past or at the time of admission. Approximate 26% neonates were admitted with bulging anterior fontanel. 40% neonates were admitted with a birth weight between 1 and 1.5 kg followed by between 1.5 and 2.0 kg which constitute around 35% of total neonates.

**Table 2: Birth weight wise distribution.**

| Birth weight | % age of neonates |
|---|---|
| 1 - 1.5 Kg | 40% |
| 1.5 - 2 Kg. | 35% |
| 2 - 3 Kg. | 25% |

Most of the neonates were admitted at the age of 15-21 days (40%) and neonates with age 7-14 days and 21-28 days were 30% each.

**Table 3: Average day of life of presentations.**

| Day of life | % age of neonates |
|---|---|
| 7-14 days | 30% |
| 15-21 days | 40% |
| 21-28 days | 30% |

CSF: CSF was abnormal in 55 patients out of 90 patients. CSF cells >100 were seen in 70%, low glucose in 60% and increased proteins in 65% of total samples. Meningitis was observed in 55 out of 90 cases (61.11%).

Out of 55 patients CSF culture was found positive in 70% cases. Most common organisms were *E. coli* in 50% cases, *Klebsiella* in 15%, *Enterobactor* in 10%, Coagulase negative staph in 15%, *Citrobactor* in 5%, *Serratia* in 2%, *Streptococcus pneumonia* in 1% and Staph aureus in 2% cases. Blood culture was positive in 35% of total cases.

CT scan was done in 55 cases with meningitis. 60% showed normal CT scan, 20% showed post meningitic hydrocephalus, 15% showed Ventriculitis and 5% showed subdural empyma. Mortality was around 45.45% n=25).

## DISCUSSION

The major burden of neonatal sepsis and meningitis occurs in developing world.[4] Meningitis is more common in neonatal period than at any other time. The new born is particularly susceptible to infection as the immature immune system is deficient in humoral and cellular immune response. Main neonatal risk factor for developing meningitis include prematurity and low birth weight (LBW), Low socioeconomic status. In our study 80% patients were LBW and 75% were having low socioeconomic status. The etiology of neonatal meningitis in the developing world differs from that of developed world. In developed countries, two predominant pathogens isolated from CSF in neonates are group *b streptococci* (GBS), *E. coli*, *Listeria monocytogens*, *streptococcus pneumonia*, *staphylococci*.[5] In our study, most common organisms were *E. coli* 50%, *Klebsiella* 15%, *Enterobactor* 10%, Coagulase negative staph 15% and *Citrobactor* 5%.

**Table 4: Aetiology of neonatal bacterial meningitis in developing countries.**

| | References | Location | Year | Patients (n) | Age (days) | Study design | Organisms (%) | Mortality (%) | Comments |
|---|---|---|---|---|---|---|---|---|---|
| Multi-centre | Who (a, b, c) | Gambia, ethiopia, philippines, papua new guinea | 1998 | 40 | 0-90 | Prospective, descriptive | *S. Pneumonia* 43<br>*E. Coli* 13<br>*H. Influenzae* 10<br>*Acinetobacter spp.* 10 | Not available | Significant inter-site variation |
| Middle east | El-said et al. | Doha, qatar | 1998–2000 | 13 | <30 | Retrospective | *S. Agalactae* 31<br>*S. Epidermidis* 31<br>*Pseudomonas spp.* 15 | 0 | Complications in 23 |
| | Al-harthi et al. | Assir, saudi arabia | 1993–1998 | 31 | N | Retrospective | *Klebsiella spp.* 31<br>*Serratia spp.* 25<br>coagulase neg. staph 9 | 48 | Most assumed nosocomial. Major congenital abnormalities in 25s |
| | Koutouby and habibullah | Dubai, united arab emirates | 1987-1992 | 10 | 0-30 | Retrospective | *S. agalactae* 70<br>*S. epidermididis* 10<br>*Pseudomonas spp.*10<br>*Klebsiella spp.* 10 | 30 | Study of sepsis – subset with meningitis. Included vlbw and premature babies |
| | Daoud et al. | Irbid, jordan | 1993-1995 | 52 | Full term neonates | Rct | *Klebsiella spp.* 48<br>*Enterobacter spp.* 17<br>*S. aureus* 8<br>*E. coli* 8 | 25 (in control group) | Clinical trial investigating steroid as adjuncts. Csf culture and latex agglutination |
| South america and the caribbean | Moreno et al. | Panama city, panama | 1975-1992 | 107 | N | Retrospective | *Klebsiella spp.* 24<br>*S. epidermidis* 19<br>*E. coli* 16 | 35 | – |
| | Ali | Trinidad, west indies | 1988-1990 | 54 | N | Retrospective | *S. agalactae* 56<br>*S. aureus* 11<br>*Enterobacter spp.* 11<br>*E. coli* 11<br>*H. influenzae* 11 | 13 | Only 9/54 had a positive csf culture |
| Asia | Chotpitaya sunondh | Bangkok, thailand | 1982-1990 | 77 | <30 | Retrospective | *Pseudomonas spp.* 17<br>*Klebsiella spp.* 13<br>*S. agalactae* 12 | 46 | With latex agglutination and counter-immunoelec trophoresis |
| Sub-saharan africa | Molyneux et al. | Blantyre, malawi | 1996-1997 | 61 | <30 | Prospective | *S. agalactae* 23<br>*S. typhimurium* 15<br>*S. pneumoniae* 11.5<br>Gram neg. rods (other) 1.5 | 34 | Subset of 0–14 year olds |
| | Milledge et al. | Blantyre, malawi | 1996-2001 | 202 | <30 | Retrospective | *S. agalactae* 30<br>*S. pneumoniae* 23<br>*Salmonella spp.* 16 | 43 | Positive gram stain or > 20 wcc/ll but no growth in 140 further cases (mortality 21) |
| | Gebremariam | Addis ababa, ethiopia | 1987-1996 | 55 | 0-28 | Retrospective | *K. pneumoniae* 30<br>*E. coli* 23<br>*Enterobacter spp.* 13 | 40 | - |
| | Campagne | Niamey, niger | 1981-1996 | 101 | <30 | Retrospective | *S. pneumoniae* 34<br>*Salmonella spp.* 15<br>*N. meningitidis* 11 | 58 | Part of larger study |
| | Longe et al. | Benin, nigeria | 1974-1982 | 53 | <30 | Prospective | *S. aureus* 29<br>*E. coli* 20<br>*Klebsiella spp.* 8<br>*S. pneumoniae* 8 | 38 | - |

**Table 4: Continue**

| References | Location | Year | Patients (n) | Age (days) | Study design | Organisms (%) | Mortality (%) | Comments |
|---|---|---|---|---|---|---|---|---|
| Airede | Plateau state, nigeria | 1988-1990 | 36 | N | Prospective | *S. aureus* 31<br>*Klebsiella spp.* 11<br>*E. coli* 8<br>*S. pneumoniae* 8 | 33 | Nine csfs suggestive of meningitis but sterile. Five grew s. Aureus on blood culture |
| Airede et al. | Maduguri, nigeria | 1992-1995 | 69 | <30 | Prospective | *S. aureus* 26<br>*E. coli* 22 | 25 | Only 50 of 69 had positive csf cultures |
| English et al. | Kilifi, kenya | 1999-2001 | 12 | <90 | Prospective | *S. pneumoniae* 33<br>*Salmonella spp.* 17 | Not available | Part of larger study, community based |
| Laving et al. | Nairobi, kenya | 1999 (6 months) | 15 | N | Prospective, cross sectional study | *E. coli* 47<br>*S. agalactae* 27<br>*Klebsiella spp.* 13 | 67 | Latex agglutination used. Only 4/15 grew on culture |
| Nathoo et al. | Harare, zimbabwe | 1987-1988 | 94 | 0–28 | Retrospective | S. agalactae 61<br>*S. pneumoniae* 8.5<br>Other strep. spp. 8.5 | 41 | - |
| Coovadia et al. | Durban, south africa | 1981-1987 | 97 | <30 | Retrospective | *K. pneumonia* 42<br>*E. coli* 17.5<br>*S. agalactae* 15.5 | 59 | 74 low birth weight |
| Adhikari et al. | Durban, south africa | 1988-1991 | 60 | N | Retrospective | S. agalactae 35<br>*Klebsiella spp.* 28<br>*E. coli* 17 | 48 | 52 low birth weight. 5/60 culture negatives were antigen + for s. Agalactae |
| Nel | Western cape, south africa | 1981-1992 | 88 | 0–28 | Retrospective | *S. agalactae* 30<br>*E. coli* 23<br>*K. pneumonia* 15 | 34 | |
| Haffejee et al. | Durban, south africa | 1986-1989 | 9 | 0–28 | Retrospective | *S. agalactae* 89<br>*S. faecalis* 11 | Not available | Asian infants only. Only 277/2171 possibly septic neonates had lp |

Our search identified 22 studies that provided data describing the aetiology of neonatal meningitis in developing countries. These are summarized in Table 4. There was significant heterogeneity between study designs, methods and quality. The overwhelming majority of studies were performed in Africa, contributing 14 to the total (Longe et al; Coovadia et al; Haffejee et al; Nathoo et al; Airede; Adhikari et al; Gebremariam; Molyneux et al; Campagne; Nel; English et al; Laving et al; Milledge et al; Airede et al); there were a single multicentre study (WHO a, b, c), four from the Middle East (Koutouby and Habibullah; Daoud et al; Al-Harthi et al; El-Said et al), two from Latin America (Moreno et al; Ali) and one from Asia (Chotpitayasunondh).

The study with the most robust methods was a WHO supported multi-centre study that attempted to determine aetiological agents responsible for serious infection in young infants (£90 days; WHO a, b, c). Study sites were in developing countries with high neonatal mortality rates, namely Ethiopia, the Gambia, Papua New Guinea and the Philippines. Unfortunately, the study only identified a total of 40 cases of neonatal meningitis, and results varied considerably between centers, limiting the conclusions that could be made. Of the other included studies, the majority were retrospective, with varying methods, often using different inclusion/exclusion criteria and sometimes using differing diagnostic methods.

Mortality in our study was 45-55% which is higher from the developed world.

## CONCLUSION

Neonatal meningitis is a major disease that results in death and significant mortality and morbidity. Every patient with late onset sepsis should undergo lumbar puncture. CSF culture and sensitivity should be performed in every newborn undergoing lumbar puncture.

*Funding: No funding sources*
*Conflict of interest: None declared*
*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Arora V, Sharma LM, Jangid D, Choudhary V, Bairwa RP, Singla S. Meningitis in late onset sepsis. Int J Contemp Pediatr 2017;4:1056-60.