MENINGITIS;
TO DETERMINE THE FREQUENCY OF MENINGITIS IN NEONATES WITH LATE ONSET SEPTICEMIA.

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ABSTRACT... Objectives: To determine the frequency of meningitis in neonates having late onset septicemia. **Study Design:** Descriptive, cross-sectional study. **Place and Duration of Study:** Department of Pediatrics, D.H.Q, Faisalabad from August, 2015 to January, 2016. **Methodology:** 105 neonates aged between 3-28 days having late onset septicemia were included in the study through non-probability consecutive sampling. Neonates having spina bifida, anencephaly and very sick neonates, after initial stabilization were excluded. For assessment of meningitis 1ml blood sample and CSF sample were sent to the hospital pathology laboratory. Meningitis was labeled if the patient had all of the following criteria: CSF glucose less than the plasma glucose by ≥50%, CSF white cell count >10/cumm and CSF protein >80 mg/dl. **Results:** Out of 105 patients, mean age was 13.53±6.99 days. 59 (56.2%) patients were male and 46 (43.8%) patients were females. The prevalence of meningitis was found to be 20 (19%). 11 (18.6%) male patients had meningitis while 9 (19.6%) female patients had meningitis with p-value = 0.905. Meningitis is more common in patients having age between 4-15 days 17 (26.6%) than the 3 (7.3%) patients having age between 16-27 days with p-value = 0.014. **Conclusion:** Meningitis is a common disorder in neonates having late onset septicemia. By knowing the magnitude of this complication preventive measure can be adopted to minimize the burden of this disease.

Key words: Meningitis, Late Onset Septicemia, Spina Bifida, Anencephaly.

INTRODUCTION

Neonatal sepsis is an important cause of neonatal morbidity and mortality.[1] In neonatal sepsis, initially there is bacteremia followed by signs and symptoms of systemic infection during first month of life.[2] Neonatal sepsis is categorized in two stages depending upon the onset, early onset sepsis (EOS) and late onset sepsis (LOS). LOS is defined as occurrence of infection after 72 hrs of life.[3,4]

Sepsis is the third most common cause of death in hospitalized patients.[5,6] The highest rate of sepsis is being observed in Africa and Asia (23-38/1,000 live births) and the lowest, in countries like the U.S. and Australia (range, 1.5-3.5 /1,000 live births).[1]

Most common organisms involved in neonatal sepsis are gram positive and gram negative bacteria and Candida. Many other organisms can also be involved depending upon time and place.[7] The signs and symptoms of neonatal sepsis consist of fever or hypothermia, cyanosis, respiratory difficulties, apnea, reluctance to feed, lethargy or irritability, hypotonia, fits, bulging fontanel, bleeding problems, abdominal distention, gauiac-positive stools, unexplained jaundice, or more importantly, "not looking well".[8]

Late-onset neonatal septicemia results in serious complications like broncho pulmonary dysplasia, short bowel syndrome, parenteral nutrition–associated liver disease, anemia of chronic disease and serious neurodevelopment sequalae. It also increases the risk of mortality.[9] Meningitis is most common cause of sepsis in neonates. In different studies, prevalence of meningitis varies from 0.3% to 3%.[10]

Meningitis is common presentation of LOS,[11] and it results in serious neurological sequale and

impairment.[12]

In a study conducted in India showed the prevalence of meningitis as 22.5% in neonates with LOS.[10]

To the best of my knowledge, there is little information in Pakistan regarding the relation of meningitis with LOS in neonates. As there is variability in literature and no attention is paid in this regard in normal practice, so I want to conduct this study to assess the exact burden of meningitis in neonates with LOS in our population for optimizing neonatal care.

The aim of the study was to determine the frequency of meningitis in neonates having late onset septicemia

METHODOLOGY

It was a cross sectional study, carried out in the Department of Pediatrics, D.H.Q Hospital, Faisalabad, on 105neonates of late onset septicemia from August 2015 to January 2016 through non-probability consecutive sampling. Permission was taken from the hospital ethical committee and informed consent was taken from all the patients.

Sample size was calculated by using WHO sample size calculator for single proportion, using Prevalence of meningitis in late onset septicemia neonates as22.5%[10] with 95%confidence level and taking absolute precision as 8%.One hundred and five patients were dealt by non-probability, consecutive sampling technique.

Neonates of both genders between the ages of 3-28 days with late onset septicemia were included in the study. Late onset septicemia was defined as neonates older than 72 hours presenting with all of following symptoms, i.e., excessive high pitched crying, cyanosis (blue coloration of lips and skin), no spontaneous movements, tachypnea (respiratory rate more than 60/min), hypothermia (temperature below 95^0 F) and CRP > 6mg/L. Patients with spina bifida, anencephaly, other neural tube defects and very sick neonates, after initial stabilization were excluded.

Demographic details of all patients were noted. For assessment of meningitis 1ml blood sample and CSF sample were sent to the hospital pathology laboratory and it was reported by pathologist. Meningitis was labeled if the patient will have all of the followings: 1) CSF glucose less than the plasma glucose by $\geq$50%, 2) CSF white cell count >10/cumm, 3) CSF protein >80 mg/dl.

All the data was entered and analyzed on SPSS Version21. Mean $\pm$ Standard Deviation was calculated for age. Frequency and percentages will be calculated for gender and meningitis. Effect modifiers like age and gender were stratified and post-stratification chi-square test was applied. A p-value $\leq$ 0.05 was considered as significant.

RESULTS

Table-I shows the demographic characteristics of the patients. Majority of the patients were between 4-15 days (61%) of age and least patients were 16-27 days old (39%) with mean age 13.53$\pm$6.99 days. While minimum age was 4 days and maximum age was 27 days. Out of 105 patients, 59 (56.2%) patients were male and 46 (43.8%) patients were females.

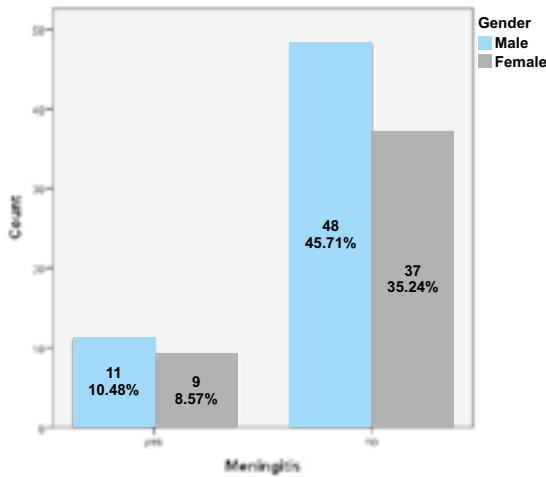| Demographic characteristics	
Age	Mean 13.53$\pm$6.99 days
4-15 days	64 (61%)
16-27 days	41 (39%)
Gender	
Male	59 (56.2%)
Female	46 (43.8%)
Table-1. Demographic characteristics	

Table-II shows the distribution of meningitis among 105 patients of late onset septicemia. 20 (19%) patients had meningitis and 85 (81%) had no meningitis.

| Presence of Meningitis (n = 105)	
Yes	20 (19%)
No	85 (81%)
Table-II. Distribution of meningitis	

Figure-1 show the distribution of meningitis among both gender. Out of 59 male patients, 11 (18.6%) patients had meningitis and 48 (81.4%) patients

had no meningitis. Out of 46 female patients, 9 (19.6%) patients had meningitis and 37 (80.4%) patients had no meningitis with p-value = 0.905.

Figure-2 show the distribution of meningitis among different age groups. Out of 64 patients having age between 4-15 days, 17 (26.6%) patients had meningitis and 47 (73.4%) patients had no meningitis. Out of 41 patients having age between 16-27 days, 3 (7.3%) patients had meningitis and 38 (92.7%) patients had no meningitis with p-value = 0.014.
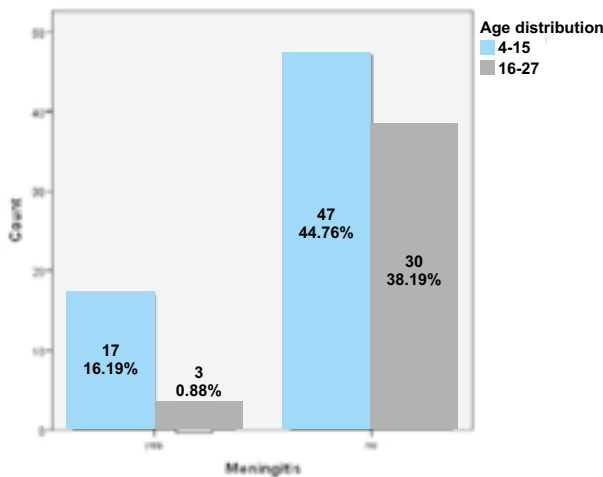
Figure-2. Distribution of meningitis among age groups p-value = 0.014

DISCUSSION
In children of less than 5 years of age, neonatal mortality every year accounts for 41% (3.6 million).[12] Most of these deaths occurred in developing and under developed countries and leading cause of deaths include pneumonia, meningitis and sepsis.[13]

Neonatal meningitis is inflammation of arachnoid and pia mater. Early detection of clinical symptoms, prompt diagnosis and early institution of medical therapy can reduce the risk of complications and mortality.[14]

Group B streptococcus (GBS) is the most common organism for sepsis and meningitis. It is usually transmitted from mother to child during childbirth. The rate of colonization in women during pregnancy is 30%, and the vertical transmission rate to the newborn is approximately 45%. The use of intrapartum antibiotic prophylaxis (IAP) has greatly reduce the rate of early onset disease (EOD) in the United States, however occurrence of late onset disease (LOD) remains unchanged.[15]

In neonates, signs and symptoms of sepsis and meningitis are nonspecific and subtle. A diagnosis of meningitis can only be made by analysis and culture of cerebrospinal fluid by performing lumbar puncture.[16]

Kaul et al[10] conducted a study in north west India on importance of lumbar puncture in neonates with late onset septicemia. According to results, prevalence of meningitis was 22.5% in late onset septic neonates. The conclusion of study is that meningitis is important cause of late onset sepsis and lumbar puncture is essential to make the diagnosis.

Shiva et al[16] conducted a study to make the diagnosis of meningitis in neonates using lumbar puncture. They found that the 3.8% neonates with late onset sepsis had meningitis. The conclusion of study was that lumbar puncture should perform in all neonates with sepsis.

Tiskumara et al[17] conducted a study in Asia on different neonatal infections. They found that the 17.2% late onset septic neonates had meningitis. According to their conclusion, the rate of meningitis is highest in Asia than the developed countries.

Da Silva et al[18] conducted a study in Salvador, Bahia, Brazilto see the frequency of newborn bacterial meningitis and sepsis during the pregnancy period. According to their results prevalence of meningitis was found to be 17% in late onset neonatal sepsis. Laving et al[19] conducted a study to observe the rate of neonatal bacterial meningitis. The results of their study showed that meningitis was found in 17.9% of septic neonates. Zea-Vera et al[20] worked on low birth weight neonates for the evaluation of meningitis in late-onset sepsis by using lumbar puncture. The results of their study showed that 17.5% neonates with late onset septicemia had meningitis. Their results favor the results of my study.

CONCLUSION

Meningitis is a common problem in late onset septic neonates. The results of my study give the local burden of this complication i.e.; 19% that can be helpful in emphasizing the importance of screening of such condition so that preventive measures should be adopted to prevent this disease. The development of meningitis in late onset septic neonates is associated within crease in age of the neonates.

REFERENCES

1. Leal YA, Alvarez-Nemegyei J, Velazquez JR, Rosado-Quiab U, Diego-Rodriguez N, Paz-Baeza E, et al. **Risk factors and prognosis for neonatal sepsis in southeastern Mexico: analysis of a four-year historic cohort follow-up.** BMC Pregnancy Childbirth. 2012; 12:48.

2. Shah AJ, Mulla SA, Revdiwala SB. **Neonatal sepsis: high antibiotic resistance of the bacterial pathogens in a neonatal intensive care unit of a tertiary care hospital.** J ClinNeonatol. 2012; 1:72–5.

3. Sivanandan S, Soraisham AS, Swarnam K. **Choice and duration of antimicrobial therapy for neonatal sepsis and meningitis.** Int J Pediatr. 2011; 2011:712150.

4. Ansari S, Nepal HP, Gautam R, Shrestha S, Neopane P, Chapagain ML. **Neonatal septicemia in Nepal: early-onset versus late-onset.** Int J Pediatr. 2015; 2015:379806.

5. Reinhart K, Bauer M, Riedemann NC, Hartog CS. **New approaches to sepsis: molecular diagnostics and biomarkers.** ClinMicrobiol Rev. 2012; 25:609–34.

6. Zea-Vera A, Ochoa TJ. **Challenges in the diagnosis and management of neonatal sepsis.** J Trop Pediatr. 2015; 61:1–13.

7. Shehab El-Din EM, El-Sokkary MM, Bassiouny MR, Hassan R. **Epidemiology of neonatal sepsis and implicated pathogens: a study from Egypt.** Biomed Res Int. 2015; 2015:509484.

8. Shah BA, Padbury JF. **Neonatal sepsis: an old problem with new insights.** Virulence. 2014; 5:170–8.

9. Ng PC, Ang IL, Chiu RW, Li K, Lam HS, Wong RP, et al. **Host-response biomarkers for diagnosis of late-onset septicemia and necrotizingenterocolitis in preterm infants.** J Clin Invest. 2010; 120:2989–3000.

10. Kaul V, Hrish R, Ganjoo S, Mahajan B, Raina SK, Koul D. **Importance of lumbar puncture in neonates with late onset septicemia a hospital based observational study from north-west India.** J ClinNeonatol. 2013; 2:83–7.

11. Ku LC, Boggess KA, Cohen-Wolkowiez M. **Bacterial Meningitis in the Infant.** ClinPerinatol. 2015; 42:29–45.

12. Gupta N, Grover H, Bansal I, Hooda K, Sapire JM, Anand R, et al. **Neonatal cranial sonography: ultrasound findings in neonatal meningitis—a pictorial review.** Quant Imaging Med Surg. 2017; 7:123–31.

13. Zaidi AKM, Ganatra HA, Syed S, Cousens S, Lee ACC, Black R, et al. **Effect of case management on neonatal mortality due to sepsis and pneumonia.** BMC Public Health. 2011; 11(Suppl 3):S13.

14. Tack DM, Holman RC, Folkema AM, Mehal JM, Blanton JD, Sejvar JJ. **Trends in encephalitis-associated deaths in the United States, 1999-2008**. Neuroepidemiology 2014; 43:1-8.

15. Manning SD, Springman AC, Lehotzky E, Lewis MA, Whittam TS, Davies HD. **Multilocus sequence types associated with neonatal group b streptococcal sepsis and meningitis in Canada.** J ClinMicrobiol. 2009; 47:1143–8.

16. Shiva F, Mosaffa N, Khabbaz R, Padyab M. **Lumbar puncture in neonates under and over 72 hours of age.** J Coll Physicians Surg Pak. 2006; 16:525-8.

17. Tiskumara R, Fakharee SH, Liu CQ, Nuntnarumit P, Lui KM, Hammoud M, et al. **Neonatal infections in Asia. Arch Dis Child Fetal Neonatal Ed.** 2009; 94:F144-8.

18. da Silva LP, Cavalheiro LG, Queirós F, Nova CV, Lucena R. **Prevalence of newborn bacterial meningitis and sepsis during the pregnancy period for public health**

care system participants in Salvador, Bahia, Brazil. Braz J Infect Dis. 2007; 11:272–6.

19. Laving AM, Musoke RN, Wasunna AO, Revathi G. **Neonatal bacterial meningitis at the newborn unit of Kenyatta National Hospital.** East Afr Med J. 2003; 80:456–62.

20. Zea-Vera A, Turín CG, Rueda MS, Guillén-Pinto D, Medina-Alva P, Tori A, et al. **Use of lumbar puncture in the evaluation of late-onset sepsis in low birth weight neonates.** Rev Peru Med ExpSaludPublica. 2016; 33:278–82.

PREVIOUS RELATED STUDY

Bashir Ahmad Kakar, Abdul Bari, Essa Khan Tareen, Raz Muhammad Kakar. ACUTE PYOGENIC MENINGITIS; INCIDENCE IN PAEDIATRICS (IN INFANTS AND CHILDREN) (Original) Prof Med Jour 14(2) 272-275 Apr, May, Jun, 2007.

Said Amin, Muhammad Usman, Muhammad Noor Wazir. Tuberculous meningitis (Original) Professional Med J Jul-Aug 2012;19(4): 449-454.

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To err is human.
To forgive is divine.

– Ancient Proverb –
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AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Shaheen Abbas	Introduction	
2	Lala Rukh Khan	Material and methods	
3	Gul Afshan	Discussion conclusion	