Original Research Article

Frequency of meningitis in patients presenting with neonatal sepsis at a tertiary care hospital: A cross-sectional study

Abstract

Aim: To investigate the prevalence of meningitis in neonatal sepsis patients at a tertiary care hospital.

Study design: A cross-sectional study

Place and Duration: Department of Paediatric, Civil Hospital Karachi from 11 – 2019 to 04 – 2020

Methodology: A total of 120 Neonates within first 28 days of life with positive blood culture were included in this study. Patient's data was collected on a predesigned proforma including demographics. Diagnosis of meningitis was done by performing lumber puncture. CSF analysis, blood, and CSF cultures were all tested in the lab.

Results: The average age of the patients was 10.75±7.24 days. There were 66(55%) male and 54(45%) female. Meningitis was found in 23.33 percent of patients with neonatal sepsis (28/120). Rate of meningitis was significantly high in late onset of sepsis as compared to early onset of sepsis (32.8% vs. 11.3%; p=0.006).

Conclusion: In this study frequency of meningitis with neonatal sepsis was high. Meningitis has a strong link to neonatal sepsis, and it must be ruled out in those babies to avoid neurological

problems. Awareness of empiric and focused antibiotic therapy can help to reduce the burden of bacterial meningitis-related morbidity and mortality.

Key Words: Neonatal sepsis, Meningitis, late onset of sepsis, early onset of sepsis

Introduction:

Newborn sepsis is a major cause of neonatal morbidity and mortality, and it is a serious global public health issue. [1] According to the World Health Organization, 4 million newborns die in the first four weeks of their lives each year, with 75 percent dying prematurely in the first week. [1-3] Infections (35 percent), premature births (28 percent), intrapartum complications (24 percent), and asphyxia were expected to be the leading causes of newborn fatalities worldwide (23 percent). Sepsis is the most common cause of newborn mortality, accounting for 30 to 50 percent of all neonatal fatalities each year. [1] Early onset sepsis (EOS) and late onset sepsis (LOS) are two types of neonatal sepsis [4]. In the first month, it is characterized by signs and symptoms of infection, with or without bacteremia in the first month of life. Septicemia, meningitis, pneumonia, arthritis, osteomyelitis, and urinary tract infections are all examples of systemic infections in newborns. [5-6]

Meningitis is a common presentation of LOS and it results in serious neurological sequelae and impairment [7-9]. The risk of newborn meningitis varies depending on where you live. When compared to earlier age groups, the neonatal era has the highest incidence of meningitis. 10 and 11] Since the early 1980s, Group B Streptococcus (GBS) has been the most common cause of newborn sepsis and meningitis, accounting for more than 40% of all early-onset infections. [12] The second most prevalent pathogen, Escherichia coli (E. coli), is isolated in 30% of all early-onset illnesses. [13-16]

Meningitis is more common in late-onset preterm babies, and the risk is directly proportional to the birth gestational age and weight. [17] Gram-negative bacteria cause it to be more severe, with a higher rate of mortality and morbidity. Both clinical symptoms and cerebrospinal fluid (CSF) examination are used to diagnose newborn meningitis. CSF culture is a great way to show that you have meningitis in a lab setting. The presence of leukocytes, glucose, and protein in the CSF can aid in the diagnosis. [18-20] With a case fatality rate of 15-25 percent and morbidity rates of 25 percent or more, neonatal meningitis has a terrible prognosis. [21]

Phiri et al. reported that 25.76% were diagnosed to have meningitis in neonatal sepsis. [22] Another study done in Lahore, Pakistan shows that the frequency of meningitis in late onset sepsis was 39.5%. [23]. For affected newborns to have a favorable prognosis and to limit morbidity, prompt identification and treatment are critical. The purpose of designing this study is to determine the magnitude of meningitis in our patients of sepsis, so that we have our local data which can be used to provide optimal neonatal care. Once we know the frequency, then we can devise protocols to keep a high index of suspicion, early recognition, early and appropriate investigations to diagnose and then manage accordingly.

Methodology

This cross-sectional study was conducted at Department of Paediatric, Civil Hospital Karachi by Non Probability Consecutive Sampling technique from 11 – 2019 to 04 – 2020. The sample size was calculated by taking prevalence of meningitis in neonatal sepsis 27.4% [21], 120 patients of neonatal sepsis were enrolled in the study at confidence interval of 95% and absolute precision 8% using WHO sample size calculator. Approval was taken from the ethical review committee of the institute.

Neonates of either gender within first 28 days of life, either full term or preterm and having positive blood culture were included in the study. Neonates with moribund condition or having any spine deformity along with negative blood culture were excluded from the study. Early Onset Neonatal Sepsis was labeled as positive if they come to us within first week of life and their Blood culture is positive for any bacteria, while the Late Onset Neonatal Sepsis was labeled if they come to us after first week of life and their Blood culture is positive for any bacteria.

Meningitis was labeled as positive if their CSF DR shows low glucose (less than two-third of serum glucose) or any of the following criteria. a. CSF white cell count >30 cells/mm3, CSF protein >100 mg/dl, With/without CSF culture positive.

Patient's data was collected on a predesigned proforma including demographics. To rule out meningitis, every patient had a lumbar puncture as part of their sepsis work up before commencing empirical antibiotics. Meningitis was diagnosed according to the operational definition. The GA, gender, birth weight, and time of onset of infection (EOS, LOS) were all documented. CSF analysis, blood, and CSF cultures were all tested in the lab. By closely adhering to the inclusion criteria, confounders and bias were avoided. The statistical package for social sciences (SPSS) Version 21 was used to compile and evaluate the patient's data.

Frequency and percentage was computed for qualitative variables like gender, sepsis (EOS/LOS), neonatal status (pre-term/full-term), Blood culture positive (Y/N), CSF culture positive (Y/N), and meningitis (Y/N). Mean ± SD was calculated for quantitative variables i.e. neonatal age, gestational age, birth weight, glucose, protein and white cell count. The Chi-square test was used to assess the effect of these modifiers on outcome based on age, gender, gestational age, neonatal status, and birth weight. Significant was defined as a P value of less than 0.05.

Results

A total of 120 Neonates within first 28 days with blood culture positive for any bacteria were included in this study. The average age of the patients was 10.75±7.24 days. There were 66 (55%) male and 54(45%) female. The average Glucose, protein and WCC was 40.97±12.13mg/dl, 109.52±48.65 mg/dl and 21.53±13.04 cells/mm3 respectively. Regarding early and late onset neonatal sepsis, 67 (55.83%) were late and 53 (44.17%) early. Out of 120 neonates, 38.33% were preterm and 61.67% full term cases. CSF culture was positive in 23.33% cases. Frequency of meningitis in patients presenting with neonatal sepsis was 23.33% (28/120). Rate of meningitis was significantly high in late onset of sepsis as compare to early onset of sepsis (32.8% vs. 11.3%; p=0.006). After controlling the effect modifiers by stratification analysis, rate of meningitis was statistically significant with low with ≤ 37 gestational age (preterm same) while it was not statistically significant with neonatal gender and birth weight. Comparison of rate of meningitis between late and early onset of sepsis was observed by gender, gestational age and birth weight.

Table 1: The demographic characteristics of the study participants n = 120

Mean age (days)	10.73 ± 7.24
Mean gestational age (weeks)	36.86 ± 2.01
Mean birth weight (Kg)	2.42 ± 0.31
Gender	
Male	66 (55.0%)
Female	54 (44.01%)
Sepsis	
Early-onset	53 (44.17%)
Late-onset	67 (55.83%)
Gestation	
Pre-term	46 (38.33%)
Full-term	74 (61.67%)
Blood Culture	
Positive	120 (100%)
CSF Culture	
Positive	28 (23.33%)
Meningitis	
Yes	28 (23.33%)
No	92 (76.67%)

Table 2: Compare the frequency of meningitis in patients with early onset vs. late onset neonatal sepsis

Meningitis	Sepsis Status		P-Value
	EOS	LOS	
Yes	6(11.3%)	22(32.8%)	0.006
No	47(88.7%)	45(67.2%)	

Chi-Square= 7.654

Table 3: Frequency of meningitis in patients presenting with neonatal sepsis by effect modifiers

n=120

Variables	Meningitis		Total	P-Value
	Yes	No		
Gender				0.765
Male	15(22.7%)	51(77.3%)	66	
Female	13(24.1%)	41(75.9%)	54	
Gestational Age				0.001
≤37	18(39.1%)	28(60.9%)	46	
38-40	10(13.5%)	64(86.5%)	74	
Birth Weight				0.331
≤2.5 kg	23(29.1%)	56(70.9%)	79	
>2.5kg	5(12.2%)	36(87.8%)	41	
Preterm				0.001
Yes	18(39.1%)	28(60.9%)	46	
No	10(13.5%)	64(86.5%)	74	

Table 4: Compare the frequency of meningitis in patients with early onset vs. late onset neonatal sepsis by gender

Gender	Meningitis	Sepsis Status		P-Value
		Early onset	Late onset	
Male	Yes	1(4.2%)	14(33.3%)	0.006
	No	23(95.8%)	28(66.7%)	
	Total	**24**	**42**	
Female	Yes	5(17.2%)	8(32%)	0.229
	No	24(82.8%)	17(68%)	
	Total	**29**	**25**	

Table 5: Compare the frequency of meningitis in patients with early onset vs. late onset neonatal sepsis by gestational age or neonatal status

Gestational age	Meningitis	Sepsis Status		P-Value
		Early onset	Late onset	
≤37 week Preterm	Yes	4(25%)	14(46.7%)	0.210
	No	12(75%)	16(53.3%)	
	Total	**16**	**30**	
>37 Weeks Term	Yes	2(5.4%)	8(21.6%)	0.041
	No	35(94.6%)	29(78.4%)	
	Total	**37**	**37**	

Table 6: Compare the frequency of meningitis in patients with early onset vs. late onset neonatal sepsis by birth weight

Birth Weight	Meningitis	Sepsis Status		P-Value
		Early onset	Late onset	
≤2.5 kg	Yes	6(16.7%)	17(39.5%)	0.026
	No	30(83.3%)	26(60.5%)	
	Total	**36**	**43**	
>2.5kg	Yes	0(0%)	5(20.8%)	0.046
	No	17(100%)	19(79.2%)	
	Total	**17**	**24**	

Discussion:

Neonatal sepsis is an important health problem resulting in high mortality and morbidity, and sometimes lifelong complications, especially neurological complications. [24] Due to its association with long term complications, morbidity and mortality, various studies have been done to find out the exact frequency of bacterial meningitis in neonatal sepsis. [25]

The average age of the patients in this study was 10.757.24 days. Males made up 66 percent of the population, while females made up 54 percent. In the Abbas et al study, newborn septic meningitis affected 65.95 percent of males and 34.05 percent of females. The patients' average age was 186.655 days. 2,500156.55 grams was the average weight. Waheed et al reported a male to female ratio of 2.1:1 in a research [26]. It was reported to be 27.4 percent in a local study

conducted in Multan [98]. Meningitis was found to be present in 23.33 percent of individuals with neonatal sepsis in this investigation

Phiri et al. reported that 25.76% were diagnosed to have meningitis in neonatal sepsis. [22] Another study done in Lahore, Pakistan shows that the frequency of meningitis in late onset sepsis was 39.5%. [23] Which is comparable to our study. For affected newborns to have a favorable prognosis and to limit morbidity, prompt identification and treatment are critical. The majority of the study results in the worldwide literature agree with our findings. In their investigation, Rasul et al found a 6-3 percent incidence of meningitis [27]. Meningitis was reported to be present in 3/1000 live births [28]. According to an Indian study, 3.3 percent of neonates with suspected clinical sepsis were identified with meningitis [29].

In contrast to our figures, others reported very few cases of septic meningitis associated with sepsis in neonates. Tsai et al [30] observed 0.68% neurological complications, while Maoulainine et al [31] reported only 3.3% meningitis in their septic patients. In a study in Taiwan Chu et al [32] observed 5.5% cases developing meningitis following septicaemia and Giannoni et al observed 6.76% case of neonatal meningitis.

In this study rate of meningitis was significantly high in late onset of sepsis as compare to early onset of sepsis (32.8% vs. 11.3%; p=0.006). Meningitis is prevalent in late-onset sepsis, according to Bhagat, et al [33], where the prevalence of meningitis was 16 percent. Visser et al. [34] (1980) found a similar finding: 24 percent of septic neonates with LOS developed meningitis. Meningitis was found to be present in 17.9% of newborns with late-onset sepsis by Laving et al. (2003), [35], Anjos De Silva et al. (2007) [36], and Tisukumara et al. (2009) [37], respectively.

Zhu et al [38] reported 92 patients of late onset and 20 patients of early onset. They reported predominance of late onset meningitis. Lower age and lower weight was observed to be predominantly affected in another study by Zhu et al.[39] In contrast to our study and some other studies, Giannoni et al [40] reported only 20% patients with early onset sepsis compared to 80% late onset sepsis but the disease was more commonly seen in those with low birth weight and median age of 9 days. Septic meningitis following septicemia is more common in underdeveloped countries compared to developed countries. Also it is commonly seen in neonates with lower birth weight. Sepsis in developing countries is more likely to be associated with meningitis as compared to the developed countries.

Conclusion

In this study frequency of meningitis with neonatal sepsis was 23.33%. Late-onset sepsis and newborns with low birth weight are linked to meningitis. Meningitis has a strong link to neonatal sepsis, and it must be ruled out in these babies to avoid neurological problems. Awareness of empiric and focused antibiotic therapy will help to reduce the burden of bacterial meningitis-related morbidity and mortality.

Permission:

It was taken from the ethical review committee of the institute

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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