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ORIGINAL ARTICLE

Frequency of Meningitis in Neonates with Late Onset Sepsis in Sharif Medical City

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ABSTRACT

Background: Bacterial sepsis and meningitis continue to be major causes of morbidity and mortality in newborns, particularly in premature infants. The present study was undertaken to know the incidence of meningitis in neonates with late onset sepsis.
Aim: To determine the frequency of meningitis in neonates with late onset sepsis.
Methods: A descriptive cross sectional study was conducted in department of pediatrics at sharif medical city Lahore, from 09-12-2019 to 08-06-2020. One hundred and forty four (144) neonates with late onset sepsis fulfilling the inclusion criteria were included in study. Meningitis was confirmed on lumbar puncture and managed as per hospital protocol. Mean & sd were presented for age, gender, duration of complain and weight. Frequency and percentage were computed for gender and meningitis.
Results: Mean age, weight and duration of symptoms in infants with late onset sepsis were 19.50±0.12 days, 3.97±1.17 kg and 4.05±1.98 days. Majority of infants were male i.e. 63.89% (m:f;1:1.7). Mean wbc count of the infants with late onset sepsis was 29.78±9.32.majority of infants had less than 75% neutrophils (68.05%), positive crp (91.67%) and negative blood culture test (52.78%). Frequency of meningitis in neonates with late onset sepsiswas 34.02%.
Conclusions: frequency of meningitis in neonates with late onset sepsis was high i.e. 34.02%.
Key words: Meningitis; neonates; late onset sepsis

INTRODUCTION

All over the world neonatal infections remains a leading cause in mortality and morbidity of newborns, even in the industrialized countries with high hygienic standards, access to antimicrobial agents for prophylaxis and deliveries at hospitals with treatment and facilities for advanced intensive care. Most studies of incidence and etiology of neonatal sepsis and meningitis come from these developed countries, while there is a lack of data from the developing countries with immensely high mortality and morbidity. In Pakistan, meningococcal meningitis goes unnoticed and kills 137 children each day.[1,2] Worldwide, every minute one individual is infected with meningitis and in Pakistan due to this infection 8% of children die after neonatal age. Most common prevalence of meningitis is found under age of one year. According to researchers, 500000 persons contact meningitis each year globally.[3] Further 10-14% of survivors of this disease develop complication including hearing loss, weakness in different body parts, and nervous complications.[4,5]

developing countries about 30-50% of the total neonatal deaths are due to sepsis.[6,7] Various community and hospital based studies have reported sepsis as a reason for neonatal death in 20-50% of patients.[8,9]

The incidence of bacterial meningitis in neoates ranges between 0.25 to 1 per 1000 live births and found in 25% of neonates with bacteremia.[10] Major strain is meningococcus which causes meningitis in neonates and adults.[11,12]

Neonatal sepsis is defined as clinical syndrome with signs and symptoms of infection with or without accompanying bacteremia in the first month of life. It involves systemic infections of the newborn such as septicemia, pneumonia, osteomyelitis, meningitis, arthritis and urinary tract infections. The frequency of late onset sepsis has increased presently, owing to the increased survival of premature infants.[13] this supports the role of hospitalization and ICU invasive treatment strategies in the pathogenesis of neonatal late onset sepsis. Strategies have been concluded for the prevention of meningitis in neonatal life. So far the only option available for prevention is hygiene protocols to be followed and minimization of invasive procedures in neonatal icu[14,15].

Late onset infections occur during the second to fourth weeks of life while infections from day 28-30 to day 120-180 are called very late onset infections. More than quarter of the patients of late onset sepsis are at high risk of meningitis. In a study Phiri et al found that out of 784 patients of septicemia, 202 were having meningitis. In early onset of sepsis, risk of meningitis is very low i.e. 1.1%. Neonatal sepsis and meningitis can co-occur in more than 30% of patients.[5] Any newborn with bacterial sepsis is also at risk of meningitis. In one study incidence of meningitis was found to be 39.5% and it was commonly associated with sepsis of late onset. Lumbar puncture is useful tool and standard protocol in newborns.[6] Infections are a leading cause of morbidity and mortality in neonatal and infant. About 30-50% of the total neonatal deaths are due to sepsis in developing countries. Upto 20% of neonates develop sepsis and 1% die of sepsis related causes.[3] In another study, 60.7% of the cases of gram negative sepsis was found to be having meningitis, and 30.7% of diagnosed gram positive sepsis have meningitis. Out of patients of meningitis, 94.5% of exclusively breastfed babies recovered, while 77% of top feeding babies recovered. Meningitis has more mortality rate than sepsis, i.e. 17.6% as compared to 4.8% respectively.[7]

So it was concluded that meningitis is really common finding in patients with late onset sepsis and associated with mortality. Patient get benefited if they are on breastfeed. An up-to-date and detailed knowledge of the epidemiology of neonatal los along with the local data base may help to reduce the burden of this disease. Objective of the study was to determine the Frequency of meningitis in neonates with late onset sepsis.

Operational definition

Diagnosis of Meningitis: Spinal tap (lumbar puncture) was done to confirm meningitis in patients having late onset sepsis.

Values found in Spinal tap (lumbar puncture) of a meningitis patient were

Glucose level: <20-30 mg/dl. It must be compared with serum glucose level. Normal CSF glucose values are two third of serum glucose value.

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Protein: usually elevated >100-150 mg/dl
WBC: 0-35 cells/mm3
Neonates: An infant less than four weeks old
Late onset Sepsis (LOS): Sepsis was described as late onset sepsis if it occurs after seven days of life.
Diagnosis of late onset sepsis: Diagnosis was made on multi variant features, according to **WHO criteria for IMCI**
•Clinical manifestations: fever (>99ºF), seizures, feeding intolerance, vomiting, lethargy, irritability, respiratory distress, apnea, cyanotic episodes poor tone. (assessed clinically and on history/ medical record)
•CBC: WBC <4 OR >30
•CRP: positive >6
•Blood culture after 48 hours (>105 organisms/ HPF)

MATERIAL AND METHODS

A Descriptive Cross Sectional Study was conducted in the nursery of Sharif Medical City, Lahore, from 09-12-2019 to 08-06-2020 after permission from IRB. One hundred and forty four (144) neonates were included in study with late onset sepsis in accordance with the inclusion criteria. Sample size calculated as% frequency of outcome factor in the population (p):39.5% 6 with Margin of error is 8% and Confidence level 95%. Sample technique was Non-probability consecutive sampling

Inclusion criteria

- Infants of age 7-28 days
- Neonates coming to Sharif Medical City with late onset sepsis (as per operational definition)
- Male & female children equally inclusive

Exclusion criteria

- Neonatal death during admission
- Low birth weight (weight less than 1000 gm on weighing machine)
- Parents/Guardians refused informed consent
- Those who already took antibiotics

Data Collection: After getting approval from advanced research committee, biomedical ethical committee, and technical review committee to conduct the study, data was collected about all those 144 neonates fulfilling the inclusion criteria presenting to the NICU of the hospital. Base line demographic information of patients (age, gender, duration of complaints, weight) was taken. Informed consent was taken from parents/guardian, ensuring confidentiality and fact that there is no risk involved to the patient while taking part in this study. Meningitis was labeled as per operational definition and managed as per hospital protocol. Data was collected and recorded by researcher herself on especially designed Proforma.

Data Analysis: Data was analyzed with statistical analysis software (IBM-SPSS-22). Mean & SD were presented for quantitative variables like age, gender, duration of complaints and weight. Frequency and percentage were computed for qualitative variables like gender, late onset sepsis, meningitis. Chi-square test was used. Data was stratified for age, gender, weight, duration of symptoms. P value of ≤ 0.05 was used as cut off point to determine the significance of test.

Results: One hundred and forty four infants with late onset sepsis were included in the study.

Distribution of patients by age: Out of 144 infants with late onset sepsis, there were 38 (26.38%) infants less than 15 days of age and 106 (73.61%) infants with more than 15 days of age. The mean age of the infants with late onset sepsis was 19.50 ± 0.12 days (Table 1).

Distribution of patients by weight: Out of 144 infants with late onset sepsis, there were 14 (9.72%) infants with weight between 3-4 Kg, 94 (65.27%) infants with weight between 4-5 Kg and 36 (25.0%) infants with weight between 5-6 Kg. The mean weight of the infants with late onset sepsis was 3.97±1.17 Kg (Table 2).

Distribution of patients by duration of complaints: Out of 144 infants with late onset sepsis, there were 46 (31.94%) infants with less than 3 days of duration of complaints and 98 (68.05%) infants with more than 3 days of duration of complaints. The mean duration of complaints of the infants with late onset sepsis was 4.05±1.98 days (Table 3).

Distribution of patients by gender: Out of 144 infants with late onset sepsis, there were 92 (63.89%) male &52 (36.11%) infants were females. The boys to girls' ratio were 1:1.7 (Table 4).

Distribution of patients by CBC: Out of 144 infants with late onset sepsis, there were 98 (68.05%) infants with less than 75% neutrophils and 46(31.94%) infants with more than 75% neutrophils. The mean WBC count of the infants with late onset sepsis was 29.78±9.32 (Table 5).

Distribution of patients by C-reactive protein: Out of 144 infants with late onset sepsis, there were 132 (91.67%) infants with Positive C-reactive protein and 12 (8.33%) infants with Negative C-reactive protein (Table 6).

Distribution of patients by blood culture test: Out of 144 infants with late onset sepsis, there were 68 (47.22%) infants with Positive blood culture test and 76 (52.78%) infants with Negative blood culture test (Table 7).

Distribution of patients by meningitis: Out of 144 infants with late onset sepsis, there were 49 (34.02%) infants with meningitis and 95 (65.97%) infants had no meningitis (Table 8).

Stratification of data (meningitis) with effect modifier (Age): Out of 38 infants with less than 15 days of age, meningitis was reported in 17 (44.73%) infants with late onset sepsis and it was not observed in 21 (55.26%) infants. Out of 106 infants with more than 15 days of age, meningitis was reported in 32 (30.18%) infants with late onset sepsis and it was not observed in 74 (69.81%) infants. The p-values was 0.291 (Table 9).

Stratification of data (meningitis) with effect modifier (gender): Out of 92 male infants with late onset sepsis, meningitis was reported in 34 (36.95%) infants and it was not observed in 58 (63.04%) infants. Out of 52 female infants with late onset sepsis, meningitis was reported in 15 (28.84%) infants and it was not observed in 37(71.15%) infants. The p-values was 0.139 (Table 10).

Stratification of data (meningitis) with effect modifier (Weight): Out of 14 infants with weight between 3-4 Kg, meningitis was reported in 6 (42.85%) infants with late onset sepsis and it was not observed in 8 (57.14%) infants. Out of 94 infants with weight between 4-5 Kg, meningitis was reported in 30 (31.91%) infants with late onset sepsis and it was not observed in 64 (68.08%) infants. Out of 36 infants with weight between 5-6 Kg, meningitis was reported in 12 (33.33%) infants with late onset sepsis and it was not observed in 24 (66.67%) infants. The p-values were 0.374 (Table 11).

Stratification of data (meningitis) with effect modifier (Duration of symptoms): Out of 46 infants with less than 3days of Duration of symptoms, meningitis was reported in 20 (43.47%) infants with late onset sepsis and it was not observed in 26(56.52%) infants. Out of 98 infants with more than 3 days of Duration of symptoms, meningitis was reported in 29 (29.59%) infants with late onset sepsis and it was not observed in 69 (%0.40) infants. The p-values was 0.902. (Table 12)

Table 1: Distribution of patient by age (n=144)

Age (days)	n	%age
<15	38	26.38
>15	106	73.61
Mean±SD	19.50 ± 0.12 days	

Table 2: Distribution of patient by weight (n=144)

Weight (Kg)	n	%age
3-4	14	9.72
4-5	94	65.27
5-6	36	25.0
Mean±SD	3.97±1.17 Kg	

Table 3: Distribution of patient by duration of complaints (n=144)

Duration of complaints	Number of patients	
	Frequency	Percentage (%)
<3 days	46	31.94
>3 days	98	68.05
Mean±SD	4.05±1.98 days	

Table 4: Distribution of patients by gender (n=144)

Gender	Number of patients	
	Frequency	Percentage (%)
Male	92	63.89
Female	52	36.11

Table 5: Distribution of patient by CBC (n=144)

Neutrophils	Number of patients	
	Frequency	Percentage (%)
<75%	98	68.05
>75%	46	31.94
WBC count (Mean±SD)	29.78±9.32	

Table 6: Distribution of patient by C-reactive protein (n=144)

C-reactive protein	Number of patients	
	Frequency	Percentage (%)
Positive	132	91.67
Negative	12	8.33

Table 7: Distribution of patient by blood culture test (n=144)

Blood culture test	Number of patients	
	Frequency	%age
Positive	68	47.22
Negative	76	52.78

Table 8: Distribution of patients by meningitis (n=144)

Meningitis	Number of patients	
	Frequency	%age
Yes	49	34.02
No	95	65.97

Table 9: Stratification of data (Frequency) by effect modifier (age) (n=144)

Age Groups	Frequency of meningitis			
	Yes		No	
	No.	%	No.	%
<15 days (n=38)	17	44.73	21	55.26
>15 days (n=106)	32	30.18	74	69.81
P value*	0.291**			

*chi square test **Not significant

Table 10: Stratification of data (meningitis) by effect modifier (gender) (n=144)

Gender	Meningitis			
	Yes		No	
	No.	%	No.	%
Boys (n=92)	34	36.95	58	63.04
Girls (n=52)	15	28.84	37	71.15
P value*	0.139**			

*chi square test **Not Significant

Table 11: Stratification of data (meningitis) by effect modifier (weight) (n=23)

Weight (Kg)	Meningitis			
	Yes		No	
	No.	%	No.	%
3-4 (n=14)	6	42.85	8	57.14
4-5 (n=94)	30	31.91	64	68.08
5-6 (n=36)	12	33.33	24	66.67
P value*	0.374**			

*chi square test, **Not Significant

Table 12: Stratification of data (meningitis) by effect modifier (duration of symptoms) (n=144)

Duration of symptoms (days)	Meningitis			
	Yes		No	
	No.	%	No.	%
<3 (n=46)	20	43.47	26	56.52
>3 (n=98)	29	29.59	69	70.40
P value*	0.902**			

*chi square test **Not Significant

DISCUSSION

In this study of 144 neonates with late onset sepsis, we determined the Frequency of meningitis in neonates. The mean age of the infants with late onset sepsis was 19.50 ± 0.12 days in our study. Majority of infants i.e. 73.61% was more than 15 days of age in our study. Similarly, in a descriptive study by Khurshid A5 et al, mean age of the infants with late onset sepsis was 10.49+7.79 days. Similarly, in a hospital based observational study by Bhagat R 7 et al, mean age of the infants with late onset sepsis was 10.8±7.05 days and 46.1% of patients were presented in the age group of 3-7 days.

The mean weight of the infants with late onset sepsis was 3.97±1.17 Kg in our study. Majority of infants i.e. 65.27% had weight between 4-5 Kg in our study. Similarly, in a descriptive study by Khurshid A et al,39.3% neonates had low birth weight (1.5-2.5 kg), however mean weight was 2.55 + 0.39 kg (range 1.8-3.6 kg). [5]Similarly, in a hospital based observational study by Bhagat R et al, mean weight of neonates was 2.61 ± 0.606 kg. The mean duration of complaints of the infants with late onset sepsis was 4.05±1.98 days in our study. Majority of infants i.e. 68.05% had more than 3 days of duration of complaints in our study. The male dominance was found in our study i.e. 63.89% with boys to girls' ratio of 1:1.7. Similarly, in a descriptive study by Khurshid A5 et al, there were 53% male, 47% female babies with M:F ratio of 1:1.1. Similarly, male dominance was found in a study by Bhagat R et al, i.e. 52.7%.The mean WBC count of the infants with late onset sepsis was 29.78±9.32in our study. Majority of infants i.e. 68.05% had less than 75% neutrophils in our study. Majority of infants with late onset sepsis i.e. 91.67% had Positive C-reactive protein in our study. Majority of infants with late onset sepsis i.e. 52.78% had Negative blood culture test in our study. Similarly, in a hospital based observational study by Bhagat R et al, Blood culture was found positive in 42.6% cases of meningitis. The frequency of meningitis in neonates with late onset sepsis was found to be34.02% in our study. Similarly, in a descriptive study by Khurshid A5 et al,27.4% infants with sepsis were diagnosed to have meningitis. Jiang Jet al, have reported that meningitis developed in 11.8% of patients in early onset and 5.2% in late onset group.[16] However, in a hospital based observational study by Bhagat R et al, frequency of meningitis in neonates with late onset sepsis was 16.07%. [7]. We cross tabulated the results i.e. frequency of meningitis with effect modifier i.e. Age and found that Frequency of meningitis was higher i.e. 44.73% in younger infants as compared to older infants i.e. 30.18%. However, the results were not statistically significant (p= 0.291). Similarly, in a descriptive study by Khurshid A et al, Majority of the neonates with sepsis i.e. 52.1% were between 1-7 days of their life. [5]

We also cross tabulated the results i.e. frequency of meningitis with effect modifier i.e. gender and found that Frequency of meningitis was higher i.e. 36.95% among male infants as compared to female infants i.e. 28.84%. However, the results were not statistically significant (p= 0.139). Similarly, in a hospital based observational study by Bhagat R et al, 57.4% males had meningitis as against 42.6% females (P >0.005). [7]

We cross tabulated the results i.e. frequency of meningitis with effect modifier i.e. Weight and found that Frequency of meningitis was higher i.e. 42.85% in low weight infants (3-4 Kg) as compared to infants with relatively more weight (>4 Kg). However, the results were not statistically significant (p= 0.374).This high incidence of meningitis in low birth weight and especially preterm has also been reported by Longe et al, [17]Moreno et al[18] and Anjos da Silva[19]. Jiang et al, [20] observed that late onset sepsis was significantly more common in very low birth weight and preterm neonates. We also cross tabulated the results i.e. frequency of meningitis with effect modifier i.e. Duration of symptoms and found that Frequency of meningitis was higher i.e. 43.47% among infants with shorter duration of symptoms (<3 days) as compared to infants with longer duration of symptoms (>3 days) i.e. 29.59%. However, the results were not statistically significant (p=

0.902).The study has certain limitations. It was carried out in single center on limited population size.

CONCLUSION

From the results of present study, it is concluded that Frequency of meningitis in neonates with late onset sepsis was high i.e. 34.02%. Frequency of meningitis was higher in younger infants, male, low weight infants and infants with shorter duration of symptoms. However, the results were not statistically significant (p>0.05).
Conflict of interest: Nil

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