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ORIGINAL ARTICLE

Risk Factors Associated with Early Onset of Sepsis

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ABSTRACT

Background: Neonatal sepsis (EOS) is among one of the leading cause of death that usually occurs due to infection in the first month of life and can be the result of various maternal and neonatal contributing factors.
Objectives: To determine maternal and neonatal contributing factors for early onset of sepsis in neonates.
Study design: cross sectional study
Period: From 13th April 2019 to 12th Oct 2019.
Settings: Neonatal units of pediatric medicine of central park teaching hospital Lahore and Bhatti international hospital Kasur.
Material and methods: After approval from hospital ethical committee total 151 neonates were selected using non-probable consecutive sampling. Neonates of both gender who were having gestational age >30 weeks with early onset sepsis were enrolled. Patients who had received antibiotics before presentation were excluded. 5ml of venous blood after proper sterilization was taken from all patients and sent to hospital laboratory for WBC count, CRP and blood culture. Data was entered in pre-designed Performa and analyzed using SPSS 20.
Results: There were total 151 patients in study, minimum and maximum age was 1 day and 7 days respectively with mean age of 3.66±1.88 days. Mean gestational age was 35.5±2.6 weeks and mean birth weight was 2.2±1.4 kg. There was slight increase in female patients 51% and 49% males. Among maternal contributing factors maternal fever was found in 64.9%, premature rupture of membrane was found in 43%, foul smelling liquor in 37.1% and meconium-stained amniotic fluid was found in 33.1% neonates. Among neonatal contributing factors prematurity was found in 66.2% low birth weight was present in 64.2%, and low APGAR score was present in 56.6 % neonates. Data was stratified for gender and contributing risk factors but p value was not statistically significant. Data was stratified for gestational age and p value was significant for prematurity, low birth weight and offensive smelling liquor.
Conclusion: Prematurity, low birth weight, low APGAR score and maternal fever were significant contributing factors in EOS.
Keywords: EOS, Neonatal contributing factors, Maternal contributing factors

INTRODUCTION

Neonatal sepsis is classified as early onset (0-7 day of life) or late onset (After 7th day of life or later). Neonates with EOS, 85% present within 1ST day of life (median age of presentation 6 hours), 5% present between 24-48 hours, and rest of percentage present between 48-72 hours. Onset of sepsis is found to be more rapid in premature babies. [1,18] Neonatal sepsis is among one of the major causes of neonatal deaths worldwide. The incidence of neonatal sepsis in Pakistan is approximately 31.3/1000 live births. [1,18] Timely diagnosis and aggressive medical care of these neonates are crucial for decreasing the burden of mortality and antibiotics resistance. [2] Blood culture are taken as gold standard diagnostic tools for diagnosis of sepsis. [3] EOS is infection that occurs within initial 72 hours of life by proven culture. [4] Bacterial organisms are hard to grow on cultures globally and more in developing countries, several studies have shown that the diagnosis of sepsis can be made by combining clinical signs and symptoms together along with some positive laboratory tests such as inflammatory markerer, C-Reactive Protein (CRP), Pro-calcitonin (PCT), Absolute Neutrophil Count (ANC), Immature to Total Neutrophil Ratio (I/T Ratio), Interleukin 6 or 8. [5]

There are various maternal and neonatal risk factors that are associated with EOS. A study conducted by Dr.Rahul V Bharad et al found that maternal fever was the most common maternal risk factor present in 67.5%. Other common risk factors were 1st pregnancy 77 (64.2%), prolonged rupture of membranes(PROM) >18 hours 49 (40.8%), meconium-stained liquor 29 (24.2%), age of mother <20 years 18 (15.0%) and foul-smelling amniotic fluid 14 (11.7%). Among neonatal risk factors 73 (60.8%) newborns were low birth weight having weight less than 2.5 Kg at birth. Prematurity was found in 71 (59.1%) patients and APGAR score <5 at 1 minute was found in 62 (51.7%) patients.[6,19]

The purpose of this study is to find the maternal and neonatal contributing factors which are associated with increased risk of early onset of sepsis in neonates presenting to remotely situated tertiary care hospital in rural areas. Identification of risk factors will help us to predict the risk of early onset sepsis in neonates and will help us to start empiric treatment early and will decrease the mortality as well morbidity that is associated with neonatal sepsis. Moreover, these risk factors can be prevented in future pregnancy to avoid risk of neonatal sepsis in next neonate and help to develop prophylactic management plan and also to establish local protocol to be followed in local hospital. In this way we can reduce the morbidity, mortality along with high expenditures on medication of these children.

MATERIAL AND METHOD

The cross-sectional study was conducted in the Pediatrics Department of Central Park Teaching Hospital, Lahore and Bhatti hospital Kasur Pakistan; after approval from institutional review board (CPMC/IRB/2015), from 13th April 2019 to 12th Oct 2019. Sample size of 151 patient was obtained by using the following formula:

$n= (Z_{1-\alpha/2})^2 \times P (1-P) / d^2$

Margin of error= 5%

$Z_{1-\alpha/2}$ = Confidence level 95%=1.96

P = Expected proportion in population = 11.7% least among all [Rahul V Bharad et al] [6]

d= absolute precision = 5%

Informed and written consent was taken from the parents or guardian of the neonates. All neonates of both gender who were more than 30 weeks of gestation presenting to neonatal unit within 7 days of life fulfilling the definition of early onset sepsis as per operational definition were included and Patients who had received antibiotics before presentation and Patients not agreed to participate in study were excluded.

Baseline demographic data like age in days, gestational age and gender was noted. Detailed history and examination were done to find maternal and neonatal risk factors. 5ml of venous

blood was taken from all patients and sent to hospital laboratory for WBC count, CRP and blood culture. All data was entered in Pre-designed Performa, All neonates were treated as per standard sepsis treatment according to hospital neonatal guidelines. Data was analyzed by SPSS version 20. Mean and standard deviation was calculated for the quantitative variables like age, gestational age and weight of neonate. Frequencies and percentages were calculated for qualitative variables like gender and neonatal and maternal contributing factors for EOS. Data was stratified for gender and gestational age. Chi square test was used and p value of ≤0.05 was considered as significant.

Operational Definitions:

1. Early onset sepsis: A neonate presenting to hospital within 7 days of life with at least one of clinical features: refusal to feed for more than 12 hours, lethargic, rectal temperature more than 38^{o}c or less than 36^{o}c, respiratory rate more than 60 breaths/min and having at least one of following lab criteria: white blood cell count more than 20000 cell/mm^3 or less than 10000 cell/mm^3, CRP more than 5mg/dl or positive blood culture.

2. Maternal contributing factors:

i. PROM: Premature rupture of membrane for more >18 hours before delivery.

ii. Maternal fever: Maternal temperature more than 38^{0}c within 24 hour before delivery.

iii. Foul smelling liquor: Determined by history from mother.

iv. Meconium stained amniotic fluid: Will be determined on history or medical record

3. Neonatal contributing factors

i. Low birth weight: Birth weight < 2.5 kg

ii. Prematurity: Less than 37 week of gestation determined on history and medical record (antenatal scan).

iii. Low APGAR score: APGAR score less than 5 determined on medical record.

RESULTS

There was total 151 patients in study, minimum and maximum age was 1 day and 7 days respectively with mean age of 3.66±1.88 days. Table 1

Mean gestational age was 35.5±2.6 weeks. Table 2

The mean birth weight was 2.2±1.4 kg. Table 3

There were 49% males and 51% females. Table 4

Among maternal contributing factors premature rupture of membrane was found in 43%, maternal fever was found in 64.9%, foul smelling liquor in 37.1% and meconium stained amniotic fluid was found in 33.1% neonates. Table 5

Among neonatal contributing factors low birth weight was present in 64.2%, prematurity in 66.2% and low APGAR score was present in 56.6 % neonates. Table 6

Data was stratified for gender and contributing risk factors but p value was not significant. Table 7

Data was stratified for gestational age and p value was significant for prematurity low birth weight and foul-smelling liquor. Table 8

Table 1: Statistics of age

Descriptive Statistics					
	N	Minimum	Maximum	Mean	Std. Deviation
Age in days	151	1	7	3.66	1.898

Table 2: Descriptive statistics of gestational age

Descriptive Statistics					
	N	Minimum	Maximum	Mean	Std. Deviation
Gestational age in weeks	151	30	42	35.5	2.6

Table 3: Descriptive statistics of weight

Descriptive Statistics					
	N	Minimum	Maximum	Mean	Std. Deviation
Birth weight in KG	151	1.2	4.2	2.2	1.4

Table 4: Gender distribution

	Frequency	Percentage
female	77	51%
male	74	49%
Total	151	100%

Table 5: Frequency of maternal contributing risk factors

Maternal contributing risk factors	Frequency	Percent
PROM	65	43
Maternal Fever	98	64.9
Foul Smelling Liquor	56	37.1
Meconium Stained Amniotic Fluid	50	33.1

Table 6: Frequency of neonatal contributing risk factors

Neonatal contributing risk factors	Frequency	Percent
Low Birth Weight	97	64.2
Prematurity	100	66.2
Low Apgar Score	84	55.6

Table 7: Data stratification for gender

		Gender						p-value
		Male		Female		Total		
		Count	%	Count	%	Count	%	
Meconium Stained Amniotic Fluid	Yes	26	52.0%	24	48.0%	50	100.0%	0.605
	No	48	47.5%	53	52.5%	101	100.0%	
Low Birth Weight	Yes	45	46.4%	52	53.6%	97	100.0%	0.389
	No	29	53.7%	25	46.3%	54	100.0%	
Premature	Yes	45	45.0%	55	55.0%	100	100.0%	0.168
	No	29	56.9%	22	43.1%	51	100.0%	
Low APGAR	Yes	40	47.6%	44	52.4%	84	100.0%	0.703
	No	34	50.7%	33	49.3%	67	100.0%	
Maternal Fever	Yes	48	49.0%	50	51.0%	98	100.0%	0.993
	No	26	49.1%	27	50.9%	53	100.0%	
Foul Smelling Liquor	Yes	27	48.2%	29	51.8%	56	100.0%	0.881
	No	47	49.5%	48	50.5%	95	100.0%	
PROM	Yes	32	49.2%	33	50.8%	65	100.0%	0.962
	No	42	48.8%	44	51.2%	86	100.0%	

Table 8: Data stratification for gestational age

		Gestational age				p-value
		Less than 37 weeks		More than 37 weeks		
		Count	Row N %	Count	Row N %	
Meconium Stained Amniotic Fluid	Yes	37	74.0%	13	26.0%	0.155
	No	63	62.4%	38	37.6%	

Low Birth Weight	Yes	97	100.0%	0	0.0%	0.000
	No	3	5.6%	51	94.4%	
Premature	Yes	100	100.0%	0	0.0%	0.000
	No	0	0.0%	51	100.0%	
Low APGAR	Yes	56	66.7%	28	33.3%	0.898
	No	44	65.7%	23	34.3%	
Maternal Fever	Yes	66	67.3%	32	32.7%	0.692
	No	34	64.2%	19	35.8%	
Foul Smelling Liquor	Yes	45	80.4%	11	19.6%	0.005
	No	55	57.9%	40	42.1%	
PROM	Yes	47	72.3%	18	27.7%	0.169
	No	53	61.6%	33	38.4%	

DISCUSSION

Neonatal sepsis is among the leading cause of mortality in the neonates. Neoborn who luckily survive can have significant neurologic damage as well multiorgan dysfunction as a consequence of central nervous system involvement, septic shock or hypoxemia secondary to severe parenchymal lung disease.

In our study among maternal contributing factors premature rupture of membrane was found in 43%, maternal fever was found in 64.9%, foul smelling liquor in 37.1% and meconium-stained amniotic fluid was found in 33.1% neonates. Among neonatal contributing factors low birth weight was present in 64.2%, prematurity in 66.2% and low APGAR score was present in 56.6 % neonates. Data was stratified for gender and contributing risk factors but p value was not significant. Data was stratified for gestational age and p value was significant for prematurity low birth weight and foul-smelling liquor.

Difference among male and female neonates human immune response is obvious; female neonates have more active cellular and humoral immune reaction so that they are more resistant to the infection.[7] In contrast to above results our study found no difference between both genders as there was almost equal number of males and females in our sample size. Shah et al have also demonstrated same result as per our study. [8] The study by Chako B et al have also shown no differences of infection rate between male and female. [9]

Study by Muhammad Hayun et al [10] showed that sample size was 221, with 44.8% male and 55.2% female. The mean of gestational age are 37 weeks and birth weight is 2596 grams. There were 11.3% with the maternal fever and premature rupture of membrane (PROM) was found in 31.2%.Meconium stained amniotic fluid (MSAF) was found in 14.5% . The demographic characteristics were same like our study and the determined risk factors were also same but in decreased frequency which can be attributed to population difference.

Low APGAR score can be due to multiple factors including the resuscitation of newborn.[11] Neonates having perinatal infection are at increased risk of having low APGAR score.[12] A study done by Chacko and Sohi also demonstrated that neonates with low APGAR score had 11 times increased risk of EOS.[13]

Shah et al study also gave the similar results of increased risk of sepsis with low APGAR score with OR of 5.7.[8] Findings by SOMAN M et al also showed 36.25 times increased risk of sepsis with low first minute APGAR score. [14] Same study shows similar results on birth weight, neonates who were low birth weight had 83 percent increased risk of sepsis that is in accordance with our study.[15] A study by Tallur et al showed association of prematurity with sepsis in 40 percent of neonates as contrast to our study which shows 66.2 percent in our study. [16] Another study shows increased risk of sepsis with PROM and prematurity. [17]

Bhutta and Yusuf [18] also found the same result as in our study of increased risk of sepsis associated with maternal fever. Proper history, physical examination and along with laboratory parameter are essential tools to predict occurrence of sepsis.

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