Acta Scientific PAEDIATRICS (ISSN: 2581-883X)

Volume 4 Issue 10 October 2021

Research Article

Clinicobacteriological Study of Neonatal Septicemia with Special Reference to Sepsis C-Reactive Protein and Procalcitonin

VL Jayasimha[1] and Shaswati Dey[2]*

[1]Professor and HOD Department of Microbiology, SSIMS and RC, Davangere, Karnataka, India

[2]Junior Resident, Department of Pediatrics SSIMS and RC, Davangere, Karnataka, India

***Corresponding Author:** Shaswati Dey, Junior Resident, Department of Pediatrics SSIMS and RC, Davangere, Karnataka, India.

Received: August 24, 2021

Published: September 29,2021

Abstract

Background: Neonatal sepsis can be described as an invasive bacterial infection which occurs within a month of life. Neonatal sepsis can present in two forms based on the age of onset, the one within 48hrs of birth is early onset sepsis (EOS) and the other late onset sepsis (LOS) which occurs after 48hrs after the birth. The incidence is 11 - 24.5/1000 live births in India.

Aim of the Study: This study aims at giving an outline of the load of bacterial sepsis in the developing countries in newborn population. The focus will be on the pathogens mostly implicated, their antibiotic susceptibility patterns, and management and finding out the diagnostic performance of procalcitonin and C-reactive protein in the intensive neonatal care unit as a early diagnostic marker.

Methodology: This study was conducted in Department of Microbiology at of S.S. Institute of Medial Science and Research Centre, Davangere. As per the criteria by Vergnano, clinically diagnosed neonates with septicaemia are included in the study. The study group comprised of 145 suspected cases of neonatal septicaemia in the neonatal intensive care unit. Blood culture by automated blood culture system was done along with C Reactive protein estimation by Nephelometry and Procalcitonin by Immunofluorometry.

Results and Discussion: In the present study out of total 145 cases, female were 64 (44%) and males were 81 (55%). In this study clinical feature like seizures and hurried breathing, grunting are seen in most of the neonates with *Klebsiella pneumoniae, E. coli* and *S. aureus* as major organisms. In this study out of 145 cases CRP positive cases were 51 (35%) and CRP negative cases were 94 (64%).

In this study out of 62 blood culture positive cases, CRP was positive in 32 cases and out of 83 blood culture negative cases 64 were negative.

In this study, among 62 positive blood cultures 48 cases had positive procalcitonin. We found positive procalcitonin in 36 cases where blood culture was negative. Out of 83 blood culture negative cases 47 had negative procalcitonin. In this study < 0.5 ng/ml PCT was found in 61 (42%), 0.5 - 2 ng/ml was found in 45 (31%), > 2 ng/ml was found in 39 (27%). It has sensitivity of 57.14% and specificity of 77.05%, positive predictive value of 77.4% and negative predictive value of 56.63%.

Keywords: Neonatal Septicemia; C-Reactive Protein; Procalcitonin; Early Onset Sepsis (EOS); Late Onset Sepsis (LOS)

Introduction

One of the important causes of morbidity and mortality in newborns is neonatal sepsis which is a systemic infection occurring within a month of life. Neonatal sepsis can present in two forms based on the age of onset, the one within 48 hrs of birth is early onset sepsis (EOS) and the other late onset sepsis (LOS) which occurs after 48 hrs after the birth. Viral or fungal sepsis may also occur at 7 days of life and must be ruled out from bacterial sepsis [1-4].

The incidence and mortality are greater among very-low birthweight (VLBW) infants are considered exclusively; for neonates with an extremely low birth weight of < 1,000g, the incidence is 26 per 1,000 and 8 per 1,000 livebirths in very low birth weight neonates of between < 1500 gms [5].

Pathogens responsible for early-onset neonatal sepsis are normal flora of the maternal genitourinary tract, which may ascend when the amniotic membranes rupture or prior to the onset of labor, leading to contamination of the amniotic fluid, causing an intra-amniotic infection [6]. Thus, the newborn may acquire the infection either *in utero* or intrapartum. Maternal risk factors for EOS includes, dietary intake of contaminated foods with *Listeria monocytogenes*, can arise before labor and delivery [7]. In pregnancy, maneuvers like cervical cerclage and amniocentesis, which increase the rates of intra-amniotic infection by rupture of amniotic cavity. Prolonged rupture of membranes, fever, vaginal colonization with group B streptococcus (GBS), and GBS bacteriuria are the important maternal factors during labor [8].

IgG antibodies in maternal serum against specific capsular polysaccharides of GBS is protective against infection with the relevant GBS strain in their neonates, whereas increased risk for GBS EOS has been shown in neonates born to mothers with low titers [9]. Chorioamnionitis, is also a major risk factor for neonatal sepsis which occurs as a result of longer length of labor and membrane rupture, repeated digital vaginal examinations, placement of internal fetal or uterine monitoring devices [10].

In utero swallowing of infected amniotic fluid by the fetus may lead to intrapartum sepsis, and colonization of the skin and mucus membranes by pathogens involved in chorioamnionitis which leads to high incidence of sepsis in newborns delivered to mothers with chorioamnionitis [11].

Infant factors leading to early-onset sepsis are prematurity/low birthweight, congenital anomalies and low APGAR scores [12]. In premature neonates immature immune system, diminished barrier function of the skin and mucus membranes, multiple invasive procedures like intravenous (i.v.) access and intubation in ill preterms are important risk factors [13]. In term and preterm infants GBS and *Escherichia coli*, which account for approximately 70% of infections are most commonly and frequently involved in EOS. Additional pathogens in minority of cases, are other *Streptococci*, *Staphylococcus aureus*, *Enterococcus* species, *Enterobacter* species, *Haemophilus influenzae* and *Listeria monocytogenes* [14].

The burden of disease attributable to *E. coli* and other gram-negative rods is increased, leading to gram-negative sepsis the most common etiology of EOS in preterm and VLBW infants when considered separately [15].

Prenatal screening and treatment with intrapartum antibiotics (IPA) has resulted in decrease in the frequency of early-onset GBS disease, however GBS remains one of the most common causes of EOS.

Acute-phase reactants: The two most commonly studied acute-phase reactants in neonatal sepsis are CRP and procalcitonin. Within 6 to 8h of infection CRP level rises and reaches maximum at 24h. Following inflammation IL-6 will be released, which stimulates an increase in CRP concentrations. A value of 10 mg/liter is the most commonly used cutoff in most published studies. CRP level is usually upto 5 mg/liter in Viral infections. When CRP measured within 24to 48h of onset of infection it gives better predictive value [16]. Increasing CRP levels is a superior predictor than individual values. Antibiotics can be safely discontinued if repeated values of CRP are normal which is strong evidence against bacterial sepsis. Procalcitonin is a propeptide of calcitonin that is significantly elevated during infections in neonates, children, and adults and produced mainly by monocytes and hepatocytes with half-life of about 24h in peripheral blood. The normal level for newborns within 72h of age is usually 0.1 ng/ml. In sepsis, PCT is synthesized by macrophages and the monocytic cells of the liver. Within 2 hours of an infectious episode PCT level increases, reaches maximum at 12 hours, and returns to normal level within 2 to 3 days in healthy adult volunteers. Procalcitonin concentration have more sensitivity less specificity than CRP concentration [17]. Definitive status of neonatal sepsis has not been established in central Karnataka as such. Little literature is available on CRP and procalcitonin levels in Neonatal sepsis.

Aim of the Study

The aim of this study is to analyse the burden of bacterial sepsis in the newborn population in developing countries with mainly focusing on the pathogens mostly implicated, their antibiotic susceptibility patterns, and management and to determine the diagnostic performance of procalcitonin and C -reactive protein as early diagnostic markers for the detection of neonatal sepsis in the intensive neonatal care unit.

Objectives of the Study

- To isolate all aerobic bacteria from blood culture of the clinically diagnosed neonates with septicemia.
- To evaluate the antibiotic sensitivity pattern in the isolated organism and drug resistance.
- To evaluate the diagnostic performance of Procalcitonin (PCT) and C-Reactive protein (CRP) as early diagnostic markers in neonatal sepsis.

Methodology

Source of data

This study was conducted in Department of Microbiology at of S.S. Institute of Medial Science and Research Centre, Davangere. As per the criteria by Vergnano, clinically diagnosed neonates with septicaemia are included in the study. The study group comprised of 145 suspected cases of neonatal septicaemia in the neonatal intensive care unit.

History of every neonate is included in the study regarding gestational age, birth weight, gender and other aspects as mentioned in the proforma. After clinical examination of the neonate by paediatrician, cases were considered for laboratory investigations.

Bacteriological culture

About 1 ml of blood was inoculated into 10 ml of brain heart infusion (BHI) broth and processed as per the protocol and incubated for one week at 37°C and was checked daily for evidence of bacterial growth in Automated blood culture system [18].

For positive broth cultures, subcultures were done next day on blood agar, Mac Conkey agar and Chocolate agar and were incubated at 37°C for 24 hours. If no growth occurred on plates after 24 hours, subsequent subcultures were done as per the standard procedures.

The grown bacteria were identified by colony morphology, Gram stain and standard biochemical tests. As per Clinical and Laboratory Standards Institute guideline (CLSI). The antibiotic susceptibility testing was performed by Kirby-Bauer disc diffusion method for the bacterial isolates. ATCC control strains were used accordingly as per standard procedures [18].

C-reactive protein

Estimation of serum CRP: Quantitative analysis was done by turbidometric method (MISPA NEPHELOMETRY).

Principle: This is a latex enhanced turbidimetric immunoassay. CRP samples attaches to specific anti-CRP antibodies, agglutinates when adsorbed to latex particles. Quantity of CRP in the sample as per Clinical and Laboratory Standards Institute guideline (CLSI) is directly proportional to the agglutination [19].

Reagent composition

- CRP R1-Glysine buffer.
- CRP R2- Latex suspension coated with anti CRP antibodies.
- Procedure done as per the guidelines in the kit.
- Measuring range -0.5 - 320 mg/l.
- Sample was considered as positive > 6 mg.

Estimation of procalcitonin

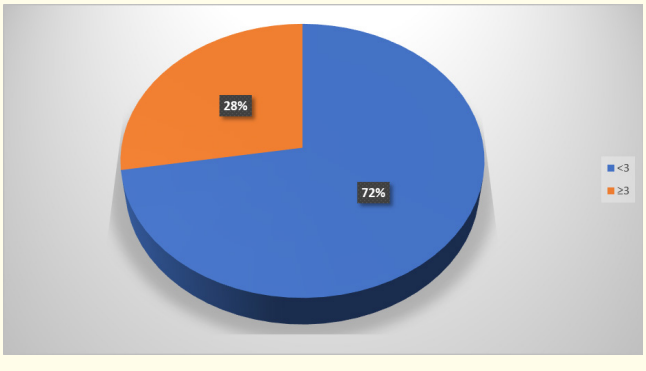
3 ml of serum sample was collected from above patients and were subjected to estimation of Procalcitonin by immunofluorescent method. The procedure for the estimation was done as per the manufacturer guidelines (Agappe Diagnostics Ltd.)

Results

Age distribution

Age (in days)	Number	Percent
< 3	105	72.4
≥ 3	40	27.6
Total	145	100.0

Table 1: Age distribution.



Graph 1: Age distribution.

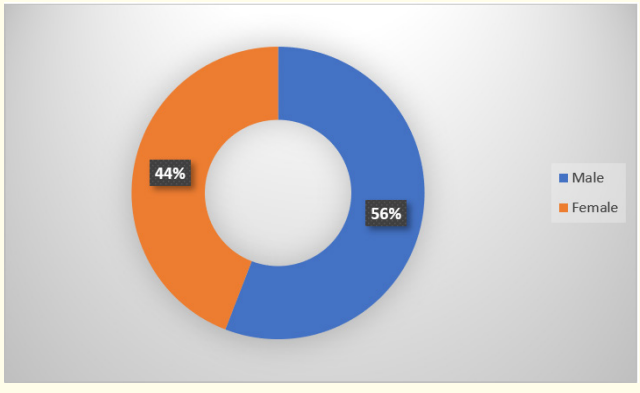
Observations

- In the present study maximum number of neonates were </= 3 days (n = 105; 72%) followed by neonates more than 3 days (n = 40; 28%).

Sex distribution

Sex	Number	Percent
Male	81	55.9
Female	64	44.1
Total	145	100.0

Table 2: Sex distribution.

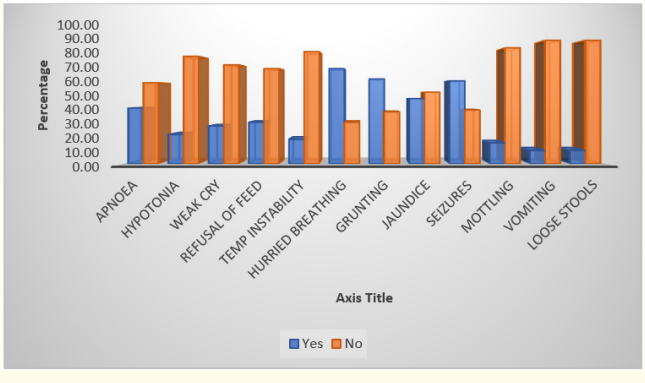


Graph 2: Sex distribution.

Observations

In the present study out of total 145 cases, female were 64 (44%) and males were 81 (55%).

Clinical features and blood culture positivity



Graph 3: Clinical features and blood culture positivity.

	Clinical feature present		Clinical feature Not present		Total	
	Number	%	Number	%	Number	%
Apnoea	59	40.70	86	59.31	145	100.00
Hypotonia	31	21.38	114	78.62	145	100.00
Weak cry	40	27.59	105	72.41	145	100.00
Refusal of feed	44	30.34	101	69.66	145	100.00
Temp instability	26	17.93	119	82.07	145	100.00
Hurried breathing	101	69.66	44	30.34	145	100.00
Grunting	90	62.07	55	37.93	145	100.00
Jaundice	69	47.59	76	52.41	145	100.00
Seizures	88	60.69	57	39.31	145	100.00
Mottling	22	15.17	123	84.83	145	100.00
Vomiting	14	9.66	131	90.34	145	100.00
Loose stools	14	9.66	131	90.34	145	100.00

Table 3: Clinical features and blood culture positivity.

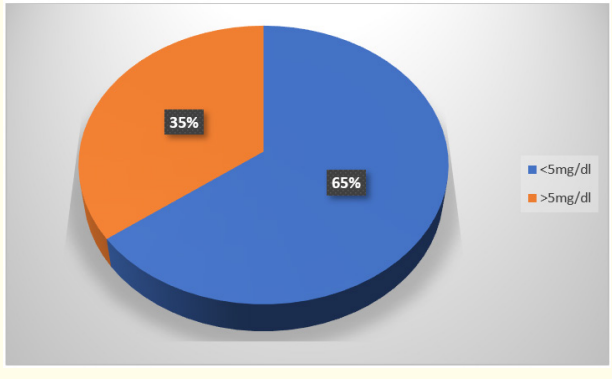
Observations

In this study clinical feature like seizures and hurried breathing, grunting are seen in most of the neonates.

CRP

CRP	No. of Neonates	Percent
< 5 mg/dl	94	64.8
≥ 5 mg/dl	51	35.2
Total	145	100.0

Table 4: CRP.



Graph 4

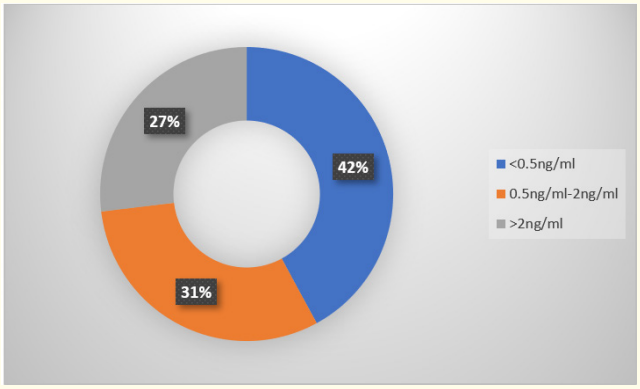
Observations

In this study out of 145 cases CRP positive cases were 51 (35%) and CRP negative cases were 94 (64%).

Procalcitonin

PCT	Number	Percent
< 0.5 ng/ml	61	42.1
0.5 ng/ml - 2 ng/ml	45	31.0
> 2 ng/ml	39	26.9
Total	145	100.0

Table 5: Procalcitonin.



Graph 5

Observations

In this study < 0.5 ng/ml PCT was found in 61 (42%), 0.5 - 2 ng/ml was found in 45 (31%), > 2 ng/ml was found in 39 (27%). It has sensitivity of 57.14% and specificity of 77.05%, positive predictive value of 77.4% and negative predictive value of 56.63%.

Clinical features and CRP

< 5 mg/dl		CRP ≥ 5 mg/dl		Total	p value
Apnoea	Yes	32	27	59	0.027
		54.2%	45.8%	100.0%	
	No	62	24	86	
		72.1%	27.9%	100.0%	
Hypotonia	Yes	15	16	31	0.031
		48.4%	51.6%	100.0%	
	No	79	35	114	
		69.3%	30.7%	100.0%	
Weak cry	Yes	25	15	40	0.717
		62.5%	37.5%	100.0%	
	No	69	36	105	
		65.7%	34.3%	100.0%	
Refusal of feed	Yes	33	11	44	0.090
		75.0%	25.0%	100.0%	
	No	61	40	101	
		60.4%	39.6%	100.0%	
Temp instability	Yes	20	6	26	0.154
		76.9%	23.1%	100.0%	
	No	74	45	119	
		62.2%	37.8%	100.0%	
Hurried breathing	Yes	66	35	101	0.843
		65.3%	34.7%	100.0%	
	No	28	16	44	
		63.6%	36.4%	100.0%	
Grunting	Yes	60	30	90	0.553
		66.7%	33.3%	100.0%	
	No	34	21	55	
		61.8%	38.2%	100.0%	
Jaundice	Yes	48	21	69	0.255
		69.6%	30.4%	100.0%	
	No	46	30	76	
		60.5%	39.5%	100.0%	
Seizures	Yes	60	28	88	0.293
		68.2%	31.8%	100.0%	
	No	34	23	57	
		59.6%	40.4%	100.0%	
Mottling	Yes	14	8	22	0.899
		63.6%	36.4%	100.0%	
	No	80	43	123	
		65.0%	35.0%	100.0%	
Vomiting	Yes	6	8	14	0.070
		42.9%	57.1%	100.0%	
	No	88	43	131	
		67.2%	32.8%	100.0%	
loose stools	Yes	9	5	14	0.964
		64.3%	35.7%	100.0%	
	No	85	46	131	
		64.9%	35.1%	100.0%	
Total		94	51	145	
64.8%		35.2%	100.0%		

Table 6: Clinical features and CRP.

Observations

In the present study, clinical features like hurried breathing (65.3%), seizures (60%) and grunting (60%) were commonly found to be associated with CRP positive cases.

Clinical features and procalcitonin

< 0.5 ng/ml		PCT			Total	p value
		0.5 ng/ml - 2 ng/ml	≥ 2 ng/ml			
Apnoea	Yes	23	17	19	59	0.490
		39.0%	28.8%	32.2%	100.0%	
	No	38	28	20	86	
		44.2%	32.6%	23.3%	100.0%	
Hypotonia	Yes	7	11	13	31	0.028
		22.6%	35.5%	41.9%	100.0%	
	No	54	34	26	114	
		47.4%	29.8%	22.8%	100.0%	
Weak cry	Yes	15	14	11	40	0.755
		37.5%	35.0%	27.5%	100.0%	
	No	46	31	28	105	
		43.8%	29.5%	26.7%	100.0%	
Refusal of feed	Yes	21	11	12	44	0.542
		47.7%	25.0%	27.3%	100.0%	
	No	40	34	27	101	
		39.6%	33.7%	26.7%	100.0%	
Temp instability	Yes	9	10	7	26	0.612
		34.6%	38.5%	26.9%	100.0%	
	No	52	35	32	119	
		43.7%	29.4%	26.9%	100.0%	
Hurried breathing	Yes	43	31	27	101	0.982
		42.6%	30.7%	26.7%	100.0%	
	No	18	14	12	44	
		40.9%	31.8%	27.3%	100.0%	
Grunting	Yes	40	30	20	90	0.266
		44.4%	33.3%	22.2%	100.0%	
	No	21	15	19	55	
		38.2%	27.3%	34.5%	100.0%	
Jaundice	Yes	27	21	21	69	0.638
		39.1%	30.4%	30.4%	100.0%	
	No	34	24	18	76	
		44.7%	31.6%	23.7%	100.0%	
Seizures	Yes	35	30	23	88	0.606
		39.8%	34.1%	26.1%	100.0%	
	No	26	15	16	57	
		45.6%	26.3%	28.1%	100.0%	
mottling	Yes	6	10	6	22	0.213
		27.3%	45.5%	27.3%	100.0%	
	No	55	35	33	123	
		44.7%	28.5%	26.8%	100.0%	
Vomiting	Yes	4	2	8	14	0.025
		28.6%	14.3%	57.1%	100.0%	
	No	57	43	31	131	
		43.5%	32.8%	23.7%	100.0%	
Loose stools	Yes	8	2	4	14	0.324
		57.1%	14.3%	28.6%	100.0%	
	No	53	43	35	131	
		40.5%	32.8%	26.7%	100.0%	
Total 42.1%		61	45	39	145	
		31.0%	26.9%	100.0%		

Table 7: Clinical features and Procalcitonin.

Observations

In our study grunting (40%), hurried breathing (43%), seizures (35%) are found in most of the neonates.

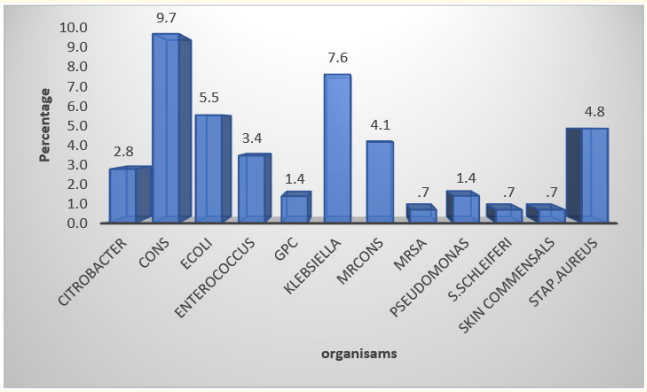
Organisms isolated in blood culture

Organisms	Neonates	Percent
Citrobacter spp	4	2.8
CONS	14	9.7
E. coli	8	5.5
Enterococcus spp	5	3.4
GPC	2	1.4
Klebsiella spp	11	7.6
MRCONS	6	4.1
MRSA	1	.7
Pseudomonas	2	1.4
S. schleiferi	1	.7
Skin commensals	1	.7
S. aureus	7	4.8

Table 8: Organisms isolated in blood culture.

Observation

In our study *Klebsiella pneumoniae, E. coli* and *S. aureus* pathogens were found to be identified in blood culture positive cases including CONS.

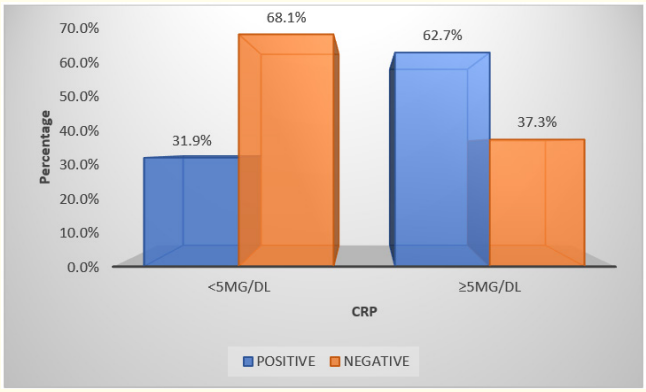


Graph 6

CRP and blood culture

CRP	Blood Culture		Total	P Value
	Positive	Negative		
< 5 mg/dl	30	64	94	0.000
	31.9%	68.1%	100.0%	
≥ 5 mg/dl	32	19	51	
	62.7%	37.3%	100.0%	
Total	62	83	145	
	42.8%	57.2%	100.0%	

Table 9: CRP and blood culture.



Graph 7

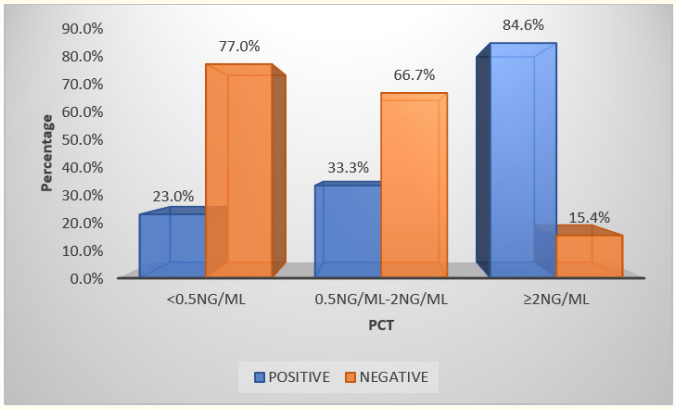
Observations

In this study out of 62 blood culture positive cases, CRP was positive in 32 cases and out of 83 blood culture negative cases 64 were negative.

Procalcitonin and blood culture

PCT	Blood culture		Total	
	Positive	Negative		P Value
< 0.5 ng/ml	14	47	61	0.000
	23.0%	77.0%	100.0%	
0.5 ng/ml - 2 ng/ml	15	30	45	
	33.3%	66.7%	100.0%	
≥ 2 ng/ml	33	6	39	
	84.6%	15.4%	100.0%	
Total	62	83	145	
	42.8%	57.2%	100.0%	

Table 10: Procalcitonin and blood culture.



Graph 8

Observation

In our study, out of 62 positive blood cultures 48 cases had positive procalcitonin. We found positive procalcitonin in 36 cases where blood culture was negative. Out of 83 blood culture negative cases 47 had negative procalcitonin.

Discussion

Sepsis is one of the most common cause of neonatal mortality and its diagnosis and management remains a challenge for health care workers [20]. Early diagnosis of sepsis and instituting antibiotic therapy at the earliest plays a crucial role in reducing the mortality rate.

Even though blood culture is the gold standard for diagnosis of neonatal sepsis, there is need of other diagnostic indicators of sepsis, as its positivity rate is low and is affected by blood volume inoculated, prenatal antibiotic use, level of bacteraemia and laboratory capabilities.

The laboratory tests are useful in evaluation of newborn with signs of infection vary. Laboratory tests like complete blood count is difficult to interpret because it varies significantly with day of life and gestational age in neonatal period. In early onset sepsis low value of white blood cells, low values of absolute neutrophil counts and high immature/total ratio are seen compared to late onset sepsis which shows high or low white blood cells counts, high absolute neutrophil counts, high immature to total ratio and low platelet counts are associated [21]. All of these findings have low sensitivities despite their association with infection.

Taking serial CRP determinations 24 - 48 hour after the onset of symptoms achieves a sensitivity of 74 - 89% and specificity of 74 - 95% compared to single value of C- reactive protein which has unacceptable low sensitivities, especially during the early stage of infection [22].

Procalcitonin increases faster than CRP, with overall sensitivity of 81% and specificity of 79% making it a very appealing biomarker.

Sex incidence

In a study done in Sion hospital Mumbai by Anuradha., *et al*. on sex incidence in neonatal sepsis found that male babies were commonly involved.

In our study also it was found that 56% were male babies whereas 44% were female. It is said that function of thymus and synthesis of immunoglobulins have a role in resistance against infection. And the genes for the same are located on X chromosome. Thus, it is found that females have double dose of genes affecting these factors compared to males [23].

Age distribution

Neonates with age 3 days or less than 3 days diagnosed with sepsis is said to be early onset sepsis. It is normally considered as a result of vertical transmission from mother during labour and delivery. Maternal risk factors include fever, urinary tract infection, colonisation with group B streptococcus, premature rupture of membranes. Foetal factors include prematurity, low APGAR score, low birth weight, male sex.

In our study also Early onset sepsis (72%) was found to be significant than late onset sepsis (27%).

Clinical features and blood culture positivity

V. Dhanalakshmi., *et al*. conducted a study in a medical college, Madurai, India had showed clinical feature correlation with neonatal sepsis. The study emphasised that the clinical features like hurried breathing, seizures, weak cry, refusal of feeds, vomiting, diarrhoea, apnoea, temperature instability, grunting and jaundice are associated with sepsis and many neonates had more than one manifestations [24].

In our study also we found that many neonates had more than one clinical manifestation among which hurried breathing, grunting, seizures and jaundice are more commonly found.

C reactive protein

Tillet and Francis in 1930 first described C-reactive protein. They concluded that it is a protein that helps in acute inflammation by complement binding to foreign or damaged cells and reaching maximum levels after fifty hours. CRP provides good idea regarding septicaemia diagnosis along with clinical evidence of the disease [25].

Effat Hisamuddin., *et al*. did a study in a neonatology unit in KRL general hospital aimed to find the time period when antibiotics treatment can be safely discontinued in case of suspected neonatal septicaemia using CRP as a tool in neonatal sepsis [26].

Singh., *et al*. observed that C-reactive protein had 80% sensitivity, 91% specificity and 92% positive predictive accuracy which was highest in their study.

In our study according to the literature and the method used to estimate CRP, value less than 5 mg/dl was taken as CRP negative cases and > 5 mg/dl was taken as CRP positive cases. And it was found that 35% were positive and 64% were negative. In this study out of 62 blood culture positive cases, CRP was positive in 32 cases and out of 83 blood culture negative cases 64 were negative. It has sensitivity of 48.39%, specificity of 20%, positive predictive value of 31.9% and negative predictive value of 37.25%. Subsequent studies have suggested that serial CRP are more reliable and useful in detection of sepsis [27].

Procalcitonin

PCT has been investigated intensively in neonatal sepsis for its diagnostic role. PCT levels were very low in those with no infections compared to high concentration of plasma PCT in infants with severe infection. Chiesa., *et al*. stated that an increase in PCT levels in early and late onset of neonatal sepsis is quite reliable. Noninfectious condition which induce abnormal values of CRP are perinatal asphyxia, respiratory distress syndrome, brain haemorrage and meconium aspiration syndrome and post surgical period [28].

PCT is a potential diagnostic variable for the diagnosis of bacterial infection because of the unique feature that PCT level increase in bacterial and fungal infections, but remain unchanged even in severe viral infections and other inflammatory diseases. Thayi S., *et al*. conducted a study in NICU of GSL Medical college, Andhra Pradesh, India. According to the study, out of 20 neonates with clinical sepsis 18 had negative PCT (0.5 ng/ml) and 2 had PCT weakly positive (0.52 ng/ml). Out of 18 blood culture positive/confirmed sepsis cases, PCT was found to be positive in 16 cases, with a sensitivity of about 88.8 percent [29].

In neonates in all sepsis groups PCT level was significantly higher compared to those in the control group ($P < 0.05$). At a cut-off of 0.5 ng/ml, the negative predictive value (NPV) of PCT was 80% and the positive predictive value (PPV) 39%.

In our study we found that out of 62 positive blood cultures 48 cases had positive procalitonin. We found positive procalcitonin in 36 cases where blood culture was negative. Out of 83 blood culture negative cases 47 had negative procalcitonin. It has sensitivity of 22.58%, specificity of 60%, positive predictive value of 22.95% and negative predictive value of 42.86%.

Spectrum of bacteria isolated

Desai K J., *et al*. showed that Gram negative bacteria were 67.85% and Gram positive bacteria were 28.57%.

Jyothi P., *et al*. in their study showed Gram negative bacteria accounted for 55.7% of cases and Gram positive 44.3% cases. *Klebsiella* spp, *Acinetobacter* spp and coagulase negative staphylococcus were most common organisms isolated [30].

According to James C, Gram negative enteric bacteria were the most common causative organisms. Several factors may be responsible for the susceptibility of the neonate to infection with these agents.

Postnatal the infant which are admitted in NICU are exposed to Gram negative organisms through humidification apparatus, resuscitation equipment and articles used in daily care. In the global perspective, group B *Streptococcus* (GBS), *Escherichia coli, Haemophilus influenzae* and *Listeria monocytogenes* are the microorganisms most commonly associated with early onset infection. In case of late onset infection causative organisms are Coagulase negative *Staphylococci, Staphylococcus aureus, E. coli, Klebsiella*, *Pseudomonas, Enterobacter, Candida*, GBS, *Serratia, Acinetobacter* and anaerobes [31].

In the present study Gram positive organisms mainly *Staphylococcus aureus* was found in most of the cultures. Gram negative organism which was more common is *Klebsiella*. The Gram positive cocci were found more than Gram negative bacilli.

Antibiotic sensitivity of bacterial isolates

The antimicrobial sensitivity pattern differs in different hospital studies as well as at different hospital studies as well as at different times in same hospital. This is because as a result of indiscriminate use of antibiotics leading to emergence of resistant strains [32]. Tsering D C., *et al*. stated in their study *Staphylococcus aureus* was the most common Gram-positive organism isolated. More than 70% of which were resistant to Penicillin, but were sensitive to Clindamycin (70%) and Vancomycin (40%). I Roy., *et al*. shown in their study that resistance to Penicillin was frequent in *S. aureus* 95% and CONS 89%, Resistant to Cefotaxime ranged from 63% to 65% and that to Ceftazidime ranged from 40% to 53% of Gram negative isolates [33]. A study by Amutha Chelliah., *et al*. showed

that there were a total of 30 (27%) *Staphylococcus aureus* isolated, out of which 17 (56%) were Methicillin resistant. Vancomycin is effective against all the MRSA strains [34]. 100% sensitive to Vancomycin is shown by *Enterococcus faecalis* and coagulase negative Staphylococci were also. In our study Linezolid was sensitive to *Staphylococcus aureus* and Meropenem sensitive to Gram negative bacilli like *Klebsiella*.

Conclusion

- Neonates who are more prone for septicemia are male, preterm and low birth-weight.
- Late-onset septicemia is less common early-onset septicemia.
- Prolonged rupture of membranes, home delivery, poor maternal health and hygiene of genitals predispose neonate to infections.
- Gram-positive septicemia is less common than Gram-negative septicemia.
- Procalcitonin rather than CRP correlates with infection positivity and can be used as a diagnostic as well as prognostic marker.
- Combination of tests like estimation of cytokines and other infection specific interleukins increases the specificity and positive predictive accuracy in diagnosis of neonatal sepsis.
- Above parameters will be used by in the second installment budget so that effectively we can identify the bacteria and the chemical mediators which predict early neonatal sepsis.

Bibliography

1. Kaistha N., *et al*. "Neonatal Septicaemia Isolates and Resistance Patterns in a tertiary care hospital of North India". *Journal of Infection in Developing Countries* 41 (2009): 557.
2. Shahla A., *et al*. "Trends in incidence of neonatal sepsis and antibiotic susceptibility of causative agents in 2 neonatal intensive care units in Tehran, Iran". *Journal of Neonatology* 1 (2012): 28-32.
3. Wagle S., *et al*. "C-reactive protein as a diagnostic tool of sepsis in very immature babies". *Journal of Pediatric Health Care* 30.1 (1994): 40-44.
4. Victor Blanchette and Alvin Zipursky. "Leucocyte disorders in new born infant". In: Gordon B Avery, editor. Neonatology. 3rd edition. Philadelphia: Lippincott (1987): 673-675.
5. Bhakoo ON. "Neonatal bacterial infections at Chandigarh. A decade of experience". *Indian Journal of Pediatrics* 47 (1980): 419-424.
6. Bhattacharyya., *et al*. "A study on blood culture positivity and C-reactive protein variability in neonatal septicaemia at neonatal intensive care unit of a tertiary care hospital". *Journal of Indian Medical Association* 110.12 (2012): 920-921.
7. Moreno MT., *et al*. "Neonatal sepsis and meningitis in a developing Latin American Country". *The Pediatric Infectious Disease Journal* 13.6 (1994): 516-520.
8. Moro ML., *et al*. "Risk factors for nosocomial sepsis in newborn intensive and intermediate care u units". *European Journal of Pediatrics* 155.4 (1996): 315-322.
9. Mehrotra N., *et al*. "Neonatal sepsis, correlation of maternal and neonatal factors to positive blood cultures". *Indian Pediatrics* 22 (1985): 275-280.
10. Ayengar Vidya., *et al*. "Neonatal sepsis due to vertical transmission from maternal genital tract". *The Indian Journal of Pediatrics* 58 (1991): 661-664.
11. Kuruvilla KA., *et al*. "Bacterial profile of sepsis in a neonatal unit in south India". *Indian Pediatrics* 35.9 (1998): 851-858.
12. Jyothi P., *et al*. "Bacteriological Profile of neonatal Speticaemia and antibiotic susceptibility pattern of the isolates". *Journal of Natural Science, Biology and Medicine* 4 (2013): 306-309.
13. Robert J and Schepal. "Increased susceptibility of male to infection". *Lancet* 2 (1969): 826.
14. Sinha N., *et al*. "Septicemia in neonate and early infancy". *Indian Journal of Pediatrics* 53 (1986): 249-256.
15. Khatua SP., *et al*. "Neonatal septicemia". *The Indian Journal of Pediatrics* 53 (1986): 509-514.
16. NNPD/AIIMS/ NF NNPD Network. National neonatal perinatal database, report 2002-2003. New Delhi: National Neonatal forum of India (2004).
17. Kaufman D and Fairchild K. "Clinical Microbiology of Bacterial and Fungal Sepsis in Very Low Birth Weight Infants". *Clinical Microbiology Reviews Journal* 17.3 (2004): 638-680.

18. Mehrotra N., *et al*. "Neonatal sepsis, correlation of maternal and neonatal factors to positive blood cultures". *Indian Pediatrics* 22 (1985): 275-280.

19. Ayengar Vidya., *et al*. "Neonatal sepsis due to vertical transmission from maternal genital tract". *The Indian Journal of Pediatrics* 58 (1991): 661-664.

20. Kuruvilla KA., *et al*. "Bacterial profile of sepsis in a neonatal unit in south India". *Indian Pediatrics* 35.9 (1998): 851-858.

21. Jyothi P., *et al*. "Bacteriological Profile of neonatal Speticaemia and antibiotic susceptibility pattern of the isolates". *Journal of Natural Science, Biology and Medicine* 4 (2013): 306-309.

22. Robert J and Schepal. "Increased susceptibility of male to infection". *Lancet* 2 (1969): 826.

23. Sinha N., *et al*. "Septicemia in neonate and early infancy". *Indian Journal of Pediatrics* 53 (1986): 249-256.

24. Khatua SP., *et al*. "Neonatal septicemia". *The Indian Journal of Pediatrics* 53 (1986): 509-514.

25. Bialkowska- Hobrzanska H., *et al*. "Molecular characterization of the coagulase-negative staphylococcal surface flora of premature neonates". *Journal of General Microbiology* 139 (1993): 2939-2944.

26. Toledano H., *et al*. "Prospective surveillance of vancomycin resistant enterococci in a neonatal intensive care unit". *European Journal of Clinical Microbiology and Infectious Diseases* 19 (2000): 282-287.

27. Stoll BJ., *et al*. "Changes in pathogens causing early onset sepsis in very low birth weight infants". *The New England Journal of Medicine* 347 (2002): 240-247.

28. Hanssler L., *et al*. "Listeriosis in newborn infants". *Klin Pad* 202.6 (1990): 379-382.

29. Ananthanarayan R. "Text book of microbiology". 6th edition. Orient Longman Limited". *Hydrabad* (2001): 70.

30. Sohn AH., *et al*. "Prevalence of nosocomial infections in neonatal intensive care unit patients: results from the first national point-prevalence survey". *The Journal of Pediatrics* 139 (2001): 821-827.

31. Papasian C., *et al*. "Transmission of Citrobacter koseri from mother to infant documented by ribotyping and pulsed field gel electrophoresis". *Diagnostic Microbiology and Infectious Disease* 26 (1996): 63-67.

32. Desai K., *et al*. "Neonatal Septicaemia: Bacterial Isolates and their antibiotics susceptibility patterns". *Gujarat Medical Journal* 66 (2011): 13-15.

33. Carivaro V., *et al*. "Pseudomonas aeruginosa in a neonatal intensive care unit: molecular epidemiology and infection control measures". *BMC Infectious Diseases* 9 (2009): 70.

34. Sharma M., *et al*. "Acinetobacter spp as Emerging Pathogen in Neonatal Septicemia". *Indian Journal of Pediatrics* 76 (2009): 861.

Volume 4 Issue 10 October 2021