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"CORRELATION OF PROCALCITONIN WITH SEPSIS SCREEN AND BLOOD CULTURE IN NEONATAL SEPSIS"

Paediatrics

Dr. Meghana SK* PG 3rd year, Department of Paediatrics, Maharashi Markandeshwar Institute of Medical Sciences And Research, MMDU, Mullana, Ambala, Haryana, India. *Corresponding Author

Dr. Praveen Kumar Reddy Mopuri PG 3rd year, Department of Paediatrics, Maharashi Markandeshwar Institute of Medical Sciences And Research, MMDU, Mullana, Ambala, Haryana,India.

Dr. A.K.Bhardwaj Professor And HOD of Department of Paediatrics, Maharashi Markandeshwar Institute of Medical Sciences And Research, MMDU,Mullana, Ambala , Haryana , India.

ABSTRACT

BACKGROUND – Sepsis in neonates may be difficult to differentiate from other conditions, because the clinical signs are non-specific. It is a common cause of morbidity and mortality amongst neonates in NICU. Neonatal sepsis is a clinical syndrome which is accompanied by signs and symptoms of infection during first 4 weeks of life. Neonatal mortality accounts for about 40% deaths under five years of age. Global incidence of neonatal deaths caused by sepsis is only 15% but in a developing country like our sepsis accounts for about 30% -50% of neonatal mortality. Delay of even few hours in initiating treatment can increase mortality and morbidity considerably.

AIMS AND OBJECTIVES-

AIM- To correlate procalcitonin with sepsis screen and blood culture in neonatal sepsis.

OBJECTIVES-

A. To compare procalcitonin and CRP with culture positivity in diagnosing neonatal sepsis.
B. To Determine sensitivity, specificity and predictive value of Procalcitonin as an indicator of neonatal sepsis in comparison with blood culture.
C. To predict the value of altered WBC and platelet counts in diagnosing neonatal sepsis.
D. To correlate culture proven sepsis with maturity of neonate, birth weight and mode of delivery.

Material: 100 clinically suspected cases of Sepsis in neonates admitted to MMIMSR, Mullana, Ambala.

Methods: All neonates who were suspected clinically as a case of sepsis based on sepsis score and categorized into (0- 72 hours PNL) EOS or LOS (>72hours PNL) depending on day of presentation of clinically suspected sepsis. Detailed history along with clinical findings of neonates were noted.

SERUM PROCALCITONIN, SEPSIS SCREEN with predetermined cut off values and during the same time blood culture was taken and sent. Depending on clinical condition CSF analysis, Urine analysis, Chest Xray were sent. Sensitivity, specificity and predictive values of procalcitonin, CRP and other parameters were assessed.

RESULTS- In this study of 100 neonates with clinical suspicion of sepsis admitted in NICU in MMIMSR over a period of 16 months from JAN 2020 to JUNE 2021. Out of 100 cases of the number of male neonates included in this study was greater than the female neonates suggesting that in clinically suspected neonatal sepsis male neonates were affected more than female neonates. Out of 100 neonates 63 neonates were male (63%) and 37 were female (37%). Laboratory finding of positive blood culture of sepsis of male neonates is 10 (56%), whereas female neonates of positive blood culture of sepsis is 8 (44%). Culture positivity showed only a slight rise in male neonates than females which was not much of a difference. . About three-fold increase in culture positivity was seen in preterm neonates (55%) when compared to term neonates (19%). Laboratory finding of positive blood culture of SGA neonates is 10 (19%), AGA is 8 (17%). Culture positivity showed SGA neonates has greater sepsis cases than AGA neonates. Association of sepsis score with procalcitonin value. On applying regression analysis, we found there is no association with R square 0.004. Association of CRP value with procalcitonin value. On applying regression analysis, it was found very mild association with R square 0.028. shows Association of absolute leucocyte count value with procalcitonin value. On applying regression analysis, we found **very mild association with R square 0.069.**

Association of blood culture with procalcitonin. On **applying t test** between positive and negative blood culture with procalcitonin value **we found significant association** of procalcitonin value (p value <0.05).

CONCLUSION-In this study the risk factors commonly associated with neonatal sepsis were found to be LBW, VLBW, ELBW, Prematurity, LSCS, instrumental delivery that is assisted vaginal. delivery. EONS was more common than LONS.

Procalcitonin was found to be a sensitive tool for diagnosis and it also helps predicting the outcome of sepsis as compared to CRP but it cannot be used as a sole marker as its neither 100% sensitive and it's not 100% specific. The predictability can be achieved by a combination of markers of neonatal sepsis rather than a single marker but as of now BLOOD CULTURE remains the gold standard in diagnosis of neonatal sepsis.

KEYWORDS

INTRODUCTION-

Neonatal sepsis (NS) is a clinical syndrome characterized by systemic signs and symptoms of infection with or without accompanying bacteremia in the first month of life. Suspected sepsis is one of the most common diagnosis in NICU owing to its vague signs and symptoms but even after improved antenatal screening, obstetric management, intrapartum screening and use of antibiotics neonatal sepsis still remains an important contributor to neonatal morbidity and mortality.[1]

Early-onset sepsis (EOS) is defined as sepsis occurring in the first 72 hours of life and that occurring beyond 72 hours is defined as late-onset sepsis (LOS). Its incidence varies from 25.3 per thousand live births in Asia of which 22.2 per 1000 live birth is EOS and 2.9 per 1000 is LOS.[1] Based on the new definition, sepsis is currently defined as "life-threatening organ dysfunction, caused by a dysregulated host immune response to infection". Currently, the World Health Assembly (WHA), the WHO's decision-making body, recognizes sepsis as a significant threat to patient safety and global health and has intensified its approach to the prevention, diagnosis, and treatment of sepsis.[2]

The immature immune system is the major contributing factor for increased neonatal susceptibility to sepsis. The immature function of polymorphonuclear neutrophils, macrophages, and T lymphocytes makes these cells incapable of carrying out a complete inflammatory response in neonates. Furthermore, neonates have a limited number of immunoglobulin at birth and cannot generate a quantitative and/or qualitative adequate mounting response against infectious agents. The insufficient time that premature has in the uterus decrease the transfer of immune globulins to the fetus. This deficiency in immunoglobulin makes premature infants at much higher risk for sepsis when compared to term infants.[3]

Unfortunately signs and symptoms of early-onset neonatal sepsis such as respiratory distress and irritability are vague and not confined to the diseases; other non- infectious processes also may present with the same manifestations. Conventional methods for diagnosis of sepsis lack enough sensitivity and specificity. A positive blood culture would be reflective of an asymptomatic underlying bacteremia with less

concern while a negative result for blood culture may not assure lack of infection[4].

There are many available markers for NS but each with limitations; Complete Blood Count (CBC), immature: total neutrophil count (I: T ratio) and absolute neutrophil count (ANC) do not have sensitivity especially if measured early in the course of sepsis. Though culture is the gold standard for confirmation, result is influenced by various factors such as prior use of antibiotics including in the prenatal period, bacterial load, laboratory standards and is time-consuming (up to 72 hours); it often fails to identify the causative organism in infected infants given low culture yields.[4]

Isolation of the causative microorganisms by using blood culture has been the gold standard method for its diagnosis. However, as pathogens in blood cultures are only detected in approximately 25% of patients, the sensitivity of blood culture is suspected to be low. Besides, Definitive culture results take at least 48–72 h, resulting in treatment delays, it is impractical to obtain blood sample for serial blood culture from infants. Therefore, there is need for newer diagnostics methods to obtain a rapid indication of the infectious status of neonates with suspected sepsis.[5]

Due to diagnostic delay suspected neonates are subjected to broad-spectrum antibiotic treatment empirically until sepsis can be excluded. The antibiotic overuse favours the development of resistance. So, improving the accuracy of the diagnostic tests may decrease the indiscriminative use of antibiotics in cases without sepsis .[6]

Hence, there is scope of using certain rapid diagnostic tests such as C-reactive protein (CRP), micro erythrocyte sedimentation rate (m-ESR), buffy coat smear examination, total white blood cell (WBC) count, absolute neutrophil count (ANC), immature/total neutrophil count ratio, and platelet (PL) count collectively termed as the "Sepsis Screen".[7]

White blood cell (WBC) counts; differential, absolute neutrophil counts; and the ratio of immature to total neutrophils in the blood are widely used as screening tests for neonatal sepsis. Unfortunately, none of these tests have been particularly useful in identifying the majority of septic infants. Normal neutrophil values are age dependent, with a peak during the first 12 to 14 h of age (range, 7,800 cells/mm^3 to 14,500 cells/mm^3). During 72 h to 240 h, the values range from 2,700 cells/mm^3 (5th percentile) to 13,000 cells/mm^3 (95th percentile) in full-term infants. Total white blood cells count have a poor positive predictive value (PPV) for sepsis. Neutropenia has greater specificity for neonatal sepsis, but the definition of neutropenia is dependent on gestational age, delivery method, and altitude. Absolute immature neutrophil counts peak at 12 h of age, from a maximum value of 1,100 cells/mm^3 to 1,500 cells/mm^3 at 12 h. In contrast, a maximum normal ratio of immature to total white blood cells (I:T ratio) of 0.16 occurs at birth and reaches a nadir of 0.12 with increasing postnatal age. A single value of the I:T ratio (>0.3) has a very high negative predictive value (NPV) (99%) but a very poor positive predictive value (25%) for neonatal sepsis. In a study of 1,539 neonates, Murphy and Weiner found that a combination of 2 serial normal I:T ratios and a negative blood culture at 24 h in a neonate shortly after birth was accurate in ruling out neonatal sepsis. Typically, neonates with viral infections, including HSV, enteroviruses, and HPV, have normal WBC counts or very mild leukopenia[8]. Platelet counts are not very sensitive or specific for the diagnosis of neonatal sepsis and not are very helpful in monitoring the response to therapy.[9]

PCT is a biomarker with a potential earlier rise in response to infection, often used to differentiate sepsis from systemic inflammation. The half-life (25-30 hours) and serum/plasma stability of PCT make it an easy parameter for routine use as compared to other inflammatory cytokines.[10]

In 1975, Moya F et al. suggested the existence of a precursor for calcitonin in chicken. The large biosynthetic molecule splits intracellularly to generate the hormone, and they named it as procalcitonin. Allison's study (1981) in RNA isolated from human medullary carcinoma demonstrated the synthesis of calcitonin as a precursor protein molecule in human. Later studies show that calcitonin is secreted after a sequential Co and post translational modification like glycosylation proteolytic cleavage, etc. In healthy individuals, PCT is produced in thyroid C cells, from a CALC-1 gene located on chromosome. The mRNA product is known as Preprocalcitonin. It is further modified to 116 amino acid procalcitonin. Finally, it is cleaved into 3 distinct molecules; active calcitonin (32 amino acid), kata calcitonin (21 amino acid) and N-terminal procalcitonin (57 amino acid). Calcitonin hormone is involved in the homeostasis of calcium and phosphorous.[11]

Normally, CALC-1 gene in thyroid C cells are induced by elevated calcium level, glucocorticoid, calcitonin gene-related peptide (CGRP), glucagon, gastrin or β-adregenic stimulations. Practically, all the PCT formed in thyroid C cells are converted to calcitonin so that no PCT is released into the circulation. Hence, the PCT level in healthy subjects is very low (0.05 ng/mL) but the inflammatory release of PCT is independent of the above regulations. During inflammation, PCT is produced mainly by two alternative mechanisms; direct pathway induced by lipopolysaccharide (LPS) or other toxic metabolite from microbes and indirect pathway induced by various inflammatory mediators like IL-6, TNF-α, etc. In bacterial septicaemia, PCT is produced by alternate pathways, either directly or indirectly. For better understanding of the pathophysiology of calcitonin precursor in sepsis, an experiment was conducted in animal (hamsters) analogue to human sepsis.[12]

During sepsis, ubiquitous and uniform expressions of calcitonin (CT) mRNA in multiple tissues were observed in hamsters. In healthy hamsters, PCT mRNA was isolated primarily from the thyroid with minute amounts of synthesis associated with lung tissue. The next set of hamsters was infected with gram-negative bacteria, and the level of PCT mRNA in various tissues and cells were observed. White blood cells (WBC), spleen, kidney, adipocytes, pancreas, colon and brain showed a significantly elevated level of PCT mRNA. Many reports are available which shows that PCT levels are elevating rapidly between 2 and 6 h which peaks within 6–24 h during bacterial infection.[11]

We had conducted this study for the comparison of procalcitonin with sepsis screen and blood culture in the diagnosis of neonatal sepsis.

AIMS AND OBJECTIVES

AIMS:

To correlate procalcitonin with sepsis screen and blood culture in neonatal sepsis.

OBJECTIVES:

A. To compare procalcitonin with CRP and culture positivity in diagnosing neonatal sepsis.
B. To correlate culture proven sepsis with maturity of neonate, birth weight and mode of delivery.

MATERIAL AND METHODS

This prospective study was conducted in the Department of Pediatrics in MMIMSR, Mullana, Ambala from JAN 2020 to JUNE 2021. Blood samples was conducted from 100 clinically suspected cases of neonatal sepsis admitted in MMU hospital. The blood samples were collected from 100 clinically suspected cases of Sepsis in neonates admitted to MMIMSR, Mullana, Ambala constituted material for the study. Detailed history and clinical findings were recorded in the Performa.

- **Inclusion Criteria:**

Neonates presenting with following:

- **Perinatal risk factors:**
- LBW
- Prematurity
- Birth asphyxia
- Home delivery
- PROM more than 24 hours
- Maternal fever
- Instrumentation
- **Clinical risk factors:**
- Poor feeding and lethargy.
- Sclerema.
- Hypothermia/Fever.
- Jaundice.
- Respiratory distress.
- Apnoea, tachypnoea.
- Feeding intolerance.
- Skin mottling.
- Bleeding tendencies.
- Seizures.

- **Exclusion Criteria**:
- Neonates who received antibiotics before admission.

METHODS:

All neonates who were suspected clinically as a case of sepsis based on sepsis score and categorized into (0- 72 hours PNL) EOS or LOS (>72hours PNL) depending on day of presentation of clinically suspected sepsis. Detailed history along with clinical findings of neonates were noted. Depending on the perinatal risk factors each baby was given a score based on the septic score below

Perinatal Infection Risk Score:[1,13,14]

SL No	Perinatal risk factor	Risk Score
1	Foul smelling liquor.	2
2.	Unclean vaginal examination done before delivery.	2
3.	Duration of labor exceeding 24 hours.	2
4.	Birth asphyxia (Apgar < 6 at 1 min).	2
5.	Birth weight 2.5 Kgs or less and/ or gestation age <37 weeks.	3
6.	Duration of rupture of membrane before delivery > 24 hours.	1
7.	Maternal pyrexia	1
Total Score		**13**

Action based on score:
Score <3: was observed clinically.
Score ≥4: was Investigated.

All neonates who are clinically symptomatic or having septic score > 4 will be screened.

SERUM PROCALCITONIN, SEPSIS SCREEN with predetermined cut off values and during the same time blood culture was taken and sent. Depending on clinical condition CSF analysis, Urine analysis, Chest Xray were sent.

The cut off values of the positive rapid screening tests in this study are as follows:[1,4,6,7]

1)	Procalcitonin	Low risk of sepsis <0.5ng/ml High risk of sepsis > 0.5ng/ml.
1)	C-Reactive protein (CRP):	> 10mg/L.
2)	Total leucocyte count (Leukopenia):	< 5,000 cells/cu.mm.
3)	Absolute neutrophil count (Neutropenia):	< 1500cells/cu.mm.
4)	Band cell count to total neutrophil count ratio (I/T):	> 0.2.
5)	Platelet count (thrombocytopenia):	< 1.5 lakhs/cu.mm

A prior approval of The Institutional Ethics committee was obtained. The study didn't impose any financial burden on the parents or guardians of the study group and an informed written consent was taken from the parents/guardians of the participants before conducting the study. All participants were ensured confidentiality. The study was not funded by any agency.

Statistical Analysis:

The data was compiled and analyzed using MS Excel (R) office 365, Graph Pad prism 8.4.2 and SPSS version 25. Descriptive statistics were presented in the form of proportions/percentages for categorical variables and mean & standard deviation for continuous data variables. Fisher Exact test/Chi square test was used for the comparison of proportions (Categorical variables). Continuous variables were analyzed using the Mann Whitney test/student T test (Independent group/Unpaired data) and Wilcoxon sign rank test/Paired T test (for paired data) based on the normality of the data. P value of <0.05 was considered significant.

RESULTS:

Table 1: Demographic profile of the study participants

Variable	Frequency (Percentage)
Female	37(37%)
Male	63(63%)
Primigravida	44(44%)
Multigravida	56(56%)
Term	31(31%)
Preterm	69(69%)
Suspected EONS	86(86%)
Suspected LONS	14(14%)

Table 2: The mean value of sepsis score and CRP level

	Mean	SD
Sepsis score	5.01	1.202
CRP level	15.66	23.01
Total leucocyte count	10702.1	5520.08
Absolute leucocyte count	5133.49	3864.77
Band cell count to neutrophil count	0.08	0.27

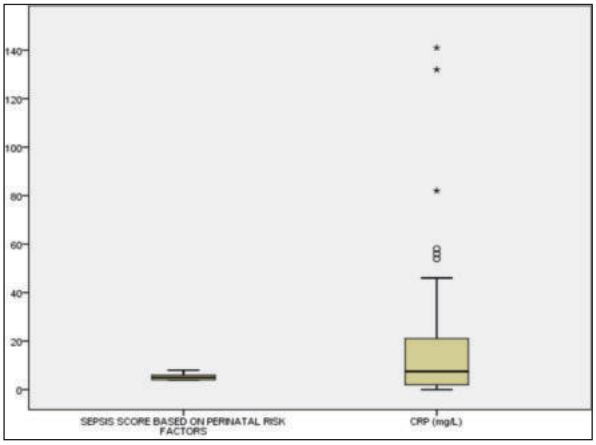

Fig1: Boxplot diagram for sepsis score and CRP level

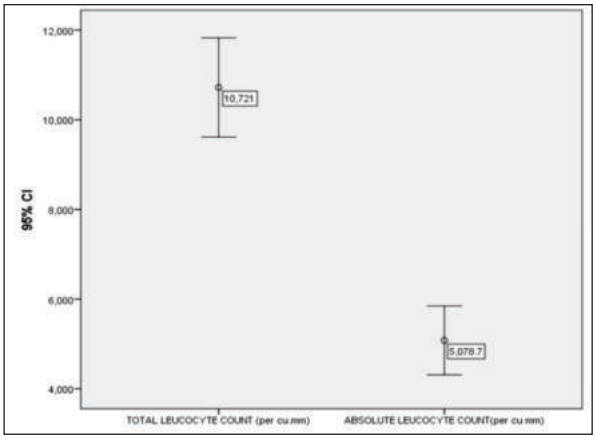

Figure2: Error diagram for TLC and absolute neutrophil count.

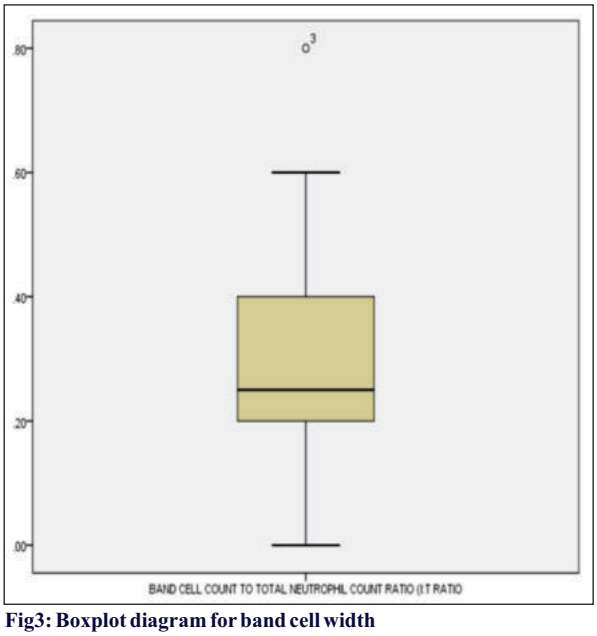

Fig3: Boxplot diagram for band cell width

Table 3: Distribution based on blood culture.

Variable	Frequency (Percentage)
Blood culture positivity	18(18%)
Blood culture negativity	82(82%)

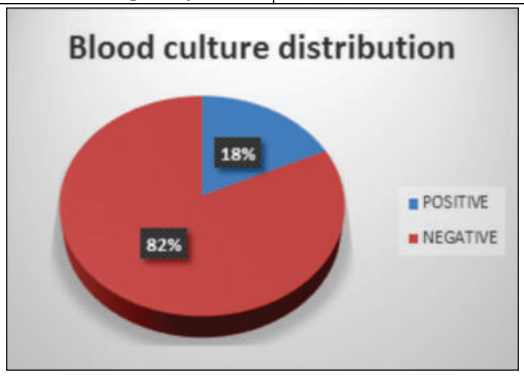

Fig 3: Distribution based on blood culture

Table 4: Distribution of different organisms found on blood culture

BLOOD CULTURE REPORT	FREQUENCY	PERCENTAGE
CONS	4	22.00%
E COLI	4	22.00%
Enterococcus faecalis	2	11.11%
Klebsiella pneumonia	3	16.67%
MRSA	5	28%
Total	18	100%

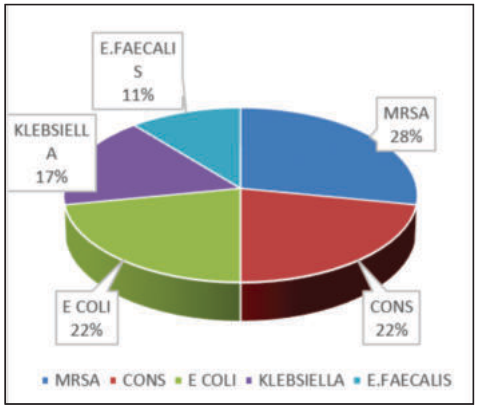

Fig 4: Distribution of different organisms found on blood culture

Table 5: Distribution Based On The Onset Of Sepsis Among Culture Proven Sepsis.

NEONATAL SEPSIS	NO OF CULTURE PROVEN SEPSIS (n=18)	PERCENTAGE (%)
EONS	**15**	**83.3%**
LONS	**3**	**16.7%**
TOTAL	**18**	**100%**

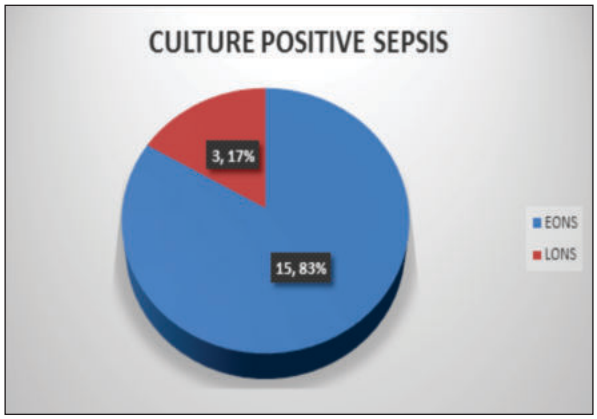

Fig 5: Distribution based on the onset of sepsis among culture proven sepsis

Correlations-

Table 6: Correlation of Gender of the Neonates with positive blood culture.

BLOOD CULTURE * GENDER CROSS TABULATION				
		GENDER		Total
		Female	Male	
Blood culture	negative	29	53	82
	positive	8	10	18
Total		37	63	100
Chi-square value- 0.52, p value – 0.47, not significant				

Laboratory finding of positive blood culture of sepsis of male neonates is 10 (56%), whereas female neonates of positive blood culture of sepsis is 8 (44%). Culture positivity showed only a slight rise in male neonates than females which was not much of a difference.

Table 7: Correlation Class of Gestation and Positive Blood Culture

CLASS OF GESTATION * blood culture Crosstabulation				
Count				
		blood culture		Total
		Negative	positive	
CLASS OF GESTATION	PRETERM	57	12	69
	TERM	25	6	31
Total		82	18	100
Chi-square value- 2.17, p value- 0.7, non-significant				

About two-fold increase in culture positivity was seen in preterm neonates 12 (67%) when compared to term neonates 6(33%).

		blood culture		Total
		negative	positive	
RESUSCITATION AT BIRTH	No	41	8	49
	Yes	41	10	51
Total		82	18	100
Chi-square value- 0.18, p value- 0.67, non-significant				

Out of 100 neonates' sepsis, 51%(n=51) of neonates had resuscitation at birth. Whereas 49% (n=49) of neonates didn't had resuscitation at birth. Laboratory finding of positive blood culture of resuscitation at birth of neonates is 10 (56%), whereas the neonates those who doesn't had resuscitation of positive blood culture of sepsis is 8 (44%). Culture positivity showed only a slight rise in resuscitation at birth of neonates than those who doesn't had resuscitation.

Table 8: Class of Birth Weight with positive blood culture.

CLASS OF BIRTH WEIGHT * blood culture Crosstabulation				
Count				
		blood culture		Total
		negative	positive	
CLASS OF BIRTH WEIGHT	ELBW	7	0	7
	LBW	39	14	53
	NORMAL BIRTH WEIGHT	24	2	26
	VLBW	12	2	14
Total		82	18	100
Chi-square value- 6.08, p value- 0.108, non-significant				

Out of 100 neonates' sepsis, 54% of neonates were under Low-Birth-Weight category. Whereas 26% of neonates were under Normal Birth Weight, 13% of neonates were under very low birth weight category and only 7% of neonates were under extreme low birth weight category. Laboratory finding of positive blood culture of LBW neonates is 14(78%), NBW is 2 (11%) and VLBW is 11%. Culture positivity of 89% (78% 0f LBW + 11% VLBW) in neonates with <2.5Kg showed that LBW neonates had greater sepsis cases than NBW neonates.

Table 9 : Weight as per Gestation with positive blood culture.

WEIGHT AS PER GESTATION * blood culture Crosstabulation				
Count				
		blood culture		Total
		negative	positive	
WEIGHT AS PER GESTATION	AGA	42	7	49
	SGA	40	11	51
Total	82	18	100	
Chi-square value- 0.898 p value- 0.343, non-significant				

Out of 100 neonates' sepsis, 52% (n=52) of neonates were under SGA category. Whereas 48% (n=48) of neonates were under AGA. Laboratory finding of positive blood culture of SGA neonates is 10 (56%), AGA is 8 (44%). Culture positivity showed SGA neonates has greater sepsis cases than AGA neonates

Table 10: Association of blood culture with procalcitonin

Report			
PROCALCITONIN QUANTITATIVE			
blood culture	**Mean**	**N**	**Std. Deviation**
negative	.77	82	1.179
positive	1.67	18	1.572
Total	.93	100	1.297
t test- 2.75, p value< 0.05, significant association			

Association of blood culture with procalcitonin. On **applying t test** between positive and negative blood culture with procalcitonin value **we found significant association** of procalcitonin value.

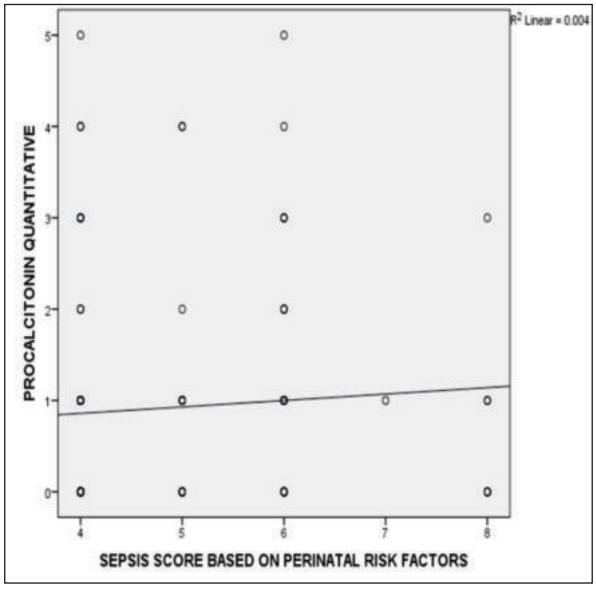

Fig 6: Association of sepsis score with procalcitonin value

Fig 6 shows Association of sepsis score with procalcitonin value. On applying regression analysis, we found there is no association with R square 0.004.

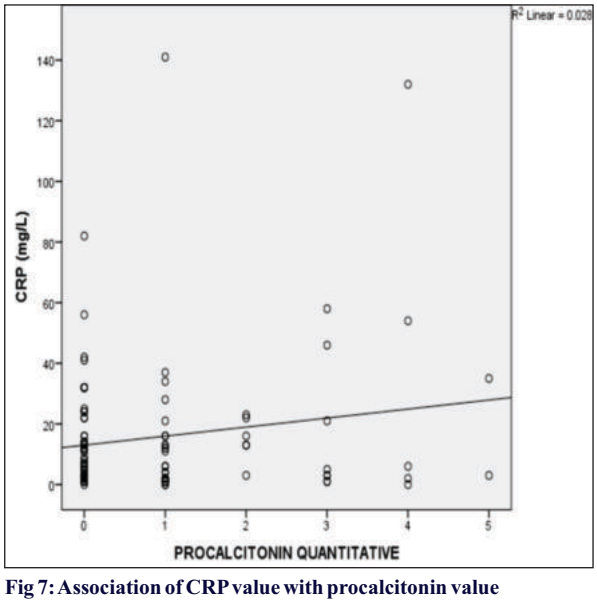

Fig 7: Association of CRP value with procalcitonin value

Fig 7 shows Association of CRP value with procalcitonin value. On applying regression analysis, it was found very mild association with R square 0.028.

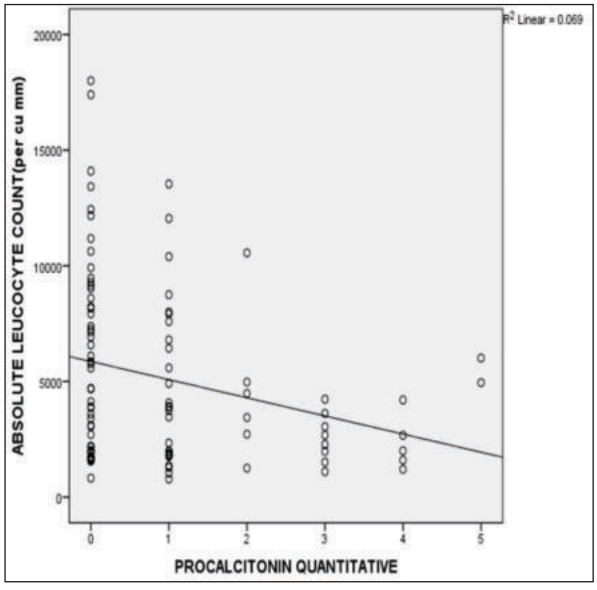

Figure8: Association of absolute leucocyte count value with procalcitonin value

Figure 8shows Association of absolute leucocyte count value with procalcitonin value. On applying regression analysis, we found **very mild association with R square 0.069.**

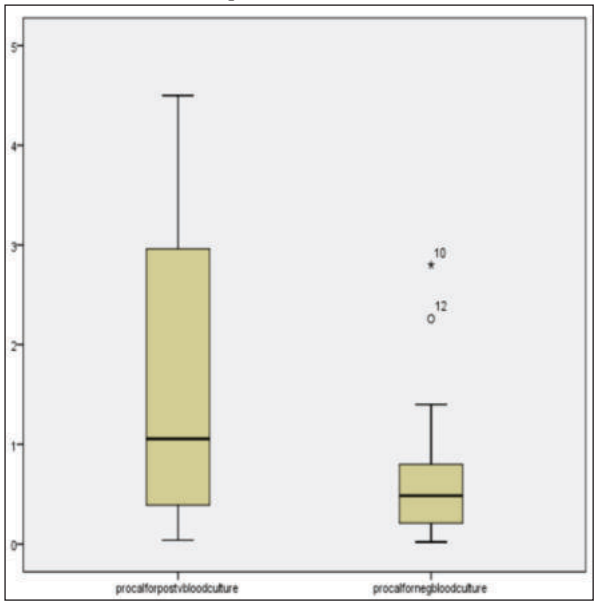

Fig 9: Association of blood culture with procalcitonin

DISCUSSION-

Gender

In the present study out of 100 clinically suspected cases of neonatal sepsis 63% were male whereas 37% were females. The male is to female population of the index study was 1.7:1, which is comparable to the studies conducted by **Abnish Kumar Bharti et al**.[1]males were 73% and females 27%; **Angadi W.A.et al**.[14]males 61.0% and females 39.0%; **Bhat AA et al**[15]males 56% and females 43%; **Harshith M. Swamy et al.**[16] 52%males and 48% females;**Emad A. Morad et al**[6] 66% males and 34% females. Unlike our study **Arowosegbe AO et al.**[5] females were 52% and males 48%.

Gestation -

In the index study out of 100 cases of suspected **neonatal sepsis** 69% cases preterm, 31% term. In similar studies **Bhat AA et al.**[16]59.3%spreterm and 40.7% term babies; **Abnish Kumar Bharti et al.**[1] 66.7% preterm and 33.3% term neonates; **Chauhan setal B et al.**[17]94% preterm. But unlike our study, **Angadi W.A.et al**.[14]37.0% preterm and 63% term; study by **Emad A. Morad et al.**[6] 38% were preterm and 62% were full term neonates.

- LBW and preterm neonates are at high risk of developing sepsis in comparison to a term neonate as they are vulnerable to sepsis due to their intrinsic susceptibility to infection owing to the immature immune system in addition to factors like prolonged hospital stay, total parenteral nutrition and exposure to invasive procedures.

Comparison of Blood culture positivity.

In our study 18% of subjects were positive for blood cultures whereas 82% negative for blood culture. This is comparable with studies by **Arowosegbe AO et al.**[5]Blood culture was positive 22.4% of the neonates in a study; by **Angadi W.A.et al**[14]9.0% positive blood culture; **Harshitha et al.**[16]20%. Higher rates of culture positivity were seen in study by **Bhat AA et al.**[15]out of 150 cases, 32% blood cultures were positive; study by **Abnish Kumar Bharti et al.**[1] blood culture was positive in 39% of cases; Blood culture positivity was 62% in a study by **Emad A. Morad et al**.[6] and 30.9% cultures in **Haniya Jafar et al.**[18] The variation in rate of isolation can be attributed to the fact that neonatal sepsis varies from place to place under the influence of factors like gestational age, birth weight of neonates, maternal health and infection, perinatal care and availability of health care facilities. Such variation could also be due to prior administration of antibiotics to the mother before the neonate was delivered or to the neonate before collecting blood sample.

Comparison of Gender of the Neonates with positive blood culture

In my study out of 18 positive blood culture cases male neonates were 56% and females 44%. Culture positivity showed only a slight rise in male neonates than females. In similar studies by; **Dr. Pearl Mary Varughese et al.**[13] 59% males and 41% females; in another study by **Dr. Angadi W.A.et al.**[14] culture positivity was 62% in males and 38% in females but higher rates of culture positivity were seen in study by **Abnish Kumar Bharti et al.**[1]76.9% culture positive cases were males and 23.1% females.

- This male preponderance in the index study may be due to x-linked immunoregulatory gene leading to host susceptibility for septicaemia.

Comparison of gestation with positive blood culture.

In the present study out of 100 neonates with suspected sepsis, 69 preterm had blood culture positivity of 55% and 31 term neonates had positivity of 19%. About three - fold increase in culture positivity was seen in preterm neonates (55%) when compared to term neonates (19%). In similar studies by **Angadi W.A.et al.**[14] 58% preterm neonates were positive for blood culture and 42% term; 67% of preterm neonates showed culture positivity **in Lakhey et al** [19]**; Harshitha M swamy et al** [16]blood culture was positive in 76% preterm and 24% term.

Comparison Birth Weight with positive blood culture-

In the present study out of 100 neonatal sepsis, 26% of neonates had normal birth weight (NBW), 74% of neonates were low-birth-weight (LBW) category.

Laboratory finding of positive blood culture of LBW is 78%, NBW 11% and VLBW11%. Culture positivity of 89% (78% of LBW + 11% VLBW). In similar studies by **Lakhey et al .**[19]LBW neonates 71% culture positivity; **Abnish Kumar et al**.[1]62% of culture positivity in LBW neonates. Unlike our study, **Angadi W.A.et al.**[14] blood culture was almost equally positive in both with 51% positivity in term and 49% preterm.

Weight as per Gestation with blood culture:

In the present study out of 100 neonates with suspected sepsis, 52% of neonates were SGA Whereas 48% of neonates were AGA. Laboratory finding of positive blood culture of SGA neonates is 61%, AGA is 39%. Culture positivity showed SGA neonates has greater sepsis cases than AGA neonates. So, we can conclude that SGA has greater chances than AGA to contract sepsis. Culture positivity showed SGA neonates has greater sepsis cases than AGA neonates. we can conclude that SGA has greater cases than AGA.**Auriti et al**.[20]have reported an increased diagnostic accuracy for PCT in neonates with birth weight lower than 1500 grams;while **López Sastre et al**.[21]concluded from one hundred infants that PCT is not sufficiently a sole marker of nosocomial neonatal sepsis and this would be a part of full sepsis evaluation.

Sepsis score and CRP levels:

In the present study the mean sepsis score was 5.01±1.2, the mean CRP levels were 15.66±23.01, total leukocyte count was 10702.1±5520.08, absolute neutrophilic count is 5133.49±3864.77, band cell count to neutrophil count 0.08±0.27mm3 ;in .In a study by **Angadi W.A.et al.**[14](81.0%) tested negative for CRP, 19.0% were positive with levels >10mg/mL, mean CRP was **10.9± 2.1**band cell ratio was < 20% in 98.6%, > 20% in 1.3%, total white blood cell count was > 5000 in 98.6% and < 5000 in 1.3%.) and mean ANC levels were 4122±1221.0 ; study by **Alireza Abdollahi et al.**[4] WBC count was 17.343 ± 1.510, mean CRP was 2.9±0.50, mean absolute neutrophil was 6601.00±1770.10, mean lymphocyte was 28.80±1.74;The mean total leukocytic count (TLC) was 22 ± 8.7 thousand/ by **Emad A Morad et al.**[6]; by **Abnish Kumar Bharti et al.**[1] there were nine cases of culture-positive sepsis accompanied; by elevated levels of procalcitonin (>0.5ng/dl) but all of which tested negative for CRP and their mean total leucocyte count was 13810.6± 4210.88 and CRP was 5.77±7.20 mean ANC was 6104.21±1645.68.

Procalcitonin:

PCT rises markedly within 6 hours of bacterial infection, peaking at 18–24 hours, remain elevated for up to 48 hours (Abnish Kumar Bharti). In this study Association of blood culture with raised procalcitonin on **applying t test** between positive and negative blood culture with procalcitonin value **we found significant association** with p value <0.05, in a similar study by **Emad et al**[6] association was significant (p value <0.01); **Alireza Abdollahi et al.**[4] (p value < 0.04); whereas **Haniya Jafar et al.**[18] (p value <0.084) insignificant rise of PCT. In the study by **Alireza Abdollahi et al**.[4]PCT was also higher in clinically proven sepsis patient compared to cases of uncertain sepsis.In a study by **Angadi W.A.et al**.[14]Forty-one (55.0%) were negative for procalcitonin and 34 (45.0%) were positive. Procalcitonin is positive in 88 cases and negative in 62 babies in a study by **Bhat AA et al**.[15]

SUMMARY

This study focused on to find out utility of procalcitonin as an indicator in neonatal sepsis vis a vis blood culture and sepsis screen.

- The present study includes a total of 100 neonates with suspected sepsis out of which 63% were Male babies and 37% Female babies, showed male predominance.
- In the index study out of 100 cases of suspected neonatal sepsis 69% cases preterm, 31% term.
- 52% of neonates were SGA and 48% AGA.
- EONS were 86% and LONS 14%
- Blood culture had grown organisms in 18%. Out of positive blood culture cases male neonates were 56% and females 44%. Culture positivity showed more in male neonates than females.
- Higher proportion of EONS 83% were culture positive as compared to LONS 17%.
- Two-fold rise in culture positivity was observed in preterm babies 67% than in term neonates 33%.
- Significant increase in culture proven sepsis was noted among LBW 89% (78%LBW +11%VLBW) than normal birth weight.
- Culture positivity in SGA 56%was more than AGA 44% neonates.
- Organisms isolated were MRSA 28%, CONS and E. coli each 22%, 18%Klebsiella, Enterococci faecalis 11%.
- Mean sepsis score was 5.01±1.2, mean CRP level was 15.66±23.01, mean total leukocyte counts were10702.1±5520.08, mean absolute eosinophil counts were 5133.49±3864.77, band cell counts to neutrophil counts were 0.08±0.27.
- Association of sepsis score with procalcitonin values, on applying regression analysis, we found there is no association (R square 0.004).
- Association of CRP values with procalcitonin, on applying regression analysis, it was found very low association (R square 0.028).
- Association of absolute leucocyte count values with procalcitonin, on applying regression analysis it was found very low association (R square 0.069).
- Blood culture positivity with procalcitonin, on applying t test between positive and negative blood cultures with procalcitonin values found significant association (p value <0.05).

CONCLUSION

In the present study there was a significant association of procalcitonin positivity with CRP. PCT is a reliable marker of inflammation in early diagnosis of neonatal sepsis both in term and pre-term babies. The combination of PCT and CRP along with validated clinical algorithm of neonatal sepsis and other factors, improves the accuracy of diagnosis.

There was significant association of procalcitonin positivity and blood culture positivity. There was a low association of absolute leucocyte

count value with procalcitonin.

The gold standard for the diagnosis of neonatal septicaemia is a positive blood culture but culture results take at least 48-72 hours, resulting in delay of treatment. Therefore, rapid diagnostic tests such as PCT, CRP, TLC, ANC and platelet count collectively can be used for early indicators of infection.

The findings of our study indicate that serum PCT, at a cut off value of 0.5ng/ml for diagnosis of sepsis. When used alone it has moderate diagnostic value but in combination with sepsis screen it has higher correlation in diagnosing of neonatal sepsis.

Limitations:

- In our study, the participants were relatively small in number. Thus, the result of this cannot be generalized for a larger population. Therefore, complementary studies with larger sample size and with diverse socio demographic profile needs to be carried out.
- We found that several factors including gender, gestational age, birth weight had no significant association with blood culture This may be associated with small sample size and could also be due to prior administration of antibiotics to the mother.

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