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Effective immunological markers for Neonatal Sepsis: Comparison of C-reactive protein with Interleukin - 6 and Blood culture

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ABSTRACT

Background: Neonatal sepsis occurs from 1 to 21 newborns out of 1 000 live births with mortality rates as high as 30% up to 69%. The most important risk factors are prematurity, low birth weight, invasive medical procedure and prolonged hospitalization in neonatal intensive care units. Infection in neonates is difficult to identify solely on the basis of physical findings, because signs are not specific. C reactive protein (CRP) is an acute phase reactant which has been used in diagnosis of bacterial infection in neonates. Interleukin-6 is a proinflammatory cytokine produced by monocytes and macrophages activated by bacterial infection. Interleukin-6(IL-6) can be detected in blood earlier than CRP during the course of bacterial infection. The objective of this study was to compare the usefulness of the level of interleukin-6 with CRP as early markers of neonatal sepsis with Blood culture.

Methods: This prospective study was carried out for a period of three months in a tertiary care hospital. Blood samples collected from 90 newborn babies were tested for Blood culture,CRP level detection by latex agglutination test and IL-6 determination by ELISA. The cut-off values recommended by the respective manufacturers were used to determine the sensitivity and specificity.

Results: Out of the blood samples collected from 90 participants, positive blood culture was found in 28 neonates(31%). *Escherichia coli* was the most common organisms for causing both Early Onset Neonatal Sepsis and Late Onset Neonatal Sepsis in the present study. Sensitivity of detection of IL-6 by ELISA method was 100% when evaluated against culture , a reference test. Specificity of this test was 41.94% compared to culture and positive and negative predictive value were 40.63% and 100% respectively. Sensitivity of CRP latex agglutination test was 64.28% when evaluated against culture, a reference test. Specificity of CRP latex agglutination test was 56.45% compared to culture and positive and negative predictive value were 40% and 77.77% respectively. The findings of the present study confirm that the serum level of IL-6 is a more reliable marker than the serum levels of CRP.

Conclusions: IL-6 was mostly positive within 24 hours of onset of sepsis in comparison with

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other tests. So IL-6 is more useful both to early (24-48 h) detection of neonatal sepsis and to monitor the antibiotic treatment while waiting for the results of cultural examinations.

Keywords: Neonatal sepsis, Blood culture,C Reactive Protein (CRP), Interleukin-6(IL-6), Sensitivity and Specificity, Positive predictive value, Negative predictive value

Introduction

Neonatal sepsis is a clinical syndrome characterized by systemic signs of infection, accompanied by bacteraemia within the first four weeks of life (28 days).Neonatal sepsis is the most common cause of morbidity and mortality in neonatal period.[1]Every year 135 million babies are born alive worldwide. Statistical data in 2011 estimated 3.0 million of these died during the first four weeks of life. Early diagnosis and prompt and appropriate treatment of all neonates with clinical suspicion of sepsis has been found to be an important strategy in preventing neonatal mortality and life threatening complications.[2]

In recent days screening of serological markers such as C-reactive protein (CRP), and various cytokines have been suggested as being useful and more sensitive indicators for early identification of sepsis in neonates. The biomarkers are classified into early phase marker (Interleukin-6, Interleukin-8, Tumour Necrosis factor-α and Interferon-γ), mid phase marker (Procalcitonin) and late phase marker (C-reactive protein).[3]

Numerous studies have reported on the effectiveness of the quantitative measurement of IL-6 for an early diagnosis of neonatal sepsis. Hence evaluation of IL-6 alone or with CRP helps in early detection of infection and effective management of neonatal sepsis. Interleukin-6 is an early phase marker. C-reactive protein is a late phase marker. The purpose of this study is to detect the role of CRP and IL-6 in the diagnosis of neonatal sepsis.

Objectives:

- To detect the bacteriological profile of neonatal sepsis and antibiotic susceptibility pattern of the isolates in Madurai Medical College.
- To determine the value of C-reactive protein and Interleukin-6 in establishing the diagnosis of neonatal sepsis.
- To compare the efficacy of C-reactive protein and Interleukin-6 with conventional blood culture method for the diagnosis of neonatal sepsis.

Methodology

This cross sectional study was conducted in Neonates who were admitted in Neonatal Intensive Care Unit with signs suggestive of sepsis, or those who developed signs of sepsis while they were in the ward for the period of three months from January 2021 to March 2021 in Institute of Microbiology, Madurai Medical College, Madurai,Tamilnadu.

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Study population:

Inclusion criteria:

Neonates who were admitted in Neonatal Intensive Care Unit at MaduraiMedical College with signs suggestive of sepsis, or those who developed signs of sepsis while they were in the ward.

Exclusion criteria:

- Neonates who were on antibiotics
- Neonates who had birth asphyxia and aspiration syndromes
- Neonates who had congenital anomalies and inborn errors of metabolism

Sample collection:

Ethical clearance will be obtained from the Institutional ethical committee before the commencement of the study. Informed consent will be obtained from reliable informants of neonates cases in neonates (0 day to 28 days) who participated in the study. Blood samples were taken from 90 clinically suspected sepsis and were tested for blood culture, detection of serum level of CRP by latex agglutination test and detection of serum level of IL-6 by ELISA.

Blood collection method:

Ideal blood sample collection should be done before initiation of anti-microbial agents. Amount of blood needed for cultures for neonates is significantly lower than that needed for adults because neonates tend to have a higher concentration of bacteria in their bloodstream than adults. Hence 2ml of blood was usually considered as the standard volume of blood adequate to detect bacteraemia in neonates. Proper aseptic precautions were undertaken during blood specimen collection to avoid sample contamination.

With clean gloved hands, preliminary aseptic precautionary steps like cleansing the venipuncture site with 70% ethanol and 2% tincture iodine and proper drying were followed. Then using a 2ml syringe with a 28G needle about 2-3 ml of blood was aspirated. Immediately and without changing or contaminating the needle 2 ml of blood sample was transferred into the top of the blood culture bottle that contains 20ml brain heart infusion broth.(HiMedia, India)Blood samples were centrifuged within 30 minutes of collection. Serum samples were immediately tested for CRP by latex agglutination method and then stored for IL-6 ELISA at -80^{o}C.

Blood culture processing procedure:

Inoculated culture bottle was incubated at 37˚C for up to 7 days. Subsequent sub culture was done in solid agar plates such as Blood agar plate, MacConkey agar plate and Nutrient agar plate after 24 hours and 72 hours with last subculture being done after seven days. The isolates were routinely identified by standard bacteriological techniques. All blood samples were subjected to the above said various tests and causative organisms for neonatal sepsis were

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identified.

Antibiotic susceptibility testing:

The antibiotic susceptibility testing was done in all isolates by Kirby Bauer disc diffusion method according to the CLSI guideline. About 3-5 colonies of the test organism were inoculated in 2 ml of peptone water and incubated for 2-4 hours at 37˚C. The turbidity of the inoculum was adjusted to 0.5McFarland standards (1.5x108 CFU/ ml). A sterile cotton swab was soaked in the inoculum and a lawn culture was made on to the Muller-Hinton agar (MHA). By rotating the swab against the inner side of the test tube, excess broth was expressed. The panel of antibiotic discs was applied and incubated at 37˚C for 18-24 hours. The zone size was recorded and interpreted as per the CLSI guidelines.
The three interpretive categories are described as follows.

Susceptible: This indicates that the recommended antibiotic in appropriate dose forrecommended period is the appropriate agent for treating the infection.

Intermediate: This indicates that the tested organism may be inhibited by possible concentrations of certain drugs if higher concentrations of the drug can be used safely.

Resistant: The antibiotic tested may not be an appropriate choice for the infection against thetested organisms either they are not inhibited by the concentration of the drug normallyachievable with the recommended dose or because the test result vastly correlates with aresistance mechanism. In this study the susceptibility for the organism was tested against following antimicrobials from Hi-media laboratories Ltd, Mumbai Gentamicin, Amikacin, Cefotaxime, Ceftazidime, Ciprofloxacin are first line drugs for gram negative organisms. Imipenem, Meropenem and Cefaperazone-sulbactum are reserved for second line drugs.

Serum CRP level detection by latex agglutination test:

All the 90 samples were tested for CRP detection by latex agglutination test with the help CRP test kit of Span Diagnostics LTD,India.

Principle:

Specially selected polystyrene latex particles are coated with monospecific goat anti human CRP antibodies. When a serum positive for C - reactive protein is mixed with the latex reagent, a positive result is indicated by a distinctly visible agglutination of the latex particles in the test cell of the slide used. In specimen negative for C –
Reactive Protein, the latex remains in a smooth suspension form in the test cell.

Materials provided:

C - reactive protein latex agglutination test kit contains the following items to perform

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the assay.Latex reagent for tests – Suspension of polystyrene latex particles, coated with monospecific goat anti-human CRP antibodies, Positive Control serum – 0.5ml,Negative Control serum – 0.5 ml,Disposable slides with 8 test cells, Disposable mixing sticks,Disposable plastic droppers with a rubber teat.C-Reactive Protein latex agglutination kit was stored at 2-8 ˚C.

Test procedure:

Qualitative analysis:

The latex reagent, controls and serum specimens were brought to room temperature. The antigen suspension was mixed thoroughly prior to use. One drop each of patient serum, positive and negative control sera were placed in respective cells of the test plate.Then one drop each of CRP latex reagent was added to each of these sera.The sera and latex reagent were mixed with separate mixing sticks and the fluid spread over the entire area of the particular cells.The test slide was tilted back and forth for two minutes so that the mixture rotates slowly inside the cells .

At the end of two minutes the results were read under bright light.

Interpretation of results:

□ □ Strong Positive– Distinct coarse agglutination occurs within 0.5 minute.

□□ Weakly Positive– Fine agglutination usually taking full 2 minutes.

□ □ Negative- No agglutination.

Distinct agglutination indicates CRP content of more than 6 mg/litre in undiluted serum specimen. Sera with positive results in the screening were tested in the titration test.

Semi quantitative analysis:

0.9% saline solution was prepared. Then the specimen was diluted with saline until the last dilution giving distinct agglutination. Titre is the last dilution step giving visible agglutination. Read the titre in the last dilution step with agglutination and multiply the titre with the conversion factor 6 to get the results in mg/litre. With the above standard guidelines, samples were tested and obtained results were documented.

Serum IL-6 level detection by ELISA:

All the 90 samples were tested for IL-6 detection by ELISA with the help of Diaclone SAS, France ELISA test kit.

Principle of the method:

A capture antibody highly specific for Interleukin-6 has been coated to the wells of the micro titre strip plate provided during manufacture. Binding of IL-6 samples and known standards to the capture antibodies and subsequent binding of the biotinylated anti-IL-6 secondary antibody to the analyte is completed during the same incubation period. Any excess unbound analyte and secondary antibody is removed.The HRP conjugate solution is then added to every well, following incubation excess conjugate is removed by careful washing. A chromogen substrate is added to the wells resulting in the progressive development of a blue

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coloured complex with conjugate. The colour development is then stopped by the addition of acid turning the resultant final product yellow. The intensity of the produced coloured complex is directly proportional to the concentration of IL- 6 present in the samples and standards. The absorbance of the colour complex is then measured and the generated OD values for each standard are plotted against expected concentration forming a standard curve. This standard curve canthen be used to accurately determine the concentration of IL – 6 in any sample.

Materials provided:

A capture antibody highly specific for IL-6 Coated Micro wells(12×8 wells),Biotinylated anti-IL-6 – 0.4ml X 1,Biotinylated Antibody diluent – 1 X 7 ml,Streptavidin – HRP : 2 x 5 µl,HRP Diluent : 1x23 ml,TMB Substrate, Stopping solution:1.6 N sulphuric acid, Standard : 200pg/ml. (2 vials),Standard Diluent: 1x7ml,Control: 2 (Freeze dried powder form),Washing Buffer: 200x concentrate dilute in distilled water.

Materials required:

□ □ □ Micro titre plate reader with appropriate filters (450 nm required with optional620nm reference filter),Micro plate washer,10, 50, 100, 200 and 1000µl adjustable single channel micropipettes with disposable tips. 50 -300 µl multi-channel pipette and reagent reservoirs, Distilled water, Vortex mixer.

Kit storage:

Store kit reagents between 2 and 8˚C. Immediately after use remaining reagents should be returned to cold storage (2-8˚C).

Preparation of Standard :

Standard vials must be reconstituted with 770 µl of standard diluent on the vial immediately prior to use. This reconstitution gives a stock solution of 200pg/ml of IL-6.Mix the reconstituted standard gently by repeated aspiration. Serial dilutions of the standard are made directly in the assay plate to provide the concentration range from 200 to 6.25pg/ml.Immediately after reconstitution add 200µl of the reconstituted standard to well's A1,
which provides the highest concentration standard at 200pg/ml.100µl of appropriate standard diluent were added to the remaining standard wells B1 to F1.100µl from wells were transferred to A1 to B1.Mix the well contents by repeated aspirations and ejections taking care not to scratch the inner surface of the wells. Continue this 1:1 dilution using 100µl from wells B1 through to F1 providing a serial diluted curve ranging from 200pgml to 6.25pg/ml.Discard 100µl from the final wells (F1) of the standard curve.

Preparation of Controls:

Freeze-dried control vials should be reconstituted with 1ml of standard diluent –Human serum. This is used as Positive control (G1). Only 100µl of standard diluent - Human serum used

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as Negative control. Biotinylated anti-IL-6 is prepared immediately before use. Dilute the biotinylated anti-IL-6 with the biotinylated antibody dilute in an appropriate clean glass vial using volumes appropriate to the number of required wells.

Preparation of Streptividin - HRP

To centrifuge vial of Streptovidin-HRP vial for a few seconds in a micro centrifuge to collect all the volume at the bottom. Then the 5 µl vial with 0.5ml of HRP diluent immediately before use. Further dilute the HRP solution to volumes appropriate for the number of required wells in a clean glass vial.

Preparation of wash buffer:

Dilute the (200x) wash buffer concentrate 200 fold with distilled water to give a 1x working solution. Pour entire contents of the washing buffer concentrate into 2000 ml graduated cylinder. Bring final volume to 2000 ml with distilled water. Mixed gently to avoid foaming. Transfer to a clean wash bottle and store at 2˚-25˚C.

ELISA Procedure:

□ □ □ 100µl of each, standard, positive control, negative control and sample were added to appropriate number of wells.50µl of diluted biotinylated anti-IL-6 were added to all wells. Cover with a plastic plate cover and incubate at room temperature (18 to 25˚C) for one hour. The wells were washed 3 times with diluted washing solution using an automatic washer. 100µl of Streptavidin-HRP solution were added into all wells. Cover with a plastic plate cover and incubate at room temperature (18 to 25˚C) for 30 minutes. The wells were washed 3 times with diluted washing solution using an automatic washer.100µl of ready to use TMB substrate solution were added into all wells. Incubate in the dark for 15 minutes at room temperature. Avoid direct exposure to light by wrapping the plate in aluminium foil. Blue colour developed in the wells.100 µl of stopping solution was pipette into each wells and mixed well and the blue colour changed to yellow. The absorbance of each well was read within 30 minutes at a wavelength of 450nm with a reference filter of 620nm.

Data analysis:

Calculate absorbance values of standards, controls and samples. Generate a linear standard curve by blotting the average absorbance of each standard on the vertical axis versus the corresponding IL-6 standard concentration on the horizontal axis.The amount of IL-6 in each sample is determined by extrapolating OD values against IL-6 standard concentrations using the standard curve.

Statistical Analysis

All the results obtained were analyzed statistically for their completeness , consistency and accuracy by the parameters like mean and percentages. The correlation of serum CRP level

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and Interleukin-6 level with blood culture for neonatal sepsis was compared statistically and results were analyzed by IBM SPSS Statistics 20. Chi-square test and Fisher Exact test were used in calculating the P-value. The P-Values of less than 0.05 were considered as statistically significant ($P<0.05$).

Results

The Study Group

A total of 90 neonates (0 to 28 days) who fulfilled the criteria of clinically suspected sepsis were analyzed. This study was conducted at the Department of Microbiology , Madurai Medical College Hospital over a period of 3 months from June 2021 to August 2021.The selected 90 study subjects were analyzed based on age and sex, The results of the analysis are tabulated in **Table 1.**

Table 1.Age and sex wise distribution in study group

Age in Days	Male		Female		Total	
	No	%	No	%	No	%
EONS (0-3days)	9	29.03%	16	27.12%	25	27.78%
LONS (4-28days)	22	70.97%	43	72.88%	65	72.22%
Total	31	100%	59	100%	90	100%

Isolated bacterial pathogens:

Out of the blood samples collected from 90 participants, positive blood culture was found in 28 neonates(31%). The organisms isolated were *Escherichia coli* in 21 neonates (75%) and *Acinetobacter* in 7 neonates(25%). *Escherichia coli* was found to be a most common organism in both early and late onset sepsis.They were resistant to third generation cephalosporins and were sensitive to Imipenem and Cefperazone-sulbactum.

Among 28 blood culture positive cases, 10 (35.7%) cases were male neonates and it contributes 35.7% of total blood culture positive cases. Another 18 cases were female neonates and it contributes 64.3% of total blood culture positive cases. There was no statistically significant difference between sex wise and culture positive cases. ('p' value is >0.05)Out of 28 blood culture positive cases, 7 cases were in the age group of 0-3 days and it contributes 25% of total culture positive cases. Remaining 21 cases were in the age group of 4-28 days and it contributes 75% of total blood culture positive cases.

C-reactive protein results in study group:

Out of 90 clinically suspected neonatal cases, 45 neonates were C-reactive protein test positive. Out of the 45 positive cases 12 neonates (26.67%) were EONS and 33

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cases (73.33%) were of LONS. **(Figure : 1)**

Figure : 1 CRP Positive cases in study group

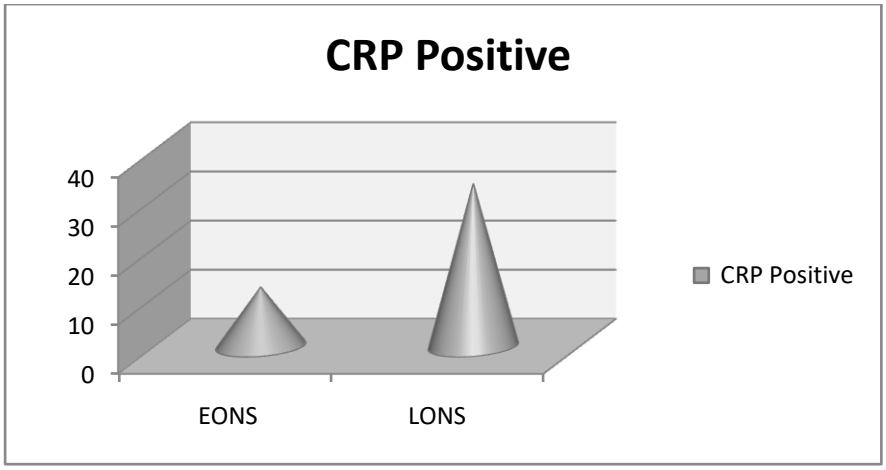

Table 2 Association between Blood culture results and CRP results

CRP	Blood Culture		Total
	Positive	Negative	
Positive	18	27	45
Negative	10	35	45
Total	28	62	90

From the above **Table : 2** Sensitivity of CRP latex agglutination test was 64.28% when evaluated against culture, reference test. Specificity of CRP latex agglutination test was 56.45% compared to culture and positive
and negative predictive value were 40% and 77.77% respectively. According to Chi-square test P-Values of less than 0.05 we**r**e considered as statistically significant (P<0.05).

Sensitivity $=TP/TP+FN=18/28\times 100 = 64.28\%$

Specificity $=TN/TN+FP=35/62\times 100 = 56.45\%$

Positive predictive value $=TP/TP+FP=18/45\times 100 = 40\%$

Negative predictive value $=TN/TN+FN=14/26\times 100 = 77.77\%$

Table:3 CRP semi quantitative Assay

CRP	No. Of cases
>6 mg/L	**27**
>12 mg/L	**1**

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>24mg/L	**6**
>48mg/L	**11**
Negative	**45**
Total	**90**

Above **Table:3** Shows, among 45 CRP positive cases, 11 cases were under serum CRP level more than 48mg/L category, 6 cases were CRP level in between 24 - 48mg/L category, one case was CRP level in between 12-24mg/L category and 27 cases were CRP level under 6 -12 mg/L category.Out of 45 CRP positive cases, 18 cases were blood culture positive. Among 18 culture positive cases, 11 cases due to gram negative organisms (high titre of serum CRP more than 48 mg/L), 6 cases due to gram negative organisms (high titre of serum CRP more than 24 mg/L) and one case due to gram Negative organism(low titre of serum CRP more than 12 mg/L)

Serum Interleukin-6 results in study group:

Out of 90 clinically suspected neonatal cases, 64 neonates were Interleukin-6 positive. Out of 64 positive cases, 18 (28.13%) neonates were EONS and 46 (71.87%) cases were of LONS.**(Figure:2)**

Figure: 2 Serum Interleukin-6 results in study group

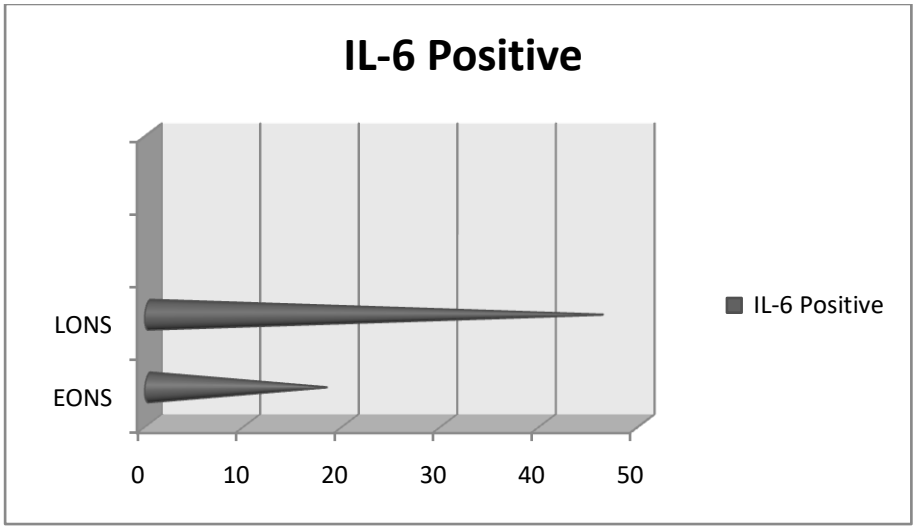

Table:4 Evaluation of Interleukin-6 with blood culture

IL-6	**Blood Culture**		**Total**
	Positive	**Negative**	
Positive	28	36	64
Negative	0	26	26
Total	28	62	90

Sensitivity $=TP/TP+FN$=28/28× 100 = 100%

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Specificity =$TN/TN+FP$=26/62× 100 = 41.94%

Positive predictive value =$TP/TP+FP$=28/64× 100 = 40.63%

Negative predictive value =$TN/TN+FN$=26/26× 100 = 100%

From the above **Table:4** Sensitivity of detection of IL-6 by ELISA method was 100% when evaluated against culture , a reference test. Specificity of this test was 41.94% compared to culture and positive and negative predictive value were 40.63% and 100% respectively. According to Chi-square test P-Values of less than 0.05 were considered as statistically significant (P<0.05).

Table:5 IL-6 Quantitative Assay

IL-6 assay by ELISA	**No. Of cases**
Highly Positive (100-200pg/ml)	**57**
Moderately Positive (50-100pg/ml)	**2**
Weakly Positive (< 50-6.25pg/ml)	**5**
Negative <6.25pg/ml	**26**
Total	**90**

Out of 64, IL-6 positive cases, 57 cases were under highly positive category (IL-6 level 100-200pg/ml, OD value 1.7-3.038), 2 cases were under moderately positive category (IL-6 level 50-100pg/ml, OD value 0.912-1.6) and 5 cases were weakly positive category (IL-6 level 6.25 - 50 pg/ml, OD value 0.236-0.911).**(Table-5)**Among 64 IL-6 positive cases, 28 cases were culture positive. All 28 neonatal cases have high titre of IL-6 level 100-200pg/ml.

Discussion

The present study shows that out of 90 clinically suspected neonatal sepsis cases,Female neonates were found to be predominant than Male neonates. Male predominance was observed in studies conducted by YR Khinchi AK *et al* and Bambala Puthattayil Zakariya *et al*.[4,5] Among 90 study cases,27.78% of cases were under the age group of 0 – 3 days(<72 hours) and remaining 72.22 % of cases were under the age group of 4-28 days.

also reported in a similar study. It was similar to the study conducted by Neema Kayange *et al* in Tanzania in which a high prevalence of LONS (60%) was reported among 300 clinically suspected neonatal sepsis cases.[6]But in contrast to Flora Chacha *et al* and Sucila Thangam *et al* studies where early onset neonatal sepsis is more prevalent than late onset neonatal sepsis.[3,7]

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The current study shows that among 90 suspected sepsis cases, blood culture was positive in 28 cases (31%).Similar positivity percentage of blood culture had been reported in the study by Shrestha R K *et al* in Nepal medical college, Kathmandu, during the period of July 2011 to January 2012 reported similar range results of 30.8% of positive blood culture.[8]Out of 90 clinically suspected neonatal cases, 45 neonates were C-reactive protein test positive. Out of the 45 positive cases 12 neonates (26.67%) were EONS and 33 cases (73.33%) were of LONS.

Sensitivity of CRP latex agglutination test was 64.28% when evaluated against culture, a reference test. Specificity of CRP latex agglutination test was 56.45% compared to culture and positive and negative predictive value were 40% and 77.77% respectively. In a similar study by Sucila Thangam *et al*, during April 2010- September 2010 showed that sensitivity of CRP were 50%, its specificity was 69.4%, its positive predictive value was 38.8% and its negative predictive value was 78.1%.[3]Another similar study done by Benitz MD *et al* from Stanford University of Medicine showed that 54.6% of sensitivity on proven neonatal sepsis and 65.5% of specificity in probable neonatal sepsis among 1002 infants.[9]

Out of 90 clinically suspected neonatal cases, 62 neonates were Interleukin-6 positive. Out of 64 positive cases, 18 (28.13%) neonates were EONS and 46 (71.87%) cases were of LONS.Out of 64, IL-6 positive cases, 57 cases were under highly positive category (IL-6 level 100-200pg/ml, OD value 1.7-3.038), 2 cases were under moderately positive category (IL-6 level 50-100pg/ml, OD value 0.912-1.6) and 5 cases were weakly positive category (IL-6 level 6.25 - 50 pg/ml, OD value 0.236-0.911).

Among 64 IL-6 positive cases, 28 cases were culture positive. All 28 neonatal cases have high titre of IL-6 level 100-200pg/ml. This finding was similar to the study of Laura LR *et al* which revealed Serum of gram negative septicemic cases had increased titre of serum IL-6 level when compared with gram positive septicemic cases. Gram negative bacterial endotoxins are potent inducer for cytokines production by leucocytes comparing with gram positive bacteria.[10]In the current study, the sensitivity of IL-6 for proven sepsis was 100% its specificity was 41.94%, its positive predictive valve was 40.63% and its negative predictive value was 100%.Shalini Tripathi *et al* investigated the role IL-6 in the diagnosis of neonatal sepsis and its correlation with the CRP. The sensitivity, specificity, positive predictive value and negative predictive value of IL-6 were 98.4%, 81.2%, 63.5% and 93.5% and those of CRP were 41%, 91%, 87% and 78% respectively.[11]

The current study confirmed the findings of various authors that IL-6 was more sensitive than CRP in detection of neonatal sepsis. In neonatal sepsis, serum IL-6 level rose earlier than the CRP level.7 So serum IL-6 level detection is mainly useful in early detection of neonatal sepsis. Detection of serum IL-6 level also detects the severity of infection and evaluation of the response to antibiotic treatment. Earlier diagnosis of neonatal sepsis by IL-6 evaluation helps to prevent neonatal mortality and morbidity and avoid unnecessary initiation of empirical

antibiotics which in turn helps in preventing drug resistance.

Conclusion

The use of high sensitivity infection markers and a negative predictive value (near 100%) are important to distinguish infected and noninfected patients before the culture results and to verify adequacy and duration of antibiotic therapy. The benefit of measuring serum IL-6 routinely in the diagnosis and follow up of neonatal sepsis, is that it reduces neonatal mortality and morbidity and also reduces the hospital stay and cost of health care. Neonatal sepsis can be prevented by proper hand washing, proper antenatal care, proper aseptic clean labour ward and proper aseptic clean NIC

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Conflicts of interest : There are no conflicts of interest.

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