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Haematological Profile in Neonatal Septiceamia

Dr.G.Vandana[1], Dr.S.Lokesh rao magar[2], Dr. Praveen[3], Dr.B .Kavita. devi[4]
Dr. sandhya rani[5], Dr.sandhya anil[6]
[1&4].Assistant.Professor, [2]Associate Professor,[3]post Graduate, [5&6]professor

Abstract:
Background: *Neonatal septicemia is defined as a bacterial infection documemted by positive blood culture in first four weeks of life. The early sepsis screen is vital as it detect earlier & enable the clinician to treat the infection timely & adequately, which in turn help to reduce the neonatal morbidity & mortality. AIMS &* ***Objective:*** *To study changes in hematological parameter in neonatal septicemia. To compare the positive predictive valve of hematological test with respective to clinical respond.*
Material & Methods: *The Study Was Conducted In Kakatiya Medical College/Mahatma Gandhi Hospital, Warangal, Telangana. During the period of two year, from jan-2014 to dec 2016.ninety four neonates below the age 28days with suspected septicemia were included in the study. Neonates were admitted & sepsis screen (total leucocytic count, band forms, toxic granules, micro-ESR,C-reactive protein) was done.*
Result: *53(56.4%) male babies were affected by neonatal septicemia. Male to female Ratio was 1.3: 1. Early onset septicemia was present in 82.8% terms babies and 86% babies with normal birth weight Commonly observed clinical manifestations in our study were refusal of Feeds (56%), temperature abnormality (46%), Pallor (36%), not doing well (24%), rash (20%) and convulsions (16%). Sepsis screen was studied in bacteriologically positive and negative cases. Combination of C-reactive protein and toxic granulation had 63.3% sensitivity, specificity of 70.8%, and 40% positive predictive accuracy. Combination of C-reactive protein and platelet count had 36.3% sensitivity, specificity of 70.8% and 27.5% positive predictive accuracy.*
Conclusion: *Sepsis screen has good sensitivity, specificity and positive predictive Accuracy and is a valuable aid in early diagnosis of neonatal septicemia. Sepsis screen is simple, cheap, less time consuming and easy to perform even at bedside. As an individual test C-reactive protein has highest sensitivity, specificity and positive predictive accuracy and is a sensitive and responsive indicator of neonatal sepsis.*
Combination of tests increases the specificity and positive predictive accuracy.

I. Introduction

" Neonatal septiceamia is defined as a bacterial infection documented by a positive blood culture in a first four week of life." Systemic bacterial infection during the first month of life has remained a major cause of infant morbidity and mortality despite the development of broad spectrum antimicrobial agents and technological advancements in life supportive therapy. The early diagnosis of neonatal septicemia still poses great difficulties as it mimicked by lot of other disorders affecting the newborn. Neonatal sepsis can be divided into two subtypes1 depending upon whether the onset of symptoms is during the first 72 hours of life or later, refer to as early onset sepsis and as late onset. Early onset sepsis is caused by organisms prevalent in genital tract or in the labour room.

Various authors have given different rate of incidence in their reviews - George H Mccrackenet.et al2. in 1981,T.Vesikari in 19853,and Lokeshwar in 19884 reported that incidence in the developing countries like ours. K. C. Buetow et.al 19655 studied septicemia in preterm babies weighing 1000-2500 grams. They concluded that incidence of septicemia was 54.3 per 1000 live preterm births. There was increasing mortality rate with decreasing birth weight.

To prevent serious morbidity and mortality caused by untreated or late treated neonatal septicemia, it is important that the diagnosis is made early and the treatment is started as early as possible. Early treatment with rational antibiotic therapy is possible with the help of certain indirect markers such as leucopenia, toxic granules, immature neutrophil to total neutrophil ratio, micro-ESR and C-reactive protein. This investigation exercise is collectively known as sepsis screen.The early diagnosis of neonatal sepsis by clinical examination is vital. 'Sepsis Screen' is an extremely reliable index of early neonatal septicemia, with less expenditure and serves as a good guide for initiating antibiotic therapy. When at least two of the indirect markers of infection are positive it give sensitivity and specificity of 93% and 88% respectively. Philip in 19806studied sepsis screen with total leucocyte count <5000/cm, band form to total neutrophil ratio>0.2,micro-ESR>15mm at the end of 1st hr. and C-reactive protein.> 0.8/100 ml, latex haptoglobin (positive>25 mg/ml) and found 93% sensitivity and 88% specificity, when two or more tests were combined.

II. Aims & Objectives

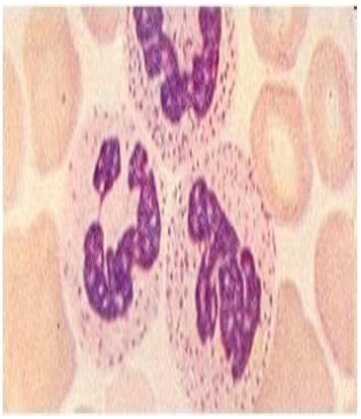
To study changes in hematological parameters in neonatal sepsis To Compare the sensitivity, specificity & positive predictive value of hematological parameter

III. Materials & Methods

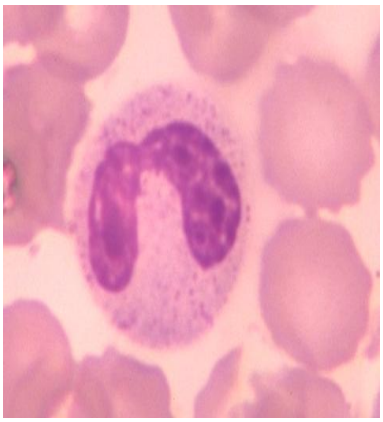
This study was conducted in KAKATIYA MEDICAL COLLEGE, WARANGAL, during study period of Two years(from january 2014 to december 2016) ,94 Neonates below the age of 28 days with suspected septicemia as per Signs and symptoms mentioned in proforma were included in this study.
Inclusion criteria - Neonates admitted to NICU with suspected sepsis
Exclusion criteria - Neonates who present with gross congenital anomalies
All neonates admitted in MAHATMA GANDHI MEMORIAL HOSPITAL were investigated as follows

1. Sepsis screen – cell counts with the help of RIPL-5000 cell counter of rayon company
2. C-Reactive protein
3. Culture reports were campare
4. Blood smear were studied after leishmann stain for Morphological features which were looked under 40X and oil immersion using cedar wood oil –

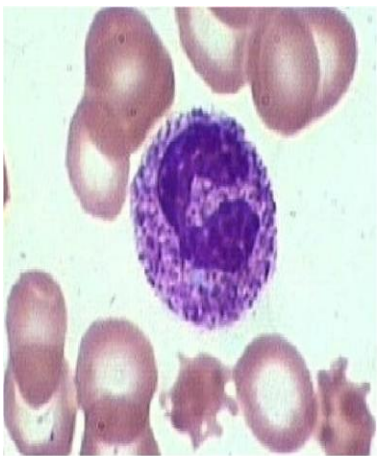
RBCs morphology
WBCs = differential count for 100 cell
Neutrophils = hypersegmented, band form. Absolute neutrophil count was calculated , toxic granules, premature cells also noted
Platelet coumt was done



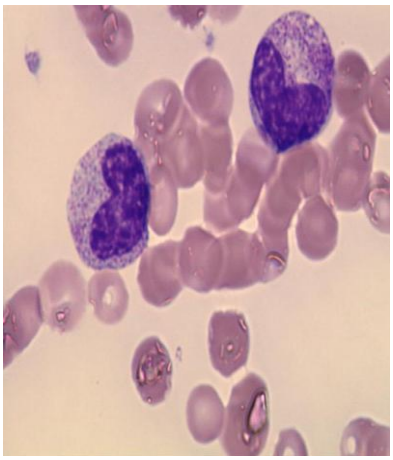
(a) Hypersegmented neutrophil



(b) band forms-left shift



(c) toxic granulation



(d)metamyelocytes

IV. Results & Discussion

The present study was conducted in kakatiya medical college/mahatama Gandhi hospital, Warangal About 94 cases was considered excluding all criteria

Table 1:- Distribution Of Cases According To Sex

SEX	male	female	total
No. of cases	53(56.4%)	41(43.6%)	94

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Male babies were more affected by neonatal septiceamia than female babies in our study which was compare with other studies. Nelson[7] stated that males have two fold increase chances of sepsis . others like Piyush Gupta et al[8],N.Somu et al[9], Khatau et al[10], observed male predominance in there study

Table Ii:- Relation Of Age Of Onset Of Septiceamia With Maturity

Age of onset	maturity		
	preterm	Term	total
<7days	23(76%)	53(82.8%)	76
>7 days	7(24 %)	11(17.2%)	18
Total	30	64	94

Early onset septiceamia was more common in term babies. Our finding was consistent with other studies. J.N.Mishra[11] observed that early onset was 71.7% in his study. T. Vesikari et.al[3]. reported early onset in most of the patients with Neonatal sepsis. In 410 cases studied onset ≤ 7 days was found in 370 cases.

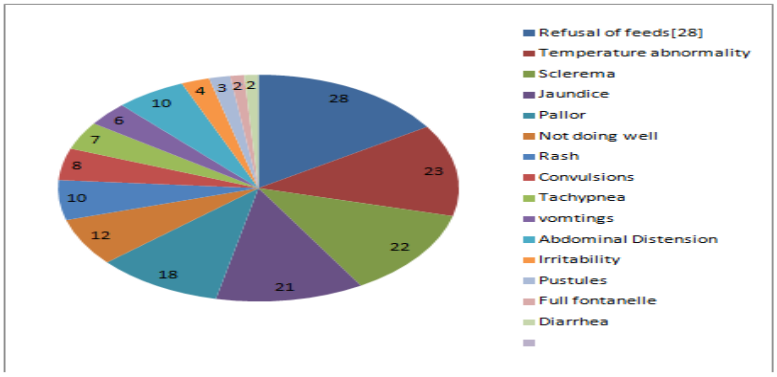
Table Iii :- Relation Of Age Of Onset With Birth Weight

Ageof onset	Birth weight		
	≤ 2000 gms	> 2000 gm	Total
≤ 7 days	33(75%)	43(86%)	76
> 7 days	11(25%)	7(14%)	18
Total	44	50	94

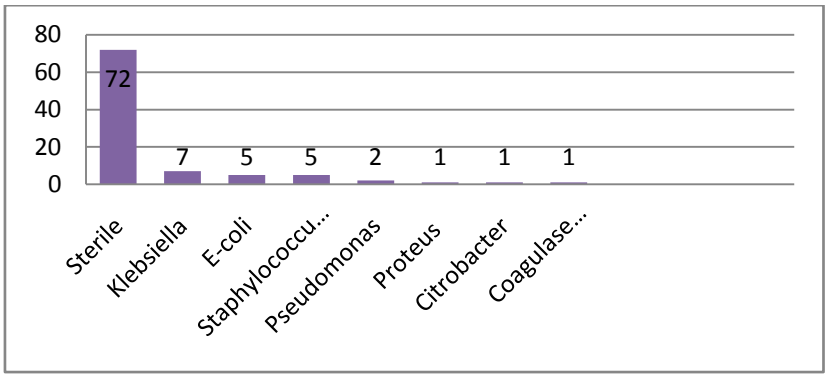
Early onset septicemia was more common in normal birth weight babies. Sucilathangam et al12,observed that 28 babies out of 50 babies were affected. Mulyani et al13 out of 99 neonates suspicious of sepsis 65 neonates had birth weight >2000gm. However various other following authors observed that onset of sepsis is More common in low birth weight babies

graph 1: clinical features in neonatal septicemia

Commonly observed clinical manifestations were refusal to feeds (56%) temperature abnormality (47%),sclerema(45%), jaundice(41%), Pallor(36%),not doing well (24%), rash (21%) and convulsions(17%) in our study and also in Khatua et al 10 that common clinical presentations were juandice, lethargy, refusal of feeds, vomiting and respiratory distress. Agarwal et.al[15], somu et al[9] and Gupta et al,[16]Observed that lethargy, feeding problems, abdominal distension, respiratory distress, hypothermia apnea and irritability were the most common presenting features lethargy, vomiting, pallor were common presenting features. Anand et. Al[17]. Observed that refusal of feed, lethargy, temperature changes, sclerema were predominant clinical features.All these studies show that clinical features of neonatal septicemia are Non specific and may be clinically indistinguishable from those occurring in non-infectious conditions during neonatal period



Graph Ii : Organisms Isolated In Culture Positive Cases



Graph shows various organisms isolated in culture positive cases. Commonest are Klebsiella(31.8%) & E.Coli (22.7%). Manroe[18]observed E.coli were commonest.

Sepsis screen = A battery of indirect markers of infection when collectively studied provide an extremely reliable index of neonatal sepsis much earlier and serve as a useful guide for initiating antibiotic therapy.

Accuracy in making early diagnosis of neonatal septicemia by any test depends on sensitivity i.e, diagnosing infection when it is not present and positive predictive accuracy ie, probability that a patient with a positive test result has, infact the disease in question. In this study sepsis screen was studied in culture positive and culture negative cases. Bacterial culture positivity gave definitive diagnosis of septicemia. In this study out of 94cases of suspected sepsis 22 cases were proved by positive culture.

Graph III :- Distribution According To Culture Positivity

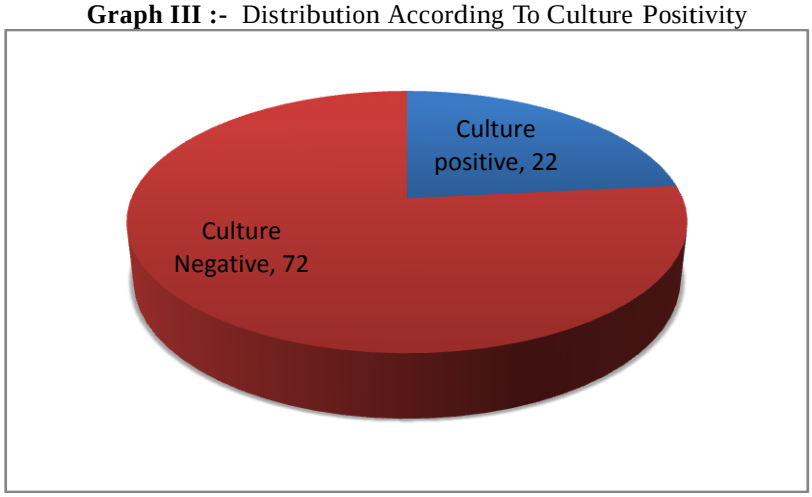


Table III- White Blood Cell Count Profile

WBC count	Culture		
	Culture positive	culture negative	total
<5000/cmm	9(40.9%)	15(20.8%)	24
>5000cmm	13(59.1%)	57(79.2%)	70
total	22	72	94

Leucopenia with count <5000/cmm was considered positive for septiceamia. In our study 9casesof culture positive & 15 cases of culture negative presented with low count. So in our study sensitivity is 40.9%, specificity is 79% & positive predictive accuracy is 48%. Alistair G.S. Philip et. Al[6]. found that leucopenia had 50% sensitivity 94% specificity and 40% positive preductive accuracy. Namedo et. al.[19] Observed that leucopenia had sensitivity of 44%, specificity of 69% and positive predictive accuracy of 48%. Unfortunately the positive predictive value of an abnormal WBC count is poor. This is not surprising since many non-infections conditions can be associated with an abnormal neonatal WBC count. Thus the initial WBC with differential cell count may not be helpful in the decision to initiate antibiotic therapy for an asymptomatic new born infant with identified risk factor for sepsis. Nevertheless it is common practice to perform these tests as a part of the immediate post natal assessment of the "at risk" infant.

In the past, the changes in the white blood cell parameters among neonates Were regarded least useful for the diagnosis of sepsis as these values were thought to be too erratic. Recently, Xanthou[20] studied these changes more precisely in healthy and diseased neonates and established its usefulness as a supportive test for the diagnosis of neonatal sepsis.

Table IV:- Cells With Toxic Granulation Profile

Toxic Granulation	Culture		
	Culture	Culture	Total
Present	15 (68.18%)	33(45.8%)	48
Absent	7 (31.82%)	39 (54.6%)	46
Total	22	72	94

So in our study toxic granulation had 68% sensitivity, 54% specificity and 31.25% positive predictive accuracy. Our studies are consistant with other studies. Namedo et. Al[19]. Observed that toxic granulation had 80% sensitivity, 70% specificity and 69% positive predictive accuracy.

Zipursky et. Al[21]. showed a very close relationship between the presence of Vacuolated neutrophils and bacterial infections. Xanthou[39] in her study of neonatal infection, described toxic granulation as an important feature. She felt that toxic granulation was invariably present 'during sepsis' a change never seen in healthy new born babies.

Table V:- Immature Neutrophil To Total Neutrophil Ratio

I/T	Culture		
	Culture	Culture	Total
I/T $\geq$ 0.2	11(50%)	17 (23.6%)	28
I/T < 0.2	11 (50%)	55(66.4%)	66
Total	22	72	94

In our study I/T had a sensitivity of 50%,specificity of 23% & positivity predictive accuracy is 31.25%. our observation were consistant with studies of M.Singh et al[22],Namedo et al[19], & Lokeshwar et al[4]. During the bacterial infections increased number of neutrophils is released from bone marrow into the blood stream providing neutrophils to migrate at the infected site.This increase in neutrophils appear essential for the host resistant to bacterial infection. As more neutrophils are released , more & more immature cell reaches the circulation, a process called as 'shift to left'. This finding have been found valuable in early diagnosis of bacterial infection.

Table VI:- Platelet Count Profile

Platelet count	Culture		
	Culture Positive	Culture negative	Total
< 1 lakh / cmm	9 (39%)	18 (25.3%)	27
> 1 lakh / cmm	14 (61%)	53 (74.7%)	67
Total	23	71	94

our study shows platelet count had sensitivity (39%), specificity (74%)a n d positive predictive accuracy of (33.33%). Our observations are consistent with other studies. Khursid S et al[23] observed in their study out of 50 neonates suspected of sepsis 22 neonates had thrombocytopenia. Out 50 neonates 21 neonates had positive blood culture of 21, 11 neonates had thrombocytopenia.in there study thrombocytopenia had sensitivity of 52%, specificity of 62%, positive predictive value of

Table VII:- C-Reactive Protein Profile

C-reactive protein	Culture		
	Culture Positive	Culture Negative	Total
Positive	20 (90.2%)	36(50%)	56
Negative	2(9.8%)	36 (50%)	38
Total	22	72	94

our study this test had 90% sensitivity,50% specificity,37.5% Positive predictive value. Our findings are consistent with other studies. Khursid S et al[23] observed 66% sensitivity,48% specificity,48% positive predictive value. Hiew T.M et al[24] in his study observed that CRP test had a sensitivity of 83%, specificity of 41%, positive predictive accuracy of 37%.

Table VIII:-Combination Of Two Test

Test	Result	Culture positive	Culture negative	Total
Toxic Granulation + Platelet Count	Positive	7(31.8%)	14(19.4%)	21
	Negative	15(68.2%)	58(80.6%)	73
	Total	22	72	94
Toxic Granulation + CRP	Positive	14(63.3%)	21(29.1%)	35
	Negative	8(36.7%)	51(71.9%)	59
	Total	22	72	94
Platelet Count + CRP	Positive	8(36.3%)	21(29.1%)	29
	Negative	14(63.7%)	51(71.9%)	65
	Total	22	72	94
Platelet Count + I/T	Positive	4(18.18%)	2(2.77%)	06
	Negative	18(81.82%)	70(97.32%)	88
	Total	22	72	94

Combination of C-reactive protein and toxic granulation gave 63.6% sensitivity, 70.8% specificity and 40% positive predictive accuracy. Combination of C-reactive protein and platelet count gave 36.3% sensitivity, 87.5% specificity and 30.76% positive predictive accuracy. Combination of platelet count and toxic granulation gave 31% sensitivity, 80.5% specificity and 33% positive predictive accuracy. Combination of immature to total neutrophil ratio and platelet count gave 18.18% sensitivity, 97% specificity and 66.7% positive predictive accuracy. In our study best combination was C-reactive protein + toxic granulation. combination immature to total neutrophil ratio and platelet count had highest specificity In our study it was observed that when two on more tests were Combined specificity and positive predictive accuracy were increased while sensitivity was decreased than the individual test. Our observations are consistant with other studies. Mishra et. Al[14].Observed that positive predictive accuracy and specificity of two test combination was higher than individual tests, at the cost of sensitivity. M Singh et. Al[22]. also found that when two or more tests were combined the specificity was increased than the individual test.

Conclusion

1. Clinical features of neonatal septicemia are non-specific
2. Male, term and normal Birth weight neonates were more prone for septicemia in our study
3. Early onset septicemia is more common than late onset septicemia
4. Gram negative septicemia is more common than gram positive septicemia
5. Gram negative septicemia is common cause of early onset septicemia & also in low birth weight babies
6. Sepsis screen is simple, cheap, less time consuming & easy to perform even at bedside with good predictive value for early diagnosis
7. Sepsis screen has good sensitivity, specificity and positive predictive a ccuracy and is a valuable aid in early diagnosis of neonatal septicemia
8. As an individual test C-reactive protein has highest sensitivity, specificity a nd positive predictive accuracy and is a sensitive and responsive indicator of neonatal sepsis
9. Combination of tests increases the specificity and positive predictive accuracy.

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