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Role Of C-Reactive Protein In Neonatal Septicemia

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Abstract
Background: *Neonatal septicemia is a major cause of mortality and morbidity, worldwide. It may manifest as early or late onset septicemia, occurring in less than 72 hours of birth or after 72 hours respectively. Risk factors predisposing to neonatal septicemia are multifactorial and include maternal, foetal and environmental factors. Isolation of bacterial agent from blood by cultural techniques serves as the "Gold Standard" for diagnosis. However, as culture results are obtained after 48 hours, many adjunctive tests, which are available, are in use and include haematological parameters, CRP, Buffy coat smear and Nitroblue Tetrazolium reduction test. The present study aimed at evaluating the usefulness of CRP in early diagnosis of neonatal septicaemia.*
Materials and Methods: *CRP test was performed on serum samples, employing the principle of rapid slide agglutination. Samples yielding a positive preliminary test were subjected to CRP test in dilutions, to obtain the titre in the sample. CRP test results were correlated with blood culture for aerobic bacteria. Various risk factors were elucidated.*
Results: *Neonatal sepsis was proved by culture in 13.3% cases. A positive CRP test was obtained in 47.8% cases, which were clinically suspected to have neonatal sepsis. Comparison of CRP test result with blood culture revealed that a positive CRP was obtained in 55% patients with culture proven sepsis. Male infants predominated (73.9%). Early onset sepsis was seen in 60.9% cases. Prematurity was evident in 56.5% babies. Prolonged labour and premature and prolonged rupture of membranes as maternal risk factors were seen in 60.9% and 52.2% neonatal sepsis cases respectively. A total of 15 babies (65.2%) with neonatal sepsis were delivered by spontaneous vaginal delivery.*
Conclusion: *CRP has a role in diagnosis of neonatal sepsis, before the blood culture results are available. However, it cannot be used as a single indicator of sepsis. It could serve as a good screening test if combined with clinical criteria and haematological parameters.*
Keyword*: Neonatal septicemia, CRP, blood culture*

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I. INTRODUCTION

Septicemia in the neonates refers to "Generalised Bacterial Infection" documented by positive blood culture in the first four weeks of life.[1] When pathogenic organisms gain access into the blood stream, they may cause an overwhelming infection without much localisation (septicaemia) or may get predominantly localised to the lung causing pneumonia or meningitis.[2]

Neonatal septicemia manifests in two forms, based on the age of onset. Early onset sepsis occurs in less than 72 hours of birth and is acquired during foetal life, delivery or at the nursery.[3] Late onset septicemia occurring after 72 hours is caused by organisms thriving in the external environment of the home or hospital.[4]

Neonatal septicemia continues to be a major cause of neonatal mortality and morbidity worldwide. In India, neonatal septicemia remains as one of the leading causes of mortality and morbidity.[5]

Risk factors predisposing to neonatal septicemia are multifactorial and include maternal, foetal and environmental factors. Predominant among maternal factors include premature rupture of membranes at any time after 37 completed weeks of pregnancy but before onset of labour.[5] Neonatal risk factors assessed include prematurity and low birth weight among others.[6]

The manifestations of neonatal septicemia are often vague and ill-defined and therefore, demand a high index of suspicion for early diagnosis.[7] Its association with high mortality and morbidity makes rapid diagnosis and prompt treatment imperative as a life saving measure.

The gold standard for diagnosis of septicemia is isolation of bacterial agents from blood by culture techniques.[8] Timely recovery of bacteria can have great diagnostic and prognostic importance.

However, as blood culture takes at least 48 to 72 hours for a positive result, many adjunctive tests have been evaluated. These tests are intended to indicate early infections, although they do not identify the inciting organisms.

Various haematological parameters such as total WBC count, band cells, absolute neutrophil count, Immature/Total neutrophil count ratio and micro ESR have been assessed for their ability to aide in diagnosing neonatal septicemia.[9] In addition; CRP, buffy coat smear and Nitroblue tetrazolium reduction test have also been tried.

The present study was aimed at determining the role of CRP and its usefulness in 'early' diagnosis of neonatal septicemia. The study also analysed maternal and foetal risk factors predisposing to neonatal infections. Finally, an attempt was made to critically analyse and assess the data obtained herein, in light of findings of other workers.

II. MATERIAL AND METHODS

The present study was conducted in the Department of Microbiology of a Tertiary Care Hospital, over a period of 3 months, extending from May to July 2021.

The subjects included in the study were inborn babies i.e. those born in the hospital and admitted to Neonatal Unit and outborn babies, who were born outside the hospital and admitted to the Neonatal Unit. Babies upto 28 days of age were included in the study. Babies who expired within 24 hours of admission, or those kept under observation for less than 24 hours and babies with birth weight of less than 1kg, who were managed with minimal handling, were excluded from the study.

Clinical features suggestive of sepsis were looked for and noted, with the help of the treating paediatrician. The time of onset of sepsis was also noted along with weight and gender of the babies.

A detailed history was obtained from the mother/guardian and with the help of the treating doctor. Maternal and foetal risk factors were sought for, from the mother, antenatal case records, referral notes and delivery notes on the following lines:

Maternal:

a) Presence of Pre eclampsia
b) History of pyrexia
c) History suggestive of Urinary Tract Infection
d) Premature or prolonged rupture of membranes
e) Prolonged labour
f) Repeated vaginal examinations
g) Mode of delivery

Foetal:

a) Prematurity
b) Weight at birth

In clinically suspected cases of neonatal sepsis, on day 2, about 1 ml of venous blood was collected with the help of the treating paediatrician, following strict precautions and put in a plain bulb. The blood was allowed to clot before being transferred to the Department of Microbiology, for conducting the CRP Test.

CRP test was performed on the serum that was obtained after the blood in the plain bulb had clotted. The test was done by Slide Agglutination method, using a commercially available kit.

One drop of test serum sample was placed on a glass slide, using a disposable dropper, provided with the kit. A drop of the CRP Latex reagent was added to the drop of the test sample, mixed well with a mixing stick. The slide was then rocked gently to and fro, for 2 minutes. Macroscopic agglutination was looked for at the end of 2 minutes. Presence of agglutination was considered as a positive test result and indicated the presence of CRP in a concentration greater than or equal to 0.6 mg/dl. When the preliminary result was positive, the serum sample was subjected to doubling dilutions. Each dilution was tested for the presence of CRP, so as to obtain the CRP titre in the sample. Positive and negative controls were incorporated with each set of tests done on a particular day.

Blood culture result of each case, included in the study was noted down.

Sensitivity, Specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) were calculated using the following formulae.[10]

1) Sensitivity = $\frac{\text{No. of true positive}}{\text{No. of true positive + No. of false negative}} \times 100$

2) Specificity = No. of true negative x 100
No. of true negative + No. of false positive

3) PPV = No. of true positive x 100
No. of true positive + No. of false positive

4) NPV = No. of true negative x 100
No of true negative + No of false negative

a) True Positive = Culture positive + CRP test positive
b) False Negative = Culture positive + CRP test negative
c) True negative = Culture negative + CRP test negative
d) False positive = Culture negative + CRP test positive

III. RESULTS

This study was undertaken over a period of 3 months, from May to July 2021. It included an analysis of CRP test in Neonatal Septicemia cases, admitted in the Neonatal Intensive Care Unit (NICU) under the Department of Paediatrics of a Tertiary Care Institution.

TABLE NO 1 : PREVALENCE OF SEPSIS DURING THE STUDY PERIOD

Category	No of cases	Percentage
Total no. of babies admitted	151	100
Suspected sepsis cases	23	15.2
Culture proven sepsis	20	13.3

During the study period, a total of 151 babies were admitted to the NICU. Suspected neonatal septicaemia cases on clinical ground, included 23 babies i.e. 15.2%. Neonatal septicemia was proved by culture in 20 cases i.e. 13.3%.

TABLE NO 2 : RESULT OF CRP TEST IN THE STUDY SUBJECTS

CRP test	Number	Percentage
Positive	11	47.8
Negative	12	52.2
Total	23	100

A positive CRP Test was obtained in 11 out of 23 babies i.e. 47.8%, while a negative result was seen in 52.2% cases (n=12).

TABLE NO 3 : COMPARISON OF CRP TEST WITH BLOOD CULTURE IN THE CASES UNDER STUDY

CRP Test	Blood culture				Total
	Positive		Negative		
	Number	Percentage	Number	Percentage	
Positive	11	55	0	0	11
Negative	9	45	3	100	12
Total	20	100	3	100	23

Comparison of CRP test result with blood culture revealed that a positive CRP was obtained in 55% patients with culture proven sepsis, while 45% babies showed a negative result. Among the culture negative, clinically suspected neonatal sepsis cases (n=3), none showed a positive CRP result.

TABLE NO 4 : SENSITIVITY, SPECIFICITY, PPV, NPV OF CRP TEST

Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
55	100	100	25

The parameters were calculated by considering a positive culture result as a "Gold standard." The Sensitivity of CRP test was 55% i.e. it correctly detected neonatal septicemia in these cases. The Specificity was 100% while the PPV and NPV were 100% and 25% respectively.

TABLE NO 5 : GENDER OF SEPTICEMIA CASES

Gender	Number	Percentage
Male	17	73.9
Female	6	26.1
Total	23	100

Male : Female ratio = 2.8 : 1; Males accounted for 73.9% of the total, showing a predominance.

TABLE NO 6 : DISTRIBUTION OF CASES ACCORDING TO ONSET OF SEPSIS

Onset	Number	Percentage
Early onset	14	60.9
Late onset	9	39.1
Total	23	100

Early onset sepsis was seen in 60.9% cases, while 39.1% cases developed sepsis after 7 days of birth (39.1%).

TABLE NO 7 : DISTRIBUTION OF CASES ACCORDING TO GESTATIONAL AGE

Gestational age	Number	Percentage
Preterm (<37 wks)	13	56.5
Term (≥37 wks)	10	43.5
Total	23	100

A total of 13 babies i.e. 56.5% were born before 37 weeks of gestation and hence premature, while 43.5% babies were born at term.

TABLE NO 8 : DISTRIBUTION ACCORDING TO BIRTH WEIGHT

Birth weight in kgs	Number	Percentage
1-1.4	3	13.1
1.5-1.9	7	30.4
2.0-2.4	4	17.4
≥2.5	9	39.1
Total	23	100

The prevalence was high in low birth weight babies. Babies weighing less than 1.4 kgs were 13.1% of the total, while those weighing between 2.0 and 2.4 kgs with neonatal sepsis were 17.4% of the total.

TABLE NO 9 : SEPSIS IN RELATION TO MATERNAL RISK FACTORS (n=23)

Risk factors	Number	Percentage
Premature rupture of membranes	12	52.2
Prolonged rupture of membranes	12	52.2
Prolonged labour	14	60.9
Repeated vaginal examinations	11	47.8
Pre-eclampsia	8	34.8
Maternal pyrexia	3	13.1
Maternal UTI	4	17.4

No obvious risk factors	6	26.1

Prolonged labour and premature & prolonged rupture of membranes as maternal risk factors were seen in 60.9% and 52.2% neonatal sepsis cases respectively. Repeated vaginal examinations were undertaken in 47.8% mothers, whose babies developed neonatal sepsis. No obvious risk factors were evident in 26.1 % mothers.

TABLE NO 10 :SEPTICEMIA IN RELATION TO MODE OF DELIVERY

Mode of delivery	Number	percentage
Spontaneous vaginal delivery	15	65.2
Lower segment caesarean section	8	34.8
Total	23	100

A total of 15 babies i.e. 65.2 % who developed neonatal sepsis were delivered by spontaneous vaginal delivery, while caesarean section had to be undertaken in 8 mothers i.e. 34.8%.

IV. DISCUSSION

Neonatal septicemia is a clinical syndrome characterised by systemic signs of infection in the first 28 days of life. It forms an important cause of mortality among neonates.[11] Many maternal and foetal risk factors contribute to the development of neonatal sepsis, most of which can be prevented.

The present study evaluated the role of CRP as a rapid diagnostic test in detecting neonatal sepsis. The study also attempted to elucidate various neonatal and maternal risk factors leading to neonatal sepsis.

PREVALENCE OF NEONATAL SEPSIS

In the present study, neonatal septicemia was suspected in 15.2% cases during the 3 months study period. Culture of blood proved sepsis in 13.3% cases (20 out of 23 cases).

This finding is in concordance with that of 10% and 15.6% in the studies of Halkaflan JSK[12] and Pawa et al.[13] Neonatal septicemia, as observed by Vinodkumar et al[11] was much higher, i.e. 53.2%.

Neonates are at a high risk for bacterial sepsis, especially in developing countries. In the recent years, invasive procedures are being undertaken more often, leading to increased sepsis in the newborn.[14] Further, with the emergence of drug resistant bacteria, the problems of septicemia are compounded.[14]

EVALUATION OF CRP AS A SCREENING TEST

Bacterial sepsis is difficult to diagnose clinically as the signs and symptoms may be non-specific. Evolution of symptoms may differ. In addition, early signs of sepsis may be minimal.[9]

In the present study, a positive CRP result was obtained in 55% cases of blood culture proven neonatal septicemia. No false positive result was obtained in the study. However, a false negative result was obtained in 45% of cases of neonatal sepsis, which were confirmed by a positive blood culture.

The sensitivity and specificity of CRP test was 55% and 100% respectively. Hisamuddin et al evaluated the validity of CRP for diagnosis of neonatal sepsis and obtained a sensitivity and specificity of 58.33% and 56.52% respectively.[15]

Chan et al found sensitivity, specificity, negative and positive predictive values of 56%, 72%, 71% and 57% respectively.[16]

Benitz et al obtained a sensitivity of 40% when the CRP was performed at onset of sepsis.[17] It takes approximately 24 hrs for serum CRP to rise, after symptoms appear. The authors opine that the sensitivity increased to 90% when performed 24 hrs later.[17] Mather et al found an increase in sensitivity from 22% to 61% as time passed after onset of sepsis.[18] Wagle and colleagues also showed a rise in CRP on day 2.[19] CRP done in the present study was on day 2. No comparison was however done with values at time of onset of sepsis.

Monitoring of CRP can be undertaken to monitor response to treatment, as was opined by Jave et al.[20] This was however not attempted in the present study.

GENDER

The present study observed a male preponderance; the male:female ratio being 2.8 :1. Similar male dominance was seen by other workers i.e. Jyoti et al, who observed their male percentage to be 65.5%.[21]

Although observations indicate that male infants develop neonatal sepsis, male gender has not been included in assessment of neonates at risk for sepsis. St. Geme et al, opine that it would be prudent to include male gender in the risk assessment for sepsis.[22]

ONSET OF SEPSIS

In the present study, early onset sepsis was suspected before 72 hours in 60.9% cases. Gandhi et al, in their study, similarly observed early onset sepsis in 59% cases.[23] However, Karambin et al observed a higher occurrence of late onset sepsis in their study.[24]

Early onset sepsis is generally acquired vertically, during birth, from the bacteria in the mother's genital tract. Infection could also occur before labour, where bacteria from the mother could ascend through the vagina upwards into the amniotic sac.

Late onset sepsis is generally nosocomial, acquired in the nursery, probably from the reservoir of early onset infected neonates.

Early onset sepsis is very often fulminant, with associated pneumonia, while late onset septicemia is slowly progressive and associated with meningitis.[25]

GESTSTIONAL AGE

Among all babies with septicemia, 56.5% babies were preterm, born before 37 weeks of gestation in the mother. Bhat et al, similarly observed that 54.7% babies with sepsis were premature.[26]

Prematurity has been accepted as a risk for development of neonatal sepsis. The immune system of a preterm baby is unable to produce immunoglobulins, phagocytose or bring about opsonisation of bacteria, culminating in infection.[27]

Premature infants generally need intravenous and endotracheal procedures, which expose them to development of sepsis, with bacteria entering through these routes.

BIRTH WEIGHT

Infants who developed sepsis and were less than 2 kgs were 43.5% of the total, in the present study.

Low birth weight has been associated with neonatal sepsis in many studies. Pal et al observed sepsis in 67.12% low birth weight neonates[28] as also Mudey et al (70 % low birth weight septic neonates).[29]

Chandra et al opine that placental protective IgG transport from maternal to foetal circulation, increases with maturity. In low birth weight infants, there is placental insufficiency. This hampers transport of IgG across the placenta, predisposing the neonate to infection.[30]

MATERNAL RISK FACTORS

Prolonged labour (60.9%), premature rupture of membranes (52.2%), prolonged rupture of membranes (52.2%) and repeated vaginal examinations (47.8%) were maternal associated risk factors in the present study.

Gandhi et al, in their study, observed that 77% neonates of mothers who had PROM developed sepsis.[23] Similar findings were also observed by Kayange et al.[31]

Prolonged leak and premature rupture of membranes carries the danger of organisms ascending from the perineal and vaginal area to cause infection in the amniotic fluid and to the fetus. This factor is often overlooked in busy obstetric wards and labour rooms.

Repeated vaginal examination favour ascent of vaginal flora towards the amniotic cavity to cause fetal infection.

Pre-eclampsia was seen in 34.8% mothers whose newborns developed sepsis in the present study. Bhaumik et al observed that mothers who had eclampsia during antenatal period had a higher risk of developing early onset sepsis.[32] Gotoff opines that neonates whose mothers had pre-eclampsia, have neutropenia in the 1st 3 days of life, which predisposes them to early onset sepsis.[33]

Fever or UTI during pregnancy, predisposes the infant to infection.[33] It is probable that the causative agents in the mother cross over through the placenta to the foetus.

MODE OF DELIVERY

In the present study, spontaneous vaginal delivery was recorded in 65.2% infants who developed neonatal sepsis. Similar observation was made by Vinodkumar et al (83.1%)[11] and Pal et al (76.9%).[34] However, Gandhi et al observed a high prevalence in infants delivered by caesarean section.[23]

Davies et al opine that vaginal delivery can cause foetal hypoxia which leads to respiratory infection and subsequent septicemia[35] A caesarean section may be safe, only if it has not been preceded by labour.

V. CONCLUSION

In the present study, CRP correctly diagnosed neonatal septicemia in 55% cases. However, the test, if done alone, would have missed 45% cases, which were blood culture confirmed at a later date i.e. 36-72 hours.

Although CRP had a role in diagnosis of neonatal sepsis, before the availability of blood culture result, it cannot be used as a single indicator of neonatal sepsis. It could serve as a good screening test if combined with other clinical criteria and haematological parameters, such as micro ESR and total WBC count.

Latex agglutination test for CRP detection is economical, easy and rapid. It can be used as a screening test if made a part of a "score" for classifying a sick neonate as having septicemia.

REFERENCES

[1]. Gomaa HHA, Udo EEE, Rajaram U. Neonatal Septicemia In Al-Jahra Hospital, Kuwait: Etiological Agents And Antibiotic Sensitivity Patterns. Med Princ Pract. 2001; 10:145-50.
[2]. Stoll BJ, Hansen NI, Adams-Chapman I. Neuro Development And Growth Impairment Among Extremely Low Birth Weight Infants With Neonatal Infection. JAMA. 2004; 292(19):2357-2364.
[3]. Eichenwald EC, Stark AR. Manual Of Neonatal Care, 6th Ed. Philadelphia: Lippincott William And Wilkins; 2008. P274-300.
[4]. Jain A, Awasthi AK, Kumar M. Etiological And Antimicrobial Susceptibility Profile Of Nosocomial Blood Stream Infections In A Neonatal Intensive Care Unit. Ind J Med Microbiol. 2007; 25:299-300.
[5]. Rohsiswatmo R, Kontrovorsi. Diagnosis Sepsis Neonatorum: Hegar B, Trihono PP, Ifran EB, Editor. Update In Neonatal Infection. Jakarta: Departmen Ilmu Kesehetan Anak FKUIRSLM. 2005; 32-43.
[6]. Shah GS, Budhathoki S, Das BK, Mandal RN. Risk Factors In Early Neonatal Sepsis. Kathmandu University Medical Journal. 2006; 4(2):187-191.
[7]. Bhakoo ON, Singh M. Perinatal Risk Factors In Neonatal Bacterial Sepsis. Indian J Pediatr. 1988; 55:941-946.
[8]. Ahmed AS, Chowdhury MA, Hoque M, Darmstadt GL. Clinical And Bacteriological Profile Of Neonatal Septicemia In A Tertiary Level Pediatric Hospital In Bangladesh. Indian Pediatr. 2002; 39:1034-39.
[9]. Parikh M, Singh N. Rapid Diagnosis Of Neonatal Septicemia. IJMM. 1995; 13:37-40.
[10]. Smith TM, Hudson AJ, Spencer RC. Evaluation Of 6 Screening Methods For Detecting Significant Bacteriuria. J Of Clin Pathology. 1988; 41:904-909.
[11]. Vinodkumar CS, Neelagund YF, Kalsurmath S, Banapurmath S, Kalappannavar NK, Basavarajappa KG. Perinatal Risk Factors And Microbial Profile Of Neonatal Septicemia. A Multicentered Study. J Obstet Gynecol India. 2008; 58(1):32-40.
[12]. Halkaflan JSK. Early Onset Neonatal Bacterial Infections. Seminar Perinatology. 1988; 22:15-24.
[13]. Pawa AK, Ramji S, Prakash K. Neonatal Nosocomial Infection: Profile And Risk Factors. Indian Pediatrics. 1997; 34:297-302.
[14]. Afsharpaiman S, Torkaman M, Saburi A, Farzaampur A, Amirsalari S, Kavehmanesh Z. Trends In Incidence Of Neonatal Sepsis And Antibiotic Susceptibility Of Causative Agents In Two Neonatal Intensive Care Units In Tehran, IR Iran. J Of Clinical Neonatology. 2012; 1(3).
[15]. Hisamuddin E, Hisam A, Wahid S, Raza G. Validity Of C-Reactive Protein (CRP) For Diagnosis Of Neonatal Sepsis. Pak J Med Sci. 2015; 31(3):527-531.
[16]. Chan DH, Ho LY. Usefulness Of C-Reactive Protein In The Diagnosis Of Neonatal Sepsis. Singaore Med J. 1997; 38(6):252-255.
[17]. Benitz WE, Han MY, Madan A, Ramachandra P. Serial C-Reactive Protein Levels In Diagnosis Of Neonatal Infection. Pediat. 1998; 102:41.
[18]. Mathers NJ, Pohlandt F. Diagnostic Audit Of C-Reactive Protein In Neonatal Infection. Eur J Pediatr. 1987; 146(2):147-151.
[19]. Wagle S, Grauang A, Kohan R, Evan. C-Reactive Protein As A Diagnostic Tool Of Sepsis In Very Immature Babies. J Pediatr Child Health. 1994; 30(1):40-44.
[20]. Jave DL, Waites KB. Clinical Applications Of C-Reactive Protein In Pediatrics. Pediatr Infect Dis J. 1997; 16(6):735-746.
[21]. Jyothi P, Basavaraj MC, Basavaraj PV. Bacteriological Profile Of Neonatal Septicemia And Antibiotic Susceptibility Pattern Of The Isolates. J Nat Sc Biol Med. 2013; 4:306-9.
[22]. St. Geme JW Jr, Murray DL, Carter J, Hobel CJ, Leake RD, Boscom FA. Perinatal Bacterial Infection After Prolonged Rupture Of Amniotic Membranes: An Analysis Of Risk And Management. J Pediatr. 1984; 104(4):608-13.
[23]. Gandhi S, Ranjan KP, Ranjan N, Sapre N, Masani M. Incidence Of Neonatal Sepsis In Tertiary Care Hospital : An Overview. Int J Med Sci Public Health. 2013; 2:548-552.
[24]. Karambin MM, Zarkesh M. Enterobacter The Most Common Pathogen Of Neonatal Septicaemia In Rasht, Iran. Iran J Pediatr. 2011; 21(1):83-7.
[25]. Kumar A, Parashar A. Clinical Approach To Neonatal Sepsis. Pediatrics Today. 2001; 4(11):493-499.
[26]. Bhat Y, Edward L, Lewis S, Vandana KE. Bacterial Isolates Of Early Onset Neonatal Sepsis And Their Antibiotic Susceptibility Pattern Between 1998 And 2004: An Audit From A Centre In India. Italian Journal Of Pediatrics. 2011; 37:32.
[27]. Yoder MC, Palko L, Milner R, Alkenzia G. Hematology Of Bacterial Infection In Premature Infants. Pediatrics. 1976; 57:829.
[28]. Pal K, Samanta AK. Bacteriological Profile And Antimicrobial Resistance Pattern In Early Onset Neonatal Sepsis : Challenge To The Physician. Int J Cur Res Rev. 2013; 5(06):51-58.
[29]. Mudey GD, Tankhiwale SN, Mudey A. Clinical Profile And Haematological Indices Of Clinically Diagnosed Early Neonatal Septicemia : A Study Conducted In Teaching Institute Attached To Rural Hospital Of Wardha District. Int. J Cur Res Rev. 2011; 3(1):4-8.
[30]. Chandra RK. Fetal Malnutrition And Post-Natal Immunocompetence. Amer J Dis Child. 1975; 129:450-454.
[31]. Kayange N, Kamugisha E, Murzamholya DL, Jeremiah S, Mushana SE. Predictors Of Positive Blood Culture And Deaths Among Neonates With Suspected Neonatal Sepsis In A Tertiary Hospital, Mwanza – Tanzania. BMC Pediatr. 2010; 10:39.
[32]. Bhaumik S, Ghosh S. Risk Of Early Onset Neonatal Septicemia In Babies Born To Mothers With Pre-Eclampsia. Indian Pediatrics. 2000, 37:775-779.
[33]. Gotoff SP. Infections Of Neonatal Infant. In, Nelson Textbook Of Pediatrics. 16th Ed, WB Saunders Company. Philadelphia, 2000; Book I (Parts I To XVIII):538-552.
[34]. Pal K, Samanta AK, Singh R. A Comparative Study Of Early Onset Versus Late Onset Neonatal Sepsis With Special Reference To Bacteriological, Demographic And Clinical Profile. Int J Cur Res Rev. 2014; 06(03):7-15.
[35]. Davies PA, Aherne W. Congenital Pneumonia. Arch Dis Child. 1962; 37:598-602.