Original Research Article

C-REACTIVE PROTEIN AS AN INDEX OF EARLY DIAGNOSIS OF NEONATAL SEPSIS

Abstracts

Introduction: Neonatal sepsis is a major cause of morbidity/mortality and the definitive diagnosis is an isolation of the pathogen from blood culture which might take 2-7 days. A test for early confirmation of infection is therefore required. C-reactive protein (CRP) is therefore suggested as an early screening tool in the diagnosis of neonatal sepsis.

Aim: To determine the usefulness of CRP in the early diagnosis of neonatal sepsis among neonates.

Study design: This was a prospective longitudinal study.

Place of the study: Department of Paediatrics, Obafemi Awolowo University Teaching Hospital Complex Ile-Ife.

Method: Consecutive neonates were recruited. Blood culture was done and CRP was done at contact and 24 hours. Data were analysed and $P < .05$ was considered significant.

Results: A total of 180 neonates comprising 106 (58.9%) males with a male to female ratio of 1.4:1 were studied. Thirty-two (17.8%) of the neonates had culture-proven sepsis with a prevalence of 10.1% among the inborn and 23.8% among the out-born with statistically significant difference ($\chi^2 = 5.638$, $P = .018$). The means of initial and repeat CRP for subjects with culture-proven sepsis were 41.4 (23.6) mg/l and 10.6 (4.3) mg/l respectively while subjects without sepsis were 9.2 (11.3) mg/l and 6.1 (2.6) mg/l respectively ($P < .001$). The CRP has a sensitivity of 93.8%, specificity 91.9%, negative predictive value 98.6%, and positive predictive value of 71.4%. The area under the curve for the receiver

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operator characteristic curve for subjects with CRP ≥ 10mg/L and positive culture was 0.909 ($P < .001$).

Conclusion: The CRP has a high sensitivity, specificity, and negative predictive value and can therefore be used to screen neonates with sepsis.

Keywords: Blood culture; C-reactive protein; Neonate; Sepsis.

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Introduction

Neonatal sepsis is a clinical syndrome of bacteraemia with systemic signs and symptoms of infection in the first 28 days of life [1]. Neonatal sepsis (NNS) is a major cause of morbidity and mortality in the newborn despite various advances in antimicrobial therapy and life supportive measures in medical practice [2]. Neonatal sepsis still remains a major contributor to infant and under-five mortality in Nigeria [3]. According to the World Health Organization (WHO), about five million neonatal deaths occur each year and 98% of this occurs in the developing countries [4]. These deaths result mainly from infections, prematurity and perinatal asphyxia [4], while neonatal sepsis alone accounts for about 1.6 million of neonatal deaths annually and about 42% of these deaths occur in the first week of life [5,6]. Recent studies in developing countries show varying incidence of neonatal sepsis, aetiological agents and antimicrobial sensitivity pattern [7-9].

A definitive diagnosis based on isolation of pathogen(s) from blood culture takes a minimum of 48-72 hours and up to seven days in most cases in the developing world, yet rapid progression of untreated infection increases the morbidity and mortality. For this reason, initiation of empirical antibiotic therapy before diagnostic results are available is recommended for neonates with clinical signs or epidemiologic factors for neonatal sepsis [10]. These clinical features are protean, often subtle, and nonspecific [11,12]. The empirical antibiotic therapy has been reported to result in treatment of as many as 30 uninfected neonates for every infected baby [13]. This has led to antibiotics wastages and unnecessary usage with its adverse effects including antimicrobial resistance [14-16]. Screening tests are now widely used in developed countries, while it is rarely used in developing world, including Nigeria, where the burden of neonatal sepsis is highest [3,6].

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C-reactive protein (CRP) is an acute phase reactant used as screening tool in the diagnosis of neonatal sepsis and various cut-off values have been used by various workers [17]. A single CRP measurement of 10mg/L and above is regarded by some authors as indicative of sepsis [17]. However, in neonates with initial normal level of CRP repeat measurement has been shown to improve the sensitivity, specificity and negative predictive values [18]. This could significantly decrease the need for unnecessary antibiotic exposure, reduce health care costs and length of hospital stay and also prevent mother-infant separation and parental anxiety [19]. Therefore, this study was carried out to determine the usefulness of CRP in early diagnosis of neonatal sepsis among neonates admitted in the Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife. The objectives were to determine the predictive value of C-reactive protein in neonatal sepsis and evaluate the value of C-reactive protein in the diagnosis of neonatal sepsis.

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MATERIALS AND METHODS

Study location: The study was carried out at the neonatal ward (NNW) of the Obafemi Awolowo University Teaching Hospital Complex (OAUTHC) Ile-Ife. The hospital serves as tertiary referral center for both urban and rural communities of Osun, Ondo and Ekiti states in the South West of Nigeria. The NNW is a 25 bedded ward and admits both inborn and out-born babies who are kept at two separate wings on the ward.

Study design: This was a prospective longitudinal study of consecutive neonates delivered both in and out of the hospital, admitted into the ward with clinical features of sepsis or risk factors for sepsis.

Study population: The subjects included all term and preterm neonates with weight greater than 1500 grammes admitted with features of sepsis or risk for sepsis.

Inclusion criteria:

- All newborn babies (both term and preterm) with weight greater than 1500 grammes admitted with features of sepsis (this is because they have comparable reference values of CRP). This includes neonate with any or combinations of the following features: fever or hypothermia, poor suck, vomiting, diarrhoea, abdominal distension, jaundice, lethargy, tachypnoea, grunting, cyanosis, respiratory distress, excessive crying or irritability and convulsion.
- Neonate with maternal risk factors for sepsis such as; peripartum pyrexia, rupture of membrane for more than 24 hours, foul smelling liquor, urinary tract infection, chorioamnionitis (foul smelling liquor with fever and tachycardia in the mother), multiple vaginal examinations (more than 3 sterile or a single unsterile examination) and delivery outside the hospital.

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- Neonate whose parent / care giver consented to take part in the study.

Exclusion criteria:

- Newborn who has had prior antibiotic therapy before admission.
- History of antepartum antibiotic therapy in the mother within a week before delivery.
- Newborn with suspected intracranial haemorrhage as this has been reported to be associated with raised CRP.
- Extreme low birth weight babies since they have a lower cut-off value of CRP.

Ethical consideration: Ethical approval with number IRB/IEC/ 0004553 was obtained from the Research and Ethics Committee of the Hospital. For each recruited neonate a signed written informed consent was obtained from the mother or guardian where mother was not available.

Sample size determination: The minimum sample size (n) was calculated using this formular:

$$n = \frac{z^2pq}{d^2}$$

The prevalence of neonatal sepsis used was from a study in OAUTHC which was 22.9% [7].

Therefore, the minimum sample size;

$$n = \frac{(1.96 \times 1.96) \times 0.229(1-0.229)}{(0.05 \times 0.05)}$$

$$n = 271$$

The average admission rate per year over the last three years into the NNW of OAUTHC Ile-Ife is 531 neonates. Applying the correction for finite population, the corrected sample size (n_c) calculated using the formula

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$$n_c = \frac{n}{1+\frac{n}{N}}$$

Where:

n_c = the minimum sample size when studying populations is less than 10,000

n = the desired minimum sample size when studying populations is more than 10,000 = 271

N= the estimate of the population size which is equal to 531

$$n_c = \frac{271}{1+\frac{271}{531}}$$

Therefore $n_c = 180$

Sample collection:

Collection of blood samples: Peripheral venous blood was obtained from the dorsum of the hand or antecubital fossa after a thorough cleaning of the site with methylated spirit (70% alcohol) and povidone Iodine applied to the site. Two milliliters (2mls) of blood were collected from each subject in 24 hours. One milliliter was inoculated into the Bactec peds plus broth for blood culture and 1ml into a plain bottle for serum CRP estimation.

The sample in the plain bottle was spun in a centrifuge at 4000 revolutions per minute for 5 minutes and the serum was thereafter separated into another clean plain bottle with a disposable bulb pipette for the estimation of serum CRP within 24 hours of collection. The same procedure was repeated 24 hours after the initial samples were collected for repeat CRP estimation if the initial CRP value was less than the cut-off value for the study.

Laboratory investigations

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C-reactive protein (CRP): The assay was carried out using a commercial kit (High-Sensitive C-reactive protein enzyme immunoassay test kit with Catalog no.5004 made in USA). This was performed at the molecular tissue culture unit of the Haematology Department of the OAUTHC. The manufacturer instruction was strictly adhered to during the procedure.

Blood culture: Blood culture was performed using the BD BACTEC PEDS PLUS^{TM}/F 1-3ml culture vials manufactured by Becton, Dickinson and company USA using one milliliter (1ml) of blood inoculated into the BACTEC peds plus blood culture broth under strict aseptic condition and incubated using the BACTEC 9050 Series which is an automated culturing machine.

Media: The general-purpose differential and selective media employed in this study include: the BACTEC ped plus culture broth, Chocolate agar, MacConkey agar, citrate agar, Urease agar, and Mueller-Hinton agar. The stains and reagents employed include the Gram's stain, Kovac's reagent and hydrogen peroxide.

For the purpose of this study subjects with a negative culture result, serial CRP less than 10mg/L were considered to be normal and values above these cut-offs with positive culture results were considered to have sepsis.

Quality control: This was ensured through the following means;

- When not in use the CRP kit components were kept in the refrigerator between 2-8^{0}C to maintain its potency.
- All samples for CRP assay and cultures were collected under strict aseptic conditions.
- Blood samples for CRP were spun and the serum separated within an hour of collection to prevent haemolysis.

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- Samples were analyzed on the same day of collection, and if not feasible samples for CRP were kept in the freezer at -20^{0}C for maximum period of 48 hours.
- Strict adherence to the manufacturer's instructions and using kits within the validity period.
- Blood culture samples were sent to the laboratory for incubation within 30 minutes of collection.
- All samples for blood film were processed by the same laboratory personnel to avoid inter-observer error.

Data analysis

Data were analyzed using the Statistical Package for Social-Sciences (SPSS) version 22.0. The mean, ranges and standard deviations of continuous variables were computed. The difference between means in continuous variables was determined using Student t-test and ANOVA while difference between proportions in categorical variables was determined using Chi-square test. Data was presented using tables, figures and charts as appropriate.

The sensitivity, specificity, positive predictive value (PPV) and the negative predictive value (NPV) were calculated for CRP against positive blood culture, which was the gold standard for the diagnosis of sepsis [20].

Receiver-operator characteristic (ROC) curves were constructed and the optimal cut-off point was determined for sensitivity and specificity. These curves were constructed by plotting the sensitivity (true positive test) on the y-axis and 1- Specificity (false positive test) on the x-axis. Statistical significance was assumed at $P < .05$ at 95% confidence interval.

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RESULTS

A total of 180 neonates were recruited into the study. Seventy-nine (43.9%) of them were delivered at the OAUTHC (inborn), while 101 (56.1%) were delivered outside the hospital (outborn).

Socio-demographic characteristics of the subjects studied

Table 1 showed the distribution of age, sex, gestational age and the weight of the subjects at admission. The ages of the neonates on admission ranged from 0 to 26 days with a mean (±SD) of 89.4 (±128.9) hours. Of the 180 subjects, 109 (60.6%) were aged ≤72 hours at admission. There were 106 (58.9%) males with a male to female ratio of 1.4:1. There were 154 (85.5%) term neonates while 26 (14.5%) were pre-term. The mean (±SD) gestational age was 38 (±1.6) weeks. The weight at admission ranged from 1.62 to 4.60kg with a mean (±SD) of 2.92 (±0.62) kg.

Of the 180 subjects, 79 (43.9%) were inborn and101 (56.1%) were out born. Out of the 101 out born neonates, 35 (19.4%) were delivered in mission homes, 10 (5.6%) in private hospitals and 24 (13.3%) at maternity centres, 27 (15.0%) by traditional birth attendants (TBAs) and 5 (2.8%) at home. The most common mode of delivery was vaginal in 118 (65.6%) while 62 (34.4%) were Caesarean section.

The 180 neonates were delivered to 175 mothers whose mean age was 28 years with range of 17 to 45 years. There were 5 sets of twins. Eighty-seven (49.7%) of the mothers were primipara, 85 (48.6%) were multipara while 3 (1.7%) were grand multipara.

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Table 1: Age at admission, sex, gestational age and weight of the neonates.

Variables	Frequency	Percentage (%)
Age at admission in hours		
≤72 hours	109	60.6
>72 hours	71	39.4
Sex		
Male	106	58.9
Female	74	41.1
Gestational age in weeks		
35 - < 37	26	14.5
37 - 42	154	85.5
Weight on admission		
1.5- <2.5	37	20.6
2.5-4.0	137	76.1
> 4.0	6	3.3

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Table 2 shows the distribution of the identified maternal risk factors. Out of the 151 neonates with risk factors for sepsis, prolonged rupture of membranes was the most common accounting for 100 (66.3%), followed by maternal peripatal pyrexia in 31(20.5%). There were 29 neonates without any maternal risk factors for sepsis.

Table 2: Maternal risk factors for neonatal sepsis.

Risk factor	Frequency (n)	Percentage
PROM*	100	66.3
Peripatal pyrexia	31	20.5
PPROM**	8	5.3
Multiple vaginal examination	7	4.7
Meconium-stained liquor	2	1.3
Antepartum haemorrhage	2	1.3
UTI***	1	0.6
Total	**151**	**100.0**

NB: Not all the neonates had maternal risk factors. *PROM-Prolonged rupture of membranes. **PPROM- Pre-labour premature rupture of membranes. ***UTI – Urinary tract infection.

Clinical features of subjects with sepsis: Table 3 showed the presenting signs and symptoms neonates with sepsis. Fever was present in 20 (62.5%), grunting and respiratory distress in 18(56.3%), and poor suck in 17(53.1%). None of the subject presented with diarrhoea.

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Table 3: The clinical features in neonates with sepsis

*Clinical features	Frequency	Percentage (%)
Fever	20	62.5
Respiratory distress	18	56.3
Poor suck	17	53.1
Depressed primitive reflexes	13	40.6
Lethargy	13	40.6
Excessive crying	12	37.5
Irritability	12	37.5
Jaundice	9	28.1
Hypothermia	8	25.0
Convulsion	7	21.9
Vomiting	3	9.4
Palor	3	9.4
Abdominal distension	3	9.4
	3	9.4

*Multiple clinical features

Culture results: Out of the 180 subjects recruited, 32 (17.8%) of them had culture proven sepsis of which 21 (65.6%) were males and 11 (34.4%) were females giving a male: female ratio of 1.9:1. Eighteen (56.3%) of the culture proven sepsis had late onset sepsis while 14

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(43.7%) had early onset sepsis; 24 (75.0%) were out born, 8 (25.0%) inborn. Twenty-eight (87.5%) were term while four (12.5%) preterm. The prevalence of culture proven sepsis among the inborn subjects was 10.1% while the prevalence among the out born was 23.8%. The difference between the prevalence of culture proven sepsis in the out born and in born was statistically significant ($\chi^2 = 5.638$, $P = .018$).

Table 4 compared the distribution of gestational age, weight and sex between the neonates with sepsis and without sepsis. Twenty-one (19.8%) of the 106 males compare to 11 (14.9%) of the 74 females that were recruited had culture proven sepsis. The difference was not statistically significant ($\chi^2 = 0.827$; $P = .35$).

Table 4: Comparison of gestational age, weight and sex between neonates with and without sepsis.

Characteristic	Subjects with sepsis (n=32)	Subjects without sepsis (n=148)	χ^2	*P* value
Gestational age				
Term	28	126		
Preterm	4	22	0.119	.201
Birth weight				
1.6 - < 2.5kg	6	31	0.077	.780
≥ 2.5	26	117		
Sex				
Male	21	85	0.827	.350
Female	11	63		

C-reactive protein (CRP) results: The mean (±SD) of initial C-Reactive protein (CRP1) and repeat C-Reactive protein (CRP2) of the entire population were 23.1±24.6 mg/l and 6.7±3.4mg/l respectively. The means of initial and repeat CRP for subjects with culture proven sepsis were 41.4 ±23.6 mg/l and 10.6 ±4.3 mg/l respectively while that of subjects without sepsis were 9.2±11.3 mg/l and 6.1±2.6 mg/l respectively. There was statistical

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difference between the mean CRP of subjects with culture proven sepsis and subjects without sepsis with *P* -values of .001 and .001 respectively at 95% confidence intervals. This is seen in table 5. The range of CRP1 was 3.6-98.0mg/l while that of CRP2 was 6.0-18.0 mg/l in culture proven neonates. The range of CRP1 was 1.0-94.0mg/l while that of CRP2 was 1.0-16.0 mg/l in neonates without sepsis.

Table 5: Comparison of the means of the C-Reactive Proteins of the subjects.

Parameters	Subjects with sepsis (n=32)	Subjects without sepsis (n=148)	*P* -value
CRP1*	41.4±23.6	9.2±11.3	.001
CRP2**	10.6±4.3	6.1±2.6	.001

*CRP1=Initial C-Reactive Protein. **CRP2= Repeat C-Reactive Protein

The sensitivity, specificity, positive predictive value and negative predictive values of C-reactive protein are shown in Table 6.

Of the 32 neonates with culture proven sepsis, 30 (93.8%) had $CRP_1 \geq 10$mg/L while two (6.2%) had $CRP_1 < 10$mg/L. Of the 148 subjects with negative culture results, 136 (91.9%) had $CRP_1 < 10$mg/L, while 12 (8.1%) had $CRP_1 \geq 10$mg/L. This was statistically significant ($\chi^2 = 9.872$, df =1, $P = .001$). The likelihood ratio of positive and negative test was 11.6 and 0.07 respectively. Eight of the 12 subjects who had $CRP_1 \geq 10$mg/L had severe birth asphyxia and four of them had acute bilirubin encephalopathy for which exchange blood transfusion was carried out.

Sensitivity = 30/32 = 93.8% Exact 95% confidence interval (79.2- 99.1%)

Specificity =136/148 = 91.9% Exact 95% confidence interval (86.3- 95.7%)

Negative predictive value (NPV) = 136/138 = 98.6%

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Positive predictive value (PPV) = 30/42 =71.4%.

Table 6: Sensitivity, specificity and predictive values of C-reactive protein and culture

CRP	Status of culture		Total
	Pos (n)	Neg (n)	
CRP ≥10mg/L	30	12	42
CRP <10mg/L	2	136	138
Total	32	148	180

Pos (n)= Total number of positive cultures. Neg (n) = Total number of negative cultures

Figure 1 showed the receiver operator characteristic (ROC) curve derived from plotting the sensitivity against 1-specificity using results of subjects with CRP ≥ 10mg/L and positive culture results. From the receiver operator characteristic (ROC) curve constructed the best point of optimal sensitivity and specificity were 87.5% and 83.1%, respectively. This gave a cut-off value of 10.3mg/L. The area under the curve (AUROC) was 0.909, *P* =.001 at 95% CI (85.0-96.9).

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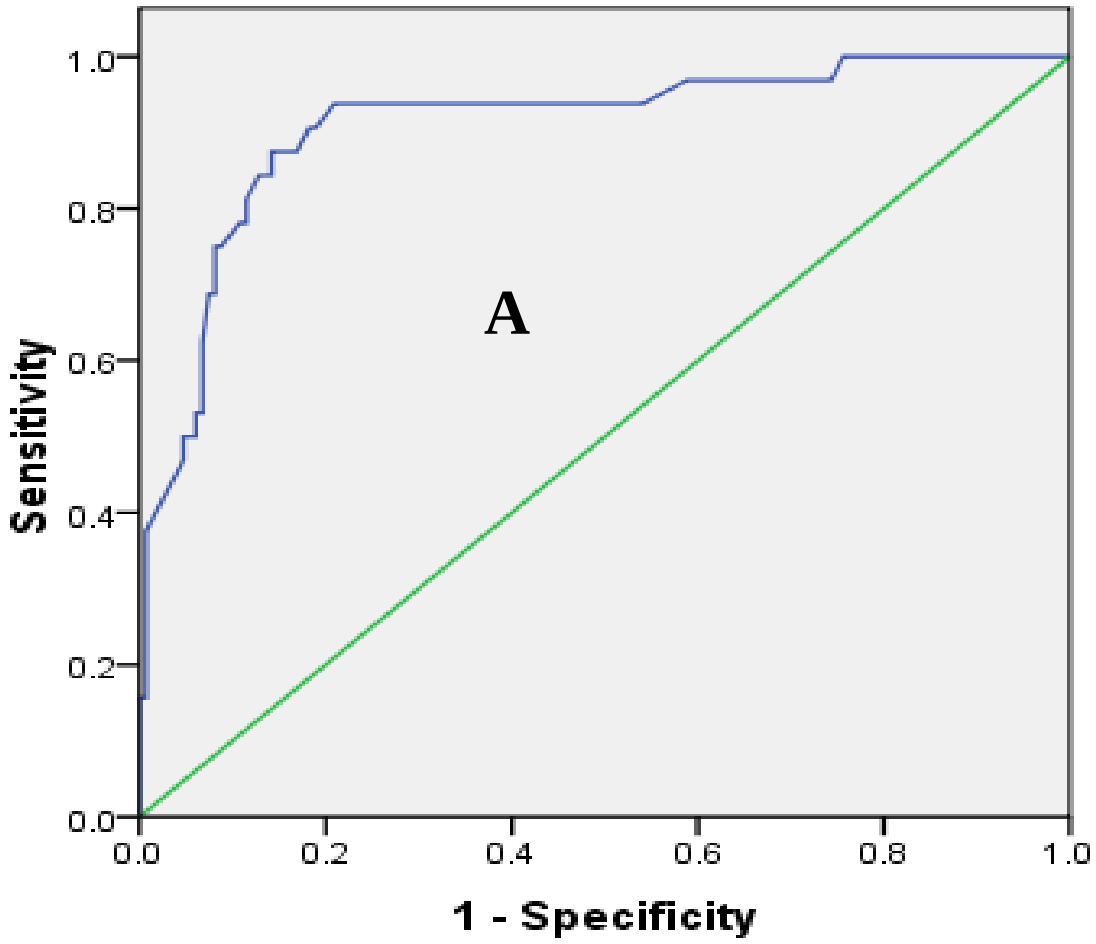

key

ROC curve

A The Area under the curve is 0.909

Useless ROC curve (A curve of a test with poor diagnostics value)

Figure 1: Receiver Operator Characteristic (ROC) curve of C-reactive protein$_1$ ≥ 10mg/L and culture results.

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DISCUSSION

Neonatal sepsis is one of the leading causes of admissions into the newborn unit in our facility and many centers in the country. In the present study 93.8% of the subjects with culture- proven sepsis had initial CRP level greater than the cut-off value of 10mg/L. This is consistent with the assertion that a CRP level of 10mg/L and above is the most reliable cut-off indicative of sepsis [20]. In the present study a high sensitivity and specificity was found at the cut-off value of 10.3mg/L from the ROC curve constructed. Similar findings have also been reported in previous studies [21]. This shows that CRP has a high level of test accuracy in this study. West et al [22], in Port Harcourt reported a moderate sensitivity and specificity with negative and positive predictive values of 79.0% and 68.4%, respectively. However, this is lower than the values recorded in the present study. The difference might have resulted from the difference in the methods of CRP estimation as quantitative measurements have been shown to have higher sensitivity when compared to qualitative ones. In the present study, serial quantitative method was used while qualitative method was used by West et al [22]. Chacha et al [23], in Tanzania, also reported values which were comparable to that observed by West et al [22], but lower than the value recorded in the present study. Qualitative method of CRP estimation has been reported to have a lower sensitivity compared to quantitative measurement [18], which was used in the present study. Majority (91.9%) of the neonates with negative culture had CRP levels less than 10mg/L resulting in a negative predictive value of 98.6% with a negative likelihood ratio of 0.07. This implies that neonates with serial levels of CRP less than10mg/L are very unlikely to have bacterial infection. Similar findings were reported by Nuntnarumit et al [18]. It was also observed that neonates with other morbidities, such as acute bilirubin encephalopathy

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and severe birth asphyxia with neonatal seizures, had elevated CRP despite negative culture results. These have been reported in some studies as non-infectious perinatal conditions that influence CRP levels in the newborn [24]. This is one of the draw backs of CRP use in the diagnosis of neonatal sepsis and this must be put into consideration when using CRP to establish the diagnosis of sepsis.

In this study, CRP has a high sensitivity (93.8%) and specificity (91.9%), along with the high negative predictive value (NPV) of 98.6% and positive predictive value (PPV) of 71.4%. This implies that CRP is able to identify over 98% of none infected neonates. This is comparable with the findings reported by Nuntnarumit et al [18] and Chiesa et al [24]. The similarities in the results of these studies could be attributed to the similarity in the methods of the CRP estimation. The implication of the finding in this study is that serial normal levels of CRP obtained 24 hours apart indicate that bacterial sepsis is unlikely in neonates with risk factors for sepsis, and, therefore, a useful test for excluding neonate without sepsis from unnecessary exposure to antibiotics. This does not imply that empirical antibiotics should not be started for neonates with suspected sepsis but that normal serial CRP level should aid in the decision to discontinue antibiotics especially if the neonate has no clinical evidence of sepsis. A study demonstrated that CRP can be a useful guide in decision making to discontinue antibiotic therapy, thus facilitating early discharge with significantly reduced health care cost, complications of treatment and family anxiety [25].

The 17.8% prevalence of culture proven sepsis observed in this study supports the fact that neonatal sepsis still remains a major challenge in newborn units. Other studies reported a higher prevalence [9,26,27]. The slightly lower prevalence of the present study may be due to the different culture technique used. In the present study Bactec Ped plus automated

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culture broth was used as against the conventional culturing broth used in the previous studies. This has been reported to have a very low false positive rate as against the traditional method used in the previous studies [28]. Also, in the present study, very low birth weight and extreme low birth weight babies were excluded while these groups were included in the studies cited. Since low birth weight and extremely low birth weight babies have been shown to be more prone to sepsis, this may also account for the higher prevalence in the other studies. However, the prevalence observed in this study is higher than 8.0% reported from Sweden [29]. The observed low prevalence in the developed countries has been attributed to access to hygienic skilled delivery for all women, risk based intrapartum antibiotic prophylaxis and high-quality intensive care for newborn [30], which is not the case in the developing countries.

In the present study, the male to female ratio of culture proven sepsis was 1.9:1. This is in keeping with the finding by McClelland and Smith who suggested that factors regulating the synthesis of immunoglobulin are located on X- chromosome, and the presence of double chromosome in female may produce greater genetic diversity in female immunologic defense against infection compared to the single X chromosome found in the male [31].

In the present study, 56.2% of the subjects had late onset sepsis while 43.8% had early onset sepsis; this is not surprising since up to 75% of subjects with sepsis were out-born. The symptoms and signs of neonatal sepsis have been well documented and found to be vague and non-specific [11,12], a feature which was evidenced in the present study. Only 17.8% of the 180 neonates with suspected sepsis in the study had culture proven sepsis. In this study, fever was the commonest symptom among neonates presenting with sepsis followed by respiratory distress. A similar finding was reported in Maiduguri by Ambe et al

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[32], while Ojukwu et al [26], in Abakaliki reported respiratory distress as the commonest symptom followed by fever. Though fever was the commonest symptom among the subjects with culture proven sepsis both in term and preterm neonates, it was observed that five out of the seven preterm subjects with culture proven sepsis had hypothermia. This difference in temperature pattern observed has been attributed to the larger body surface area, smaller body mass and low subcutaneous fat in preterm neonates [33].

It is therefore, recommended that C-reactive protein ELISA Kit should be made available in the institution as part of routine screening test for neonates at risk of sepsis and antibiotics can be successfully discontinued by 72 hours in subjects with two levels of CRP < 10mg/L taken 24 hours apart with no clinical evidence of sepsis. The limitation of this was the inability of the Bactec culture broth to support the growth of anaerobic organisms which might be responsible for some false negative results recorded in this study. Similarly, a single blood culture sample was taken in this study rather than two which has been found to improve the yield of organisms in neonatal sepsis.

CONCLUSION

The sensitivity, specificity and negative predictive value of C-reactive protein (CRP) in the diagnosis of neonatal sepsis were 93.8%, 91.9% and 98.6%, respectively. Therefore, the CRP can be used to safely identify neonates in whom sepsis is unlikely, thus leading to shorter duration of admission and antibiotics exposure.

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