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## PEDIATRICS | RESEARCH ARTICLE

# Procalcitonin in the diagnosis of early-onset neonatal infection in resource-limited settings

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**Abstract:** *Objectives*: To study the usefulness of procalcitonin (PCT) in comparison to C-reactive protein (CRP) in diagnosis of early onset neonatal infection (EONI) in resource-limited setting. *Methods*: Admitted newborns to two big neonatal units in Khartoum were investigated for EONI including CBC, urine analysis, blood culture, CRP and PCT. They were given Ampicillin and Gentamycin which were changed as per blood C/S results or according to clinical progress. CRP and PCT were done initially. PCT was repeated 8 h and CRP 36 h later. Decision to continue antibiotics was taken after getting results of 2nd CRP. Three categories were identified: Confirmed EONI were those with positive blood culture, non-infected were asymptomatic with negative blood culture/ other lab support; and the 3rd were those with negative blood culture but non-conclusive clinical/lab results. The 1st and 3rd categories were continued on antibiotics for 7–14 days. PCT levels were compared to CRP levels in the three categories. *Results*: Fifty-nine newborns were included: mean weight 3.18 kg and mean age 11 hours. Twenty-one infants were confirmed EONI. Isolated organisms were: 9 *Staphylococcus epidermidis*, 7 *Esherishia coli*, 3 *Klebsiella*, one *Proteus* and one Group B haemolytic streptococcus. Twenty-eight were not infected and ten were nonconclusive. Repeat PCT had better positive and negative predictive values than CRP, at 88.2%, and f 96% respectively. *Discussion*: Both CRP and PCT were good to guide management of EONI but one test of PCT taken 8 h after initiation of antibiotics treatment might be enough; especially in resource-limited settings.

**Subjects:** Infectious Diseases; Tropical Medicine; Perinatal & Neonatal Medicine

**Keyword:** neonatal infection; diagnosis; procalcitonin; Sudan

## ABOUT THE AUTHOR

Senior paediatrician/neonatologist with wide experience in neonatology starting in Fazakerly hospital in Liverpool and other UK hospitals. Added experience in the subject in Oman and lastly in Sudan. Wrote about neonatal jaundice. Sepsis, breast feeding and preterm growth and congenital herpes infection. He also wrote extensively in the problem of scorpion stings in children brucellosis, bacterial meningitis and the causes of coma in febrile children. He is still active in research and the academic life.

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## PUBLIC INTEREST STATEMENT

Bacterial infections in the newborn are dreadful and often lead to death or severe mental handicap. They either occur while the baby is in the womb or after its delivery but they are difficult to diagnose. The tools available for diagnosis take time before confirmation of the infection and the baby should be kept in hospital till confirmation or refute of infection. The aim of this study was to use a blood test (procalicitonin level) so as to get a quick and reliable answer to this problem. We reached at encouraging results but probably more wider research is needed.

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## 1. Background

There is a consensus that early-onset neonatal infection (EONI) refers to infection arising within first 72 h after birth (Goldstein, Giroir, & Randolph, 2005; Vergnano, Sharland, Kazembe, Mwansambo, & Heath, 2005) although previous attempts to extend this to 7 days in term newborn were made (Vergnano et al., 2005). Neonatologists have struggled for years to find ways of identifying the handful of newborns with serious illnesses among the thousands who present with the clinical setting of EONI (Chiesa et al., 2003). It has often been the case that accurate histories, careful examination and clinical acumen are not enough and newborns with serious illnesses are missed while others are unnecessarily treated (Dellinger et al., 2013). The risk factors for EONI are well known as infections during pregnancy with mainly group B streptococci (GBS) (Lachenauer & Wessels, 2011), preterm labour (Polin, 2012), premature rupture of membranes (PROM) (Caughey, Robinson, & Norwitz, 2008) and chorioamnionitis (Stoll, 2011). The problem arises when attempts to confirm infection are made. EONI is difficult to confirm (Stocker, Hop, & van Rossum, 2010) and yet it contributes to about 16% of all neonatal mortality (Altunhan, Annagür, Örs, & Mehmetoğlu, 2011).

Diagnostic investigations are many but none is conclusive. Blood culture is considered the gold standard (Altunhan et al., 2011; Stocker et al., 2010) but requires a minimum of 1–2 mL of blood obtained via umbilical artery catheter or peripheral veins. Results take 24–48 h and is hampered by administration of antibiotics to mothers. Even in children when blood extraction is easy the yield of blood culture was not great (Tripathi, Cotten, & Smith, 2012). White blood counts and platelets as biomarker for EONI have yielded poor predictive values in newborns (Chiesa et al., 2003; Le Doare et al., 2014; Polin, 2012) and children (Baraff, Oslund, Schriger, et al., 1992; De et al., 2014). Interleukins are good markers but their short life in blood circulation limits their diagnostic value (Chiesa et al., 1998, 2003). Both C reactive protein (CRP) and procalcitonin (PCT) seem to be more useful for detecting serious illness than WBC but their ability to identify all children with serious bacterial infection was doubted (Chiesa et al., 1998, 2003). PCT, a precursor of calcitonin, is a 116 amino acid protein secreted by the C cells of thyroid gland in normal situation but its levels may increase during septicemia, meningitis, pneumonia and urinary tract infection (Ming & AI, 2010; van Rossum, Wulkan, & Oudesluys-Murphy, 2004). This marker also is produced by macrophage, and monocyte cells of various organs in severe bacterial infection and sepsis (Assicot et al., 1993; Carrol & Thomson, 2002; Gendrel & Bohuon, 2000). The reported diagnostic accuracy of PCT and CRP for the diagnosis of bacterial infections has varied across studies (Assicot et al., 1993; Chiesa et al., 2003; Ming & AI, 2010). Usefulness of PCT for early diagnosis of neonatal sepsis is well studied but its clinical use is lagging behind the use of CRP. This may be due to its cost (López Sastre et al., 2007; Simon, Gauvin, Amre, & Saint-Louis, 2004) or that evidence for its usefulness has not yet gained momentum. The current British (NICE) guideline for dealing with EONI is to measure CRP twice and decide about continuity of antibiotics at 36 h of age (Neonatal NICE, 2012). This has resulted in doing more lumbar punctures and more hospital admissions (Mukherjee, Ramalingaiah, Kennea, & Duffy, 2014). Failure to reach an early decision about treating EONI will result in: inappropriate antibiotics use, emergence of resistance (Hyde et al., 2002; Le Doare et al., 2014; Shah, Mulla, & Revdiwala, 2012; Vernet et al., 2014), increased health care cost (Gray, 2007) and increased mortality (Afroza, 2006). These effects are felt more in resource limited countries where budgets for health are very minimal (Vernet et al., 2014). There is a need to look into the WHO suggested diagnostic point-of-care testing to make a quick clinical decision and consequently saving on health budget (Drain et al., 2014). Two tests of CRP in Sudan cost 25 US dollars while a single PCT costs 15 dollars. If the extra cost of inpatient care while waiting to decide by the results of repeat CRP is taken, the benefit of choosing PCT will be clear.

The purpose of this study was to compare between PCT and CRP in the early diagnosis of EONI. It was a prospective study and the main outcome was the position of PCT at presentation and on its repeat in the early diagnosis of EONI. This is expected to reduce expenditure on health.

## 2. Objectives

(1) To study a series of term newborns suspected for EONI for their risk factors, clinical characteristics and the laboratory confirmation of their infection.

(2) To compare between PCT and CRP as biomarkers for early diagnosis of EONI.

## 3. Design

Prospective, observational, study of a series of newborns admitted with EONI to two SCBUs in Khartoum, Sudan.

## 4. Setting

This study was done in SCBU in the National Ribat Teaching Hospital (NRTH) and in Dream Specialized Hospital (DSH), Khartoum. The hospitals are 2 km apart with total annual deliveries of about 2,000 in NRTH and 1,500 in DSH. NRTH is a government hospital and DSH is a private hospital. Each of them has facilities for intensive care and good laboratory back-up but all investigations in this study were done in Dream specialized hospital for the period May to November 2015.

## 5. Sample size

Since there were no previous reports of incidence it was decided to take a convenience sample of all cases admitted for six months which was a series of 59 cases.

## 6. Inclusion criteria

All term newborns with risk factors for EONI and those who developed clinical features of infection within 72 h of birth were subjects of study: The risk factors considered were: GBS infection during pregnancy, membrane rupture before onset of uterine contractions, prolonged PROM >18 h, offensive odor of amniotic fluid and the clinical syndrome of maternal intrauterine infection. Clinical features considered for suspected EONI were: hypothermia or hyperthermia, irritability, lethargy, apnea, and bradycardia.

## 7. Exclusion criteria

(1) Newborns who were started on antibiotics before admission to SCBU.

(2) Newborns with major congenital anomalies, proven inborn errors of metabolism or hypoxic ischaemic encephalopathy.

(3) Newborns whose parents refuse consent.

## 8. Main outcome measures

(1) Confirmed cases of invasive bacterial infections in newborns suspected for EONI.

(2) Comparison between the levels of PCT and CRP in confirmed cases of EONI.

(3) Comparison between levels of PCT and CRP in suspected non confirmed cases of EONI.

(4) Analysis of cost incurred in over-treating suspected cases of EONI.

## 9. Methods

Newborns admitted to SCBU with the provisional diagnosis of EONI, as described in inclusion criteria, were recruited for the study. A study questionnaire was filled for each patient documenting the risk factors, clinical features for EONI and results of their investigations. Initial investigations included CBC, blood culture, CRP and PCT in serum. Their urine was also taken for routine analysis and cultured if it contained >5 WBC/HPF. Cultures from other sites (including CSF), Chest X Rays and imaging were done as appropriate. Newborns were started on Ampicillin and Gentamycin as first line antibiotics awaiting blood culture results. PCT test (ichroma™ PCT, Boditech Med Incorporated, Revision No.7, 2014, Republic of Korea) was repeated 8 h after the initial test. Procalcitonin was measured using a quantitative fluorescence immunoassay (BRAHMS, Hennigsdorf, Germany). This is based on the use

of a sandwich immunodetection method; the detector antibody in buffer binds to antigens in a fresh serum sample forming complexes that migrate onto nitrocellulose matrix to be captured by the other immobilized—antibody on test strip. In this assay, the donor molecule was Cryptate labeled polyclonal sheep antibody recognizing epitopes in the immature CT region, while the acceptor molecule was an XL665 labeled monoclonal antibody raised against the CCP-1 region of PCT.[18,19]. Pooled sensitivity for PCT markers was 92% (95% CI, 86–95%), compared with 86% (95% CI, 65–95%) for CRP markers; taking values of >2 ng/ml as severe sepsis with a working range of 0.1–100 ng/ml.

CRP (Fortress diagnostics, Unit 2C Antrim Technology, UK) was repeated 24 h after the initial test. Significant levels to support EONI was taken as >10 mg/L for CRP and >2.6 ng/ml for PCT according to manufacturer's inserts. Manual broth-based blood culture systems was used, namely non-selective blood agar media. Growth of any organism in samples taken from symptomatic newborns was taken significant. CSF was tested guided by the clinical situation and antibiotics were changed guided by blood culture results and the clinical scenario. Levels of CRP and PCT, both initial and repeat, were compared in relation to the three categories.

By the end of the first 36 h newborns were labeled proven infected if their blood culture showed growth of organisms; and were continued on antibiotics treatment. Another category were labeled infected but not proven if: one of their CRP is positive, their total WBC count was less than 5,000/mm³ or more than 30,000/mm³, or clinically ill. The third category were the rest of newborns suspected for EONI but no further evidence was documented and their antibiotics were discontinued and labeled suspected only.

## 10. Data analysis
The EPI info programme was used for data entry and analysis. Chi square test was used for calculation of significance and predictive value test was deployed for comparison between outcomes.

## 11. Ethical clearance
The committee for ethics in research in the National Ribat University cleared and approved the study with the condition of taking written consent from the newborns' parents.

## 12. Results
Fifty-nine newborns fulfilled the study criteria; 34 females and 25 males. Their mean weight was 3.18 kg (range 2.6–4.8 kg) and the mean age of presentation was 11 h (range 1–70) hr. Fifty newborns (84.7%) presented within 24 h of age and forty-four of them (88%) presented in the first 12 h; out of whom 30 newborns were admitted at birth due to prolonged rupture of membranes (18 h and more). That was the main maternal risk for EONI followed by maternal fever (12/59 = 20%) and maternal leukocytosis in 11/59 (18.6%). Foetal tachycardia, uterine tenderness and smelly liquor were documented in ten, six and five cases respectively. The clinical features documented in newborns on admission to SCBU are shown in Table 1.

The mean WBC count was 16.36 (SD 9.619), the mean neutrophils count was 10.66 (SD 10.33) and the platelets mean was 174.22 (SD 72.76).

Band forms were looked for in 36 samples of blood and only four showed band forms. Urine microscopic examination showed more than 10 pus cells per HPF in three newborns and Proteus was grown from one of them.

Blood culture grew 21 organisms: 9 *Staph epidermidis, 7 E. coli, 3 Klebsiella, one Proteus and one Group B haemolytic Streptococcus.* That comprised the category of proven infection. The Staph epidermidis group was considered infected because seven of them actually presented with the clinical syndrome of sepsis from the start. There were ten newborns who belonged to the infected but not proven and the remainder 28 were the suspected only. Lumbar puncture was done for 10 newborns from the proven category and four of the spinal fluids contained more than 5 pus cells per HPF; one

| Table 1. The clinical features of newborns suspected for EONI (*N* = 59) | | |
|---|---|---|
| **Clinical feature** | **No** | **%** |
| Tachypnoea | 51 | 88 |
| Tachycardia | 48 | 81.4 |
| Grunting | 44 | 74.6 |
| Refusal of feeds | 37 | 62.7 |
| Added respiratory sounds | 35 | 59.3 |
| Depressed moro reflex | 28 | 47.5 |
| Fever | 22 | 37.3 |
| Jaundice | 16 | 27.1 |
| Ileus | 9 | 15.3 |
| Full fontanelle | 4 | 6.8 |
| Infected umbilicus | 1 | 1.7 |

CSF grew Proteus, another *E. coli* and a third *Staph epidermidis*. The baby who had Proteus grown in his urine and blood also had the organism in his CSF. CSF was also obtained from two newborns belonging to the infected not proven and they were sterile.

The initial CRP (CRP 1) was non- reactive in 25 newborns (42.1%), <10 in 19 (32.2%), 10–20 in 10 (16.9%) and more than that in 5 newborns (8.5%). The repeat CRP (CRP 2) was nonreactive in three newborns, <10 in 13 (22%), 10–20 in 18 (30.5%) and more than 20 in 25 newborns (33.9.1%). Initial PCT (PCT 1) was nonreactive in 21 newborns (35.5), <2.6 in 27 (45.8%), 2.6–10 in 7 and more than 10 in 4 newborns (6.8%). The repeat PCT (PCT 2) was non-reactive in 2 newborns (3.4%), <2.6 in 32 (54%), 2.6–10 in 11 (18.6%) and more than 10 in 14 newborns (23.7%).

Results of CRP 1/PCT 1 in newborns with proven EONI are shown in Table 2 and those for the not infected in Table 3. CRP 2/PCT 2 for the two categories are shown in Tables 4 and 5. Table 6 shows results for CRP 1/ PCT 1 in newborns who were treated for EONI without blood culture proof (3rd category). All CRP 2 results for this category were positive but only 5/10 were positive for PCT 2.

| Table 2. The results of CRP 1 and PCT 1 in newborns with proven EONI | | | |
|---|---|---|---|
| | **Positive** | **Negative** | **Total** |
| CRP 1 | 14 | 7 | 21 |
| PCT 1 | 17 | 4 | 21 |
| Total | 31 | 11 | 42 |

Notes: The $\chi^2$ statistic is 1.1085. The *p*-value is 0.292407. This result is not significant at $p < 0.05$.

| Table 3. The results of CRP 1 and PCT 1 in newborns without EONI | | | |
|---|---|---|---|
| | **Positive** | **Negative** | **Total** |
| CRP 1 | 4 | 24 | 28 |
| PCT 1 | 2 | 26 | 28 |
| Total | 6 | 50 | 56 |

Notes: The $\chi^2$ statistic is 0.7467. The *p*-value is 0.387534. This result is not significant at $p < 0.05$.

| Table 4. The results of CRP 2 and PCT 2 in newborns with proven EONI | | | |
|---|---|---|---|
| | **Positive** | **Negative** | **Total** |
| CRP 2 | 19 | 2 | 21 |
| PCT 2 | 20 | 1 | 21 |
| Total | 39 | 3 | 42 |

Notes: The $\chi^2$ statistic is 0.359. The *p*-value is 0.549076. This result is not significant at $p < 0.05$.

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### Table 5. The results of CRP 2 and PCT 2 in newborns without EONI

|  | Positive | Negative | Total |
|---|---|---|---|
| CRP 2 | 14 | 14 | 28 |
| PCT 2 | 4 | 24 | 28 |
| Total | 18 | 38 | 56 |

Notes: The $\chi^2$ statistic is 8.1871. The *p*-value is 0.004219. This result is significant at $p < 0.05$.

### Table 6. The results of CRP 1 and PCT 1 in newborns with EONI not proven by blood culture

|  | Positive | Negative | Total |
|---|---|---|---|
| CRP 1 | 4 | 6 | 10 |
| PCT 1 | 2 | 8 | 10 |
| Total | 6 | 14 | 20 |

Notes: The $\chi^2$ statistic is 0.9524. The *p*-value is 0.329114. This result is not significant at $p < 0.05$.

### Table 7. The predictive value for CRP 2 and PCT 2 in diagnosis of EONI

|  |  | Treated group | Not treated group | Total |
|---|---|---|---|---|
| CRP 2 | Positive | 29 | 14 | 43 |
|  | Negative | 2 | 14 | 16 |
| PCT 2 | Positive | 30 | 1 | 31 |
|  | Negative | 4 | 24 | 28 |

Notes: CRP 2: Sensitivity = 93.5%, Specificity = 50%. PPV = 67.4%, NPV = 87.5%.

PCT 2: Sensitivity = 96.8%, Specificity = 85.7% PPV = 88.2%, NPV = 96%.

In Table 7 the predictive values of CRP 2 and PCT 2 were worked out and will be compared in discussion.

Managing infants in the three categories resulted in 264 inpatient days. The category of blood culture-proven infection were admitted for 10–14 days but two of them needed more than two weeks of inpatient management and one of them died on day 20 due to Proteus meningitis. Three more of this group died: one of *E. coli* meningitis on day four, one of respiratory failure on day 12 and the 3rd died due to severe necrotizing enterocolitis on day eight. One infant had repeated chest infections and another had repeated convulsions. The 2nd category of twenty-eight newborns (45%) were discharged within 3 days of admission and they did well on follow up at four weeks after discharge except for three infants who did not show up. The 3rd group was treated with antibiotics for 7–14 days and they did well on follow up but one of them had repeated admissions for chest infection and one had obstructive hydrocephalus secondary to clinical meningitis (PCT 2 was positive).

## 13. Discussion

It is clear that more than half of the newborns in this study were born after prolonged rupture of membranes and those were really the ones that needed early decision-making with regard to EONI in order to avoid their unnecessary stay in hospital. The most important warning risk factors before delivery were maternal/foetal tachycardia and maternal fever as shown in Table 1. This emphasizes the need to adopt the risk-factor—based approach to prevent EONI (Dellinger et al., 2013; Goldstein et al., 2005; Stoll, 2011), although it does not work well for GBS (Bekker, Bijlsma, van de Beek, Kuijpers, & van der Ende, 2014). Prematurity is a known risk factor (Heath et al., 2004) but this study did not include this category. The findings on CBC indices were congruous with previous studies (Altunhan et al., 2011; Baraff et al., 1992; Chiesa et al., 2003; De et al., 2014; Polin, 2012) and they were poor indicators of EONI. In fact the British evidence update advisory group (Mirrett, Weinstein, Reimer, Wilson, & Reller, 2001) did not recommend CBC in the battery for diagnosis of EONI. Band forms in the blood

film were not useful either. Urine microscopy was positive for infection in three newborns and one of them grew Proteus species—both in urine and the blood. That newborn in fact had overt features of bladder outlet obstruction. Organisms grown from the blood were 21/59 (35.6%0) and they were mainly *Staphylococcus epidermidis* (CoNS) and *E coli*. The large number of CoNS is probably due to our open system blood collection technique and this calls for observing scrupulous technique in taking blood (Bedford Russell & Kumar, 2015). The clinical scenarios supported infectivity of the newborns whose blood grew CoNS in spite of them being term infants. Similar findings were reported from a cohort study in adults (Bedford Russell & Kumar, 2015). Strikingly GBS were grown only from one blood sample while they accounts for 43% in USA (Altunhan et al., 2011) and 58% in the UK (Stocker et al., 2010). This could not be explained but it has been our local observation. In fact the isolation rate of blood culture in this study was high compared with others, quoting the large South London study where 46,039 infants and children were prospectively studied for bacterial infections and, almost half of them (44.7%) were suspected for invasive bacterial infections. Blood and CSF cultures were positive in 1,442 (7.9%) and 88 (4.0%), respectively. (Tripathi et al., 2012) Blood culture-proven EONI is found to be <1% (Stocker et al., 2010). The difference in infection rate could be due to the difference in hygiene levels.

Tables 2 and 3 compare the results of CRP 1 and PCT 1 in the category of proven infection and the not infected. In both categories there was no significant difference between CRP 1 and PCT 1 in the ability to support the diagnosis of EONI or refute it. Repeating CRP over 24 h was suggested previously to increase its reliability (Blommendahl, Janas, Laine, Miettinen, & Ashorn, 2002; Hengst, 2003).

Analysis of Table 4 and comparing that to Tables 2 and 3 reveals that both CRP 2 and PCT 2 tests were able to differentiate more between infected and not infected newborns but there was no significant difference between the two tests. Applying this to the category of newborns who did not have EONI as shown in Table 5 it is clear that PCT 2 test significantly distinguished between the infected and not infected (*p-value is .004219)*. Again in Table 6 CRP 1 and PCT 1 were unable to furnish diagnosis in those who were clinically ill but their blood culture was negative. CRP 2 and PCT 2 were both high enough in all of them to support the diagnosis of infection. In a recent meta-analysis on the subject PCT markers were found significantly better than CRP markers at differentiating bacterial infections from viral infections (Blommendahl et al., 2002; Ming & AI, 2010; Simon et al., 2004). Pooled sensitivity for PCT markers was 92% (95% CI, 86–95%), compared with 86% (95% CI, 65–95%) for CRP markers, and the difference was statistically significant (6%; 95% CI, 5–11%;). How-ever, pooled specificities were comparable for PCT vs. CRP markers (Assicot et al., 1993; Ramirez, 2014).

It was clear then that PCT 2 was a good tool to help in decision-making in case of suspected EONI. That was also shown in Table 7 which compares predictive values for CRP 2 and PCT 2 with better sensitivity, stronger specificity and high predictive values for PCT 2. If PCT 2 was deployed, probably we could have lessened the number of days in inpatient-care, would have done less lumbar punctures and saved more in the health budget. This stand point is also supported by observations on the current clinical management of EONI (Mukherjee et al., 2014). It is also probably possible that only one PCT test done six hours after suspecting EONI may suffice; but this needs more research at a larger scale.

WHO and others have called for new clinical diagnostic methods that can function in settings with restricted access to a central laboratory (Drain et al., 2014; Hay Burgess, Wasserman, & Dahl, 2006; Institute of Medicine & Forum on Microbial Threats, 2007; Mabey, Peeling, & Perkins, 2001; Urdea et al., 2006). The fundamental advantage of such point-of-care testing in resource-limited settings is to provide clinicians and patients with an immediate test result, the primary outcomes should be based on the most relevant clinical decisions. WHO developed the ASSURED criteria for an ideal point-of-care test in resource-limited settings (Mabey, Peeling, Ustianowski, & Perkins, 2004; Peeling, Holmes, Mabey, & Ronald, 2006) taking its accuracy and reliability as the main features. (Peeling, Smith, & Bossuyt, 2006). PCT fulfils these criteria and its cost is equivalent to one fifth of the admission cost of a newborn in special care baby unit (SCBU) for one day. If results of PCT 2 in this study

were deployed at least one admission day per patient in the 2nd category could have been saved. Also, five of the ten infants in the 3rd category could have been discharged earlier saving about 80 admission days.

Thus making use of PCT 2 could have possibly saved about 108/264 (40.9%) of the total admission days. Comparing this to the cost of PCT the benefit is clear.

## 14. Limitations of the study
The sample size is appropriate for this study but it would have been even better if it were larger. Blood culture was not selective and this probably could have eliminated some of the non-pathological Streptococci. The costing of case management was based on estimates and probably it was not very accurate.

## 15. Conclusion
This series study compared between CRP and PCT in the diagnosis of EONI and it revealed that both tests are good to help in decision-making about EONI. Probably PCT, especially done some hours after suspecting EONI, is more helpful and it may be sufficient on its own; which may reduce expenditure on health to a great extent in resource-limited settings

### Contributor ship statement
EO El-Amin conceived the idea of the work and shared it with BE Mustafa and MA Gamal Eldin and the three wrote the proposal and involved FAM Salih who agreed to do the necessary investigations and verify their results. HF Salih agreed to join the group and included his patients from Dream hospital. OE Elamin read and understood the work, designed the research questionnaire and collected most of the samples. Recruitment of subjects was done by all except FAM Salih.

Analysis of data and writing up the manuscript was shared by all members of the group as well as revising the final version and agreement for its submission.

**Competing Interests**
The authors declare no competing interest.

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