

# Procalcitonin in Sepsis: A Biochemical Aspect

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## Abstract

The diagnosis of severe bacterial infection particularly in neonates is often difficult because the clinical signs are non-specific and subtle. Hence, this study is undertaken to determine the performance of procalcitonin in biochemical point of view to diagnose sepsis. Procalcitonin has been determined in 70 neonates with suspected sepsis and compared with 70 normal neonates, with similar demographic characters. Procalcitonin values are significantly higher in the cases of neonates with clinically suspected sepsis ( $132\text{pg/dl} \pm 167.09$ ) compared to the control neonates ( $63\text{pg/dl} \pm 47.32$ ) which is statistically significant.

This result shows that the serum procalcitonin level seems highly significant and increased in clinically suspected sepsis. Hence, this research paper is an attempt to highlight biochemical aspects of procalcitonin in sepsis.

**Key words:** Procalcitonin, Sepsis, neonates.

## I. INTRODUCTION

Neonatal sepsis is one of the topical problems in modern medicine that is related to the increasing amount of infants with sepsis and high mortality rate. In India, it contributes to 19% of all neonatal deaths.[1] Sepsis is a complex, multifactorial and rapidly progressing disease characterized by an excessive inflammatory response to the infection that can lead to organ failure and eventually death. Timely diagnosis of neonatal sepsis is extremely important.

Though various diagnostic modalities are present for neonatal sepsis, yet blood culture is the gold standard. But it does not have high sensitivity and specificity. C-reactive protein has been one of the parameters used for detection of sepsis but has limited use.[2] Currently, no single test can be considered as an ideal diagnostic test so, need of new laboratory markers for diagnosis of neonatal sepsis. Recently some studies reported serum procalcitonin as a measurable laboratory marker in inflammatory response to infection. Serum procalcitonin levels seem to be significantly greater in proven sepsis and decrease dramatically in all types of sepsis after appropriate treatment.[3] Due to lack of definite data regarding PCT in developing countries[1], present study is undertaken to determine the concentration of

PCT in neonates with suspected sepsis and try to highlight its biochemical role.

## II. MATERIALS AND METHODS

This study is case-control study and conducted on cases of suspicious infants with clinical sign and symptoms of sepsis and hospitalised in Neonatal Intensive Care Unit of Bharati Vidyapeeth Deemed University Medical College & Hospital, Sangli, Maharashtra, India from 2015-2016. Cases are compared with controls who not having symptoms of sepsis.

Clinical criteria for diagnosis of sepsis in neonates are- 1) Maternal risk factors- fever, use of alcoholic beverages, premature rupture of water sac (PROM), Urinary Tract Infection.

2) Neonatal risk factors- low birth weight, poor cry, brady/tachycardia, respiratory distress, apnea and gasping respiration.

Before starting antibiotic treatment, blood sample is collected by responsible physician for routine tests to diagnosis of sepsis. Simultaneously, 2 ml of clotted blood is sent for the determination of PCT concentration. After centrifugation serum sample get isolated and is kept in deepfreeze.

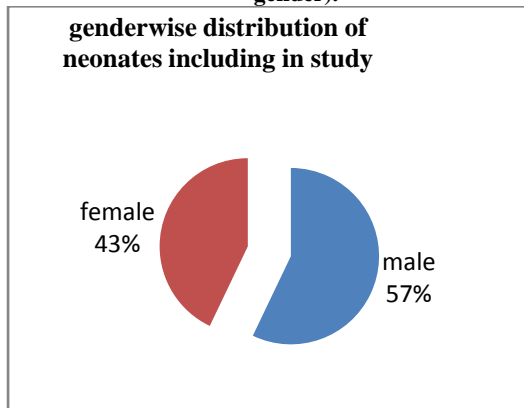
Measurement of PCT is performed by commercial available ELISA kit (RayBio\_ELISA Kit-Cat#: ELH-PROCALC-001). The mean absorbance is calculated for each set of duplicate standards, controls and samples, and subtracted the average zero standard optical density. The standard curve was plotted on log-log graph paper or using Sigma plot software, with standard concentration on the x-axis and absorbance on the y-axis. The best-fit straight line was drawn through the standard points.

Written consent is taken from mothers or guardians of neonates for the tests. SPSS software is used for the data analysis. Values of PCT of the cases are compared to controls that studied equally.

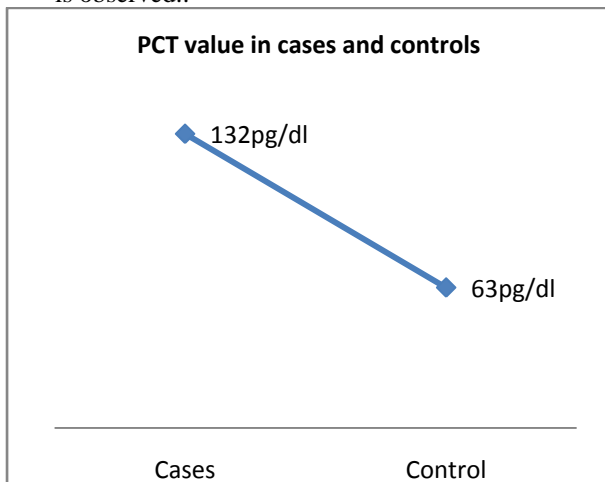
## III. OBSERVATIONS AND RESULTS

In this research study, based on clinical symptoms, seventy infants are suspected with sepsis out of which forty cases (57.1%) are male. In addition to that 94% infants are premature. These characters have been presented further in Graph -1.

**Graph No.1:- Distribution of Neonates (according to gender).**



Furthermore, PCT concentration, in both cases and controls, is presented through graph-2. Statistically, highly significant difference between cases and controls regarding PCT values ( $p < 0.001$ ) is observed..



**Graph 2:- PCT concentration in cases(neonates with suspected sepsis) are compared to control neonates (without sign and symptoms of sepsis).**

#### IV. DISCUSSION

Untreated infection may end tragically; newborns with “suspected sepsis” are often subjected to a battery of extensive diagnostic procedures and unguided systemic antibiotic therapy pending further laboratory results<sup>4</sup>. The clinical signs of the infection and routine laboratory tests of sepsis, such as CRP and the number of leucocytes are not specific and sometimes false.

Blood culture still gold standard for diagnosis of neonatal sepsis but has limited utility because of delayed reporting, frequent use of maternal antibiotics, low neonatal sample volume[5].

In this study, sepsis is more common in males (57.1%) which is similar to Neeraj Kumar et al (2014)[1] and others. It may be linked due to the X linked immunoregulatory gene making male neonates more sensitive to infection. Also this can be, probably, due to the attitude of parents who seek medical services more for their male child than females. Premature babies are more commonly

infected also due to low complement levels, hypogammaglobulinemia.

In the present study, the result of values of procalcitonin have increased with a higher statistical significance in neonates with suspected sepsis (median 132 pg/ml) in comparison with normal controls (median 63pg/ml).

Eminent authors like Assicot et-al first time described increased PCT levels in the blood of patients with sepsis & systemic infection in 1993[6]. Since then, several clinical studies have been investigated the role of PCTs in patient with systemic infection & sepsis.

The molecular structure of PCT was first described in 1981[7]. It was shown that PCT was a glycoprotein consisting of 116 amino acids with a weight 13 KDa which was encoded by CALC-1 gene on short arm of chromosome-11[8] and processes from its own precursor preprocalcitonin.[9]

Under physiological conditions, PCT is produced only by thyroidal c-cells & in small amounts in neuroendocrine cells of lung & small intestine respectively. Here it is further processed into its effective hormone calcitonin & stored in cellular vesicles until released in conditions of high serum Ca level. Hence, PCT is nearly not detectable in serum of normocalcaemic patients[10]. Production of PCT does not necessarily correlate with calcitonin secretion.[11]

In the absence of infection, the production of PCT outside of the neuroendocrine cells of the thyroid and the lung is suppressed. In the presence of sepsis or in infection, all tissues produce PCT. Because of this dual role, PCT is considered a “homokine”<sup>12</sup>. Homokines can either act as a hormone as in the normal physiologic state or as a cytokine during inflammatory processes.[12] Till the date, no other causes of PCT increase have been determined. The factors mediating the production of homokines are as however unknown. It may be induced either by toxins produced by bacteria or by humoral- or cell-mediated host response.

The primary pathophysiological trigger for increase of serum PCT is infection. This often results in the appearance of circulation of Lipopolysaccharide which is one of the constituent of microorganisms. Soon thereafter, there is a secondary release of putative principal pro-inflammatory and anti-inflammatory cytokine messengers. [13]

As with other cytokines, there is little intracellular storage of PCT during sepsis, whereas, synthesis of PCT is necessary for the production of calcitonin.[12]

PCT has a better association with bacterial sepsis and is superior to currently available biomarkers in the clinical setting. [14]

In the biochemical point of view, exact mechanism of action of PCT in sepsis is not properly known but it is imagined that proteolysis of PCT to calcitonin must have been blocked by cytokines.[15] But, the site of production of PCT is different and hence, possibilities of its regulation must be diverse[8].PCT may be reduces calcium availability to cell and thus, trying to reduces cell death during infection.

## V. CONCLUSION

In respect to the results, observations and findings of the present research study, PCT has proved its efficacy as a biomarker of bacterial infection. It should be supported widely and should be accepted this marker in routine practice.

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