



**PRESEPSIN (SCD14-ST) - A NOVEL BIOMARKER OF NEONATAL SEPSIS**

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**ABSTRACT**

**Introduction-**Despite the continuous research and advances in laboratory services diagnosis of neonatal sepsis remains challenging because of non specific clinical signs and symptoms and unavailability of specific accurate biomarker. **Aims & objectives-**The present study was undertaken to evaluate the usefulness of new biomolecule Presepsin as diagnostic tool. **Material and methods -**Study comprises with 140 neonates, out of which 70 neonates were with suspected sepsis and 70 served as full term healthy controls. From birth history it was noted that out of 70 patients 42 were delivered as preterm while 28 were as full term babies. **Observation & results-**Serum Presepsin was measured from all subjects and found that mean concentration of Presepsin in control group was  $318 \pm 192.92$  pg/ml and that of in study group was  $909 \pm 207.03$  pg/ml which was significantly high than control. The meta-analysis showed the Presepsin levels in preterm patients  $913 \pm 209.92$  pg/ml while in full term sepsis neonates values were  $866.75 \pm 168.62$  pg/ml. **Discussion-**Statistically high concentration of Presepsin in study group than control can be justified on the basis of release of Presepsin from breakdown of membrane CD14 and lipopolysaccharide binding protein complex enter into phagosomes and involve in destruction of bacteria by phagocytosis. Concentration of Presepsin released in circulation may have close relation with bacterial count. Full term patients showing low concentration of Presepsin may be due to well developed immune system can control bacterial growth. **Conclusion-**Our findings offer good support to establish Presepsin as a new reliable biomarker for diagnosis of neonatal sepsis and may serve as reliable diagnostic tool to save these budding lives!

**KEYWORDS:** Neonatal sepsis, Presepsin, Preterm, Full term.

**INTRODUCTION**

Neonatal sepsis represents a diagnostic burden with non specific signs and symptoms. The clinical course can be fulminate and fatal if treatment is delayed. Therefore, it is crucial to establish early diagnosis and initiate adequate therapy.<sup>[1]</sup> Blood culture 'Gold' standard takes up 7 days for results and may be confusing; so there is need of a specific marker for early diagnosis.

Although many laboratory biomarkers are useful for diagnosis of sepsis, but sometimes shows drawbacks like some biomarkers elevated in non septic conditions like trauma, surgery, Myocardial infarction, Systemic Inflammatory Response Syndrome.<sup>[2]</sup> Currently, not an ideal marker is found which has better diagnostic power than other conventional one. In this aspect a new valuable marker Presepsin as diagnostic and prognostic marker of sepsis found recently.

By giving particular attention on Presepsin it is found with other name as – soluble CD 14 subtype (sCD14-ST) which is a 13 kD, soluble type of CD-14 with 64 amino acid residues.<sup>[3,4]</sup>

Preliminary studies suggest that the concentration of Presepsin normal in healthy individuals and has been shown to increased in response to bacterial infections and with severity of disease.<sup>[5]</sup>

Currently, Presepsin is under investigation in clinical practice as a reliable marker of adult and neonatal sepsis and for the postmortem diagnosis of sepsis related death.<sup>[6,7]</sup>

Yageshi and coworkers observed that the concentration of Presepsin was increased in patients with sepsis compared to healthy individuals and patients with systemic inflammatory response syndrome (SIRS).<sup>[8]</sup>

Analogous results were obtained by Endo et al<sup>[9]</sup> in a multicentre prospective study where systemic and localized bacterial infection significantly raised than patients with non bacterial infectious disease. Performance of Presepsin significantly estimated in burn sepsis patients by Ozlemetal.<sup>[10]</sup>

Vodnik et al found higher Presepsin values in sepsis than healthy and SIRS.<sup>[11]</sup> According to these above several studies, Presepsin could be seen as valuable marker of sepsis. Hence, the goal of the present study is to evaluate the diagnostic role of Presepsin in neonates with suspected sepsis.

## MATERIALS AND METHODS

After Institutional Ethical Committee (IEC) approval, this research study was conducted at Department of Biochemistry, in association with Department of Pediatric, Bharati Vidyapeeth (Deemed to be University) Medical College & Hospital, Sangli. Out of total 140 neonates, 70 were included as cases with clinical signs and symptoms of sepsis suggested by Pediatrician and 70 were as control with no clinical signs of sepsis. From birth history of neonates, it was noted that out of 70 patients 42 were delivered as preterm while 28 were as full term babies

## OBSERVATIONS AND RESULT

**Table 1: Concentration of Serum Presepsin in the study and control group.**

Groups	Conc. Of Presepsin (pg/mL) (Mean ± S.D.)
Study Group (N=70)	909 ± 207.03
Control Group (N=70)	318 ± 192.92
*P value	0.000

\*P value = 0.000 – Highly significant

**Table 2: Concentration of Serum Presepsin in control, Preterm and Full term neonates with sepsis.**

Groups	Conc. Of Presepsin (pg/mL) (Mean ± S.D.)
Pre term (N=42)	913 ± 209.92
Full term (N=28)	866.75 ± 168.62
Control Group (N=70)	318 ± 192.92
*P value of control against Pre term & Full term	0.000
**P value of Pre term against Full term	0.638

\*P value = highly significant, \*\*P value < 0.005 = non significant

## DISCUSSION

Neonatal sepsis is a life threatening condition and continues to be a major challenge for pediatricians. Early diagnosis of neonatal sepsis is required for treatment to improve survival of patients.<sup>[12]</sup>

Presepsin was thought to be a new biomarker of sepsis. In the study of Mehmet Agilli, concentration of Presepsin in sepsis was found to be significantly raised in patients with Systemic Inflammatory Response Syndrome (SIRS) than healthy peoples.<sup>[13]</sup> Similarly, increased level of Presepsin was observed than

Before starting antibiotic treatment, blood sample was collected from all cases of neonatal sepsis by pediatrician for routine laboratory investigations. Simultaneously 2 ml blood was collected in plain container. Also 2 ml blood was collected from all 70 controls. Serum was separated and used for the determination of Presepsin concentration.

Measurement of Presepsin was performed by commercial available ELISA kit (SINCERE™ – Human Presepsin [sCD14-ST] – ELISA Kit, Cat no. E13652093, Lot no. E150705211). The mean absorbance was calculated for each set of duplicate standards, controls and samples, and was subtracted the average zero standard optical density. The standard curve was plotted on log-log graph paper 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 was taken from parents or guardians of all these neonates for involving them in the study. Values of Presepsin compared between controls and neonatal sepsis. The data was collected, tabulated and analyzed by SPSS software and Microsoft Excel.

Interleukin-6 and D- dimer levels as a result of bacteremia in animal model.<sup>[14]</sup>

Presepsin was considered to be more precious than PCT in diagnosis of sepsis.<sup>[15]</sup> Ulla and co-workers suggested Presepsin as promising marker, correlates with the early stages of the septic process among the different molecules suggested as sepsis molecule in recent days.<sup>[12]</sup>

David Giavarina determines the reference intervals of Presepsin which help to distinguish and rule out healthy

subjects from patients with inflammatory & infectious diseases.<sup>[16]</sup>

In our study, we measured the concentration of Presepsin in neonates with suspected sepsis and compared with normal healthy controls. Values of Presepsin in study group were found significantly raised ( $p=0.000$ )  $909\pm 207.03$  pg/ml (Mean and SD) than those of control  $318\pm 192.92$  pg/ml.

Increased concentration of Presepsin in sepsis can be explained by on the basis of work of Yageshi.<sup>8</sup> Presepsin is subtype of CD14 so called as sCD14ST. CD14 or membrane CD14 (mCD14) is a glycoprotein expressed on the membrane of monocytes and or macrophages. These cells can respond to endotoxin lipopolysaccharide (LPS) through mCD14 as a high affinity receptor for LPS-LBP complex. LPS- mCD14 internalized via a macropinocytosis (phagosome), during this lysosome get fused with phagosome forms phagolysosome. Lysosomal enzyme cathepsin D causes degradation of mCD14 into small molecule soluble CD14 subtype (sCD14ST) i.e. Presepsin which is released into the blood circulation along with undigested cell debris.

Simultaneously, mCD14 can be shedded from cell membrane into circulation forming sCD14 which on proteolysis by plasma protease converted into smaller molecule sCD14ST or Presepsin.

On the basis of patient's history data, neonates of suspected sepsis have been categorized as preterm and full term delivered babies. Meta-analysis of observations and results was done (Table-2) which showed significantly raised value of Presepsin in all sepsis neonates, as well as Preterm and Full term than control. Though non significant, elevated levels of Presepsin were noted in Preterm groups ( $913 \pm 209.92$  pg/ml) than full term ( $866.75 \pm 168.62$ pg/ml) which can be explained as- Presepsin released in circulation may have close relationship with bacterial count. Full term patients showing low concentration of Presepsin may be due to well developed immune system that control bacterial growth.

## CONCLUSION

Significantly raised levels of Presepsin in patients of suspected neonatal sepsis showed relationship with maturity terms when compared with control was observed. Evaluation of results in present study and its comparison with previous studies offers strong support for suggestive role of Presepsin as more specific reliable biomarker may be used for diagnosis of neonatal sepsis. Further investigations in large scale and in depth are needed to establish this biomarker in diagnostic as well as prognostic role.

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