Study of Serum Presepsin as Diagnostic &Prognostic Marker in Early Onset Neonatal Sepsis

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

(قَالُوا سُبْحَانكَ لاَ عِلمَ لَنَا إِلاّ مَا
عَلّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيم)

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Abstract

Background: Sepsis is a complex clinical condition caused by dysregulated immune response to an infection resulting in multiorgan failure with a fatal outcome. More than 90% of neonatal deaths occur in the poorest countries of Asia and Africa. There is no gold standard for diagnosing sepsis as clinical and laboratory signs are neither sensitive enough nor specific enough. Biomarkers have shown great promise in diagnosis of sepsis and guiding appropriate treatment of neonates. Among these, soluble CD 14 sub-type (presepsin) has been suggested as a novel diagnostic and prognostic marker to identify high-risk patients, and may be useful for the clinical management of serious infectious diseases. However, few studies addressed the value of presepsin as a sepsis biomarker in neonates and data on its prognostic value in septic neonates are still lacking. **Aim:** We assessed presepsin levels as a potential early diagnostic and prognostic marker for early onset neonatal sepsis. **Methods:** A total of 60 full term neonates was enrolled; 40 neonates with clinical and laboratory signs of EONS and 20 healthy controls. Complete blood count, high sensitivity C-reactive protein (hs-CRP) and sepsis score including clinical and laboratory indicators were assessed. The diagnosis was verified thereafter by blood culture. According to the results of blood cultures, the studied septic neonates were classified into 2 groups: the culture-proven septic group and culture-negative septic one. presepsin levels were measured on initial sepsis evaluation and at 72 hours after antibiotic therapy. For ethical reasons, cord blood samples were collected from control neonates and only samples from neonates that proved to be healthy by clinical examination and laboratory analysis were further analyzed for presepsin. **Results:** Initial presepsin levels were significantly elevated in all neonates with EONS compared with healthy controls. Patients with culture-proven and

culture-negative sepsis had higher presepsin compared with controls while no significant difference was found between both septic groups. Elevated initial presepsin levels were associated with the occurrence of septic shock, high mortality rate and a worsening clinical course of the disease. Presepsin decreases significantly after 72 hours after antibiotic therapy in neonates. Presepsin was positively correlated to hs-CRP and sepsis score. ROC curve analysis revealed that presepsin cutoff value of 1400 pg/mL could be predictive of mortality among neonates with sepsis with 100% sensitivity and 88.5% specificity while the cutoff value of 480 pg/mL could be predictive of clinical course of sepsis with 100% sensitivity and 95% specificity. Neither baseline hs-CRP levels nor sepsis score had a prognostic utility in relation to mortality or clinical course of the disease. **Conclusions:** presepsin could be considered an early diagnostic marker for EONS before culture results. Elevated presepsin levels reflect sepsis severity and poor prognosis more accurately than CRP or sepsis score. Thus, it could a valuable biomarker to monitor the disease course.

Keywords: early onset neonatal sepsis, presepsin, mortality, septic shock, CRP.

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List of abbreviations

• AAP	American academy of pediatrics
• APPs	Antimicrobial proteins and peptides
• AUC	The areas under the ROC curve
• BP	Blood pressure
• BSI	Blood stream infection
• CBC	Complete blood count
• CD	Cluster of differentiation
• CNS	Central nervous system
• CoNS	*Coagulase-negative Staphylococcus*
• CRP	C-reactive protein
• CS	cesarean section
• CSF	Cerebrospinal fluid
• DIC	Disseminated intravascular coagulation
• DM	Diabetes mellitus
• DNA	Deoxyribonucleic acid
• E coli	*Escherichia coli*
• ECG	Electrocardiography
• EDTA	Ethylenediaminetetraacetic acid
• ElISA	Enzyme-linked immuno assay

• EONS	Early Onset Neonatal Sepsis
• ESR	Erythrocyte Sedimentation Rate
• GA	Gestational age
• GBS	*Group B streptococcus*
• G-CSF	Recombinant Granulocyte-colony stimulating factor
• G-CSF	Granulocyte colony-stimulating factor
• GI	Gastrointestinal tract
• GM-CSF	Granulocyte-macrophage stimulating factor
• GPI	Glycosyl-phosphatidyl inositol
• HCT	Haematocrit
• HLA	Human Leukocyte Antigen
• HR	Heart rate
• HRC	Heart rate characteristics
• HRP	Horseradish peroxidase enzyme
• HSS	Hematological scoring system
• HSV	*Herpes simplex virus*
• I/M	Immature-to-mature neutrophil ratio
• I/T	Ratio of immature to total neutrophils
• IAP	Intrapartum antibiotic prophylaxis
• IFN	Interferon
• Ig	Immunoglobulin

• IL	Interlukin
• IMV	Invasive mechanical ventilation
• IV	Intravenous
• IVIG	Intravenous immunoglobulin
• K.pneumonia:	*Klebsiella pneumonia*
• KDa	kilodalton
• LBP	lipopolysaccharide-binding protein
• LFTs	Liver function tests
• LONS	Late Onset Neonatal Sepsis
• LPS	Lipopolysaccharide
• mCD14	Membrane-bound CD14
• MD2	Myeloid Differentiation Protein-2
• MODS	Multiple Organ Dysfunction Syndrome
• MW	Molecular weight
• nCD	Neutrophil expression of CD64
• NFκB	Nuclear Factor kappa B
• NICUs	Intensive Care Units
• NK	Natural Killer
• OD	Optical density
• P value	Probability value
• PAF	Platelets activating factor
• PAMP	Pathogen-Associated Molecular Patterns

• PCR	Polymerase chain reaction
• PCT	Procalcitonin
• PMNs	Polymorphonuclear leukocytes
• PPHN	Persistent pulmonary hypertension of the newborn
• PPV	Positive predictive value
• PROM	Premature rupture of membrans
• PRRs	Pattern-Recognition Receptors
• rG-CSF	Recombinant Granulocyte-colony stimulating factor
• rhG-CSF	Recombinant Human G-CSF
• ROC	Receiver operating characteristic curves
rRNA	Ribosomal ribonucleic acid
RSV	Respiratory syncytial virus
S. aureus	*Staphylococcus aureus*
SABC	HRP-Streptavidin Conjugate
sCD14	Soluble CD14
sCD14-ST	sCD14 subtype
SD	Standard deviation
SIRS	Systemic Inflammatory Response Syndrome
SST	Serum separator tube
SVD	Spontaneous vaginal delivery
Temp	Temperature

• THP1	Human cell line of monocytic cells
• TLC	Total leucocytic count
• TLRs	Toll-like receptors
• TMP	Tetramethylbenzidine substrate
• TNF-α	Tumor Necrosis Factor –α
• TPN	Total parentral nutrition
• UNICEF	Unaited Nation Children's Emergency Fundation
• UTI	Urinary tract infection
• VLBW	Very low birth weight infants
• WBCs	white blood cells

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