

# بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ





# شبكة المعلومات الجامعية التوثيق الالكتروني والميكروفيلم



# جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

## قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها  
علي هذه الأقراص المدمجة قد أعدت دون أية تغييرات



## يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار



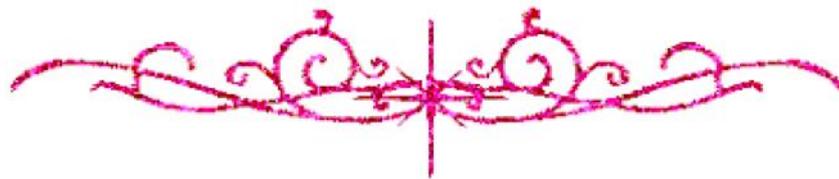


# بعض الوثائق الأصلية تالفة





# بالرسالة صفحات لم ترد بالأصل





*Faculty of postgraduate childhood Studies*

*Department of Medical Studies for Children*

# **Serum Presepsin and Amyloid-A as Early Markers in the Diagnosis of Neonatal Sepsis and their Relation to Anthropometric Assessment**

## **Thesis**

*Submitted for fulfillment of PhD in Childhood Studies  
(Child Health and Nutrition)  
Medical Studies Department for Children*

**Presented by**

**Mai Mohsen Badie Hassen**

M.B.B.CH,MSc. of Pediatrics

Assistant Researcher at Biological Anthropology Department,  
Medical Division,  
National Research Centre

**Under Supervision of**

**Prof. Dr. khalad Hussien Taman**

Professor of Pediatrics(God Bless His Soul)  
Postgraduate Childhood Studies Faculty  
Ain Shams University

**Prof.Dr. Asharf Hamed Shaalan**

Professor of Biological Anthropology  
President of National Research Centre

**Prof. Dr. Howaida Hosny El Gebaly**

Professor of Pediatrics  
Dean of Postgraduate Childhood Studies Faculty  
Ain Shams University

**Prof.Dr. Rokia Abd-El Shafy Soliman**

Professor of Biological Anthropology  
National Research Centre

**Dr. Samer Hamed El Khayat**

Lecturer of Pediatrics of  
Postgraduate Childhood Studies faculty  
Ain Shams University

**Faculty of Postgraduate Childhood Studies  
Ain Shams University**

**2020**

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالَ مَوْلَا

لَسْبَدَانِكَ لَا أَعْلَمُ لَنَا  
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ  
الْعَلِيمُ الْعَظِيمُ

صدق الله العظيم

سورة البقرة الآية: ٣٢

# *Dedication*

*I would like to dedicate this work to my **mother**, **husband** and my **sons**, for their continuous support, encouragement and motivation not only through my whole life but also because they endured all my negligence towards them throughout the period of that thesis. If it weren't for you I wouldn't be.*



## **Acknowledgments**

Thanks are all to **Allah**, to whom I related any success in achieving any work in my life and for blessing me throughout my life by HIS Compassion and Generosity.

I would like to convey special appreciation and sincere thanks **Prof. Dr. Khalad Hussien Taman (god bless his soul)** Professor of Pediatrics & Dean of Postgraduate Childhood Studies faculty, Ain Shams University for her supervision, giving the idea of research.

I should state my deep thanks to **Prof. Dr. Howaida Hosny El Gebaly**, Professor of Pediatrics & Dean of Postgraduate Childhood Studies faculty, Ain Shams University for her supervision, giving the idea of research, helpful guidance and advices. It is mainly due to her generous effort; this work could be possible.

I would like to convey special appreciation and sincere thanks to **Prof. Dr. Asharf Hamed Shaalan**, Professor of Biological Anthropology National Research Centre for his advices and keen concern throughout work.

I am also grateful to **Prof. Dr. Nyera EL Morsy & Prof. Dr. Muhammad Al-Tohamy**, Professors of Biological Anthropology National Research Centre for their steady help in writing thesis

I'm extremely appreciating **Dr. Samer Hamed El Khayat**, Assistant Professor of Pediatrics, Postgraduate Childhood Studies faculty, Ain Shams University, for his great care, valuable instructions.

I would like to express my real appreciation to **Prof. Dr. Abd El Rahman Galhom**, Professor of Pediatrics, El Warrak hospital for providing all facilities not only for fulfillment of all applied clinical & official information needed for cases recruitment but also for learning me all clinical skills that's were helpful in clinical practice and enormous efforts, supportive suggestions, standing beside me and helping me at any time.

I would also like to thank **Prof. Dr. Rokia Abd-El Shafy**, Professor of Biological Anthropology, and National Research Centre for being a main part of this thesis team.

Many thanks and appreciation to all neonatal parents who have been convinced of the value of this study and approved to join it.

✍ **Mai Mohsen Badiaa Hassen**

# Abstract

**Background:** Neonatal septicemia causes significant morbidity and mortality. Early accurate diagnosis and treatment are fundamental. Presepsin and serum amyloid-A (SAA) biomarkers could be two of the earliest markers that aid in the diagnosis of sepsis. **Aim:** To investigate the role of presepsin and SAA as simple applicable tests for early prediction and diagnosis of neonatal sepsis and to correlate between both presepsin and SAA, in one hand, and total leukocytic count, immature/total leukocyte ratio, CRP and blood culture, on another hand. **Patients and Methods:** Case control study comprising 90 neonates with gestational age  $\geq 36$  weeks; 60 pediatrics and 30 controls. Presepsin, SAA, total leukocytic count, immature/total leukocyte ratio, CRP and blood culture were measured during first and third days of admission for patients while were measured once on admission for controls. **Results:** Mean serum presepsin and SAA levels were not only significantly higher but also detected earlier in patients than controls. Presepsin was the most sensitive (93.3%) followed by SAA and lastly CRP (85.0%). With regard to specificity; presepsin and SAA came first, equally, by (100%) then CRP (86.7 %). As regard to positive predictive value of the markers presepsin and SAA came first equally by (100%) then CRP (92.7 %). Finally, presepsin had the highest negative predictive value (88.2%) followed by SAA (85.7 %) compared to CRP (74.3 %). **Conclusion:** Presepsin and SAA are accurate, highly sensitive and specific markers either for prediction or diagnosis of early onset sepsis in contrast to CRP or hematological scoring system (HSS).

**Keywords:** Neonatal sepsis, Presepsin, Amyloid A

## List of Contents

<i>Subject</i>	<i>Page No.</i>
<b>List of Abbreviations.....</b>	<b>i</b>
<b>List of Tables.....</b>	<b>iii</b>
<b>List of Figures .....</b>	<b>iv</b>
<b>Introduction .....</b>	<b>1</b>
<b>Aim of the Work.....</b>	<b>4</b>
<b>Review of Literature</b>	
Neonatal Sepsis .....	5
Biomarkers of Sepsis .....	49
Serum amyloid A and Its relation with Neonatal sepsis .....	61
Serum Prespsin and its Relation with Neonatal sepsis .....	71
Neonatal Anthropometry.....	79
<b>Patients and Methods.....</b>	<b>99</b>
<b>Results.....</b>	<b>111</b>
<b>Discussion .....</b>	<b>146</b>
<b>Summary .....</b>	<b>162</b>
<b>Recommendations .....</b>	<b>166</b>
<b>References .....</b>	<b>167</b>
<b>Arabic Summary .....</b>	<b>—</b>

---

## **List of Abbreviations**

<b>AAP</b>	: American Academy of Pediatrics
<b>AGA</b>	: Appropriate-for-gestational age
<b>APRs</b>	: Acute-phase reactants
<b>AUC</b>	: Area Under the Curve
<b>AUC</b>	: Area under curve
<b>BMI</b>	: Body mass index
<b>BPD</b>	: Broncho-pulmonary dysplasia BPD
<b>BS</b>	: Biceps
<b>BSF</b>	: Estimate of Body Surface
<b>BSF</b>	: Body surface
<b>BW</b>	: Birth weight
<b>CDC</b>	: Center for Disease Control
<b>CHL</b>	: Crown-heel length
<b>CoNS</b>	: Coagulase negative Staphylococci
<b>CRP</b>	: C reactive protein
<b>CS</b>	: Caesarean section
<b>CSFs</b>	: Colony stimulating factors
<b>CVC</b>	: central venous catheters
<b>DEMPU</b>	: Diabetes Endocrine and Metabolism Pediatric Unit
<b>EMR</b>	: Eastern Mediterranean region
<b>EOS</b>	: Early-onset sepsis
<b>FFM</b>	: Fat-free mass

<b>GA</b>	: Gestational age
<b>GBS</b>	: Group B streptococcus GBS
<b>G-CSF</b>	: Granulocyte colony stimulating factor
<b>GIT</b>	: Gastrointestinal tract
<b>GM-CSF</b>	: Granulocyte macrophage colony stimulating factor
<b>HC</b>	: Head Circumference
<b>HDL</b>	: High Density Lipoprotein
<b>HRC</b>	: abnormal HR characteristics
<b>HSS</b>	: Hematological Scoring System
<b>HSS</b>	: Hematological sepsis score
<b>I/T</b>	: Immature/Total
<b>IL-1b</b>	: Interleukin- 1b
<b>IMCI</b>	: Integrated Management of Childhood Illness
<b>IUGR</b>	: Intrauterine growth restriction
<b>IVIG</b>	: Intravenous immunoglobulin
<b>LBW</b>	: Low birth weight
<b>LCAT</b>	: Lecithin cholesterol acyl transferase
<b>LGA</b>	: Large-for-gestational age
<b>LOS</b>	: Late-onset sepsis
<b>LP</b>	: Lumbar puncture
<b>LPBP</b>	: Binding protein
<b>LPS</b>	: Lipopolysaccharides
<b>LT</b>	: Length
<b>MAC</b>	: Mid Arm Circumference

<b>MAC/HC</b>	: Mid-arm circumference/head circumference index
<b>MDG4</b>	: Millennium Development Goal
<b>MDR</b>	: Multiple drug resistant
<b>MRSA</b>	: Methicillin Resistant Staphylococcus Aureus
<b>NICU</b>	: Neonatal intensive care unit
<b>NICU</b>	: Neonatal Intensive Care Unit
<b>NM</b>	: Neonatal mortality
<b>NPV</b>	: Negative predictive value
<b>NRN</b>	: Neonatal Research Network
<b>OD</b>	: Optical density
<b>PCT</b>	: Procalcitonin
<b>PGE2</b>	: Prostaglandin E2
<b>PI</b>	: Ponderal index
<b>PLT</b>	: Platelets
<b>PMN</b>	: poly morphonuclear cells
<b>PPV</b>	: Positive predictive value
<b>Presepsin</b>	: Soluble CD14 subtype
<b>pro-ADM</b>	: Proadrenomedullin
<b>pro-ADM</b>	: Proadrenomedullin
<b>PROM</b>	: Prolonged premature rupture of membranes
<b>PROM</b>	: Prolonged rupture of membranes
<b>PSPN</b>	: Human Presepsin
<b>PT</b>	: Prothrombin Time

<b>PTT</b>	: Partial Thromboplastin Time
<b>RDS</b>	: respiratory distress syndrome
<b>ROC</b>	: Receiver Operating Characteristic
<b>SAA</b>	: Serum Amyloid-A
<b>SAA</b>	: Serum Amyloid A
<b>SBS</b>	: Subscapular skinfold
<b>SDG</b>	: Sustainable Development Goals
<b>SGA</b>	: Small-for gestational-age
<b>SIRS</b>	: systemic inflammatory response syndrome
<b>SPS</b>	: Suprailiac
<b>sTREM-1</b>	: Soluble triggering receptor expressed on myeloid cells-1
<b>suPAR</b>	: Soluble urokinase-type plasminogen receptor
<b>suPAR</b>	: Plasminogen activator receptor
<b>SVD</b>	: Spontaneous vaginal delivery
<b>TLC</b>	: Total Leucocytic count
<b>TLR4</b>	: Toll-like receptor 4
<b>TNF</b>	: Tumor necrosis factor
<b>TRACE</b>	: Time-Resolved Amplified Cryptate Emission
<b>TS</b>	: Tricipital skin fold
<b>uPAR</b>	: Urokinase-type plasminogen activator receptor
<b>UTI</b>	: urinary tract infection