بسم الله الرحمن الرحيم

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بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى مسئولية عن محتوى هذه الرسالة.

ملاحظات: ....

Pentraxin-3 in Diagnosis of Early Onset Neonatal Sepsis

Thesis

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سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم
صدق الله العظيم
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Mohamed Elsayed Abd Rabou

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List of Abbreviations

Abbr.		Full-term
CBC	:	Complete blood count
CDC	:	Centers for Disease Control and Prevention
CHIKV	:	Chikungunya virus
CMV	:	Cytomegalovirus
CNS	:	Central nervous system
COL	:	Collagen
CONS	:	Coagulase-negative staphylococci
CRP	:	C-reactive protein
CSF	:	Cerebrospinal fluid
CT	:	Computed tomography
DC	:	Dendritic cells
ECM	:	Extracellular matrix
ECs	:	Endothelial cells
EEG	:	Electroencephalogram
ELBW	:	Extremely low birth weight
ELISA	:	Enzyme-Linked Immunosorbent Assay
EOS	:	Early onset sepsis
FG	:	Fibrinogen
FGFs	:	Fibroblast growth factors
GBS	:	Group B streptococcoi
HA	:	Hyaluronic acid complex
HC	:	Heavy chain
HCC	:	Hepatocellular carcinoma
HDL	:	High density lipoprotein
HPeV1	:	Human parechovirus 1
HSV	:	Herpes simplex virus
i.v	:	Intravenous
IAP	:	Intrapartum antibiotic prophylaxis
IFN-γ	:	Interferon gamma

IL-12	:	Interleukin-12
Ip	:	Intraperitoneal
IRF3	:	Interferon regulatory factor 3
IV	:	Intravenous
IVA	:	Influenza virus type A
LE	:	leukocyte esterase
LOS	:	late onset sepsis
LOX-1	:	low-density lipoprotein receptor-1
LP	:	lumbar puncture
LPS	:	Lipopolysaccharides
MABP	:	Mean arterial blood pressure
MHV-1	:	Murine hepatitis virus strain 1
MRI	:	Magnetic resonance imaging
NETs	:	Neutrophil extracellular traps
NICU	:	Neonatal intensive care unit
OMVs	:	Outer membrane vesicles
ox-LDL	:	Oxidized low density lipoproteins
PCR	:	Polymerase chain reaction
PIC	:	Preinitiation complex
Plg	:	Plasminogen
PSA	:	prostate-specific antigen
PTX 3	:	Pentraxin 3
ROS	:	Risk of sepsis
RRV	:	Ross River virus
RSV	:	Respiratory syncytial virus
SCLC	:	Small-cell lung carcinoma
SEM	:	Skin, eye, and mouth
SIRS	:	Systemic inflammatory response syndrome
SMCs	:	Smooth muscle cells
SNAP11	:	Score for neonatal acute physiology-II
SREC-I	:	Scavenger receptor expressed by ECs I
TF	:	Tissue factor
Th	:	T helper

TNF-α	:	Tumor necrosis factor alpha
UTI	:	Urinary tract infection
WBCs	:	White blood cells

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ABSTRACT

Background; Neonatal sepsis is one of the most important causes of neonatal morbidity and mortality. Symptoms and signs of neonatal sepsis can be silent; therefore, laboratory investigation is necessary in cases of doubt or if there are risk factors. Pentraxin 3 is a prototype of the long pentraxin family. It is effective in the early phase of inflammation and it is detected as an early marker of sepsis in neonates, **Aim and objectives;** to evaluate the diagnostic value of Pentraxin 3 in early neonatal sepsis, **Subjects and methods;** This study is a prospective cohort study, was carried out on 80 neonates with risk factors for early-onset sepsis at Ain Shams University hospital, **Result;** Pentraxin 3 in sepsis group positive in 91.2% (sensitivity 91.2% -- specificity 82.6%), Rodwell score (sensitivity 79.4% -- specificity 82.6), Score for Neonatal Acute Physiology II (SNAP II)score (sensitivity 76.5% -- specificity 82.6%) so these scores were significant independent predictors for sepsis, **Conclusion**; PTX 3 could be used as a new biomarker of neonatal sepsis with high sensitivity and specificity. It is already elevated in the umbilical cord, so measuring serum PTX3 might be useful in the prediction of infection in newborns

Keywords: Diagnosis, marker, neonate, pentraxin 3, Early onset sepsis.

Introduction

Globally, sepsis is still one of the major causes of morbidity and mortality in neonates, despite recent advances in healthcare units. The estimated global burden for neonatal sepsis was 2,202 (95% CI: 1,099–4,360) per 100,000 live births, with mortality between 11% and 19% **(Fleischmann-Struzek et al., 2018) (Wu et al., 2009)**. More than 40% of under-five deaths occur in the neonatal period, resulting in 3.1 million newborn deaths each year **(UNICEF et al., 2011)**.

Two types of neonatal sepsis have been observed: early-onset sepsis when features of sepsis present within 24 hours in 85%, between 24-48 hours in 5% and a smaller percentage of patients present within 48-72 hours **(Klinger et al., 2009)**; and late-onset sepsis where the disease manifests beyond 72 hours **(Van den Hoogen et al., 2009)**. Early treatment of neonatal sepsis is associated with improved outcomes, so that rapid diagnosis is the key to reducing this burden **(Obiero et al., 2015)**.

The most common risk factors associated with early-onset sepsis (EOS) are preterm delivery, low birth weight, premature rupture of membranes, maternal urinary tract infection, and maternal group B Streptococcal colonization while late-onset sepsis (LOS) is associated with central/umbilical catheters, mechanical ventilation and parenteral nutrition **(Cortese et al.,**

2016). Clinical manifestations of neonatal sepsis are nonspecific. These include temperature instability, respiratory distress, apnea, poor feeding, lethargy, irritability, convulsions, hypotonia, poor perfusion, and abdominal distension **(Shah & Padbury, 2014)**.

Pentraxins are an evolutionarily conserved group of pattern recognition glycoproteins which share a pentraxin-like domain in the C terminus. The pentraxin family has been implicated in humoral innate immunity. Depending on their structure, pentraxins are divided into short and long pentraxin families. C-reactive protein (CRP) and serum amyloid P-component (SAP) are the two short pentraxins, while long pentraxins include pentraxin 3 (PTX3) and neuronal pentraxins **(Liu et al., 2014) (Cie´ Slik and, Hrycek, 2015)**.

PTX3 acts as an acute phase reactant protein as its blood levels, which is low in normal conditions (less than 2 ng/ml), increase dramatically to a peak of 200–800 ng/ml within 6–8 hours during endotoxic shock, sepsis and other inflammatory conditions **(Mantovani et al., 2008)**.