بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

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MONA MAGHRABY

Role of Urinary Intestinal Fatty Acid Binding Protein in Prediction of Necrotizing Enterocolitis and Its Correlation with GutCheck Score

Thesis

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Abb.	Full term
AUC	*Area under curve.*
CI	*Confidence interval.*
COX	*Cyclo-oxygenase.*
CpG	*Cytosine phosphate guanine.*
EGF	*Epidermal growth factor.*
ELISA	*Enzyme-linked immunosorbent assay.*
Fibrinogen-γ	*Fibrinogen gamma.*
GA	*Gestational age.*
GIT	*Gastro-intestinal tract.*
IAIP	*Inter-Alpha Inhibitor Protein.*
IL	*Interleukin*
kDa	*Kilodalton.*
MV	*Mechanica ventilator.*
NCPAP	*Nasal continuous positive airway pressure.*
NEC	*Necrotizing enterocolitis.*
ng/ml	*Nannogram per millimeter.*
NICU	*Neonatal intensive care unit.*
NPO	*Nil per os (nothing by mouth)*
OR	*Odds ratio*
PDA	*Patent ductus arteriosus.*
rhEPO	*Recombinant human erythropoietin.*
rhG-CS	*Recombinant human granulocyte colony-stimulating factor.*
ROC	*Receiver operating curve.*
RPM	*Round per minute.*
SIP	*Spontaneous intestinal perforation.*
TGF	*Tissue growth factor.*
TNFα	*Tumor necrosis factor alpha*
u-IFAB	*Urinary intestinal fatty acid binding protein*
VlBW	*Very low birth weight.*

INTRODUCTION

Necrotizing enterocoitis (NEC) is a severe devastating inflammatory condition affecting the gastrointestinal tract of neonates especially preterm babies, it is the most common GIT emergency in preterm babies with high morbidity and mortality.

The definite etiology of NEC is still not completely understood, However it is strongly associated with gut hypoxia-ischemia and increased bacterial colonization and translocation in the immature gut, thus the most important risk factors are prematurity, low gestational age, hemodynamic instability leading to gut ischemia caused by large pataent ductus arteriosus (PDA) or congenital heart disease and sepsis ***(Gephart et al., 2014).***

Early manifestations of NEC are usually subtle resembling sepsis (temperature instability, hypotension, bradycardia or tachycardia) even though it can turn into severe disease leading to intestinal gangrene without implementing early management plan including gastric decompression, withholding feeding and aggressive antibiotic therapy ***(Gephart and Hanson, 2017).***

It affects 7 of each 100 neonate admitted in NICUs worldwide with high mortality reaching up to 100% in late cases ***(Ginglen and Butki, 2020).***

Mortality rate in NEC ranges from 10% to more than 50% in infants who weigh less than 1500 g, depending on the severity of disease, compared with a mortality rate of 0-20% in babies who weigh more than 2500 g. Extremely premature infants (1000 g) are still particularly vulnerable, with reported mortality rates of 40-100%. It ranges from 4.7% in term infants and 11.9% in premature babies ***(Wiswell et al., 1988).***

Early diagnosis of NEC plays a fundamental role in management and improves outcome, However it remains challenging due to lack of confidential laboratory biomarkers that can detect NEC before the appearance of radiological signs which indicates disease progression, and lack of diagnostic tools that indicate neonates with high risk of developing the disease as well ***(Sharma and Hudak, 2013).***

Many studies has been carried out to investigate the most specific and sensitive tool for early detection of NEC.

Many non-invasive biomarkers are used to reflect the early steps of disease before the appearance of radiological changes for early diagnosis and intervention, One of the most promising biomarkers is urinary intestinal fatty acid binding protein u-IFABP that can detect early NEC with high sensitivity and specificity, Also the urinary level is correlated with the severity of the disease and length of bowel resected in NEC patients that needed surgical intervention ***(Gregory et al., 2014).***

Urinary intestinal fatty acid binding protein (u-IFABP) is a small cytoplasmic protein with high organ sensitivity located in small intestinal enterocytes brush border involved in the uptake and transport of polar lipids. IFABP In the context of progressive gut wall barrier failure in NEC is released in the circulation with subsequent secretion by the kidneys. IFABP can be measured in serum and urine. An elevated urinary IFABP is a sensitive and specific non-invasive predictor of impending NEC 1day prior to the first clinical manifestation urinary iFABP screening might identify infants at high risk ***(Golin et al., 2014).***

On the other hand a number of tools have been formulated to detect the risk for NEC development and facilitate interpersonal data interpretation, the most important is the GutCheck ^{NEC} tool which is formulated of ten items each of them reflects an independent risk factor for developing NEC, these factors are gestational age, NICU-specific NEC rate, black or Hispanic race, outborn status, multiple infections, metabolic acidosis, Packed red blood cell (RBC) transfusion, and two risk reducers: human milk fed at both day 7 and 14, intake of probiotics ***(Gephart et al., 2013).***

GutCheck^{NEC} score has underwent many stages of refinement to detect the most specific risk factors affecting NEC occurrence and prognosis and demonstrated very good (B-range) prediction for infants who developed surgical NEC and

those who died and (C-range) prediction of medical NEC ***(Gephart 2012).***

The score is one of the most promising tools for early detection of the disease and still needs further studies and prospective clinical testing to confirm its sensitivity and specificity ***(Gephart et al., 2014).***