

*Research Article***Role of Resistin Versus C Reactive Protein (CRP) in Diagnosis of Neonatal Sepsis.****Magdy M. Kamel , Mohammed A. Bahaa El-Din, Mostafa A. El-Sayed and Ayman H. Abbas Mohamed**

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Abstract

Introduction: Sepsis is a systemic inflammatory response to infection occurring in infants at ≤ 28 days of life. **Aim of the work:** So, the present study aims to: 1) Study role of resistin as a diagnostic biomarker in neonatal sepsis. 2) Compare between resistin and CRP in neonatal sepsis. **Subjects and methods:** This study was conducted in neonatal intensive care unit (NICU), Minia Children University Hospital, in the period from March 2016 till March 2017. **Results: Results of Demographic Data** Comparison of group 1 (proved sepsis) and group 2 (suspected sepsis) as regards demographic data (Table 2) revealed statistically insignificant differences in age, gender, weight, gestational age, prematru rapture of membranes and history of maternal fever. **Discussion:** Despite improved neonatal care over the past decades, infections remain common and sometimes life-threatening in neonates admitted to the neonatal intensive care unit (NICU). **Recommendations:** Serum resistin level can be used in diagnosis of neonatal sepsis. Further studies are needed to detect diagnostic value of serum resistin level in neonatal sepsis in preterm babies in comparison with full term babies. Serial measurements of serum resistin level at different time intervals to follow up septic conditions of neonates.

Keywords: AST: aspartate transaminase. AUC: area under the curve. , CAMP: cyclic adenosine monophosphate.

Introduction

Sepsis is a systemic inflammatory response to infection occurring in infants at ≤ 28 days of life⁽¹⁾.

Neonatal sepsis remains one of the leading causes of morbidity and mortality both among term and preterm infants (Camacho-Gonzalez et al., 2013). Although advances in neonatal care have improved survival and reduced complications in preterm infants, sepsis still contributes significantly to mortality and morbidity among very-low-birth-weight (VLBW, <1500 g) infants in Neonatal Intensive Care Units (NICUs)⁽²⁾.

Compared with the clear and valuable therapeutic options, the diagnosis of suspected neonatal sepsis is challenging. In preterm infants, the diagnosis of sepsis is more difficult, because of the nonspecific clinical presentation and the lack of reliable diagnostic tests .Blood culture is the gold standard for the diagnosis of

sepsis in newborns. However, technical problems such as insufficient blood sample or maternal antibiotic usage can be a barrier in isolating the responsible pathogens⁽³⁾.

For many years, a search has been ongoing to find predictor for neonatal sepsis that identify effectively neonates who are at risk of infection⁽⁴⁾.

Although infection markers might help in the diagnosis because they can indicate the presence or absence or severity of sepsis and can differentiate bacterial from viral and fungal infection, and systemic sepsis from local infection. However, the exact role of biomarkers in management of septic patients remains undefined and no single lab test provides rapid and reliable identification of early infected neonates. C reactive protein (CRP), Procalcitonin (PCT) and Interleukin 6 (IL-6) are the most widely used markers for neonatal sepsis⁽⁵⁾.

Resistin is a newly discovered metabolic hormone and it has been implicated in adipogenesis and in the development of insulin resistance⁽⁶⁾. Resistin is called FIZZ3 (found in inflammatory zone) or ADSF (adipose specific secretory factor) was identified as 12.5 kDa polypeptide, and is expressed and secreted by white adipose tissue⁽⁶⁾.

Resistin has recently been recognized to act as a proinflammatory cytokine in humans. Patients with severe sepsis or septic shock had significantly elevated systemic levels of resistin which correlate with severity of disease⁽⁷⁾.

The initial studies showed the relationship between resistin levels and anthropometric parameters in neonates, and resistin was suggested to be involved in the maintenance of neonatal metabolic homeostasis (Ng PC et al., 2005). Recent studies have shown that resistin might also play a role in inflammation and autoimmunity. Although resistin is predominantly expressed in adipocytes from rodents, analysis of resistin gene expression across a wide array of human tissues has revealed that peripheral blood mononuclear cells (PBMCs), macrophages and bone marrow cells are a major source of human resistin⁽⁸⁾.

Aim of the work

So, the present study aims to:

- 1) Study role of resistin as a diagnostic biomarker in neonatal sepsis.
- 2) Compare between resistin and CRP in neonatal sepsis.

Subjects and methods

This study was conducted in neonatal intensive care unit (NICU), Minia Children University

Hospital, in the period from March 2016 till March 2017.

The present study was approved by the local ethics committee. Informed consents were obtained from families of the infants included in the study. Confidentiality of patients is saved by keeping their records anonymous.

Subjects:

This study included one hundred neonates admitted to NICU were recruited for the study. They were divided into three groups:

Group 1: (proved sepsis) It included forty neonates diagnosed as having proved early onset neonatal sepsis based on clinical and laboratory data.

Group 2: (suspected sepsis) It included forty neonates diagnosed as having early onset neonatal sepsis based on clinical data only and the laboratory results were free

Group 3: (control group) It involved twenty non septic term newborns.

Inclusion criteria:

Patients admitted to NICU were included in the study provided they fulfill the following criteria:

- 1- G.A ≥ 37 wk, 2- Body weight ≥ 2.500 kg.
- 3- signs of neonatal sepsis.

Exclusion criteria:

- 1- major congenital anomaly, 2-Chromosomal abnormality, 3- major surgical problems

Results

Comparison of group 2 and control group as regard laboratory data.

Variables	Group 2 (n=40) Mean±SD	Control (n=20) Mean±SD	t-value	P-value
CRP (ng/ml)	4.15±1.65	0±0	11.15	0.0001**
Hb (gm/dl)	15.77±2.46	16.10±1.31	0.55	0.58
TLC (x10 ³ /mm ³)	15.48±9.13	10.18±1.37	2.57	0.01*
Platelets (x10 ³ /mm ³)	195.75±121.57	350±60.02	5.34	0.0001**

*Significant difference. **Highly significant difference. CRP: C-reactive protein; Hb: Hemoglobin; TLC: Total Leukocyte count

Discussion

Despite improved neonatal care over the past decades, infections remain common and sometimes life-threatening in neonates admitted to the neonatal intensive care unit (NICU)⁽⁹⁾.

Early recognition and diagnosis of neonatal sepsis are difficult because of the variable and non specific clinical presentation of this

condition. It is extremely important to make an early diagnosis of sepsis, because prompt institution of antimicrobial therapy improves outcomes⁽⁹⁾.

Globally, sepsis is still one of the major causes of morbidity and mortality in neonates, in spite of recent advances in health care units⁽¹⁰⁾.

Diagnosis and management of sepsis are a great challenge facing neonatologists in NICU, clinical diagnosis of presentation is difficult due to nonspecific signs and symptoms and laboratory diagnosis is time consuming, this matter necessitates the initiation of empirical antibiotic therapy till the suspected sepsis is ruled out. At the same time, increased multidrug resistant organisms make the treatment options fewer and the effective treatment is delayed⁽¹¹⁾.

Sepsis is one of the most important diseases in preterm babies and is responsible for 45% of late deaths in the neonatal intensive care units, early diagnosis and treatment of the newborn infant with suspected sepsis are essential to prevent severe and life-threatening complications⁽¹²⁾.

Recommendations

- Serum resistin level can be used in diagnosis of neonatal sepsis.
- Further studies are needed to detect diagnostic value of serum resistin level in neonatal sepsis in preterm babies in comparison with full term babies.
- Serial measurements of serum resistin level at different time intervals to follow up septic conditions of neonates.

References

1. Lin FY, Weisman LE, Azimi P, Young AE, Chang K, Cielo M, Moyer P, Troendle JF, Schneerson R and Robbins JB (2011). Assessment of intrapartum antibiotic prophylaxis for the prevention of early-onset group B Streptococcal disease, *Pediatr Infect Dis J.*; 30(9):759-63.
2. Michael CW, Daniel KB, and Edmund C (2009). Immunotherapy in Neonatal Sepsis: Advances in Treatment and Prophylaxis; *Curr Opin in Pediatr.*; 21(2): 177-81.
3. Nagaev I, Bokarewa M, Tarkowski A and Smith U (2006). Human Resistin Is a Systemic Immune-Derived Pro-inflammatory Cytokine Targeting Both Leukocytes and Adipocytes. *PLOS ONE*; 1(1):e31.
4. Nogueiras RM Barreiro ML, Caminos JE, Gaytan F, Suominen JS, Navarro VM, Casanueva FF, Aguilar E, Toppari J, Dieguez C and Tena-Sempere M (2004). Novel expression of resistin in rat testis: Functional role and regulation by-nutritional status and hormonal factors. *Journal of Cell science*; 1 (117): 3247-57.
5. Pagano C, Marino O, Calcagno A, Schiappelli P, Pilon C, Milan G, Bertelli M, Fanin E, Andrighetto G, Federspil G and Vettor R (2005). Increased Serum Resistin in Adults with Prader-Willi Syndrome Is Related to Odesity and Not to Insulin Resistance. *J Clin Endocrin Metab*, 90(7): 4335-40.
6. Peters RP, Van-Agtmael MA, Danner SA, Savelkoul PH and Vandenbroucke- Grauls CM (2004). New developments in the diagnosis of blood stream infections. *Lancet Infect Dis.*; 4: 751-60.
7. Shalini Tand Malik GK (2010). Neonatal Sepsis: past, present and future . *Internet Journal of Medical Update*, 5(2):45-54.
8. Silswal N, Singh AK, Aruna B, Mukhopadhyay S, Ghosh Sand Ehtecham NZ (2005). Human resistin stimulates the pro-inflammatory cytokines TNF-alpha and IL-1;2 10 macrophages by NF-kappaB-dependant pathway. *Biochem Biophys Res Commun*; 334(4): 1092-1101.

9. Steppan CM and Lazar MA (2002). Resistin and obesity-associated insulin resistance. *Trends Endocrinol. Metab*, 13: 18-53.
10. Yura S, Sagawa Nand Itoh H (2003). Resistin is expressed in the human placenta. *J Clin Endocrinol Metab.*; 88: 1394-7.
11. Zhou F, Peng Z, Murugan R, and Kellum JA (2013). Blood purification and mortality in sepsis: a meta-analysis of randomized trials. *Crit Care Med.*; (41): 2209-20.
12. Zaidi AK, Tikmani SS, Warraich HJ, Darmstadt GL, Bhutta ZA, Sultana S (2012). Community-based Treatment of Serious Bacterial Infections in Newborns and Young Infants: A Randomized Controlled Trial Assessing Three Antibiotic Regimens. *Pediatr Infect Dis J*. 31(7):667-72.