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Role of neutrophil CD11b expression in diagnosis of early-onset neonatal sepsis in full-term infant

To the editor,

Neonatal sepsis is a major cause of death or disability in neonatal age population despite suitable therapy and optimal care.[1] The early recognition and diagnosis of neonatal sepsis are difficult because of the nonspecific clinical presentation that mimics other illnesses. For fear of neglecting an actual case of sepsis, antibiotics are administered to all suspected septic neonates.[2] This empiric therapy may result in antimicrobial overexposure and resistance and increase healthcare costs.

A definite diagnosis of sepsis is made by the isolation of pathogenic organisms by blood culturing. However, the procedure is time consuming and its sensitivity is suspected to be low. A number of cell surface antigens have been used as diagnostic markers of neonatal sepsis.[3] Cluster differentiation (CD) 11b, a member of the β-integrin family of adhesion proteins, is expressed at very low levels on the surfaces of unstimulated neutrophils.[4]

Our research question was as follows: Can CD11b detect sepsis in full-term infants with suspected sepsis? We hypothesized that the expression of CD11b would be increased in full-term neonates with early-onset sepsis. The study aimed to evaluate the diagnostic value of neutrophil CD11b in the early diagnosis of sepsis in full-term newborn infants (as the majority of studies focused on preterm infants) and determine the correlation between CD11b expression and conventional markers as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) in the diagnosis of neonatal sepsis. The study also examined the diagnostic utility of CD11b combined with CRP and ESR.

This analytical case-control study included 75 full-term infants who were hospitalized in neonatal intensive care unit (NICU) of Al-Zahraa University Hospital. The patients were classified into three groups: Sepsis group (n=25), neonates with proven sepsis based on clinical manifestations of sepsis and positive blood culture; Suspected sepsis group (n=25), neonates with suspected sepsis based on strong persistent clinical signs of infection, elevated CRP and ESR, and negative blood culture; and Control group (n=25) neonates with no clinical signs and symptoms suggestive of sepsis, no maternal risk factors, and normal CRP level.

Exclusion criteria included:

- Congenital anomalies
- Inborn error of metabolism
- Birth asphyxia
- Administration of antibiotics prior to inclusion

All groups underwent history taking, clinical examination, and laboratory investigations including complete blood count, CRP, and ESR. CD11b levels were measured using enzyme-linked immunosorbent assay. The statistical analysis was done using IBM SPSS Statistics ver. 25.0 (IBM Co., Armonk, NY, USA).

Our study revealed no significant intergroup differences in gestational age (GA), sex, admission weight, head circumference, body length, or postnatal age among the study groups.

The percentage of neutrophils expressing CD11b was significantly upregulated in the sepsis and suspected sepsis groups versus the control group. Our results were similar with those of previous studies.[5,6] CD11b increases markedly within a few minutes after the cell encounters bacteria or endotoxins. This unique property enables the use of CD11b as an early warning marker for the detection of bacterial infection.[7]

In this study, CD11b levels were higher in the sepsis group than in the suspected sepsis group; this finding was contradictory to those reported by Adib et al.[4] This contradiction might be due to differences in the timing of blood collection in relation to infection phase.

The best cutoff point of CD11b was >0.695 ng/ml; it had a sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 100% in the sepsis group. In the suspected sepsis group, CD11b showed 88% sensitivity and 80% specificity with a PPV of 81.5% and an NPV of 87% at a cutoff point >2.0009. Similar values were detected by one study, [6] while other studies reported different values.[4] The different findings might be explained in several ways, such as differences in GA or CD11b measurement methods.

The total leukocyte count, absolute neutrophil count, and CRP and ESR levels were less useful as markers for early diagnosis of sepsis.[8] CRP can be used as a late indicator of neonatal sepsis because it increases slightly in the initial disease phase. Unlike CRP, CD11b does not required newly formed protein synthesis. The combination of CD11b with CRP improved the sensitivity and NPV to 100%, but the specificity and PPV remained nearly the same in the suspected sepsis group. The combined use of CD11b and ESR improved the sensitivity and NPV to 100% and enhanced the specificity and PPV to 96% and 96.2%, respectively.

This study demonstrated insignificant differences in CD11b expression between male and female newborn infants in the studied groups. CD11b expression showed a significant increase

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in neonates with positive culture compared to neonates with negative culture results; this finding explained the increase in CD11b expression in the sepsis group versus the suspected group. This finding agreed with those of Lai et al.[9)]

The absence of a correlation between CD11b and other hematological parameters indicated that CD11b is a sensitive marker whose level increased early in the disease process while the other parameters remained unchanged.[9)]

The clinical practice of treating infants with suspected infection using broad-spectrum antimicrobials increases the risk of invasive fungal infection and promotes the development of resistant bacterial strains. The use of a preventive strategy and application of safe standards can decrease the infection rate within the NICU.[10)]

Although the incidence of sepsis is lower in term infants than in preterm infants, the potential for serious adverse outcomes, including death, is of great consequence; thus, caregivers should have a low threshold for evaluation and treatment for possible sepsis in any infant regardless of GA.[8)]

The limitation of this study was its lack of including fungal pathogens and classifying bacterial infections into gram-positive or -negative organisms. However, we used other conventional tools such as clinical sepsis score, hematological picture, CRP, and ESR to confirm the diagnosis.

Our findings suggest that CD11b is a sensitive marker for sepsis and suspected sepsis in full-term neonates and that it may be added to sepsis markers. This information would allow the neonatologist to confidently discontinue antibiotic use as long as the neonate is clinically stable.

Key message

Question: Can CD11b detect sepsis in full-term infants with suspected sepsis?

Finding: The percentage of neutrophils expressing CD11b was significantly upregulated in the sepsis and suspected sepsis groups versus the control group.

Meaning: CD11b is a sensitive marker for sepsis and suspected sepsis in full-term neonates and it may be added to sepsis markers. This information would allow the neonatologist to confidently discontinue antibiotic use as long as the neonate is clinically stable.

The study protocol (No. 382) was approved by the committee council of Faculty of Medicine for Girls, AL-Azhar University (ethical committee No. 202001013).

Informed consent was obtained from the parents after the aim of the study was explained.

Conflicts of interest

No potential conflicts of interest relevant to this article are reported.

Safaa ELMeneza, MD[1], Walaa Mohamed, MS[1], Iman Elbagoury, MD[2], Karima Bahagat, MD[1]

[1]Department of Pediatrics, Faculty of Medicine for Girls, AL-Azhar University, Cairo, Egypt
[2]Department of Clinical pathology, Faculty of Medicine for Girls, AL-Azhar University, Cairo, Egypt

Corresponding author: Safaa ELMeneza, MD
AL-Azhar University, Faculty of Medicine for Girls, AL-Azhar University Campus Elmokaiam Eldaym Street, Six district, Nasr city 1141, Cairo, Egypt
✉E-mail: safaa5@hotmail.com, safaaelmeneza@azhar.edu.eg
https://orcid.org/0000-0002-4853-4648

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