Pentraxin 3 as a marker of early-onset neonatal sepsis

To the editor,

Neonatal sepsis remains one of the leading causes of morbidity and mortality among term and preterm infants. The traditional markers of leukocyte count and C-reactive protein (CRP) levels are not reliable in determining the severity of disease and mortality risk. Pentraxin3 (PTX 3) is a prototype of the long Pentraxin family. It differs from CRP in terms of gene organization localization and production location. It is sensitive in the early phases of inflammation. PTX 3 was used as an early marker of sepsis in adults with an earlier increase level than CRP, but still not fully studied in neonates.

The research question of this study was as follows: can PTX 3 act as a diagnostic marker for early-onset neonatal sepsis? We also hypothesized that PTX 3 can provide early diagnosis of neonatal sepsis as in the adult population. The study aimed to evaluate the role of the serum PTX 3 in the diagnosis and prognosis of early-onset neonatal sepsis in full-term patients. We conducted a case-control study over a period from October 2020 to July 2021 and this study included 2 groups: group I, comprised 40 neonates with early-onset sepsis (EOS), started within the first 72 hours. They were diagnosed by clinical and laboratory findings and then confirmed by positive blood culture. Group II (control) included 40 neonates. They had no signs of infection and nonsuggestive laboratory results.

History, clinical examination, and sepsis workup as well as serum PTX 3 were done on all the studied cases. The process of measuring PTX 3 was achieved by using enzyme-linked immunosorbent assay from Cloud-Clone Corp. (Katy, TX, USA) with catalogue number; SEK411Hu 96 test. The data were collected, verified, validated, and statistical analysis was done using IBM SPSS Statistics ver. 20.0 (IBM Co., Armonk, NY, USA).

Our results showed that there were no significant differences between the EOS group and control regarding the gestational age (GA), sex, length, and head circumference, the P value was 0.424, 0.823, 0.089, and 0.311 subsequently. However, there was a significant decrease in the birth weight as well as postnatal age and a significant increase in the abdominal circumference clinical and hematological sepsis scores in the EOS group as the P value was 0.001. PTX 3 median and interquartile range was 4.12 (3.26–5.25) ng/mL in the EOS group and 0.63 (0.45–1.29) ng/mL in the control group, the P value was 0.001 (Table 1). Analysis of covariance showed that PTX values among the EOS group were not affected by GA, postnatal age, birth weight, and gender as P values were 0.799, 0.564, 0.095, and 0.205 subsequently (Table 2).

The current study showed that there was a significant increase in the mean value of PTX 3 among newborn infants with EOS compared to normal neonates. This increase may

Table 1. Comparison between early-onset septic (EOS) newborn group and control group according to demographic data

<table>
<thead>
<tr>
<th>Variable</th>
<th>EOS (n=40)</th>
<th>Control (n=40)</th>
<th>Test of significance</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>22 (55.0)</td>
<td>23 (57.5)</td>
<td>χ²=0.051</td>
<td>0.823</td>
</tr>
<tr>
<td>Female</td>
<td>18 (45.0)</td>
<td>17 (42.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestational age (wk)</td>
<td>37.63±0.81</td>
<td>37.78±0.86</td>
<td>t=0.804</td>
<td>0.424</td>
</tr>
<tr>
<td>Birth weight (kg)</td>
<td>2.72±0.16</td>
<td>3.28±0.23</td>
<td>t=12.543*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Length (cm)</td>
<td>47.79±1.17</td>
<td>48.25±1.24</td>
<td>t=1.723</td>
<td>0.089</td>
</tr>
<tr>
<td>Head circumference (cm)</td>
<td>34.78±0.84</td>
<td>34.94±0.56</td>
<td>t=1.020</td>
<td>0.311</td>
</tr>
<tr>
<td>Abdominal circumference (cm)</td>
<td>32.05±1.15</td>
<td>30.85±1.23</td>
<td>t=4.499*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Postnatal age (hr)</td>
<td>9.50 (4.50–39.0)</td>
<td>48.0 (14.0–60.0)</td>
<td>U=439.50</td>
<td>0.001</td>
</tr>
<tr>
<td>Clinical sepsis score</td>
<td>10.70±1.29</td>
<td>0.75±0.67</td>
<td>U=0.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hematological sepsis score</td>
<td>4.0 (4.0–4.0)</td>
<td>0.0 (0.0–1.0)</td>
<td>U=0.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pentraxin3 (ng/mL)</td>
<td>4.12 (3.26–5.25)</td>
<td>0.63 (0.45–1.29)</td>
<td>U=4.0</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are presented as number (%), mean±standard deviation, or median (interquartile range). χ², chi-square test; t, Student t test; U, Mann Whitney U test.

Boldface indicates a statistically significant difference with P<0.05.

Received: 17 October 2023, Revised: 27 January 2024, Accepted: 7 March 2024

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be because PTX 3 is a part of the PTX superfamily and is produced after recognition of microorganism particles or response to an inflammatory stimulus, tissue damage, or inflammation. It is formed by innate immune cells and primary proinflammatory cytokines interleukin-1β (IL-1β) and tumor necrosis factor α. Our results are complemented by the previous studies. However, these 2 studies did not specify the type of sepsis whether early or late onset sepsis, also the GA was not uniform as they included preterm, late preterm and full term. In our study, we included full term infants with confirmed late onset sepsis by blood culture. PTX3 may be useful in early detection of sepsis as it works in a way like acute phase reaction protein, it was shown to increase from 6–8 hours after insult, whereas CRP requires more duration after 24–30 hours. PTX 3 is stored in specific granules in neutrophils, while CRP is systemically formed by the liver in response to IL-6, with a process that requires a longer time. Thus, in sepsis, PTX3 plasma levels are associated with the severity of the condition, patient survival, and response to therapy. PTX3 may also be an acute phase biomarker.

This study determines the best cutoff point of PTX 3 to detect EOS in neonates to be >1.52 ng/mL with sensitivity of 97.5%, specificity of 92.50%, whereas the positive predictive value (PPV) and the negative predictive value (NPV) were 92.9% and 97.4% correspondingly. These results indicate the ability of the PTX 3 to be a good marker for sepsis. In previous studies, we reported that total leukocyte count, absolute neutrophil count, and CRP and erythrocyte sedimentation rate levels were less useful as markers for early diagnosis of sepsis. CRP can be used as a late indicator of neonatal sepsis because it is increased slightly in the initial disease phase.

Our study suggested that PTX 3 has prognostic value as there was a significant increase of PTX 3 among nonsurvival cases, P value was <0.003. Receiving operating curve demonstrated that the best cutoff point of PTX 3 to detect mortality was >4.8 ng/mL with a sensitivity of 92.3%, specificity of 100%, PPV of 100%, and NPV of 98.5%. This indicates that PTX 3 increased with the acceleration of the disease and worsening of the tissue damage. Other studies have demonstrated the association of high levels of PTX3 with organ dysfunction, activation of markers of coagulation, and poor outcome.

PTX 3 can be an ideal marker as there was no significant difference between mean values in male and female newborn infants; the mean values were not affected by GA, sex, postnatal age, and birth weight in LOS groups, this makes PTX 3 independent for diagnosis of sepsis although its level may be affected in normal control by GA.

Furthermore, in the sepsis group, PTX 3 showed a significant positive correlation with the duration of premature rupture of membranes, clinical sepsis score, immature to mature ratio, CRP, and hemolytic sepsis score.

Additionally, the study reveals that there was no considerable difference in the release of PTX 3 to various bacterial species; there was no difference either in cases of Klebsiella pneumoniae compared to other organisms.

PTX 3 can be used as a trustworthy marker for diagnosis and prognosis of early-onset neonatal sepsis owing to its high sensitivity, specificity, and positive and negative predictable values in full term newborn infants. It can predict nonsurvivor septic neonates; its value is not affected by GA, postnatal age, birth weight, and sex. Therefore, it can promote early diagnosis and better outcomes of neonatal sepsis; meanwhile, further studies are needed to standardize its values between different laboratories for different age groups.

The study was approved by the ethics committee of the Faculty of Medicine for Girls, AL-Azhar University. Informed consent was obtained from the parents before recruitment in the study. The approval number is 202006288.
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Footnotes

Conflicts of interest: No potential conflict of interest relevant to this article was reported.

Funding: This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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How to cite this article: ELMeneza S, El-Bagoury I, Rayes H, Hassan A. Pentraxin 3 as marker of early-onset neonatal sepsis. Clin Exp Pediatr [Epub ahead of print]. https://doi.org/10.3345/cep.2024.00409