

## Evaluation of natural killer cells as diagnostic markers of early onset neonatal sepsis: comparison with C-reactive protein and interleukin-8

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This study was conducted on thirty-seven neonates and healthy neonates (sixteen full term and fourteen preterm). The study aimed at revealing the role played by the NK cells in neonatal sepsis and evaluating the sensitivity of NK cell number and cytotoxicity as diagnostic markers in infants with suspected early neonatal sepsis compared with the circulating cytokine IL-8 and CRP levels. All samples of peripheral blood lymphocytes were subjected to determination of CD16 and CD56 positive cells using flow cytometry and NK cytotoxicity using the standard 4h <sup>51</sup>Cr release assay. Sera were separated to measure IL-8 using ELISA. Determination of CRP, using turbidimetric assay, as well as blood cultures were done for patient's group only. Out of the 37 cases of suspected early neonatal sepsis, 16 were given final diagnosis of sepsis. Seven infants (43.8%) in the sepsis group had culture-proven diagnosis, one of which had meningitis. The median CRP value was significantly higher in sepsis group (88 mg/L; range: 17-159 mg/L) compared with that in non-septic group (15.4 mg/L; range: 7.6-23.2 mg/L,  $p < 0.001$ ) only 12-60 h after admission. On the other hand, newborns in the sepsis group had significantly higher serum levels of IL-8 (median 310 pg/mL; range: 37-583 pg/ml) at study entry than that in the non septic group (median 63 pg/mL; range: 32-94 pg/ml,  $P < 0.001$ ). On admission, the NK activity, rather than the number of CD16 and CD56 positive cells was much affected where NK cytotoxicity was significantly lower in sepsis group (3.4 +/- 2.1%, range 0.9-7%) than that of the nonseptic group (18.3 +/- 6.7%: range 10.7- 25.3%,  $p < 0.01$ ) and healthy neonates (23.8 +/- 4.7%: range 12.2-32.3%,  $p < 0.001$ ). We may conclude that defective NK cell activity rather than NK cell number plays an important role in susceptibility to early onset neonatal sepsis. Evaluation of NK cytotoxicity as a marker in early diagnosis of neonatal sepsis reveals that the sensitivity, specificity and predictive values of reduced NK cytotoxicity (10% killing) was higher than both of CRP and IL-8, either individually or in combination. Additionally, reduced NK cytotoxicity showed high correlation with the severity and outcome of neonatal sepsis. Our data raise the possibility that the addition of NK cell activity to the standard work-up of critically ill patients with suspected sepsis could increase diagnostic certainty and generate an improved patient management.