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IL-6 and associated immune markers in acute pancreatitis: potential for monitoring disease severity

Maimela, Murunwa Grace

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ABSTRACT

Numerous scoring systems for diagnosing, stratifying, and prognosticating acute pancreatitis (AP) have been developed; however, these systems do not fully reflect the evolving understanding of AP immunopathogenesis. Assessment of AP severity and possible complications using inflammatory mediators such as cytokines and dysregulated immune cells may serve as a better option in choosing rational and effective therapeutic options. This study aimed to monitor inflammatory mediators such as interleukin-6 (IL-6), chemokine ligand 4 (CXCL-4), reactive oxygen species (ROS) and associated immune cells to assess their potential in predicting AP severity and determining outcomes of severe AP patients for better management. Twenty-four AP-patients, 17 mild AP (MAP), four moderately severe AP (MSAP), and three severe AP (SAP) patients were recruited from the Chris Hani Baragwanath Academic Hospital (CHBAH), Johannesburg, South Africa. Approximately 16mL of blood was collected on days (D) 3, 5, 7, 9, 13 and 15 post-epigastric pain. These samples were assayed with once-off samples from eight age- and sex-matched healthy controls (HCs). ROS were studied using a spectrophotometric assay, and IL-6 and CXCL4 were analysed by intracellular cytokine staining (ICS) and enzyme-linked immunosorbent assays (ELISA). Among the 24 patients, biliary AP (n=14, 58%) was the predominant aetiology. IL-6, CXCL4 and ROS increased with increasing AP severity (SAP>MSAP>MAP), especially from D9-D15. These findings agreed with routine clinical biochemical test results such as C-reactive protein (CRP), which were shown to increase with severity ($p=0.019$). Additionally, natural killer cells (NKs) and activated $CD62p^{+}$ platelets were expressed more in the severe patient group and further linked to IL-6 and CXCL4 secretion in AP patients, respectively. Statistically significant differences were only observed on D9 and D13 for the ROS data between SAP patients and HCs, $p=0.0050$ and $p=0.0071$, respectively. These preliminary findings further support that IL-6, CXCL4 and ROS combined with clinical parameters may be useful in monitoring and predicting the outcome of patients, especially in SAP, for improved care and better AP management. Importantly, for the SAP patient who enters a second phase of disease, the findings provide important implications of early intervention and can potentially inform management guidelines.