IMPA CT OF NEUTROPHIL APOPTOSIS ON HAEMOSTATIC ACTIVATION IN CHRONIC LIVER DISEASE PATIENTS

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ABSTRACT

Background and Aim: Recent studies suggest the impact of apoptosis on the mechanisms leading to hypercoagulability. We aimed to clarify the potential role of neutrophil apoptosis in neutropenia and hypercoagulable state encountered in chronic liver disease patients.

Materials and Methods: This study was conducted on fifteen normal controls and forty five patients with chronic liver disease classified according to modified Child Pugh classification into, Child A, B and C groups (15 cases each). Studied Haemostatic parameters include, prothrombin time, partial thromboplastin time, tissue factor, protein C antigen, protein S antigen, and markers of haemostatic activation (prothrombin fragment 1+2, thrombus precursor protein and D-dimer). Flowcytometric study was done for quantitative assay of neutrophil apoptotic subpopulations to detect the percentage of early and late apoptotic, and necrotic neutrophils using AnnexinV-FITC/Propidium iodide dye. Semiquantitative assay of apoptotic neutrophils showing DNA fragmentation was performed on neutrophil culture using terminal deoxynucleotidyl transferase mediated deoxyuridine triphosphate nick end labeling (TUNEL) test. In addition to enzyme linked immunosorbent assay for soluble Fas (APO-1/CD95) in culture supernatant. The results revealed a rise in the neutrophil apoptotic and necrotic markers with progression of the disease, and they were inversely correlated with the absolute neutrophil count. The apoptotic neutrophil cells showed a significant positive correlation with several haemostatic parameters (tissue factor, prothrombin fragment 1+2, thrombus precursor protein and D-dimer), which further incriminate the apoptotic mechanisms in the hypercoagulable state encountered in this clinical setting. Conclusion: Enhanced neutrophil apoptosis and necrosis in patients with chronic liver disease may explain in part the mechanism of neutropenia in these patients and may be one of the important factors which drive the haemostatic balance towards the hypercoagulable state.

Keywords: Neutrophil apoptosis, neutropenia, hypercoagulability, liver disease.