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TGF-beta1 and C-erb-B2 neu oncoprotein in Egyptian HCV related chronic liver disease and hepatocellular carcinoma patients

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Transforming growth factor beta (TGF-beta), a pro-fibrogenic cytokine, has several polymorphism in humans with difference in activity levels. Hepato-carcinogenesis involves alterations in the action of protooncogenes such as the; neu (C-erb-B2) oncogene. Overexpression of the neu-oncogene has been implicated in experimental cellular transformation and tumorigenesis in a wide range of human cancer. We examined TGF-beta1 and C-erb-B2 mRNA expression and their protein levels in hepatitis C virus (HCV) patients and those developing Hepatocellular carcinoma (HCC). Sixty patients (30 HCV and 30 HCC) and 30 controls were enrolled. HCV patients were classified into mild, moderate, marked and no fibrosis. HCC patients were categorized into grade I, II, III. TGP-beta1 and C-erb-B2 expression were studied. Messenger RNA was extracted using the guanidinum thiocyanate phenol chloroform method, and used of RT-PCR. Protein serum levels were estimated by (EIA). Significant difference were obtained when comparing TGF-bet1 and C-erb-B2 mRNA in HCV and HCC $P = 0.0076$, and controls. The HCV group revealed significant difference with C-erb-B2 but not TGF-B1 mRNA as compared to controls $P < 0.005$ and $P > 0.05$ respectively. Serum protein levels demonstrated difference increase significance shown when comparing their levels in both studied groups $P < 0.001$, $P < 0.05$ respectively and when compared to controls ($P < 0.001$). TGF-beta1 serum levels in HCV patients showed increase with degree of fibrosis ($P = 0.003$) while, C-erbB-2 serum levels showed no significance ($P = 0.089$). In different grades of HCC patients, TGF-beta1 levels showed no significant difference ($P = 0.769$). However, C-erb-B2 levels revealed significant difference ($P = 0.002$) between grade I & III and grade II &. III ($P < 0.001$). Positive correlations to protein serum level were obtained with TGF beta1mRNA in HCV group, while, C-erb-B2 mRNA in HCC patients. In conclusion, TGF-beta1 upregulation in HCC suggests its role in hepatic carcinogenesis. Elevated expression of C-erb-B2 may reflect pre-neoplastic liver cell proliferation, cellular necrosis associated with chronic liver disease and alternatively from HCV carcinogens which enhance malignant transformation. Correlation of both parameters with their protein levels might rise using their antibodies in immunotherapy for HCC.