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OXIDATIVE STRESS INDUCED CYSTEINYLATED PLASMA ALBUMIN IN THE PATIENTS WITH NONALCOHOLIC FATTY LIVER DISEASE

Abhishak C Gupta
Indian Institute of Technology Delhi, India

Backgrounds & Aim: In the absence of any symptomatic clinical features, liver biopsy remains the gold standard to assess disease progression in non alcoholic fatty liver disease (NAFLD) patients. Oxidative stress is postulated to play an important role in liver disease progression. Albumin is the most abundant plasma protein with antioxidant activity. The degree of oxidized cysteine 34 (Cys34) in human serum albumin (HSA) is correlated with oxidative stress related pathological conditions and modulates its physiological function, as well as serves as a biomarker for oxidative stress. The aim of the present study was to develop a noninvasive diagnostic plasma marker for NAFLD by studying the differential modification pattern of plasma albumin in NAFLD patients.

Patients & Methods: We analyzed purified plasma albumin from 46 biopsy-proven NAFLD patients (17 with benign fatty liver and 29 with NASH) and 21 healthy non-smoker/ non-alcoholic blood donors matched with age and BMI. The structural modifications of albumin were analyzed by direct measurement of plasma albumin using liquid chromatography coupled with electrospray ionization time-of-flight mass spectrometer (ESI-TOF/MS). Relative percent abundance of unmodified (intact) and modified isoforms of albumin was compared between patients and controls.

Results: Three most prominent isoforms of albumin were observed in the deconvoluted ESI spectrum with molecular masses of 66.438±2.8, 66.559±4.8 and 66.603±6 Da in controls and NAFLD patients represents intact, cysteinylated and glycated isoforms of albumin respectively. Unmodified albumin was the predominant peak with 100% relative abundance in healthy subjects in perfect agreement with calculated theoretical mass (66.438 Da, 542aa). In contrast, the relative abundance of modified form with addition of +119Da (cysteinylation) of albumin was predominant (100%) in NAFLD patients. Cysteinylated isoform of albumin (cys-Alb) was significantly higher in NAFLD patients than controls [100% vs. 52% ($p<0.01$)]. Although NAFLD showed 100% relative abundance of cys-Alb isoform, further fatty liver and NASH patients differ on the basis of unmodified albumin isoforms [82% vs. 60% ($p<0.05$)] suggesting varied oxidative stress.

Conclusion: Our results showed that sustained oxidative stress is reflected by high levels of cysteinylated albumin in NAFLD patients. The measurement of cysteinylated albumin in suspected NAFLD patients might prove to be a useful marker to assess the degree of oxidative damage, inflammation and severity of the disease.

Biography

Abhishak C Gupta is working in Indian Institute of Technology, Delhi. He is a Project Scientist in Department of Textile Technology, IIT, Delhi.

abhigupta78@gmail