Hepatic Enzymes are Associated with Insulin Resistance and Impaired Fibrinolysis in Drug Naïve, Recently Diagnosed Type 2 Diabetes Subjects

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In the general population, hepatic enzymes (alanine aminotransferase (ALT) and aspartate aminotransferase (AST)) are associated with insulin resistance (IR) and increased hepatic fat. Little data exists on abnormalities in hepatic enzymes in type 2 diabetes (T2DM) subjects who tend to be insulin resistant, obese and have impaired fibrinolysis. We examined the relationship of ALT and AST to variables associated with IR and the metabolic syndrome in 4356 (57.7% M; mean age 56.5yrs; mean BMI 31.9 kg/m^2; geometric mean HOMA IR 6.32 μU/mL*mmol/L) recently diagnosed, drug naïve T2DM subjects in ADOPT (A Diabetes Outcome Progression Trial).

Median ALT was 23 IU/L (IQR; 17, 32) and AST 20 IU/L (16, 25). After adjustment for age, gender and alcohol intake (yes/no), ALT correlated with waist circumference (WC) ($r=0.09$; $p=0.008$) and log HOMA IR ($r=0.22$; $p<0.001$) but not log triglycerides (TG) ($r=0.03$). Similarly, AST correlated with WC ($r=0.09$; $p=0.015$) and log HOMA IR ($r=0.21$; $p<0.001$) but not log TG ($r=0.01$). Neither ALT nor AST were correlated with HbA_{1c}.

Fibrinolysis and inflammatory factors were measured only in the cohort from the United States (n=918). After adjustment for age, gender and alcohol intake, both ALT and AST correlated weakly with log PAI-1 activity ($r=0.13$ and 0.15, respectively) and log PAI-1 antigen ($r=0.12$ and 0.14, respectively) (all p-values ≤0.001). No correlation was seen between ALT or AST and log CRP, log fibrinogen, log WBC or HbA_{1c}.

In summary, ALT and AST are weakly but significantly related to some aspects of the metabolic syndrome (WC, insulin resistance and PAI-1) independently of age, gender and alcohol intake, but not to glycemic control. In conclusion, hepatic enzymes within the normal range are associated with central adiposity and insulin resistance and through these intermediates may be related to impaired fibrinolysis in T2DM.