

Metabolic Associated Fatty Liver Disease (MAFLD) Associated with Diabetes Mellitus, Overweight, and Metabolic Dysregulation as an Inflammatory Cascade

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Abstract: Background: Metabolic Associated Fatty Liver Disease, MAFLD, is a new nomenclature proposed to replace the old term NAFLD. MAFLD is a new challenge in modern medicine, due to its progressively increasing global prevalence and its associated multiple sequels. The diagnosis of MAFLD relied upon on presence of both hepatic steatosis and any of the following three metabolic conditions: overweight/obesity, type 2 diabetes mellitus, or evidence of metabolic dysregulation (MD) in lean individuals. **Aim:** This study aimed to investigate some markers of inflammation in patients with MAFLD with/or without diabetes mellitus and with/or without overweight/obesity. **Methods:** This prospective study recruited patients with MAFLD as diagnosed by presence of hepatic steatosis detected by abdominal ultrasound. A group of apparently healthy individuals without hepatic steatosis were included as controls. Confirmation and grading of steatosis was done by conventional and Dixon MRI at 1.5 Tesla system. Liver fibrosis staging was done by Shear Wave Elastography. All participants of the study were subjected to: anthropometric studies, HCVAb, HBsAg, complete blood picture, liver biochemical profile, renal biochemical profile, s. ferritin, s. Ceruloplasmin, thyroid hormones profile, fasting blood glucose and fasting insulin levels with mathematical determination of HOMA-IR. TNF- α , IL-6, and Cytokeratin-18, (CK-18), were assayed as specific markers of inflammation. **Results:** Eighty patients with MAFLD compared to twenty apparently healthy controls were included in this prospective study. Our results indicated significantly higher values of TNF- α , IL-6, and CK-18 in MAFLD patients compared to controls, ($p < 0.001$). The presence of diabetes mellitus with obesity confers more

significant higher values of these inflammatory markers in MAFLD patients than in the group of obesity without diabetes, ($p < 0.001$). Total cholesterol, s. triglycerides, total leucocytes count, and serum ferritin were significantly increased in MAFLD patients than controls. Fasting blood glucose, fasting serum insulin, and HOMA-IR were significantly higher in patients compared to controls, ($p < 0.001$). TSH serum levels were significantly higher in MAFLD patients than controls, ($p < 0.001$). Both TSH and HOMA-IR were positively correlated with the grade of steatosis, ($p < 0.001$). On linear regression analysis, waist circumference, waist hip ratio (WHR), TSH, TNF- α , IL-6, and CK-18 were significant predictors for moderate/severe grades of steatosis, ($p < 0.001$). On multiple stepwise regression analysis, both fasting serum insulin and TNF- α , were the significant predictors of moderate /severe steatosis, ($p < 0.013$ and $p < 0.001$, respectively). On multiple stepwise discriminant functional analysis, TSH was found to be the most significant predictor in discriminating the grade of steatosis in MAFLD patients. Utilizing TSH serum levels, a discriminant score was obtained to predict advanced grades of steatosis with AUC of 0.99 and total accuracy of 87.5%. **Conclusion:** Our study has elucidated the inflammatory nature of MAFLD and its associated components in the form of diabetes mellitus, overweight/obesity, and metabolic dysregulation by finding out significant higher values of multiple markers of inflammation in MAFLD patients compared to controls. Furthermore, our results have indicated a critical role displayed by the thyroid axis in MAFLD associated syndromes.

Keywords: MAFLD, Diabetes Mellitus, HOMA-IR, TSH, TNF- α , IL-6, and CK-18.