ABSTRACT

Non-alcoholic fatty liver disease (NAFLD) is a chronic liver disease with hepatic histology that resembles alcoholic liver disease. It is a frequent cause of chronic liver disease and is attracting increasing scientific attention worldwide. I explored the possibility that increased gastrointestinal alcohol production may have a role as a “second hit” in the pathogenesis of NAFLD in study subjects with the metabolic syndrome. In an attempt to investigate this hypothesis, this study looked at blood, urine and breath levels of alcohol in patients with the metabolic syndrome versus matched age and ethnic group healthy controls. Of the twenty study subjects, 80% had dyslipidaemia, 60% had hypertension and 70% had type 2 diabetes mellitus. Their mean BMI was 35.1±8.2 kg/m² (mean ± SD, $P < 0.0001$ versus controls). The serum aminotransferases were significantly elevated in the study subjects, their ALT levels being 57.4±44.79 U/L versus 17.4±4.60 U/L in the controls (95% CI 18.02 – 61.42, $P < 0.001$), and their AST levels 52.5±36.21 U/L versus 23.4±4.86 U/L in the controls (95% CI 11.99 – 46.20, $P < 0.01$). Seventy five percent of the study group had sonar features suggestive of fatty liver disease. Two adipocytokines, adiponectin and leptin, mediators of insulin resistance, an important factor in the

development and progression of NAFLD, were also measured. Adiponectin levels were significantly lower (6875 ng/L versus 15475 ng/L; median value, $P < 0.01$), and leptin concentration levels significantly higher (13.56 ng/L versus 3.05 ng/L; median value, $P < 0.05$) in the study subjects than in the control group.

Alcohol was detected in 60% of the study subjects, of which 35% tested positive for ethanol, 55% tested positive for methanol, and 30% tested positive for both ethanol and methanol. This was a statistically significant result, as none of the control group tested positive for any of the alcohols. The ethanol concentration in the study subjects' blood was 7.14±3.28 mg% (mean ± SD), in their urine 3.71± 12.87 mg% (mean ± SD) whilst none was detected in their breath. The methanol concentration in the study subjects' blood was 16.17±17.95 mg% (mean ± SD), in their urine 6.8± 13.58 mg% (mean ± SD) while their breath level was 2.05±3.19 mg (mean ± SD).

This study therefore suggests that endogenous alcohol production may be indeed be involved in the pathogenesis of NAFLD in subjects with the metabolic syndrome. Not only ethanol but also methanol was detected in the subjects tested. Endogenous alcohol may therefore be responsible for the 'second hit' theory in the pathogenesis of NAFLD, and it is likely that

formaldehyde, the metabolite of methanol may be a more potent toxin of hepatocyte injury as opposed to acetaldehyde, the metabolite of ethanol. The most likely source of the alcohol is from intestinal bacterial flora. These findings provide further insight into the pathogenesis of NALFD, suggesting other therapeutic alternatives such as the use of antibiotics and probiotics as a potential treatment strategy for NAFLD.