normal liver enzymes in the treatment group, or the possibility to undergo phlebotomy in the controls. Nevertheless, in a per-protocol analysis of patients who completed the study, amelioration of histological damage was demonstrated in 7/11 (64%) phlebotomized patients vs. 1/8 (12%) controls ($p = 0.026$).
Conclusions: Phlebotomy is well tolerated in patients with NAFLD and increased iron stores, effectively reduces iron stores, and results in an improvement in ALT and AST levels. These preliminary results suggest that iron depletion may possibly improve liver damage in patients with NAFLD and increased iron stores.

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ANA POSITIVITY IDENTIFIES A SUBGROUP OF NAFLD PATIENTS WITH DISTINCT METABOLIC PROFILE AND IMPAIRED HISTOLOGICAL RESPONSE TO WEIGHT LOSS

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Background: Obesity is often accompanied by comorbidities including metabolic and liver disturbances. Antinuclear (ANA) and anti smooth muscle (ASMA) antibodies can be expressed in various clinical settings including liver diseases.
Aim: To evaluate the clinical significance of the expression of ANA and ASMA in the assessment of obese patients.
Patients and Methods: 522 obese patients were consecutively enrolled, with a one year follow up in 166 patients. Serum tests, including ANA and ASMA, glucose, insulin and c-peptide levelus during oral glucose tolerance test (OGTT), ultrasound and fat measurement at CT scan were performed at baseline and at 12 months follow up. A liver biopsy was performed in 314 patients at baseline and in 86 at follow up.
Results: at baseline ANA+ patients presented sgnificantly lower levels of glucose at 180′ ($p = 0.023$), insulin at 0′ ($p = 0.017$) and at 180′ ($p = 0.039$) and c-peptide at 0′ ($p = 0.020$) and at 180′ ($p = 0.010$) during OGTT when compared to ASMA+, ANA+/ASMA+ and ANA−/ASMA− patients. At 12moths a significant decrease of BMI, NAS score and presence of histologically proven NASH was detected in all groups ($p < 0.05$), with a reduction of BMI significantly higher in ANA− patients with respect to ANA+ patients ($p = 0.006$). The extent of BMI reduction was similar in ASMA+ and ASMA− patients. A significant decrease of glucose, c peptide and insuline levels during OGTT, ALT, GGT, grade of stetosis and lobular inflammation at histology was observed in ANA−, ASMA+ and ASMA− patients ($p < 0.05$) but not in ANA+ patients. Balooning was significantly decreased in ANA− ($p < 0.001$) and in ASMA− ($p < 0.001$) patiens but not in ANA+ and ASMA+ patients. Fat measurement at CT scan showed a significant reduction of both total and visceral fat in all groups ($p < 0.05$) except ANA+ where a significant reduction of total fat ($p = 0.021$) but not of visceral fat was observed.
Conclusion: In our obese population, ANA positivity seams to identify a subset of patients with a lower glucose metabolism disturbance at baseline and an impaired improvement of glucose metabolism, visceral fat and histological features of NAFLD/NASH at follow up, suggesting a different pathogenetic profile.

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BARIATRIC SURGERY REDUCES ADIPOCYTE SIZE, IMPROVES LIVER INJURY AND COUNTERACTS LIPOTOXICITY VIA CHANGES IN SERUM FATTY ACID COMPOSITION AND ADIPONECTIN LEVELS

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Background and Aims: Obesity is a growing worldwide pandemic and a risk factor for non-alcoholic fatty liver disease (NAFLD). Recently identified adipokines were found to promote the crosstalk of adipose tissue and the liver, which may play a pivotal role in the development of NAFLD. With the present study, we aimed to explore the interplay of adipose and liver tissue addressing the short-term effects of bariatric surgery.
Patients and Methods: Blood, visceral adipose tissue, and liver tissue samples were obtained from 160 morbidly obese patients undergoing bariatric surgery. Liver and adipose tissue were scored histopathologically. Blood samples taken before and 6 weeks after surgery were analyzed for routine parameters of liver injury and lipid metabolism. In a sub-cohort, the composition of free fatty acids and apolipoproteins were assessed at both time points.
Results: The 160 severely obese patients (34 male/126 female) had a mean age of 43 years (range 19–65) and mean BMI of 52kg/m^2 (35–78kg/m^2). Adipocyte cell size significantly correlated with AST and ALT blood levels as well as steatosis, ballooning, and NAS score in liver biopsies. Furthermore, serum triglyceride and free fatty acid composition were correlated with liver injury. Bariatric surgery improved levels of stearic acid and dihomo-gamma-linolenic acid as early as 6 weeks after surgery. Several apolipoproteins (ApoAI, ApoAII, ApoCIII) were significantly associated with serum and histological parameters of liver injury. Serum markers improved at 6 weeks after surgery, including serum triglycerides, ApoCIII, and cell death markers (M30, M65). Plasma levels of adiponectin at baseline correlated with hepatic steatosis, ballooning and NAS-score. 6 weeks after surgery, adiponectin levels were significantly increased independent of the type of surgery.
Conclusions: Adipocyte cell size and serum levels of free fatty acids correlate with histological and serological markers of liver injury. Moreover, our findings reveal that bariatric surgery has beneficial effects on liver injury as soon as 6 weeks after the procedure which may be due to the observed changes in lipid metabolism and adiponectin levels. Collectively, these findings underline a crosstalk between adipose tissue and the liver which could be therapeutically targeted by bariatric surgery.

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GALLSTONE DISEASE IS NOT ASSOCIATED WITH LIVER FIBROSIS AND NONALCOHOLIC STEATOHEPATITIS IN NONALCOHOLIC FATTY LIVER DISEASE

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Background and Aims: GD is the most common disorder of the gastrointestinal tract and it is strongly associated with metabolic

risk factors. GD and nonalcoholic fatty liver disease (NAFLD) have a similar risk factor profile and frequently coexist. We sought to examine whether the presence of GD in patients with biopsy-proven NAFLD is associated with hepatic fibrosis and the histological nonalcoholic steatohepatitis (NASH) score.
Methods: This is a retrospective review of a prospective database of patients with biopsy-proven NAFLD enrolled from four different gastroenterology clinics in Turkey. A total of 441 Turkish patients were included in the analysis. GD was diagnosed in the presence of sonographic evidence of gallstones, echogenic material within the gallbladder with constant shadowing and little or no visualization of the gallbladder, or absence of gallbladder at ultrasonography, coupled with a history of cholecystectomy.
Results: Fifty-four patients of the 441 NAFLD patients (12.2%) had GD (GD+ subjects). Compared with GD− subjects, GD+ patients were older, had a higher BMI, and showed a higher prevalence of female subjects and the metabolic syndrome. However, GD+ patients did not have a higher risk of advanced fibrosis or definite NASH on liver histology. After adjustment for potential confounders, the prevalence of GD in NAFLD patients was not associated neither with severe fibrosis (≥2) (odds ratio [OR] = 1.06, 95% confidence interval [CI] = 0.53–2.21, p = 0.68) nor with definite NASH (OR = 1.03, 95% CI = 0.495–2.12, p = 0.84).
Conclusions: The results of this multicenter cross-sectional study conducted in Turkey indicated that patients with histology-proven NAFLD and GD were older, had a higher BMI, and showed a higher prevalence of female subjects and the MS compared with those without GD. However, we did not find any significant association of GD with neither liver fibrosis nor definite NASH both at univariate and multivariable analysis. The presence of GD is not independently associated with advanced liver fibrosis and definite NASH in adult patients with biopsy-proven NAFLD.

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HYPOTHYROIDISM IS NOT ASSOCIATED WITH SPECIFIC HISTOLOGICAL FEATURES OR SEVERITY OF NON-ALCOHOLIC FATTY LIVER DISEASE

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Background and Aims: Recent evidence derived from epidemiological studies has suggested that hypothyroidism can act as a risk factor for non-alcoholic fatty liver disease (NAFLD) as diagnosed by ultrasonography. However, it is currently uncertain whether there is a significant association between hypothyroidism and the severity of liver histology among patients with NAFLD. In this multicenter study, we assessed whether there is a significant relation between liver histology and hypothyroidism among patients with biopsy-proven NAFLD.
Methods: A total of 483 patients with NAFLD (263 males and 220 females, mean age, 45±10 years) were recruited in this study. The NAFLD diagnosis was based on liver biopsy and exclusion of other known etiologic factors of chronic liver disease. An experienced pathologist blinded to clinical data scored the liver biopsies according to the National Institute of Diabetes and Digestive and Kidney Diseases NASH Clinical Research Network scoring system. The diagnosis of hypothyroidism was based on a previous history of hypothyroidism (use of T4 replacement therapy) or according to theTSH value. In multivariable-adjusted linear logistic regression models, each histological feature of NAFLD was considered as the dependent variable.
Results: A total of 64 NAFLD patients (13%) had hypothyroidism. The distribution of subjects with hypothyroidism was not different in NAFLD patients classified according to liver histopathology (steatosis alone, borderline steatohepatitis, definite steatohepatitis). Notably, the presence of hypothyroidism was not associated with the degree of hepatic steatosis ($P = 0.31$), lobular inflammation ($P = 0.52$), hepatocyte ballooning ($P = 0.74$), portal inflammation ($P = 0.33$), fibrosis ($P = 0.33$), and the NASH score (0.48) among patients with NAFLD.
Conclusions: This study has shown for the first time that the histological severity of NAFLD is not independently predicted by hypothyroidism. Future follow-up studies are necessary to validate these findings and better estimate the risk of disease progression in relation to hypothyroidism among patients with biopsy-proven NAFLD.

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DEVELOPMENT AND VALIDATION OF NASH DIAGNOSTIC INDEX AS A NON-INVASIVE MODEL FOR DIAGNOSING NON-ALCOHOLIC STEATOHEPATITIS (NASH)

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Background and Aims: Non-alcoholic fatty liver disease (NAFLD) is recognized as a common cause of chronic liver disease, worldwide. Distinguishing the progressive non-alcoholic steatohepatitis (NASH) from the benign simple steatosis requires a liver biopsy. Fatty Liver Index (FLI) is a non-invasive test that has been developed to diagnose NAFLD. FLI is calculated using BMI, waist circumference, triglycerides, and gamma-glutamyl transpeptidase. FLI has not been validated for diagnosing NASH. A non-invasive test to simultaneously diagnose both NAFLD and NASH will be clinically useful. The aim of this study was to validate FLI and to develop a biomarker for establishing the diagnosis of NASH.
Methods: For this study, we used two patient cohorts. First, we used a population-based cohort with clinical, laboratory and hepatic ultrasound data from National Health and Nutrition Examination Survey (NHANES-III) database to validate FLI. Subsequently, we used the same database to develop a new predictive index called NASH Diagnostic index (NDI). Finally, we validated both indices using a second patient cohort for whom liver biopsy, clinical and laboratory data were available. Multivariate logistic regression was performed to build the predictive model. The model's linearity was ascertained by Box-Tidwell while adjusting for study weight and clustering. Final models were examined by goodness-of-fit test.
Results: NHANES-III cohort included 4,458 individuals. Using NHANES-III, FLI's diagnostic accuracy for NAFLD showed positive predictive value (PPV) of 42% and negative predictive value (NPV) of 89%. NDI is calculated by insulin, glucose, triglycerides (mg/dL), alanine aminotransferase (U/L), and waist-to-hip ratio. Using NHANES-III, NDI's predictive accuracy for NAFLD had a PPV of 43% and NPV of 90%. We then validated both FLI and NDI using a biopsy-proven NAFLD cohort (N = 78). Since 95% of NAFLD patients had a FLI score>91, FLI was not able to distinguish simple steatosis from histologic NASH. On the other hand, using a threshold ≥22, NDI had a specificity of 82% for establishing a diagnosis of simple seatosis, while for a threshold ≥50, NDI had a specificity of 86% for diagnosing histologic NASH.
Conclusions: FLI and NASH-I have good NPV for NAFLD. NDI can diagnose histologic NASH with good accuracy.