

Nonalcoholic Fatty Liver Disease Digestive Disease Week

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The relationship between Insulin Resistance and nonalcoholic fatty liver disease is independent of obesity.

KC Sung, MC Ryan, BS Kim, et al. Div Medicine, Stanford University, Stanford, CA, USA, Div Medicine, Kangbuk Samsung Hospital, Sungkyunkwan Univ Sch Med, Seoul, South Korea

Nonalcoholic fatty liver disease (NAFLD) is emerging as a major health problem in parallel with an increasing prevalence of obesity. Insulin resistance and abdominal and overall adiposity are both closely associated with NAFLD; however, the interplay between the two in the relationship with NAFLD is unclear. To address this question, measurements were made in 56,249 Korean subjects of abdominal ultrasound, fasting plasma insulin (FPI) and lipid concentrations, hepatitis serology, overall obesity (body mass index, BMI) and abdominal obesity (waist circumference, WC). After rigorous exclusion criteria, 28,249 nondiabetic subjects (44% men) were available for study. Subjects were divided into controls (no steatosis on ultrasound and a serum ALT<30 U/L), steatosis (with an ALT<30U/L) and “nonalcoholic steatohepatitis” or NASH (steatosis and an ALT>30 U/L). After adjusting for age, BMI and WC, FPI concentrations and the concentration ratio of triglyceride/high density lipoprotein cholesterol (TG/HDL-C) were still significantly higher in the steatosis group and higher again in the NASH group. Odds ratios for the presence of steatosis and NASH with increasing quartiles of FPI and TG/HDL-C ratio were increased 5-7 fold over controls, independent of age, BMI and WC. ROC curves for the presence of steatosis showed a sensitivity and specificity of 68% with a FPI concentration of 8.4 μ U/ml for men, and 9.0 μ U/ml for women. Similar results were seen with a TG/HDL-C ratio of 2.8 for men and 2.0 for women. In conclusion, we have demonstrated in this large, nondiabetic population-based study, that surrogate estimates of insulin resistance, FPI concentration and the TG/HDL-C ratio, predict features of NAFLD independent of age, BMI and WC.

Apneic-hypopneic episodes during Obstructive Sleep Apnea can be associated with histologic nonalcoholic steatohepatitis (NASH).

P Mishra, C Nugent, A Afendy, et al. Center Liver Diseases, Inova Fairfax Hospital, Annandale, VA, USA

Nonalcoholic fatty liver disease (NAFLD) and obstructive sleep apnea (OSA) are associated with obesity and metabolic syndrome. A strong association between sleep-disordered breathing, NAFLD and atherosclerotic disease has been observed. Theoretically, hypoxemic episodes during sleep apnea may predispose patients to oxidative stress as the “second hit” in the pathogenesis of NAFLD. **Objectives.** To evaluate the association between different subtypes of NAFLD and polysomnographic parameters. **Methods.** 238 patients who underwent bariatric surgery were selected. 174 had biopsy-proven NAFLD (41 NASH, 133 non-NASH). 125 had sleep study with 62 patients having complete polysomnographic (PSG) data for analysis. Demographic, clinical, laboratory and liver biopsy data were available. Excess alcohol intake and other causes of liver disease were excluded. Apnea was defined as the complete cessation of airflow \sim 10 seconds. Hypopnea was defined as a 30% or greater reduction in airflow or respiratory effort \sim 10 seconds accompanied by a 4% or greater desaturation. The average number of episodes of apnea and hypopnea per hour of sleep (apnea-hypopnea index, AHI) was calculated as a summary measurement of sleep-disordered breathing. AHI > 5 is considered abnormal according to the American Academy of Sleep Medicine (AASM) consensus. **Results.** Clinico-demographic data for the study cohort are as follows: age 43.7 \pm 12.3 years, BMI 51.6 \pm 11.1 kg/m², fasting serum glucose 114.8 \pm 49.4 mg/dl, fasting serum triglycerides 167.3 \pm 76.3 mg/dl, 39% hypertension and 31% diabetes mellitus. Liver histology showed that 28% of patients had NASH, 65% had steatosis with or without non-specific inflammation and 7% had normal histology. The lowest desaturation (nadir oxygen saturation) was 77.4 \pm 18.9%. Patients with NASH had significantly higher ALT values (40.3 vs. 28.4, p=0.03) compared to non-NASH. Mean AHI was 54.4 \pm 34.3 in NASH group vs. 32.8 \pm 37.1 in Non-NASH (p=0.07). **Conclusions.** Our results suggest that the

frequent nocturnal hypoxic episodes in patients with OSA is a risk factor for developing steatohepatitis. Whether correction of hypoxemia results in regression of any of the histologic changes, requires further study. Additionally, a longitudinal study following patients with NAFLD and OSA may provide important insight into the association between these two diseases.

Outcome of Japanese patients with cirrhosis due to nonalcoholic steatohepatitis (NASH) and hepatitis C. S Yatsuji, E Hashimoto, A Kabutake, et al. Dept Internal Med and Gastroenterol, Tokyo Women's Medical University, Tokyo, Japan

Background and aims. Ethnic differences in the prevalence and features of NASH are well-documented. But, there is no information on the outcome of Japanese NASH patients. In this study we compared the outcome of Japanese with liver cirrhosis due to NASH (LC-NASH) with that of those with LC associated to hepatitis C virus infection (LC-HCV). **Patients and methods.** We investigated the long-term morbidity and mortality of 48 patients with biopsy proven LC-NASH and 60 with biopsy proven LC-HCV who were not treated or did not respond to interferon. The end-points were survival, appearance of varices and HCC. Time to failure analysis (Kaplan-Meier) and log-rank analyses were used for across-group comparisons. The impact of baseline risk factors on survival and the development of specific complications were evaluated by logistic regression. Specific categorical features across different subsets were compared using χ^2 test. Mann-Whitney test was used for across-group comparisons of numerical data. The patients were monitored every 4-6 months clinically, biochemically and ultrasonographically. **Results.** LC-NASH group: the median age was 64 y.o. (18-89 y.o.). There were 27 women (56%); 12 patients (25%) had a BMI >30, 32 (67%) a BMI >25, and 29 (60%) had diabetes. Thirty four (71%) patients were in Child-Pugh class A. During follow up (median 32.5 months; range 0.8-199), 11 patients developed some disease. Three died from HCC and 3 from a liver unrelated cause. Five patients developed HCC, 5 esophageal varices, 5 ascites, and 4 developed hepatic encephalopathy. The 5-year survival rate was 83%, and the cumulative probability of developing HCC at 5 years was 11%. LC-HCV group: the median age was 58 y.o. (33-73 y.o.). There were 31 women (52%); 2 patients (3%) had a BMI >30, 20 (33%) a BMI >25, and 16 (27%) had diabetes. Forty-three (72%) patients were in Child-Pugh class A. During follow up (median 50.7 months; range 0.4-189), 19 patients developed some disease. Six died from HCC and 2 from a liver unrelated cause. Fifteen patients developed HCC, 17 esophageal varices, 15 ascites, and 8 developed hepatic encephalopathy. The 5-year survival rate was 79%, and the cumulative probability of developing HCC at 5 years was 20%. There were no significant differences between the two groups regarding any parameter. **Conclusions.** In this prospective study, we found no significant differences between LC-NASH and LC-HCV concerning morbidity, including HCC and mortality.

Hepatocellular carcinoma (HCC) in biopsy proven non-alcoholic steatohepatitis (NASH). AL Chagas, LO Kikuchi, DP Vezozzo, et al. Univ São Paulo Sch Med, São Paulo, Brazil, Gastro-enterol Hepatol, Univ of Virginia, Charlottesville, VA, USA

Background. Nonalcoholic steatohepatitis (NASH) is a well-recognized cause of cirrhosis and has been increasingly associated with hepatocellular carcinoma (HCC) most often arising in the late stage of NASH represented by cryptogenic cirrhosis. The aim of this study was to better characterize patients with HCC and active, histologically defined NASH. **Methods.** Between April 1998 and August 2006, among 408 patients with HCC detected at the time of ultrasound imaging, we identified 7 (1.7%) with HCC occurring in the setting of active biopsy proven NASH based on the presence of steatosis, ballooning degeneration and pericellular fibrosis. HCC was diagnosed based on at least two imaging techniques showing characteristic features in a focal hepatic lesion >2cm, with arterial hypervascularity. Six of seven HCC were confirmed histologically. All patients were negative for markers of viral hepatitis, Wilson's disease, hemochromatosis and autoimmune diseases and had current and past daily alcohol intake less than 100 g/week. **Results.** There were 4 males and 3 females with a mean age of 63±13.9. Overweight (BMI 25-29.9 kg m²) was present in 4 (57%) and obesity (BMI > 30) in 3 (43%). 57% were diabetic and 28.5% had dyslipidemia. Cirrhosis was present in 6 of 7 patients - one had HCC and NASH with fibrosis stage 1 and absence of cirrhosis based on liver biopsy. Among the cirrhotic patients, 71.4% were Child class A and 14.2% Child B. Lesions were evident by ultrasound in all patients. Tumor size ranged from 1.0 to 5.2 cm and 8 of 14 (57%) were <3cm. The majority of lesions (46%) were hyperechogenic by ultrasound. The HCC was well differentiated in 1/6 (16.6%), moderate differentiated in 5/6 (83.3%) and poorly differentiated in none. HCC had focal steatosis within the cancer and this appears to be associated with milder histological grades. AFP was < 100 in all patients. **Conclusion.** The association of NASH with HCC is not limited to patients with NASH-related 'cryptogenic' cirrhosis. We observed HCC in earlier stages of NASH including one patient without apparent cirrhosis. Cancer, in this setting, was often multifocal, preceded clinically advanced disease and occurred with non-diagnostic levels of alpha-fetoprotein. Further investigation of these relationships is warranted to determine relative risk and the possible need for more aggressive screening in NASH patients.

Orlistat (Xenical) in the treatment of overweight patients with nonalcoholic steatohepatitis (NASH): a multi-centered, randomized, prospective trial. SA Harrison, EM Brunt, WJ Fecht, BA Neuschwander-Tetri. Medicine, Brooke Army Med Center, Fort Sam Houston, TX, Saint Louis University, Saint Louis, MO, USA

Treatment options for NASH remain limited but evidence suggests that obese patients who are able to lose between 5-10% of body weight may have histopathologic improve-

ment. Orlistat, a reversible inhibitor of gastric and pancreatic lipase, is associated with modest weight loss and preliminary studies have demonstrated that orlistat is well tolerated and results in improvement in liver enzymes and liver pathology in patients with NASH. **Aims.** Determine if orlistat therapy and caloric restriction in overweight patients causes weight loss and improvement in the underlying steatosis, necroinflammatory and fibrotic changes of NASH. **Methods.** 50 overweight patients (BMI = 27) with NASH diagnosed by liver biopsy from two academic medical centers were enrolled. Patients were randomized to receive either orlistat 120mg po TID with meals and a 1400 Kcal/day diet plus vitamin E 800 IU daily or a 1400 Kcal/day diet and vitamin E 800 IU daily for 36 weeks. Vitamin E was included to avoid deficiencies associated with orlistat use. Patients using metformin or a thiazolidindione at the start of the trial were excluded. Biopsies were repeated at week 36. **Results.** 37 patients have completed the trial and all patients will complete the study by Jan 2007; 21 patients received orlistat/diet/vitamin E and 16 received diet/vitamin E alone. Mean age: 47.3±9.2 (SD), mean BMI: 36.3±6.5, mean weight: 225.7±42.5 lbs. The orlistat group lost a mean of 8.2% and the diet alone group lost 6% body weight. Both groups had similarly improved steatosis, necroinflammation, ballooning and NAFLD Activity Score (NAS). Comparing all patients losing ~ 9% of body weight (n=14), to those that did not (n=23), significant improvement in QUICKI (p=0.003), AST (p=0.02), adiponectin (p=0.03), steatosis (p=0.009), inflammation (p=0.02), and NAS (p=0.01) was seen but there was no difference in ballooning or fibrosis. Total serum PAI-1 decreased significantly in this group as well. Among patients losing ~5% of body weight (n=21), significant improvement in QUICKI (p=0.001), cholesterol (p=0.02) and steatosis (p=0.04) only. **Conclusions.** Patients losing ~ 5% of body weight over 9 months improved insulin resistance and steatosis, but only those patients losing ~ 9% achieved improvement in insulin resistance, steatosis, inflammation, and NAS. Xenical use did not enhance weight loss in this cohort, nor did it enhance outcomes in enzymes or histopathology.

Global gene expression profile analysis in NASH related cirrhosis. MS Kubrusly, Sandra VS, ML Correa-Giannella, D Giannella-Neto, T Bacchella, MCC Machado. Gastroenterology LIM37, Univ Sao Paulo, Endocrinology LIM25, Univ Sao Paulo, Sao Paulo, Brazil

Nonalcoholic steatohepatitis (NASH) is the progressive form of nonalcoholic fatty liver disease (NAFLD) that carries a risk for fibrosis, cirrhosis, and end-stage liver disease. The high-throughput gene expression technology provides simultaneous investigation of thousands of genes, showing a snapshot of the transcription state of diseased liver tissue. **Aim.** With a complete coverage of the liver transcriptome by microarray using normal liver tissue as controls (CTRL), we searched for differences in mRNA abundances between CTRL and NASH related cirrhosis. **Casuistic and method.** We obtained liver specimens from three patients with NASH

related cirrhosis diagnosis and three CTRL tissue samples from donor liver during transplantation procedure. Samples were evaluated for differentially expressed mRNAs by using CodeLink™ Human Whole Genome Bioarrays (GE Healthcare, USA). **Results.** Gene ontology (GO) analysis by GenMAPP software identified 778 statistically significant GO terms containing genes assigned to biological processes (92%), molecular function (5%) and cellular components (3%). Transcriptional levels of 444 annotated genes were changed in at least 2 fold with statistically significant ratio: 229 up-regulated in NASH related cirrhosis and 215 up-regulated in CTRL. A more detailed GO analysis were employed using GeneSifter microarray data software (VizX Labs LLC, Seattle, WA, USA; <http://www.genesifter.net>), based on KEGG public pathway resource. Ten statistically significant pathways were identified containing differentially expressed genes including biosynthesis of steroids, phosphatidylinositol signaling system, pyrimidine metabolism, mTOR signaling pathway, T cell receptor signaling pathway, epithelial cell signaling in Helicobacter pylori infection, ECM-receptor interaction, cytokine-cytokine receptor interaction, regulation of actin cytoskeleton, complement and coagulation cascade. **Conclusion.** This study reveals significant gene expression alterations in key biological pathways and provides potential insights into understanding the molecular mechanisms involved in the pathogenesis of NASH related cirrhosis.

Prevalence of fatty liver and associated morbidity in adults: results from coroner's cases in San Diego County. HM Patton, C Behling, A Unalp-Arida, FY Kim, C Stanley, JE Lavine. Univ of California, San Diego, CA, Pacific Rim Pathology, San Diego, CA, Johns Hopkins Sch Public Health, Baltimore, MD, San Diego County Medical Examiner's Office, San Diego, CA, USA

Background. Estimation of fatty liver prevalence is hindered by the impracticality of biopsy on a population basis. Previous autopsy studies have been conducted in hospital-based case series that were selected for obesity, thus making it difficult to extrapolate findings to the general population. The aim of this study was to evaluate the prevalence and risk factors for fatty liver among unselected coroner's cases. **Methods.** The study cohort consisted of 283 consecutive subjects with liver tissue available from autopsies performed by the San Diego County Medical Examiner's Office from January through March 2000. Autopsy records and investigative reports were reviewed to extract pertinent demographic and clinical data. The study pathologist (C.B.), masked to all clinical information, reviewed liver specimens for scoring of features of nonalcoholic steatohepatitis including steatosis [0 (<5% macrovesicular fat), 1 (5-33%), 2 (33-66%), 3 (>66%)], lobular inflammation (0-3), hepatocyte ballooning (0-2), and for staging of fibrosis (0-4). **Results.** The study population was predominantly Caucasian (72.8%) and male (72.4%) with a mean age of 48.1 years. Mean body mass index (BMI) was 27.2 kg/m² and mean abdominal fat layer was 3.4 cm. The

overall prevalence of steatosis was 137/283 (48.4%) with 146 grade 0 (51.6%), 87 grade 1 (30.7%), 23 grade 2 (8.1%) and 27 grade 3 (9.5%). The fibrosis stage was >1 in 47/264 (17.8%) with 22 (8.3%) having advanced fibrosis (stage 3-4). BMI >25 kg/m² [OR=3.73, 95% CI: 2.26-6.18] and abdominal fat layer >3.0 cm [OR=3.34, 95% CI: 2.04-5.45] were both associated with steatosis. Abdominal fat layer >3.0 cm was also associated with a NASH Activity Score (NAS)>4 [OR=4.87, 95% CI: 1.39-17.11]. Individuals with a NAS >4 were more likely than those with a NAS <4 to have died from cardiovascular causes or have a history of diabetes, hypertension, or dyslipidemia [OR=4.86, 95% CI: 1.10-21.48]. Individuals with steatosis [OR=2.87, 95% CI: 1.08-7.62] and individuals with fibrosis [OR=6.91, 95% CI: 2.74-17.43] were more likely to have had a death that was categorized as alcohol-related. **Conclusion.** Utilizing histological determinants, the prevalence of fatty liver (48%) in this cohort is much higher than previous estimates using serum transaminases as a surrogate. Central obesity and alcohol consumption are both associated with histological severity. NAS >4 was significantly more common among those who died due to cardiovascular disease suggesting that those with steatohepatitis may be at increased risk for adverse cardiovascular outcomes.

Gender-specific clinicopathological features in nonalcoholic steatohepatitis. M Tobari, E Hashimoto, A Kabutake, et al. Dept Internal Medicine Gastroenterology, Tokyo Women's Medical University, Tokyo, Japan

Background and aims. Nonalcoholic steatohepatitis (NASH) is strongly associated with obesity. In Japan, the prevalence of obesity shows a significant gender difference. Therefore, it is speculated that the clinicopathological features of NASH differ between men and women. The present study was performed to clarify the gender specific clinicopathological features of NASH. **Patients and methods.** Two hundred and twelve patients, who had at least one manifestation of metabolic syndrome, were diagnosed as having biopsy-proven NASH at Tokyo Women's Medical University from 1990 to 2006. Their clinical data were collected prospectively. Informed consent was obtained from each patient. NASH was diagnosed based on clinicopathological criteria: steatohepatitis on liver biopsy, intake of less than 100 g of ethanol per week, exclusion of other liver diseases. The patients were divided into four groups: premenopausal women, postmenopausal women, <50 y.o. men, and >50 y.o. men. These four groups were compared for clinicopathological features, development of hepatocellular carcinoma (HCC) and mortality. **Results.** There were 20 patients in premenopausal women, 77 patients in postmenopausal women, 73 patients in <50 y.o. men and 42 patients in >50 y.o. men. The number of patients was the smallest in the group of premenopausal women (p<0.01). Concerning obesity, its prevalence was significantly higher in premenopausal women and <50 y.o. men (p=0.05). Regarding metabolic syndrome, the prevalence of diabetes mellitus (DM) and hypertension was significantly higher in

postmenopausal women (p=0.04, p=0.03, respectively). Histologically, the prevalence of severe grade was high in premenopausal women and <50 y.o. men. On the contrary, that of advanced fibrosis was high in postmenopausal women and >50 y.o. men (p=0.01). Five patients in postmenopausal women and seven patients in >50 y.o. men were diagnosed HCC and NASH simultaneously. Three patients in postmenopausal women and three patients in >50 y.o. men developed HCC during the follow-up period. Three patients in postmenopausal women and 4 patients in >50 y.o. men died (cirrhosis; 3, HCC; 4). Significant differences were seen between pre- and postmenopausal women in the prevalence of obesity (p=0.05), hypertension (p=0.002) and advanced fibrosis (p=0.02). **Conclusions.** According to our study, several gender-specific differences were detected among NASH patients. DM and hypertension were more common in postmenopausal women, and the risk factors for NASH in females were different before and after menopause. These facts may be important for prevention and treatment of NASH.

Usefulness of contrast-enhanced endoscopic ultrasonography for the initial diagnosis and long-term follow-up of intraductal papillary mucinous neoplasms of the pancreas. E Ohno, Y Hirooka, A Itoh, et al. Gastroenterology, Nagoya Univ Sch Med, Endoscopy, Nagoya University Hospital, Nagoya, Japan

Background. Intraductal papillary mucinous neoplasms of the pancreas (IPMNs) vary from hyperplasia to invasive cancer pathologically, and the timing to treat surgically remains difficult in clinical settings. Endoscopic ultrasonography (EUS) is one of the most reliable diagnostic modalities to diagnose IPMNs. As already reported, contrast-enhanced EUS (CE-EUS) reveals the characteristic vascularity of pancreatic diseases including IPMNs. The purpose of this retrospective study is to verify our diagnostic strategy and to elucidate the natural course of long-term followed cases. **Patients and methods.** Two hundred twenty-six patients with IPMNs were examined by CE-EUS as the initial study since January, 2001. Our indications for resection were as follows: the case of main-duct type, existence of mural nodule with blood flow signal in CE-EUS (regardless of the nodule size) and coexistence of ductal cancer cases. Target lesions were observed by EUS, then, the contrast agent (Levovist; Schering, Japan) was adjusted to 300mg/ml in concentration, and was injected intravenously at a rate of 1ml/sec, and enhancement effect was estimated. The endoscopes used was EG-3630UR (Pentax) and ultrasound systems were EUB-6000,8500 (Hitachi). As to the follow-up cases (patient refusal of operation, mural nodule lacking color signals and under our operative indications, and so on.), EUS and/or CT was performed every 6 months. We investigated the pathological diagnosis of surgically removed cases according to our operative indications, and assessed the clinical course of follow-up cases. **Results.** Fifty seven patients (21.4%, 57/266) were resected (main-duct type, 13; branch-duct type,

44). Nine far advanced cases were inoperable. There were 25 with adenoma, 18 with carcinoma in situ, 11 with invasive carcinoma derived from IPMN and 3 with coexistence of pancreatic ductal cancer and there was no hyperplasia case. Mural nodule with enhanced effect by CE-EUS was regarded as the presence of nodule with atypical epithelium indicating precise malignant indicator. One hundred seventy patients had been followed. Ten cases (6.2%, 10/170) out of follow-up cases were resected. Median follow-up term was 16months (5-58months). The criteria or sign to resect of those cases were nodule enlargement with increased color signals (9 cases), furthermore, appearance of color signals of septum in 6 cases. **Conclusion.** Our diagnostic strategy was appropriate because there were no hyperplasia cases pathologically. As to follow-up study cases, the nodule enlargement and increased blood flow in the lesions may be a useful indicator to determine the timing of surgical treatment.

Evaluation of small intestinal bacterial overgrowth in nonalcoholic steatohepatitis by jejunal aspirate and quantitative culture. SB Chalamalasetty, U Ghoshal, UC Ghoshal, G Alexander, A Misra, G Choudhuri. Dept Gastroenterology, Dept Microbiology, Sanjay Gandhi Post Graduate Inst Med Sciences, Lucknow, India

Background. Pathogenesis of non-alcoholic steatohepatitis (NASH) is still unclear. NASH in jejuno-ileal bypass surgery seems to be associated with small intestinal bacterial overgrowth (SIBO). A single human study using breath tests has shown increased prevalence of SIBO in patients with NASH. We did this study to evaluate frequency of SIBO in NASH using quantitative culture of jejunal aspirate (currently the gold standard method) and hydrogen breath tests. **Methods.** NASH was diagnosed based on presence of fatty liver on ultrasonography and alanine amino-

transferase (ALT) 1.5 times above upper limit of normal for a period of more than 6 months. Other causes of chronic hepatitis have been excluded by viral and autoimmune markers, copper and iron studies. Historical controls with no clinical evidence of fatty liver were taken as controls. Jejunal aspirate was collected using a standard technique, with a catheter assembly during esophago-gastroduodenoscopy, was cultured for aerobic and anaerobic bacteria and colony count was determined using serial dilution technique. Glucose and lactulose hydrogen breath tests (GHBT and LHBT) were also performed in a subset of patients. SIBO was diagnosed if aspirate grew >105 colony forming unit/ml (CFU/ml) of bacteria in the aspirate or breath H₂ rise > 14 ppm on GHBT. **Results.** Jejunal aspirate could be obtained in 35 of 38 patients with NASH. Culture was sterile in 14 (40%) and bacteria were isolated in 21 (60%), one of whom also grew anaerobes. In contrast, bacteria were isolated in 3/12 historical controls (25%) (p=ns). The median colony counts in patients whose culture was positive was 103-105 CFU/ml. SIBO was present in 7/35 (20%) patients with NASH (5 by jejunal aspirate culture and 2 on GHBT) in contrast to none of the controls (p=ns). On culture of the aspirate in patients with SIBO, 2 patients had 2 types of organisms and 3 had one organism isolated. The various organisms grown in SIBO were Streptococcus in 2, Acinetobacter baumannii in 2, Enterococcus fecalis, Enterobacter aerogenes and Proteus mirabilis in one each. On comparison of patients with and without SIBO, no significant difference in their age, anthropometric measurements or ALT was found. **Conclusion.** Small intestinal bacterial overgrowth as diagnosed using quantitative jejunal aspirate culture is uncommon in patients with NASH. Therefore, it is unlikely to play major role in pathogenesis of this disorder.

Ofelia Mosteanu
Cluj-Napoca