INNOVATIONS IN NAFLD CARE 2022

HYBRID WORKSHOP

6-7 May 2022 | BARCELONA, SPAIN

Programbook

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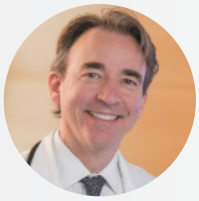

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Abstracts
Accepted abstracts are published in this program book.

Certificate of Attendance
Certificates of attendance will be sent by e-mail after completion of the post-meeting survey.

Feedback
Your feedback is very valuable to us and enables us to further improve this workshop. After each day a survey will be sent to you via email and we would like to ask you to complete it.

Networking
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Make use of the options to network during the coffee breaks and lunch.

Virtually
The Meeting Hub allows you to connect and communicate with other attendees. Once you have located an attendee you want to connect with, click the Connect button. Once the other attendee accepts your request, you can choose to interact by starting a live chat or live video call. You can also schedule a meeting at a later time, send messages and take notes. Contact information for all attendees you have connected with will be included when you export contacts.

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Webcasts of the presentations along with the PDF presentations will be available on **www.AcademicMedicalEducation.com** 3 weeks after the workshop. You will be able to watch the presentations on the virtual portal until 3 weeks after the workshop.

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We encourage you to post news and tweet about #NAFLDCare to your social media accounts as often as you like during the workshop.
You can either post your own tweets to your followers using the hashtag #NAFLDCare or retweet a message through the official @Academic_MedEdu.

Time Zones
Times are in Central European Summer Time. If you need to convert the times to your timezone, this website might be of interest to you:
www.worldtimebuddy.com

Venue
The Innovations in NAFLD Care Workshop 2022 will be held in the Sercotel Caspe Hotel in Barcelona, Spain. To attend in person, you must have an "in-person registration".

Virtual Platform
OnAIR is the virtual platform being used for the Innovations in NAFLD Care Workshop 2022 for those attending virtually. A video tutorial on how to use the portal can be found here.

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Friday, 6 May 2022

Central European Summer Time (CEST)

Session 1	**NAFLD - Epidemiology and Disease Burden; Measuring a Silent Condition** *Session Chairs: Jeffrey Lazarus & Alina Allen*
13:40	**Opening of the Workshop** **Jeffrey Lazarus, PhD, MIH, MA** Barcelona Institute for Global Health (ISGlobal), Spain **Jörn Schattenberg, MD** Johannes Gutenberg-Universität Mainz, Germany
13:50	**Is NASH/NAFLD a Public Health Challenge in 2022?** **Zobair M. Younossi, MD, MPH, FACG, FACP, AGAF, FAASLD** Inova Health System, United States
14:15	**The Liver-Heart Axis – Does NASH Drive Cardiovascular Disease?** **Sven Francque, MD, PhD** Antwerp University Hospital, University of Antwerp, Belgium
14:40	**Fatal Triple – Linking Obesity, Type-2 Diabetes, and NASH** **Cyrielle Caussy, MD, PhD** Lyon University and Lyon South Hospital, France
15:05	**Discussion**
15:25	Break & Networking
Session 2	**Screening and Risk-Stratifying for NAFLD – Who and Where?** *Session Chairs: Kenneth Cusi & Helen Jarvis*
15:55	**Opening of the Session**
16:00	**Clinical Care Pathways for the Risk Stratification of Patients** **Emmanuel Tsochatzis, MD, MSc, FEBTM, FRCP, PhD** Royal Free Hospital, United Kingdom
16:25	**Use of Intelligent Liver Function Testing in General Practice** **John Dillon, MB, BS, MD** University of Dundee / Ninewells Hospital and Medical School, United Kingdom
16:50	**Why and How to Identify NALFD in Primary Care?** **Jean Muris, MD, PhD** Maastricht University, The Netherlands
17:15	**Discussion**
17:35	Break & Networking
Session 3	**How to Manage Patients with NAFLD in Different Healthcare Facilities** *Session Chairs: John Dillon & Emmanuel Tsochatzis*
17:55	**Opening of the Session**
18:00	**The Central Role of Primary Care in the NASH Epidemic: Opportunities and Challenges** **Helen Jarvis, MD** Newcastle University, United Kingdom
18:25	**Nutritionists Perspective: Lifestyle and Behavioral Structured Interventions** **Shira Zelber-Sagi, BSc, RD, PhD** University of Haifa / The Tel-Aviv Medical Center, Israel
18:50	**Pushing for Weight Management: Bariatric Interventions Benefits and Considerations** **Jörn Schattenberg, MD** Johannes Gutenberg-Universität Mainz, Germany
19:15	**Discussion**

Friday, 6 May 2022

Central European Summer Time (CEST)

	Closing
19:35	**Closing of Day 1** **Jeffrey Lazarus, PhD, MIH, MA** Barcelona Institute for Global Health (ISGlobal), Spain **Jörn Schattenberg, MD** Johannes Gutenberg-Universität Mainz, Germany

Saturday, 7 May 2022

Central European Summer Time (CEST)

	Patient Organization Session *Session Chair: Jörn Schattenberg*
09:00	**Opening of the Session**
09.05	**Roundtable Discussion: the NAFLD Continuum of Care** **Achim Kautz** Kautz[5] gUG, Germany **Fernando García Pérez** FNETH, Spain **Donna R. Cryer, JD** Global Liver Institute, United States **José Willemse, MSc** Dutch Liver Patients Association, the Netherlands
09:45	Break & Networking
Session 4	**Multidisciplinary Management of NAFLD – How to Manage Our Patients Today?** *Session Chairs: Jörn Schattenberg & Shira Zelber-Sagi*
10:15	**Opening of the Session**
10:20	**The Road to Comprehensive Models of Care for NAFLD - What Are the Endpoints?** **Jeffrey Lazarus, PhD, MIH, MA** Barcelona Institute for Global Health (ISGlobal), Spain
10:45	**Integrating Non-Invasive Tests for NAFLD in Clinical Practice Outside the Liver Space - Which Test and at What Level?** **Alina Allen, MD** Mayo Clinic Rochester, United States
11:10	**Using the Power of Digital Innovation - Apps Transforming Weight Management** **Marcus Ranney, MD** Human Edge, India
11:35	**Discussion**
12:05	Break & Networking
	Industry Session *Session Chairs: Jörn Schattenberg & Jeffrey Lazarus*
12:30	**Opening of the Session**

Saturday, 7 May 2022

Central European Summer Time (CEST)

12:35	**Roundtable Discussion: Industry Developments Advancing Comprehensive Care Models for NAFLD** **Peter Rydqvist, MSc, MPharm** Madrigal Pharmaceuticals, Sweden **Laurent Sandrin, PhD** Echosens, France **Ahsan Shoeb, MBBS, MD, DPMM** Novo Nordisk A/S, Denmark
13:15	Lunch Break
Session 5	**Future Pharmacotherapeutics for NASH - Defining Mechanisms, Drug Safety, and Efficacy** *Session Chairs: Sven Francque & Cyrielle Caussy*
14:15	**Opening of the Session**
14:20	**Pharmacotherapy for Obesity - Improving Body Weight and NAFLD** **Naim Alkhouri, MD** Arizona Liver Health, United States
14:45	**How to Use Diabetes Drugs for Liver Benefit in Patients with NAFLD** **Kenneth Cusi, MD, FACP, FACE** The University of Florida, United States
15:10	**Liver-Directed Drugs in the Pipeline for Fibrotic NASH** **Stephen Harrison, M.D, FACP, FAASLD Col (ret.)** University of Oxford / Pinnacle Clinical Research / Summit Clinical Research, United Kingdom / United States
15:35	**Discussion**
15:55	Break & Networking
Session 6	**Round Table Discussion on the Public Health Roadmap to Comprehensive Care for NAFLD/ NASH** *Session Chairs: Jörn Schattenberg & Jeffrey Lazarus*
16:20	**Opening of the Session**
16:25	**Exchanging and Sharing Ideas on the NAFLD/NASH Roadmap Including Social Media and Digital Transformation of Health Care** **Roger Green, MBA** *(moderator)* SurfingNASH / HEP Dynamics, United States **Kenneth Cusi, MD, FACP, FACE** The University of Florida, United States **Marcus Ranney, MD** Human Edge, India **Shira Zelber-Sagi, BSc, RD, PhD** University of Haifa / The Tel-Aviv Medical Center, Israel
	Closing
17:10	**Closing Words** **Jeffrey Lazarus, PhD, MIH, MA** Barcelona Institute for Global Health (ISGlobal), Spain **Jörn Schattenberg, MD** Johannes Gutenberg-Universität Mainz, Germany
17:20	End of the Workshop

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Driving the Discussion in Fatty Liver Disease

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EATAN European African Treatment Advocates Network

Erasmus MC Universitair Medisch Centrum Rotterdam

GHASSA Gastroenterology & Hepatology Association of Sub Saharan Africa

GISH

GLI Global Liver Institute

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1

Prevalence of Liver Fibrosis is More Common in Endocrinology Clinics than in Primary Care or Family Medicine Setting: Implications for Patient Care

Godinez Leiva E1, Lomonaco R1, Shrestha S1, Rodrigues Silva-Sombra L1, Mansour L1, Shetty S1, Kalavalapalli S1, Dillard R1, Marangi S1, Gonzalez M1, Valdez Saenz E1, Barb D1, Cusi K1
1University Of Florida, Gainesville, United States

Background: In 2019, the ADA recommended screening for NASH and liver fibrosis patients with T2DM and steatosis or elevated plasma aminotransferases (AST and/or ALT). However, most patients with diabetes are believed to not have elevated plasma aminotransferases. As the true prevalence of liver steatosis and fibrosis in unselected patients with T2DM in the United States is uncertain, the aim of this study was to examine their prevalence in the outpatient setting of a tertiary academic medical center.

Materials and methods: We screened patients with T2DM attending either endocrinology (E), internal medicine (IM) or family medicine (FM) outpatient university clinics, where patients and their physicians were unaware of having NAFLD. Screening for fibrosis (1º outcome) was performed by vibration-controlled transient elastography (VCTE), and for steatosis by controlled attenuation parameter (CAP) (2º outcome). We also measured routine chemistries and diagnostic panels of fibrosis (APRI and FIB-4).

Results: A total of 586 patients (E: 174; IM: 129; FM: 283) were recruited (age: 60±12; 55% females; 57% non-Hispanic whites, 29% African Americans, 5% Asian; BMI: 33±6 kg/m2; A1c: 7.5±1.7%; AST: 21±10 U/L; ALT: 23±16 U/L). Patients in the 3 settings were matched for major clinical characteristics. Overall, only 10% of patients had an AST or ALT ≥40 IU/L. In 80% patients with clinically significant liver fibrosis (≥F2) AST or ALT were ≤40 IU/L. The prevalence of NAFLD (CAP: ≥274 dB/m) was similar among clinical settings (E: 74%, IM: 71%, FM: 65%, NS). In contrast, the prevalence of clinically significant fibrosis (LSM ≥8.0 kPa or ≥F2) was higher in E: 19% compared to IM and FM, 8% and 11%, respectively (both $p<0.05$). Based on LSM, patients with stage F3-4 were almost 2- to 4-fold higher in E (11%) vs. IM (3%) or FM (6%) clinics. An AST cutoff of >40 IU/L had low sensitivity to identify patients with LSM ≥8.0 kPa (E: 4%; IM: 2%; FM: 1%), improved if >30 IU/L (E: 6%; IM: 3%; FM: 2%), but still missed most patients (~80%). Mean FIB-4 among those without fibrosis (LSM <7.0 kPa) was 1.18±0.52 versus ≥F2: 1.33±0.58. APRI was 0.22±0.10 and 0.34±0.20 in the group with LSM ≥8.0 kPa, confirming the low sensitivity and PPV of both tests. Glycemic control (A1c) was not correlated with the presence or not of steatosis or fibrosis. However, among patients in endocrine clinics, duration of diabetes (>10 vs. <10 years) was associated with steatosis (61% vs. 39%; $p<0.05$) and with a doubling in the prevalence of clinically significant fibrosis (41% vs. 16%; $p<0.01$). Obesity (BMI) correlated with steatosis ($r = 0.44$; $p<0.001$) and with clinically significant fibrosis ($r = 0.23$; $p<0.05$), but not with glycemic control (A1c).

Conclusion: There is a high prevalence of undiagnosed NAFLD and of clinically significant fibrosis in patients with T2DM, which may warrant implementation of systematic screening. Endocrinologists must be aware that they concentrate patients at the highest risk in their outpatient clinics, and have the opportunity to prevent cirrhosis in a large number of people.

2

External Validation of a Clinical Care Pathway to Risk Stratify Patients with NAFLD and Determine if Hepatology Referral Is Warranted

Leff P2, Polanco P1, Kundu R1, Raman A1, Garg P1, Choudhri S1, Chatha Y1, Kahlon N1, Patel S1, Kolli N1, Lantz K1, Ahmed R1, Gupta J1, Dharia A1, Kohli A1, Alkhouri N1
1Arizona Liver Health, Chandler, United States, 2Des Moines University College of Osteopathic Medicine, Des Moines, United States

Background: As NAFLD and NASH continue to increase globally, more straight forward algorithms are needed to help primary care and endocrine specialist manage these patients. A NAFLD clinical care pathway was recently proposed by a multiple-disciplinary task force from the American College of Gastroenterology (AGA) to help primary care physicians screen patients at risk for fibrotic NASH (NASH with significant fibrosis F2-F4) to determine if secondary care to a hepatologist is needed. We aimed to externally validate the performance of this pathway using liver histology as the gold standard.

Methods: Consecutive patients seen at a tertiary care center for suspected NAFLD were included. NASH, NAS, and fibrosis stage were assessed using the Kleiner's histology score. Liver stiffness measurement was based on vibration-controlled transient elastography (VCTE). VCTE probe sizes were chosen based on automated recommendations. Liver biopsies were conducted within 6 months of laboratory tests and VCTE. Risk stratification was determined based on the publication by the AGA. Metabolic risk factors, alcohol intake, CBC, and liver function tests were determined based on chart review. FIB-4 was calculated based on age, AST, ALT, and platelet count.

Results: 333 patients were included. The mean age was 57.45 years and 243 (72.97%) were female. 192 (57.66%) had diabetes mellitus, 134 (40.24%) had dyslipidemia, 187 (56.16%) patients had hypertension. 100 (30.03%) had F0-F1, 233 (69.97%) with F2-F4. 6 (1.80%) patients were excluded due to the presence of other etiologies of chronic liver disease. 327 (98.20%) patients were evaluated using FIB-4 and VCTE based on the AGA pathway. 133 (40.67%) patients had FIB-4 <1.3, 66 (49.62%) had F0-F1, 67 (50.38%) had F2-F4. FIB-4 >2.67 was present in 61 (18.65%) patients where 5 (8.20%) had F0-F1 and 56 (91.80%) had F2-F4. 133 (40.67%) patients had FIB-4 =1.3-2.67 (Indeterminate) requiring further assessment with VCTE. Out of these patients, 34 had VCTE < 8 kPa (including 9 with F2-F4). A total of 76 (23.2%) patients that will be considered as low risk based on the AGA pathway had significant fibrosis (F2-F4) and would have been missed.

Conclusion: Although the AGA clinical care pathway algorithm provides as a good first step in screening patients who are at risk of having significant fibrosis (F2-F4), almost one quarter of patients with significant fibrosis on liver biopsy would have been missed. The main limitation of this study is the high prevalence of F2-F4 in our cohort given the fact that these patients were seen in hepatology practice and had liver biopsy done.

3

Biomarkers, Imaging and Safety in Resmetirom 52 Week Non-Cirrhotic NASH Phase 3 Clinical Trial, Completed Open-Label Arm of Maestro-NAFLD-1

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1Radcliffe Department of Medicine, University of Oxford; , Oxford, United Kingdom, 2Duke University, Durham, United States, 3Madrigal Pharmaceuticals, West Conshohocken, United States, 4Covenant Research and Clinic, LLC, Fort Myers, United States, 5Arizona Liver Health, Chandler, United States

Background: MAESTRO-NASH NCT03900429 and MAESTRO-NAFLD-1 NCT04197479 are 52-week Phase 3 registrational double-blind placebo controlled clinical trials to study the effect of resmetirom, a selective thyroid receptor beta agonist in more than 2000 NASH patients. A goal of MAESTRO-NAFLD-1, a 1200 patient "real life" NASH study is to identify non-invasive markers that correlate with patient response to resmetirom treatment. The 171 patient 100 mg open label (OL) arm completed the 52-week study in July 2021.

Methods: Eligibility required at least 3 metabolic risk factors (Metabolic syndrome), fibroscan kilopascals (kPa) consistent with ≥F1 fibrosis stage, and MRI-PDFF≥8%. The primary and key secondary endpoints of MAESTRO-NAFLD-1 including safety, relative percent reduction of MRI-PDFF (week 16), LDL cholesterol (LDL-C) (week 24), Apolipoprotein B and triglycerides, fibroscan and 52-week endpoints were analyzed in the OL arm.

Results: Mean age was 55.6 (11.5 (SD)), female 69%, BMI 36.1 (6.3), diabetes 48%, hypertension 68%, dyslipidemia >70%, ASCVD score 11.6%; fibroscan (kPa 7.7 (3.3)), and MRI-PDFF 17.8% (7%). Statistically significant (p<0.0001) reduction of MRI-PDFF -53% (3.3% (SE)) overall, and in several subgroups were observed at week 52 (figure). Liver volume (LV) was elevated at baseline (2202 cm (535)) by ~50% relative to normal controls and ~15% after correction for BMI (Euro J of Radiol 106, 2018, 32–37). Resmetirom reduced LV-21% (1.0%), -23% (1.0%) respectively, at weeks 16 and 52 (p<0.0001), in all demographic groups (figure). LV reduction was greater than predicted by % reduction in MRI-PDFF, a measure of liver fat content (Clin Gastroenterol Hepatol. 2015 13: 561–568); LV-corrected mean MRI-PDFF reduction at Week 52 was -61% (2.4%). Weight loss ≥5% occurred in ~21% and was linked to resmetirom exposure (SHBG). At week 52, MRE (-0.34, p=0.03); fibroscan CAP (-39(4.6)) and VCTE (-1.87; -20%) (p<0.0001) were reduced relative to baseline. LDL-C (-21% (1.9%)), apolipoprotein-B (-22% (1.6%)) and triglycerides (-22% (2.6)) were statistically significantly reduced (p<0.0001). Decreases from baseline in liver enzymes were ALT -20 IU, AST -11 IU, GGT -25 IU (p<0.0001). Significant reductions in inflammatory and fibrosis biomarkers, reverse T3, ELF, and M30 and an increase in adiponectin were observed. No safety flags were identified; BP (systolic, diastolic) was reduced by ~2-4 mmHg, (p=0.02); bone mineral density (DEXA) was unchanged at 52 weeks.

Conclusion: In this 52-week Phase 3 OL study, noninvasively identified NASH patients treated with 100 mg per day of resmetirom for up to 52 weeks demonstrated rapid and sustained reduction in 1) hepatic fat and liver volume 2) fibrosis as assessed by biomarkers, MRE and fibroscan; 3) LDL and atherogenic lipids, 4) liver enzymes and inflammatory biomarkers, providing support for the use of non-invasive tests to monitor individual NASH patient response to resmetirom treatment.

4

Lean patients with NAFLD have lesser metabolic risk factors but similar liver disease severity as non-lean patients with NAFLD

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1Department of Hepatology, Post Graduate Institute of Medical Education and Research, Chandigarh, India

Background: Non-alcoholic fatty liver disease (NAFLD) has emerged as a major cause of chronic liver disease globally. While majority of patients with NAFLD are overweight or obese, around 10-20% patients are lean with a normal body mass index (BMI). The objective of the study was to assess the differences in the clinicopathological profile and liver disease severity among lean and non-lean patients with NAFLD.

Methodology: We reviewed the records of 1040 Indian patients with NAFLD [age: 40.9± 11.34 years, 604 (58%) males] managed prospectively in a real-life fashion in the last 10 years. Asian BMI cut-offs were used for categorizing lean (<23kg/m2) and non-lean (overweight: 23-24.9 kg/m2 and obese: ≥25 kg/m2). Metabolic syndrome risk factors were defined as per the NCEP-ATP III criteria with Asian cut-offs for abdominal obesity (males ≥90 cm, females ≥80 cm). Significant elevations in transaminases were defined as >2 × ULN. Non-invasive assessment of fibrosis was done using FIB-4 with a cut-off of <1.3 being used for ruling-out advanced fibrosis. Histology was reported using the NASH-CRN system and non-alcoholic steatohepatitis (NASH) was defined as NAFLD activity score (NAS) ≥ 5. Significant and advanced fibrosis were defined as ≥F2 and ≥F3, respectively.

Results: One hundred and forty-nine (14.3%) patients were lean while 891 (85.7%) patients were non-lean [overweight: 194 (18.6%), obese: 697 (67%). Age of lean and non-lean patients were similar [38.5± 12 years vs 41.46 ± 11.1 years, p=0.96]. Type 2 diabetes mellitus [25 (16.7%) vs 152 (17.05%), p>0.99], elevated triglycerides [81 (54.3%) vs 525 (58.9%), p=0.33] and low HDL [71(47.6%) vs 479(53.7%), p=0.18] were observed in a similar proportion of lean and non-lean patients with NAFLD. However, patients with lean NAFLD were less likely to have central obesity [72 (48.3%) vs 788 (88.4%), p<0.001], hypertension [6 (4.02%) vs 239(26.8%), p<0.001], and metabolic syndrome [21 (14.09%) vs 290 (32.5%), p<0.001] compared to non-lean patients. Significant elevations in AST [29 (19.4%) vs 170 (19.04%), p=0.9] and ALT [57 (38.2%) vs 350 (39.2%), p=0.85] were observed in a similar proportion of lean and non-lean patients. FIB-4 scores were similar in lean (1.49 ± 1.27) and non-lean patients (1.5 ± 1.3, p=0.9) and advanced fibrosis was ruled-out in 87 (58.3%) lean patients compared to 516 (57.9%, p=0.92) non-lean patients.
Liver biopsy data was available in 149 patients [lean: 19 (12.7%), non-lean: 130 (87.3%)]. There was no difference in mean NAS [3.26 ± 1.54 vs 3.47 ± 1.26, p=0.87) or the proportion of patients with definite NASH [4 (21.05%) vs 20 (15.3%), p=0.51] among lean and non-lean patients. Further, the proportion of patients with significant [2 (10.5%) vs 32 (24.6%), p=0.25] and advanced [1 (5.26%) vs 18 (13.84%), p=0.47] fibrosis was similar between lean and non-lean patients with NAFLD.

Conclusion: Lean patients with NAFLD are less likely to have abdominal obesity, hypertension and metabolic syndrome compared to their non-lean counterparts. However, there is no difference in biochemical parameters, non-invasive assessment of fibrosis and the histologic presence of NASH and significant or advanced fibrosis among lean and non-lean patients with NAFLD.

5

Type 2 Diabetes and Abdominal Obesity Are Risk Factors for Liver Fibrosis Progression in Subjects With NAFLD: A Population Based-Study

Pérez A1, Julián M1, Pera G2, Ballesta S1, Caballeria L2, Cusi K3, Genua I4, Mauricio D4, Alonso N1
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Objective: To investigate the longitudinal changes in the liver stiffness measurement (LSM) in the general adult population without known liver disease and to describe its association metabolic risk factors, with special focus on subjects with NALFD and T2D.

Design and methods: A longitudinal adult population-based cohort study was conducted in Catalonia. LSM was measured by transient elastography (TE) at baseline and follow-up (mean: 4.2 years). Subjects with a current history of liver disease, including cholestasis, hepatitis C or B virus infection, and high-risk alcohol consumption were excluded from the study. Subgroups with non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes (T2D) were also analyzed. Moderate and advanced liver fibrosis was defined as LSM ≥ 8.0 kPa and ≥ 9.2 kPa, respectively. These cut-offs have been shown to predict significant liver fibrosis in large populations of subjects.

Results: Among 1,478 subjects, the median LSM value was 4.8 ± 2.2 kPa at baseline and 4.9 ± 2.0 kPa at the follow-up. The cumulative incidence of LSM ≥8.0 kPa and ≥ 9.2 kPa at follow-up was 2.8% and 1.9%, respectively. The multivariate analyses showed that T2D and abdominal obesity were significantly associated with progression to moderate-to-advanced liver fibrosis, in the whole cohort as well as in subjects with baseline NAFLD. Female sex was negatively associated with progression. In subjects with T2D, abdominal obesity was associated with increase in LSM over time. On the other hand, a decline in LSM value < 8 kPa was observed in 66% of subjects with baseline LSM ≥ 8.0 kPa. Also, change in LSM value from ≥ 9.2 kPa to < 9 kPa was observed in 62% of the cohort.

Conclusions: In this prospective cohort study, minimal changes in baseline LSM value were observed at follow-up in subjects without previously known liver disease. In NAFLD subjects, type 2 diabetes and abdominal obesity were associated with moderate-to-advanced liver fibrosis development over time. The optimization of these associated metabolic risk factors may have contributed to regression in LSM.

6

The Effect of Saroglitazar Along With Lifestyle Advice vs. Only Lifestyle Advice in the Management of NAFLD/NASH: A 24 Week Retrospective, Real World Experience

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Background and Aims: Non-alcoholic fatty liver disease (NAFLD) is emerging as a global pandemic and the most prominent forms of chronic liver disease (CLD) lead to end-stage liver disease. Lifestyle changes are the cornerstone in the management of NAFLD, but poor patient compliance to healthy lifestyle changes is the major practical hurdle in real-life settings. The study was done to analyze the effect of only Lifestyle advice compared with lifestyle advice along with standard therapy (Saroglitazar 4mg OD, the only approved therapy for NAFLD/NASH by DCGI), in routine clinical practice on NAFLD/ NASH patients.

Methods: A total of 58 documented fatty liver patients (Males 57.4%) (mean age 46.6 ± 13.3 years and weight 70.2 +10.6 kg) with baseline Fibroscan™ imaging for both CAP and LSM parameters are categorized into two groups (Group A & B), based on the disease severity, associated co-morbid conditions, and best suitable clinical judgments. The majority of patients were non-diabetic (73.8%) and Non-Hypertensive (88.5%). One group was only advised with standard dietary and lifestyle changes (Group A, n=25) and the other group was prescribed standard pharmacotherapy as Saroglitazar 4 mg OD along with dietary and lifestyle advice (Group B, n=33). The baseline median values with range for CAP in dB/m and LSM in KPa, in Group A, was 260 (145 - 383) and 4.4 (3.2 - 12.4) and in Group B was 280 (202 - 386) and 9.2 (4.0 - 35.4), respectively. Repeat Fibroscan™ imaging was done at the follow-up after 24 weeks, and the improvement in steatosis and fibrosis was measured as percentage changes in corresponding mean values. The data were analyzed and statistical significance for improvements in CAP and LSM, in each group was established using paired sample T-test.

Results: The study shows the highly significant ($p<0.001$) decrease in LSM by 20.1%, with mean ± SD changes (from 12.2 ± 7.7 to 9.7 ± 5.1 KPa), and in CAP by 9.83% (from 282.0 ± 43.5 to 254.3 ± 31.9 dB/m), from baseline in Group B, which was prescribed with both Saroglitazar 4mg OD along with dietary and lifestyle changes. Group A, which was only advised with dietary and lifestyle changes has shown an increase in both LSM and CAP by 4.8%, with mean ± SD changes (from 5.2 ± 2.0 to 5.5 ± 1.6 KPa) and 3.7% (from 261.8 ± 57.1 to 271.6 ± 45.7 dB/m) respectively, after 24 weeks. There were no treatment-related side effects among the study population.

Conclusions: The study shows that Saroglitazar 4mg OD along with Lifestyle changes are much more efficacious strategies than only lifestyle advice. Also, in the study, Saroglitazar was found extremely safe and effective treatment option for NAFLD/NASH. More studies and well-designed double-arm clinical trials will warrant more emphasis on this outcome.

7

Perceptions and Awareness About the Non-alcoholic Fatty Liver Disease (NAFLD) Among Patients With NAFLD

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Background: Globally, 25% of population is estimated to have underlying non-alcoholic fatty liver disease (NAFLD). Sedentary lifestyle, easier access to high caloric food and the ongoing pandemics of Type 2 diabetes mellitus and obesity is expected to catapult NAFLD into a substantial public health problem. Assessment of the perception and knowledge of the disease among patients with NAFLD is urgently needed to better design public health initiatives.

Aim: To assess the perceptions and awareness regarding NAFLD among Indian patients with NAFLD.

Methods: In this ongoing cross-sectional survey, all patients with NAFLD attending the Liver Clinic or tele hepatology services of our institute from Sep 2021 onwards are being interviewed using a pre-specified questionnaire about their perceptions and awareness of NAFLD, its risk factors, complications, and management.

Results: Of 106 participants interviewed so far [mean age 47.5±12.6 years] majority [64 (60.4%)] were men. The majority of patients were graduates [n=48.9 (46.2%)] or post-graduates [n=15(14.2%)] and belonged to the upper-middle and lower-middle economic classes [n=75 (70.8%) and n=27 (25.5%) respectively]. All patients were aware that they had fatty liver disease (100%) and 79 (74.5%) patients were aware about the terminology of NAFLD. None of the patients however were aware of the term MAFLD (metabolic-dysfunction associated fatty liver disease). All patients opined that the nomenclature of NAFLD or MAFLD was of no significance to them. Only 18 (17%)] patients were aware of the full form of non-alcoholic steatohepatitis (NASH) and that it was a severe form of NAFLD. All patients were aware that NAFLD is not a contagious disease (100%). None of the patients were bothered about the prefix 'non-alcoholic' attached to their disease and no one felt stigmatized by the term NAFLD. The majority of the patients were aware that NAFLD is a lifestyle disease [n= 103 (98.1%)] related to a lack of physical activity and improper diet [n=105 (99.1%)] and is associated with overweight/obesity [n=103 (98.1%)], diabetes mellitus and hypertension [n=99.9 (94.3%)]. Most of the patients were aware that NAFLD can cause scarring/ cirrhosis of the liver [n=92.9 (87.7%)] and liver cancer [n=61 (57.7%)]. Practically all the patients were aware that fatty liver can be diagnosed by ultrasound [n=105 (99.1%)], CT-Scan/ MRI [n=101 (95.3%)], and Fibroscan [n=106 (100%)]. Most of the patients were aware that NAFLD can be controlled if diagnosed at an early stage with the combination of regular exercise and calorie restriction [n=106 (100%)] together with control of diabetes mellitus, hypertension, or dyslipidemia [n=105 (99.1%)]. Only 41 (39%)] patients were aware of the fact that endoscopy and surgery are available treatment options for patients with obesity who are not able to lose weight with lifestyle modifications. One hundred and five (99%) patients were aware that drugs are available for the treatment of NAFLD/NASH while n=62 (58.3%) patients were aware of liver transplantation as a treatment option for patients with NAFLD related cirrhosis or hepatocellular carcinoma.

Conclusion: Most Indian patients are aware of the risk factors, complications, and management options of NAFLD and are not stigmatized by its nomenclature.

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The Unfavorable Metabolic and Lipidomic Profile of Patients with NAFLD is Reversed by Bariatric Surgery

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Background: Bariatric surgery is known to induce weight loss and improve insulin resistance, cardiovascular risk factors, and steatohepatitis in patients with type 2 diabetes (T2D). Total ceramides (Cer) and diacylglycerols (DAGs) have been implicated in the development of insulin resistance and nonalcoholic fatty liver disease (NAFLD). The impact of bariatric surgery on lipidomic profile in NAFLD has not been fully examined. The aim of this study was to assess at baseline, and 3-6 months after bariatric surgery, changes in the plasma lipidome, in particular Cer and DAGs profile, of patients with NAFLD.

Materials and methods: We recruited 17 patients with NAFLD who underwent bariatric surgery (age: 47±3 years, BMI: 46±2 kg/m2, T2D: 13 of 17 patients). Post-surgical data is available in 10 patients (ongoing). Six patients served as controls without T2D or NAFLD for the baseline data (age: 47±6 years, BMI: 31.2±2.1 kg/m2). Ultra-high-performance liquid chromatography coupled to Thermo Q-Exactive Orbitrap mass spectroscopy was used for global lipidomic profiling. Data from positive and negative ion modes were analysed using LipidMatch software.

Results: Patients with NAFLD at baseline had severe insulin resistance (measured by HOMA-IR and Adipo-IR), with significantly higher cytokeratine (CK)-18 and lower plasma adiponectin levels. Compared to controls, patients with NAFLD had a worse lipidomic profile, with higher plasma levels of total lipids (34%; p=0.01), Cer (20%; p=0.31), DAGs (50%; p=0.03) and total triglycerides (TG) (79%; p=0.01). Before surgery, patients with T2D (vs. without) had the worst profile, with higher total plasma lipids (28%; p= 0.01) and DAGs (41%; p= 0.04) and TGs (75%; p = 0.01). Bariatric surgery improved the metabolic profile, with a reduction in HOMA-IR, Adipo-IR, CK-18 and increase in adiponectin levels (all $p<0.05$ vs. baseline), as well as the lipidomic profile, reducing total plasma lipids, Cer, DAGs, TG, cholesterol esters (CE), phosphatidylcholine (PC) phosphatidylinositol (PI) levels, (all $p<0.05$). In patients with T2D, bariatric surgery led to a marked reduction in plasma levels of total lipids (-29%; $p<0.01$) and TG (-75%; $p<0.01$), and in DAGs (-41%; p=0.02), key mediators in hepatic and muscle insulin resistance. Moreover, reduction in total body weight after bariatric surgery correlated with lower DAGs (r=0.81; p=0.03) and TG (r=0.66; p=0.07) and correlated with improvement in HOMA-IR after surgery (DAGs: r= 0.81; p = 0.014 and TGs: 0.85; $p \leq 0.01$). Ceramides did not correlate with improved HOMA-IR or Adipo-IR.

Conclusion: Patients with type 2 diabetes and NAFLD have an extremely unfavorable metabolic and lipidomic profile. Both are rapidly improved after bariatric surgery, in particular plasma ceramides and DAGs levels, known to be linked to “lipotoxicity” and insulin resistance in type 2 diabetes and in NAFLD. Assessment of the lipidomic profile before and after bariatric surgery may provide further insights into the mechanisms related to insulin resistance in patients with NAFLD and be an early signature of treatment response.

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Determinants of Association Between Non Alcoholic Fatty Liver Disease (NAFLD) and Coronary Artery Disease (CAD)

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Background & aim: NAFLD is closely related to the multiple potential risk factors of cardiovascular diseases and thought to be an independent risk factor for cardiovascular events as both share similar risk factors. This study was conducted to explore the impact of presence and severity of Non-alcoholic Fatty Liver Disease (NAFLD) on the prevalence and severity of Coronary artery Disease (CAD).

Methods: A cross-sectional observational study was conducted between From April 2020 to December 2021 ,to explore the relationship between NAFLD and risk of CAD in our patients who are, unlike western countries, mostly non-obese. We have planned for a bidirectional approach, one in subjects with NAFLD (135 patients) and another in subjects with CAD(91 patients) , keeping them in two separate groups. NAFLD was diagnosed by USG fatty liver grading & Coronary artery disease was diagnosed by multi detector CT Coronary angiogram to find out the coronary artery calcium score , degree of stenosis & plaque character . Invasive angiogram was done for known coronary artery Disease patients . Known cirrhotics , alcoholics > 20 gm in males & > 10 gm in females, CKD. Pregnancy & known chronic inflammatory diseases were excluded . Fibroscan was done in all patients to exclude cirrhosis along with upper GI endoscopy.

Results: The prevalence of CAD in NAFLD group was found to be 71.9% which was significantly higher (Z=6.50;p<0.0001). On CT coronary angiogram, proportion of patients with no calcification (83.7%) was significantly higher (p<0.0001). There was significant association between CAC scores and USG grade of NAFLD of the patients (p=0.043). No plaque (72.6 %), soft non calcified plaque (10.4%), calcified (7,4%), mixed plaque (9.6%) & there was significant association between plaque Character and USG grade of NAFLD of the patients (p=0.023). 68.9% of the patients were with CAP>259 which was significantly higher than other CAP (Z=6.67;p<0.0001) & there was significant association between CAP and USG grade of NAFLD of the patients (p=0.019).52.8% of the patients were having obesity which was significantly higher than other BMI group (Z=5.01;p<0.0001). 2.2 % of the total population were underweight & 16.4% were of normal weight pointing towards increased prevalence of CAD in lean NASH patients .There was significant association between APRI scores and USG grade of NAFLD of the patients (p<0.001). Multiple Logistic Regression was used to estimate the risk factors after adjusting different risk factors under study .Alcohol, obesity, Diabetes with physical activity <30 minutes per day, Hypertension and habit of smoking were considered to be independent risk factors of CVD in NAFLD population, after adjusting the affect of metabolic syndrome.

Conclusions: Patients with NAFLD are at increased risk for coronary artery diseases independent of classical risk factors including smoking, diabetes, hypertension, decreased physical activity. This shows that NAFLD might be an independent risk factors for coronary artery disease.

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Urinary Alpha 1 Microglobulin in Non Alcoholic Fatty Liver Disease and Its Association With Liver Fibrosis

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Background: Non Alcoholic Fatty Liver Disease (NAFLD) is now being recognised as the most common cause of chronic liver disease worldwide with definite diagnosis based on Liver Biopsy. However, there are very few non invasive markers for detection of liver fibrosis in NAFLD.
Recent studies have provided a strong insight into the liver kidney cross talk between NAFLD and Chronic Kidney Disease (CKD). Alpha-1 Microglobulin (A1M) is a glycoprotein secreted by liver (MW-30kDa). Glomeruli freely filter the unbound form of A1M, which is virtually completely reabsorbed and broken down by proximal tubular epithelial cells. Hence elevated A1M levels in urine strongly suggest defective reabsorption capacity of proximal tubules and hence kidney function decline. Further, it also has reductase properties and it acts as a radical scavenger by protecting against oxidative tissue damage.

Methods: A total of 30 NAFLD cases with normal range Glomerular Filtration Rate (GFR) and urine routine microscopy and age and sex matched controls were enrolled into the study. Urinary Alpha 1 Microglobulin (A1M) levels were estimated in both the groups. Subjects were further divided into 3 groups based on grades of fatty liver on ultrasonography and FIB-4 score was calculated. The relationship of Urinary A1M with grades of fatty liver and FIB-4 index was estimated.

Results: Urinary A1M was significantly higher in cases as compared to controls (W= 899.0, p=<0.001). Urinary levels of A1M positively correlated with grade of fatty liver with highest values being in grade III fatty liver group($\chi 2$=23.701, p <0.001), and with FIB-4 index (rho = 0.87, p = <0.001) respectively. All our patients had normal eGFR, normal Urine routine microscopy which indicates that Urinary alpha 1 microglobulin acts as an important marker to detect early renal injury in NAFLD as compared to eGFR and urinary proteinuria. There was a strong negative correlation between eGFR (mL/min/1.73m2) and Urine $\chi 1$-Microglobulin (mg/L), and this correlation was statistically significant (rho = -0.72, p = <0.001).

Conclusion: Oxidative stress plays a major role in the liver injury in NAFLD, thus liver produces antioxidant molecule A1M in response to oxidative damage. Our study showed promising results regarding the role of Urinary A1M in detecting fibrosis as well as renal injury in NAFLD. Based on our findings, it is suggested that urinary A1M may be used in assessing fibrosis and renal injury in NAFLD, even with normal range eGFR.

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The Complexity of NASH Cirrhosis Clinical Trials: Screen Failure Reasons and Baseline Patient Characteristics

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Background: Patients with NASH cirrhosis have the highest likelihood of developing major adverse liver related events and an unmet need in terms of therapeutic options. Several drugs are being tested in patients with NASH cirrhosis in phase 2 trials. Screen failure (SF) reasons in non-cirrhotic NASH trials have been described; however, limited data exists on the reason for screen failure reasons in NASH cirrhosis trials. The aim of this study was to understand the reasons for screen failure in 3 NASH cirrhosis trials and to describe the patient's characteristics of both screens failed subjects and those who randomized.

Methods: Data on patients who presented for screening visits for three phase 2 NASH cirrhosis trials at one research site were analyzed. The reasons for screen failure were divided into 4 major categories: 1. Biopsy, 2. Laboratory tests, 3. Imaging tests, 4. Other. Baseline characteristics including demographics, clinical history, lab values, findings from imaging tests and biopsy were collected. Characteristics of patients that screen failed were compared to those who randomized using 2-sided t-test, p value < 0.05 was considered statistically significant.

Results: 43 patients were included in the analysis. 16 randomized (37%) and 27 screen failed (63%). The mean age was 58 ± 9.1 years with 39.5% of the population being male. Mean BMI in the whole population was 39.6 Kg/m2. 54.8% of the patients were found to have type 2 diabetes. The reasons for screen failure were as follows: 2 (7.5%) on biopsy, 8 (30%) on labs, 7 (25.5%) on imaging tests, 10 (37%) for other reasons. Top 3 causes included in the other category were patients out of the screening window, dropping out of the trial, or using prohibited medications. There was no significant difference between the screen failure group and the randomized group in terms of platelet count, INR, bilirubin, FIB4 score and AGILE4 score ($p > 0.05$ for all).

Conclusions: NASH cirrhosis trials have similar screen failure rates compared to non-cirrhotic trials; however, the reasons for screen failure are different. In NASH cirrhosis trials, fewer patients screen failed because of not meeting histologic criteria on liver biopsy which has been the major reason for screen failure in non-cirrhotic trials. Baseline laboratory and imaging tests were not different between patients who screen failed and those who randomized.

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Metabolomic Techniques to Extract and Equate Phyllanthin From P.niruri and to Study if Phyllanthin Regulates the Expression of NFKB/PI3K/AKT Pathway in Improving the Liver Histology in Animal Model of NAFLD: A Preliminary Study

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Introduction: Dysregulation of PI3K/AKT pathway contributes to the development of NAFLD. Aim of the study was to evaluate the hepatoprotective effect and efficacy of P.niruri in improving the liver histology in a mice model of NAFLD and to assess if it is related to the regulation of NFKB/PI3K/AKT pathway.

Methodology: To extract and equate the Phyllanthin from P. niruri we used the HPTLC, NMR, FTIR and GCMS technique in our plant products. In mice Group A C57BL/6 mice were given normal chow diet. Group B were fed MCDD for 4 weeks to make NAFLD model. Control as well as MCDD mice were also administered plant crude extracts i.e., 200 mg/kg & 400mg/kg (group C and group D). Control as well as MCDD mice administered commercially available Phyllanthin (2mg/kg & 4mg/kg) (group E and group F). RT-PCR expression of NF-KB, AKT, PI3K and IRS-1 genes was studied and relative expression was calculated using 2^-ΔΔCt method. All further groups were evaluatued for improvement in NAS.

Results: In HPTLC – CAMAG Linomat, out of all seven peaks in the spectrum, single peak was identified which was compared to standard spectrum (Phyllanthin). We found Phyllanthin was equivalent to 1.48χg/ml dry weight of P.niruri . Similarly in case of FTIR, spectra were composed among wavelength numbers of 3500 and 700 cm-1 for all extracts. The standard samples P. niruri and commercial samples like alcohols, phenols, aromatics, and alkanes showed more powerful absorption than the other samples analysed. GC–MS technique useful for the alteration that reported by the study of Phyllanthin there in the crude extract samples. The 1H-NMR data of phyllanthin was represented by distinctive region, alkenes and methyl aldehydes are common in both the groups.
C57BL/6 mice with different group when compare with MCDD (group 4) had 4.63-fold higher expression of IRS, 2.2. Fold higher expression of PI3K, 5.89 Fold higher expression of AKT gene, 4.78 fold higher expression of NF-Kχ m RNA in comparison to control. Of all mice with NAFLD, lobular inflammation was seen in 37 (62%) and hepatocyte ballooning in 6 (10%) mice. As per NAS, 28 (46.6%) mice had no NASH (score 1 or 2), 19 (31.6%) had borderline NASH (score 3 or 4) and 13 (21.6%) mice had definite NASH (score 5 or more). Fibrosis staging showed F0 in 28 (47%), F1 in 23(38%), F2 in 7(11.6%) and F3 in 2(3.3%). NAS scoring in different groups Group 1, II, III, VI, VIII & X was significant (p=0.001) when compared with MCDD Group.

Conclusion: The results of our study demonstrate that the hepatoprotective effect of crude extract of P.niruri in a mice model of NAFLD is related to the regulation of NFKB/PI3K/AKT pathway and both crude extract and commercial Phyllanthus niruri is effective in improving the liver histology in MCDD mice model of NAFLD.

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Accuracy of Enhanced Liver Fibrosis (ELF) Test for the Prediction of Advanced Liver Fibrosis in Unselected Individuals With Chronic Liver Disease

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Background and Aims: Non-invasive tools (NITs) are needed to define liver fibrosis stages and replace histology in clinical practice. Liver Stiffness Measurement (LSM) has a high accuracy to detect advanced fibrosis and is used in specialized clinics. Enhanced Liver Fibrosis (ELF) test is a blood-based tool that has been shown to have prognostic value in patients with Non-Alcoholic Fatty Liver Disease (NAFLD) and other liver diseases. The current presentation aims to explore the concordance of the ELF test and LSM patients to detect advanced fibrosis in a tertiary care setting and represents interim analyses from an ongoing study.

Method: Outpatients referred for suspected liver disease were consecutively enrolled at their first presentation. Clinical data, LSM, regular laboratory and ELF test were collected at the same time. ELF values > 11.3 and LSM > 10 kPa were defined as cut-off to identify patients with high risk for liver disease.

Results: 50 patients were included, of which 42% were male with median age of 53 years [IQR 40 – 63]. The predominant etiologies of liver disease were NAFLD (62.5%) and autoimmune/cholestatic (12.5%). Median BMI was 31.6 [IQR 28 – 35.1] and type 2 diabetes was present in 32.4% of patients. Median LSM was 8.3 kPa [IQR 5.3 – 15.3] and 38% had LSM> 10 kP. Median ELF score was 9.5 [IQR 8.2 – 10.9] and 20% of the cohort had values > 11.3. ELF score showed a good correlation with LSM (r = 0.75, p < 0.001) and individuals with ELF > 11.3 had higher values of LSM when compared to those with ELF < 11.3 (median 24.1 kPa [IQR 11.8 – 51.6] versus 7.1 kPa [IQR 5.1 – 9.3], p = 0.002). 10 patients had discordant values, of which 9 had low ELF but high LSM values. At multivariate logistic regression analysis, ELF test predicted advanced fibrosis after adjustment for age, gender and type 2 diabetes (aOR 29.8, 95% CI 1.5 – 591, p = 0.025).

Conclusion: ELF test shows a good correlation with LSM. In tertiary clinical care, the majority of patients with high risk for liver disease were identified with ELF values > 11.3 and LSM >10. In discordant cases, most patients had low ELF and high LSM values. Both NITs are useful in identifying patients with advanced liver disease.

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The Level of Neuron- and Astrocyte-Specific Proteins in the Rat Brain under Experimental Nonalcoholic Steatohepatitis

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During the nonalcoholic steatohepatitis (NASH) patients have hepatic encephalopathy (HE) - complex of psychical and neurological violations. Traditionally, development of HE relates to increasing the neurotoxic metabolites' concentration. One of the main objects of action of these metabolites is astroglia and neurons of CNS. The functional state of these cells is correlated with level of specific proteins like neuronal cell adhesion molecules (NCAM) and glial fibrillary acidic protein (GFAP).

Nonalcoholic steatohepatitis was induced by prolonged methionine-choline deficient diet (MCCD). The 16 Sprague-Dawley (Mol:SPRD Han; Taconic M&B A/S, Ry, Denmark) rats were used for experiment according to ethical rules. The rats were decapitated under Isofuran anesthesia according to ethical rules; the brain was quickly removed and divided into different regions.

NASH induced 80% loss of bodyweight during 6 weeks of experiment (99±3.98 g compared to 478±12.22 g in control group). However, the weight of brain in a NASH group was decreased on 22% (1.66±0.04 g compared to 2.13±0.027 g in control group). Obtained data indicate that protein biosynthesis affected by NASH conditions is most protected in the brain.

The locomotor activity and study interest were much decreased in rats at MCCD.

The NCAM level in the membrane fraction of rat brain proteins decreased by 40% in the cerebellum. The level of soluble GFAP in the rat's cerebellum did not differ from control animals. In the posterior part of hemispheres, the absolute level of soluble GFAP was decreased by 21%. The most significant changes were recorded in the amount of filament GFAP at the NASH modelling, which was reduced in the cerebellum by 75% and almost unchanged in the posterior part of hemispheres.

NCAM decreasing in cerebellum indicates drop of interneuron interaction ability. A significant reduction in filament GFAP in the cerebellum indicates that in this part of the rat's brain under the influence of long-term MCDD degenerative changes in astroglia cells occurred.

Immunohistochemical study confirmed significant degradation of astrocytes during the development of experimental NASH in rats - a decrease in the size of astrocytes, a loss of their stellar shape.
The obtained results show the development of intense encephalopathy with significant suppression of the locomotor and interest functions of the animals because of chronic impairment of the detoxication function of the liver.

The obtained data allow suggesting that changes of GFAP level can reflect the complex of the cytoskeleton modification under NASH condition.

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To Study the Relationship Between Hepatic Iron Deposition and Histologic Severity in Nonalcoholic Fatty Liver Disease

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Introduction: Nonalcoholic fatty liver disease (NAFLD) is the most common liver disease and is present in up to 9-32% of the general population in India. Hepatic iron overload may be present in various chronic liver diseases and associated with the risk of toxicity and severity of the liver disease. The aim is to study the relationship between hepatic iron deposition and serum iron biomarker with histologic severity in NAFLD patients.

Methods: It is an interim analysis of a prospective study involving thirty adult subjects with metabolic syndrome and USG s/o fatty liver with or without deranged LFT. Other common causes of NAFLD were ruled out. These subjects underwent liver biopsy. On histopathological examination Hepatic iron staining, hepatic steatosis, hepatic inflammation, ballooning degeneration, Hepatic fibrosis were noted. Serum iron biomarkers were measured prospectively.

Results: Mean age of the study population was 45.5±23.4 years. M: F was 1.3:1. Out of 30 patients, Nonalcoholic steatohepatitis(NASH) patients was 19/30(63.3%) and Nonalcoholic fatty liver (NAFL) was 11/30(36.6). Increase S. Ferritin was found in 26/30(86.66%) of NAFLD in which 15/26(57.7%) of NASH and 11/26(42.3%) of NAFL. Fibrosis was present in 18/30(60%) of NAFLD, in which mild fibrosis (F0-F1) 10/18(55.5%) and moderate-severe fibrosis (≥F2) 8/18(45.5%). S.ferritin was raised in 15/18(83.3%) of patients with fibrosis (p value=0.03). Hepatic iron staining was present in 8/30(26.6%) of NAFLD patients in which 5/19(26.3%) of NASH and 3/11(27.2%) of NAFL. Hepatic iron staining was present in 5/18(27.7%) of patients with fibrosis (p value=0.65). However, there was no association between the presence of hepatic iron deposits and serum ferritin with the NASH (p value=1.0 and 0.53 respectively). Noninvasive markers of fibrosis (NFS, FIB 4, and APRI) correlated with biopsy-proven hepatic fibrosis.

Conclusion: Our study did not confirm the association between the presence of hepatic iron and serum ferritin and the severity of NASH in NAFLD.

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