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Original Research Article

A Prospective Study of the Prevalence of Non-Alcoholic Fatty Liver Disease and Non-Alcoholic Steatohepatitis in Adults

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Conflict of interest: Nil

Abstract:

Objectives*:* The study aims to assess the prevalence of NAFLD and NASH, along with associated risk factors in adults. Additionally, it seeks to explore potential gender disparities and offer insights into the epidemiology of these conditions.

Methods: The study, conducted at a tertiary care centre over one year, employed a prospective design with 164 participants aged 18 to 70. Patients underwent right upper quadrant ultrasound examinations and liver biopsies for the diagnosis and inclusion of those with NAFLD or NASH. The biochemical parameters of the participants were extensively analyzed and correlated with the identification of NASH.

Results: The study involved 164 participants, in which Group B (NAFLD patients) exhibited notable distinctions from Group A (non-NAFLD), showcasing higher mean age (56.49 vs. 51.56 years), elevated body mass index (31.4 vs. 23.7), and significantly increased prevalence of diabetes (26.3% vs. 7.9%) and hypertension (68.2% vs. 33.9%). Group B also demonstrated higher rates of non-diet soda consumption (48.3% vs. 39.5%) and lower levels of regular exercise (>30 min/week). The comparative analysis further highlighted variations in metabolic parameters between individuals with and without nonalcoholic steatohepatitis (NASH), emphasizing distinct features in mean age, hemoglobin A1c, prevalence of hypertension, and lipid profiles.

Conclusion: The study reveals a substantial prevalence of NAFLD and NASH, particularly among middle-aged adults, highlighting the critical role of lifestyle factors in their development. The findings emphasize the urgency of implementing targeted interventions and screening strategies to address these prevalent liver conditions.

Recommendation: The study recommends the implementation of targeted lifestyle interventions and systematic screening for early detection of NAFLD and NASH in middle-aged adults.

Keywords: NAFLD, NASH, Middle-aged adults, Risk factors.

Introduction

The rates of obesity and diabetes are witnessing alarming rise in the global number of cases. As per recent data, 44% of the worldwide adult population is grappling with obesity, while in the Indian subcontinent, the prevalence stands at 40% for women and 12% for men [1]. Additionally, the occurrence of diabetes in individuals aged 15 years and above is reported at 16.1 % in the Indian subcontinent [2]. The incidence rates of metabolic syndrome, which is a collection of clinical manifestations like diabetes and obesity, has also been on the upswing owing to this.

Non-alcoholic fatty liver disease (NAFLD), a component of metabolic syndrome, has become a major cause of abnormal levels of liver enzymes. This disease has also been associated with an elevated risk of getting diabetes and coronary artery disease [3]. Global estimates indicate that the prevalence of NAFLD is 32%, with a higher incidence in men (40%) compared to women (26%) [3]. This prevalence usually changes with the study cohort and the methods used for diagnosis, which include imaging techniques or biopsy of the liver.

Establishing the incidence rates of non-alcoholic steatohepatitis (NASH), a significant subset within NAFLD, has proven to be challenging owing to the need for a liver biopsy for diagnosis. In contemporary health settings, the reported incidence rates of NASH in the overall population stands at 5.27% [4]. It is crucial, however, to approach this statistic with caution, considering the lack of available data on population-based prevalence for NASH in the general populace. This, therefore, emphasizes the need for a nuanced interpretation of

the reported figures to better comprehend the broader implications of NASH within the broader public health landscape.

Prevalence rates of both NAFLD and NASH vary among different patient groups. For instance, in patients undergoing bariatric surgery for obesity, the estimated rates of NAFLD and NASH is around 91 % and 37 %, respectively [5,6]. In diabetic patients, however, the rates of NAFLD lies from 40-69%, while no data is available on incidence rates of NASH [5]. The current study aims to prospectively determine the incidence rates of both NAFLD and NASH in adults with no known history of liver disease.

Materials and Methods

Study Design

The study employs a prospective observational design, targeting individuals aged 18 to 70 years evaluated at a tertiary care centre for a period of 1 year.

Inclusion and exclusion criteria

Participants, aged between 18 and 70 years, who had hepatic steatosis on sonography were a part of the study. Patients with a history of chronic liver disease, HIV, or on certain medications were excluded from the study. Individuals consuming over 20 grams of alcohol daily were also not included in this investigation.

Study Size

The study included 164 patients who displayed signs of NASH or NAFLD.

Study Setting

The study was conducted at a tertiary care centre, where right upper quadrant ultrasound examinations were performed utilizing advanced ultrasound units. Skilled sonographers and a seasoned radiologist assessed images for hepatic steatosis. Percutaneous liver biopsies, when needed, were carried out in collaboration with an expert hepatopathologist.

Right Upper Quadrant Ultrasound

Ultrasound examinations of the right upper quadrant were conducted using suitable ultrasound systems such as ATL HDI 5000 equipped with a compatible transducer. Experienced sonographers performed the examinations by adjusting the technical parameters based on the set protocol to get the ultrasound of the right upper quadrant. The ultrasound images were then independently assessed and evaluated for steatosis of the liver. The presence of a homogeneous echotexture, clear portal veins, with echogenicity resonating with or slightly higher than that of renal parenchyma distinguished the healthy liver. In contrast, fatty liver was characterized by the presence of an increased echogenicity, an indistinct diaphragm, or less visible echogenic walls of portal veins. Centricity PACS was used to review the generated images and there was no grading of the severity of the hepatic steatosis.

Percutaneous Liver Biopsy

Liver biopsy was done on patients with positive ultrasound results. The serum collected was stored for subsequent biochemical analysis. Those with a negative ultrasound result, did not undergo a biopsy, and were categorized as the control group participants. The liver biopsy was done using a 14-gauge BARD Monopty biopsy instrument. All liver biopsies were reviewed with the help of the Brunt system to ensure the grading as well as staging of hepatic steatosis when present.

Bias

The potential bias in this study may arise from the exclusion of patients with a history of chronic hepatic disease, limiting the generalizability of findings to a broader population. Additionally, the reliance on ultrasound for hepatic steatosis assessment may introduce observer bias due to subjective interpretation.

Ethical Consideration

The study upholds ethical standards by obtaining informed consent, ensuring voluntary participation, maintaining confidentiality, and receiving approval from the Institutional Review Board.

Statistical Analysis

The statistical analysis involved descriptive statistics, $\chi 2$ or Fisher exact tests for proportions, and t or Mann–Whitney tests for continuous variables. Logistic regression models were constructed to assess predictive factors for the development of NASH.

Results/Outcomes

Participants

Among the 164 participants enrolled in this study, 89 were categorized into Group A and 75 were categorized into group B based on ultrasound findings. Participants belonging to group A showed negative ultrasound results indicating the absence of NAFLD while those in group B showed positive signs of NAFLD. In the comparative analysis between Group A (non-NAFLD) and Group B (NAFLD patients), significant differences were observed in various characteristics. Group B had a higher average age (56.49 vs. 51.56 years) and a significantly greater body mass index (31.4 vs. 23.7) when compared to Group A. The prevalence of diabetes mellitus (26.3% vs. 7.9%), hypertension (68.2% vs. 33.9%), and regular consumption of non-diet soda (48.3% vs. 39.5%) were also markedly

higher in Group B, demonstrating statistically significant differences. Additionally, Group B exhibited a higher frequency of fast-food consumption (>1/week) and lower rates of regular exercise (>30 min/week) compared to Group A (Table 1).

Table 1: General demographic traits of study cohort

Characteristics	Group A (non-NAFLD) (n = 89)	Group B (NAFLD patients) (n = 75)	*p*-value
Mean age (yrs)	51.56	56.49	0.003
Body mass index	23.7	31.4	<0.006
Men	36 (40.7 %)	44 (58.9%)	0.318
Diabetes mellitus	7(7.9 %)	20 (26.3 %)	<0.00005
Hypertension	30 (33.9 %)	51 (68.2 %)	<0.00005
Non-diet soda (> 1/week)	35 (39.5 %)	26 (48.3 %)	<0.00005
Fast food (> 1/week)	54 (60.5 %)	53 (70.9 %)	0.049
Exercise (> 30 min/ week)	61 (68.9 %)	42 (56.3 %)	0.02

Furthermore, within the NAFLD group, a comparative analysis was performed to distinguish the individuals with and without non-alcoholic steatohepatitis (NASH). In this attempt, several noteworthy variations emerged across key parameters, shedding light on the different metabolic disparities within the cohort. Participants with NASH displayed a slightly elevated mean age (58.1 vs. 55.8 years) and a higher mean hemoglobin A1c (6.15 vs. 6.02), indicative of potential differences in metabolic profiles. Moreover, a higher prevalence of high blood pressure (77.6% vs. 62.4%) and mean glucose levels (108.2 vs. 102.7 mg/dL) were observed in the NASH group. The NASH group also displayed distinctive lipid profiles, with lower mean levels of high-density lipoprotein (44.7 vs. 48.5 mg/dL) and higher levels of low-density lipoprotein (112.6 vs. 111.2 mg/dL) (Table 2).

Table 2: Comparative Analysis of Participants with and without Non-alcoholic Steatohepatitis (NASH)

N = 164	Not NASH (n = 49)	NASH (n = 26)	*p*-value
Mean age (yrs)	55.8	58.1	0.041
Body mass index	30.7	35.1	0.645
Men	29 (59.6 %)	17 (65 %)	0.541
Women	20 (40.4 %)	9 (35 %)	0.512
Diabetes mellitus	11 (23.5 %)	6 (25.1 %)	0.068
Hypertension	30 (62.4 %)	20 (77.6 %)	0.024
Quantitative Insulin-Sensitivity Check Index, mean	0.35	0.33	0.126
Glucose, mg/dL, mean	102.7	108.2	0.042
Insulin, uIU/mL, mean	15	24.1	0.284
Hemoglobin A1c, mean	6.02	6.15	0.004
Alanine aminotransferase, U/L, mean	35.9	48.6	0.075
Aspartate aminotransferase, U/L, mean	24.1	34.3	0.214
Alkaline phosphatase, U/L, mean	83.4	87.1	0.076
Total cholesterol, mg/dL, mean	188.9	185.6	0.076
Low-density lipoprotein, mg/dL, mean	111.2	112.6	0.033
High-density lipoprotein, mg/dL, mean	48.5	44.7	0.024
Free fatty acid, mEq/L, mean	0.61	0.60	0.884

Discussion

This prospective study's most compelling revelation is the substantial incidence rates of non-alcoholic fatty liver disease (NAFLD) which stands at 45.7% and non-alcoholic steatohepatitis (NASH) which is estimated to be 15.8% within the study cohort. Despite utilizing a less sensitive test and stringent alcohol consumption criteria, our findings align with the escalating rates of obesity and diabetes globally [7-10]. Significantly higher occurrences of both diabetes and obesity have been observed in individuals with fatty liver compared to those without in this study.

The present study also identified stark differences in the lifestyles of individuals with NAFLD and those without the disease. Those with NAFLD exhibited a higher frequency of fast-food consumption and less regular exercise compared to the non-NAFLD participants. This association between fatty liver disease and lifestyle corroborates previous research findings [11-13]. This includes studies conducted by Krasnoff et al., discovered that a majority of patients with biopsy-confirmed NAFLD did not adhere to

recommended physical activity guidelines [11]. Additional studies have also highlighted dietary patterns among NASH patients, indicating higher consumption of simple carbohydrates and reduced ratios of polyunsaturated to saturated fatty acids, along with drop in the intake of fibre, vitamin C, and vitamin E [12, 13].

These findings hold significance as it underscores the link between obesity and poor lifestyle habits, which could potentially lead to more severe consequences. Existing literature has revealed that the survival rates of individuals with NAFLD are lower than that of the general population, as the NAFLD patients often succumb to cardiovascular-, malignancy-, and liver-related diseases [14-17]. This alarming revelation is particularly concerning as nearly half of the asymptomatic adults in our study population were identified with NAFLD.

The present study further reveals a significant sex disparity, with higher rates of NAFLD (59.6% vs. 40.4%) and NASH (65% vs. 35%) observed in men when compared to women. This aligns with previous findings, suggesting a potential role of sex hormones in NAFLD development [18, 19]. Male patients with NAFLD exhibited distinct metabolic markers and lifestyle differences, including increased soda consumption. Among diabetic patients, the study establishes a NASH prevalence of 23.5%, emphasizing the need for proactive screening and potential liver biopsy in those with steatosis on imaging. This underscores the importance of the potential role of sex hormones and underscores the need for gender-specific considerations in understanding and managing these liver conditions. Additionally, the study's unique prospective assessment of NASH prevalence in diabetic patients emphasizes the clinical significance of screening and addressing fatty liver disease within this high-risk population.

Conclusion

The present study reveals a significant prevalence of NAFLD and NASH, particularly among males, pointing towards the impact of gender-specific factors. The results emphasize the crucial role of lifestyle factors and advocate for targeted screening efforts, especially among diabetic individuals who exhibited a heightened prevalence of NASH. These specific insights enhance our understanding of NAFLD epidemiology and underscore the need for precise interventions tailored to high-risk groups. In essence, the study emphasizes the urgency of targeted awareness campaigns, early identification, and tailored management approaches to address the escalating burden of fatty liver diseases.

Limitations

The study's reliance on ultrasound for NAFLD detection may underestimate prevalence, as liver biopsy, the gold standard, was not universally applied. Additionally, the study's focus on a specific demographic limit the generalizability to broader populations.

Recommendations

The study recommends incorporating liver biopsy alongside imaging for precise NAFLD diagnosis in future investigations. Additionally, expanding research to encompass diverse age groups and geographic regions is advised to enhance the generalizability of findings and inform more comprehensive preventive strategies.

Generalizability

While the study's concentration on adults within a specific hospital may limit its generalizability to broader geographic regions and demographics, the results provide valuable insights into NAFLD prevalence and risk factors within this specific group.

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List of Abbreviations

NAFLD - Non-Alcoholic Fatty Liver Disease

NASH – Non-Alcoholic Steatohepatitis

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