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Original Article

Factors Predictive of Non-Alcoholic Fatty Liver Disease in Non-Obese Pakistani Population

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ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD) is one of the most prevalent causes of chronic liver disease worldwide, with a rising incidence in developing countries. In Pakistan, the estimated prevalence ranges from 14-47%. Studies have shown that NAFLD is also not uncommon among the non-obese lean population.

Objective: The aim of this study was to evaluate the factors predictive of non-alcoholic fatty liver disease in a non-obese Pakistani population, defined by a body mass index (BMI) of less than 23 kg/m².

Methods: This cross-sectional study was conducted at the Department of Hepatogastroenterology, Sindh Institute of Urology and Transplantation from November 1, 2020, to October 31, 2021. A total of 194 patients with BMI < 23 kg/m² presenting with abdominal pain were included. Exclusion criteria were viral hepatitis, significant alcohol intake, hepatocellular carcinoma, or other malignancies. Data collection involved recording demographic information, medical history, and clinical parameters. Ultrasound abdomen examinations were performed after 8-10 hours of fasting to diagnose NAFLD. Clinical assessments included history of hypertension and smoking, and laboratory tests such as liver function tests, fasting blood sugar levels, and lipid profiles. The primary outcome was the presence of fatty liver on ultrasound. Statistical analysis was conducted using SPSS version 25.0. Continuous variables were analyzed using the Student t-test and categorical variables using the Chi-square test. Significant variables in univariate analysis underwent multivariate logistic regression to identify independent predictors of lean NAFLD. A p-value ≤ 0.05 was considered significant.

Results: Out of the 194 patients, 107 (55.2%) were females. The mean age was 36.1 ± 9.6 years, and the mean BMI was 21 ± 1.7 kg/m². NAFLD was detected in 48 (24.7%) patients. Among the study population, 78 (40.2%) were hypertensive, 40 (20.6%) were diabetic, 49 (25.3%) were smokers, and 54 (27.8%) had increased triglyceride levels. Decreased HDL-C levels were observed in 72 (37.1%) patients. Univariate analysis identified hypertension ($p \leq 0.001$), diabetes ($p \leq 0.001$), smoking ($p \leq 0.001$), hypertriglyceridemia ($p \leq 0.001$), and decreased HDL-C levels ($p \leq 0.001$) as significant factors. Multivariate logistic regression showed that diabetes (OR: 9.4, $p = 0.037$), smoking (OR: 46.4, $p \leq 0.001$), hypertriglyceridemia (OR: 4.75, $p = 0.016$), and decreased HDL-C levels (OR: 36.8, $p \leq 0.001$) were independently associated with lean NAFLD.

Conclusion: Non-obese individuals with a BMI less than 23 kg/m² can develop NAFLD and related complications. The study identified diabetes, smoking, hypertriglyceridemia, and decreased HDL-C levels as significant predictors of lean NAFLD. Further studies are needed to enhance the understanding of the disease's risk factors and behavior in this population.

Keywords: Non-alcoholic fatty liver disease, lean NAFLD, body mass index, diabetes, smoking, hypertriglyceridemia.

Journal of Health and Rehabilitation Research 2791-156X JHRR

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is characterized by hepatic steatosis identified either through imaging or histology in the absence of significant alcohol consumption, use of steatogenic medications, or hereditary disorders (1). NAFLD encompasses a spectrum ranging from simple steatosis to non-alcoholic steatohepatitis (NASH) with or without fibrosis, and cirrhosis (2). The global prevalence of NAFLD is approximately 25%, with variability observed across different regions, including 15-45% in Asian countries (3, 4). In Pakistan, the prevalence estimates range between 14-47%, indicating a significant burden (5-8). Traditionally, NAFLD is closely associated with obesity, diabetes mellitus, dyslipidemia, and metabolic syndrome (9, 10). Body mass index (BMI) is a key parameter in assessing obesity and is considered an important predictor of NAFLD (11). However, it is noteworthy that South Asians, compared to their European counterparts, tend to have higher body fat percentages, particularly abdominal fat, which increases the risk of metabolic syndrome even at lower BMI levels (12, 13). This disparity suggests that BMI may not be a fully accurate measure of body adiposity in the Asian population.

Several studies have highlighted the occurrence of NAFLD in individuals with low BMI, a phenomenon observed in South Asia as well. For instance, Das et al. reported a 5.1% prevalence of lean NAFLD in a community-based study, despite the majority of participants having a BMI below 25 kg/m2 (17). In Pakistan, Abbas et al. documented a 15.3% prevalence of NAFLD in a hepatitis awareness program, where 22.5% of the population had a BMI below 25 kg/m2, although a higher BMI cut-off was used (5). A study by Khan RTY et al. revealed that approximately 33% of the non-obese Pakistani population presented with NAFLD, further underscoring the significance of lean NAFLD (18). These findings highlight the need for a nuanced understanding of NAFLD prevalence among non-obese individuals in Pakistan, using the Asian population standard BMI cut-off of less than 23 kg/m2.

Given the multifactorial nature of NAFLD, which encompasses various metabolic and cardiovascular risk factors, it is crucial to explore these associations in the context of lean individuals. Studies have shown that even with a low BMI, Asians possess a higher percentage of body fat, which may contribute to NAFLD development (14-16). The interplay between visceral adiposity and metabolic disorders like diabetes and hypertension has been well-documented, suggesting that these factors may be pertinent even in non-obese individuals (20-22). This association is particularly relevant in the Asian population, which exhibits a higher predisposition to insulin resistance and type 2 diabetes at lower BMI thresholds compared to other ethnic groups (25, 26).

Therefore, this study aims to determine the factors predictive of NAFLD in the non-obese Pakistani population, defined by a BMI of less than 23 kg/m2. The study focuses on identifying the metabolic and lifestyle variables that may contribute to NAFLD in this demographic, thereby providing a comprehensive understanding of the disease's behavior in a population that is not typically associated with obesity. Identifying these factors is critical for early diagnosis and intervention, which could mitigate the risk of progression to more severe liver conditions such as cirrhosis. By addressing the gap in current knowledge regarding lean NAFLD in Pakistan, this research seeks to contribute to the broader epidemiological understanding of NAFLD and inform targeted public health strategies.

MATERIAL AND METHODS

This descriptive, cross-sectional study was conducted at the Department of Hepatogastroenterology, Sindh Institute of Urology and Transplantation (SIUT), from November 1, 2020, to October 31, 2021. The study population included patients of either gender, aged 18-70 years, who presented with abdominal pain and had a body mass index (BMI) less than 23 kg/m2. Patients with a history of viral hepatitis, significant alcohol intake, hepatocellular carcinoma, or any other malignancy were excluded to ensure the specificity of the study for non-alcoholic fatty liver disease (NAFLD).

Ethical approval for the study was obtained from the Ethical Review Committee of SIUT (approval number: ERC-SIUT-217), and all participants provided informed consent in accordance with the Declaration of Helsinki. Data collection involved recording demographic information, medical history, and relevant clinical parameters. Ultrasound abdomen examinations were performed by a single consultant radiologist with over five years of experience to minimize inter-observer variation. The ultrasound examinations utilized the TOSHIBA Aplio 50 model (MCM17545TS) and were conducted after ensuring a fasting period of at least 8-10 hours. NAFLD was defined by the presence of a hyperechoic liver on ultrasound.

Clinical assessments included recording the history of hypertension and smoking. Laboratory investigations were performed at the time of presentation and included liver function tests, fasting blood sugar levels, and fasting lipid profiles. The primary outcome was the presence or absence of fatty liver on ultrasound. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages.

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 25.0. Continuous variables were analyzed using the Student t-test, while categorical variables were analyzed using the Chi-square test. Variables that were statistically

Journal of Health and Rehabilitation Research 2791-156X JHRR

significant on univariate analysis underwent multivariate logistic regression analysis to identify independent predictors of lean NAFLD. A p-value of ≤ 0.05 was considered statistically significant.

A total of 194 patients with a BMI of less than 23 kg/m2 were included in the study. Of these, 107 (55.2%) were females and 87 (44.8%) were males, with a mean age of 36.1 ± 9.6 years. The mean BMI was 21 ± 1.7 kg/m2. The socioeconomic status of the participants was predominantly middle class, with 127 (65.5%) patients. On ultrasound, 48 (24.7%) patients were diagnosed with NAFLD. The prevalence of hypertension, diabetes, and smoking was recorded as 40.2%, 20.6%, and 25.3%, respectively. Additionally, 27.8% of the patients had increased triglyceride levels, while 37.1% had decreased high-density lipoprotein (HDL) levels.

The univariate analysis identified hypertension, diabetes, hypertriglyceridemia, decreased HDL levels, and elevated alanine transaminase (ALT) levels as significant factors associated with NAFLD. However, multivariate logistic regression analysis revealed that diabetes, smoking, hypertriglyceridemia, and decreased HDL levels were independently associated with lean NAFLD. The study's findings underscore the importance of recognizing and addressing these risk factors in the non-obese Pakistani population to mitigate the risk of NAFLD and its potential complications.

RESULTS

A total of 194 patients with a BMI less than 23 kg/m2 were included in the study. Of these, 107 (55.2%) were females and 87 (44.8%) were males. The mean age of the patients was 36.1 ± 9.6 years, and the mean BMI was 21 ± 1.7 kg/m2. The socioeconomic status of the participants predominantly fell within the middle class, comprising 127 (65.5%) patients.

On ultrasound examination, NAFLD was detected in 48 (24.7%) patients. The distribution of clinical characteristics and laboratory findings in the study population is presented in Table 1. Among the participants, 78 (40.2%) were hypertensive, 40 (20.6%) were diabetic, and 49 (25.3%) were smokers. Additionally, increased triglyceride levels were noted in 54 (27.8%) patients, while decreased high-density lipoprotein (HDL) levels were observed in 72 (37.1%) patients.

Table 1: Baseline Characteristics of Study Population

Characteristic	Total (n=194)	NAFLD Present (n=48)	NAFLD Absent (n=146)	p-value
Gender				
- Male	87 (44.8%)	17 (35.4%)	70 (47.9%)	0.130
- Female	107 (55.2%)	31 (64.6%)	76 (52.1%)	
Socioeconomic Class				
- Upper class	26 (13.4%)	8 (16.7%)	18 (12.3%)	0.476
- Middle class	127 (65.5%)	28 (58.3%)	99 (67.8%)	
- Lower class	41 (21.1%)	12 (25.0%)	29 (19.9%)	
Smoking				
- Yes	49 (25.3%)	35 (73.0%)	14 (9.6%)	≤0.001
- No	145 (74.7%)	13 (27.0%)	132 (90.4%)	
Hypertension				
- Yes	78 (40.2%)	30 (62.5%)	48 (32.9%)	≤0.001
- No	116 (59.8%)	18 (37.5%)	98 (67.1%)	
Diabetes				
- Yes	40 (20.6%)	24 (50.0%)	16 (11.0%)	≤0.001
- No	154 (79.4%)	24 (50.0%)	130 (89.0%)	
Hypertriglyceridemia				
- Yes	54 (27.8%)	32 (66.7%)	22 (15.1%)	≤0.001
- No	140 (72.2%)	16 (33.3%)	124 (84.9%)	
Decreased HDL-C levels				
- Yes	72 (37.1%)	36 (75.0%)	36 (24.7%)	≤0.001
- No	122 (62.9%)	12 (25.0%)	110 (75.3%)	
Mean Age (years ± S.D)	36.1 ± 9.6	35.4 ± 8.5	36.3 ± 10	0.570
Hemoglobin (g/dL ± S.D)	13 ± 1.2	12.9 ± 1.1	13.1 ± 1.3	0.321
Total Leucocyte Count (x10^9/L ± S.D)	4.5 ± 4.2	4.8 ± 4.3	4.3 ± 4.1	0.473

Journal of Health and Rehabilitation Research 2791-156X JHRR

Characteristic	Total (n=194)	NAFLD Present (n=48)	NAFLD Absent (n=146)	p-value
Platelet Count (x10^9/L ± S.D)	299 ± 135	295 ± 136	301 ± 134	0.764
Total Bilirubin (mg/dL ± S.D)	0.77 ± 0.35	0.69 ± 0.26	0.79 ± 0.37	0.080
Aspartate Transaminase (IU ± S.D)	33.4 ± 33	41.1 ± 59.7	30.8 ± 15.9	0.650
Alanine Transaminase (IU ± S.D)	44.4 ± 24.3	51 ± 34.6	42 ± 19.4	0.030
Alkaline Phosphatase (IU ± S.D)	126.9 ± 67.5	147.6 ± 119.1	120 ± 35	0.020
Gamma-Glutamyl Transferase (IU ± S.D)	35.7 ± 40.2	36 ± 72	35.6 ± 20.8	0.956

Univariate analysis identified hypertension, diabetes, smoking, hypertriglyceridemia, decreased HDL levels, and increased alanine transaminase (ALT) levels as significantly associated with the presence of fatty liver in non-obese patients. These associations are detailed in Table 2.

Table 2: Comparison of Variables in Predicting NAFLD in Non-obese Population

Variable	Fatty Liver Present (n=48)	Fatty Liver Absent (n=146)	p-value
Hypertension	30 (62.5%)	48 (32.9%)	≤0.001
Diabetes	24 (50.0%)	16 (11.0%)	≤0.001
Smoking	35 (73.0%)	14 (9.6%)	≤0.001
Hypertriglyceridemia	32 (66.7%)	22 (15.1%)	≤0.001
Decreased HDL-C levels	36 (75.0%)	36 (24.7%)	≤0.001
Alanine Transaminase (ALT)	51 ± 34.6 IU	42 ± 19.4 IU	0.030
Alkaline Phosphatase	147.6 ± 119.1 IU	120 ± 35 IU	0.020

Multivariate logistic regression analysis revealed that diabetes, smoking, hypertriglyceridemia, and decreased HDL levels were independently associated with lean NAFLD, as shown in Table 3.

Table 3: Multivariate Logistic Regression Analysis of Independent Predictors of NAFLD in Non-obese Population

Variable	p-value	Odds Ratio	95% Confidence Interval
Diabetes	0.037	9.4	1.1 – 76.5
Smoking	≤0.001	46.4	8.4 – 256.2
Hypertriglyceridemia	0.016	4.75	1.3 – 16.9
Decreased HDL-C levels	≤0.001	36.8	6.2 – 218.5

These findings indicate that in a non-obese Pakistani population, diabetes, smoking, hypertriglyceridemia, and decreased HDL levels are significant predictors of NAFLD. These results underscore the importance of monitoring these factors to identify individuals at risk and to implement early interventions to prevent the progression of NAFLD and its associated complications.

DISCUSSION

The study demonstrated a notable prevalence of non-alcoholic fatty liver disease (NAFLD) among non-obese individuals in a Pakistani population, with significant associations identified between lean NAFLD and factors such as diabetes, smoking, hypertriglyceridemia, and decreased HDL-C levels. These findings align with previous research highlighting that NAFLD is not confined to obese populations but also affects individuals with a lower body mass index (BMI) (1). This study contributed to the understanding of lean NAFLD, emphasizing the need for vigilance in non-obese individuals who may be at risk of developing this condition.

The prevalence of lean NAFLD observed in this study (24.7%) was higher than previously reported figures in other Asian populations. For instance, Das et al. found a 5.1% prevalence of lean NAFLD in an Indian community-based study (17). The higher prevalence in this Pakistani cohort underscores regional variations and potentially different genetic or lifestyle factors contributing to the development of NAFLD. Additionally, the findings are consistent with studies showing that South Asians have a higher propensity for visceral adiposity and metabolic abnormalities, even at lower BMI thresholds (12, 13).

The independent association of diabetes with lean NAFLD observed in this study is consistent with the literature, where insulin resistance and type 2 diabetes mellitus (T2DM) are well-documented risk factors for NAFLD (25, 26). The significant correlation between smoking and NAFLD also corroborates findings from studies in Japanese and Chinese populations, where smoking was associated with an increased risk of fatty liver disease (30, 32). Hypertriglyceridemia and decreased HDL-C levels as independent predictors further highlight the role of dyslipidemia in the pathogenesis of NAFLD, aligning with previous research (33, 34).

This study had several strengths, including a well-defined cohort of non-obese individuals and the use of ultrasound, a non-invasive and widely available diagnostic tool, to detect hepatic steatosis. The inclusion of a comprehensive set of metabolic parameters allowed for a detailed analysis of potential risk factors. However, the study also had limitations. The cross-sectional design precluded the establishment of causality. The reliance on ultrasound for diagnosing NAFLD, while practical, may not be as definitive as liver biopsy, which remains the gold standard (35, 36). Additionally, the single-center nature of the study and the relatively small sample size limit the generalizability of the findings. Selection bias may also have influenced the results, as the study was conducted in a tertiary care setting, potentially skewing the sample towards more severe cases.

Future research should focus on longitudinal studies to elucidate the causal pathways linking these risk factors to lean NAFLD. Larger, multicenter studies could provide more generalizable data and help identify regional variations in the prevalence and risk factors of lean NAFLD. Moreover, incorporating more advanced imaging techniques and biomarkers could enhance diagnostic accuracy and provide deeper insights into the disease's pathophysiology.

The study highlighted the importance of recognizing lean NAFLD as a significant clinical entity. Healthcare providers should be aware that non-obese individuals are not immune to NAFLD and should consider screening for NAFLD in patients with diabetes, smoking habits, hypertriglyceridemia, or low HDL-C levels. Early identification and management of these risk factors are crucial to preventing the progression of NAFLD and its complications, such as cirrhosis and hepatocellular carcinoma.

CONCLUSION

In conclusion, this study provided valuable insights into the prevalence and predictors of lean NAFLD in a Pakistani population. It underscored the importance of metabolic health, even in individuals with a lower BMI, and highlighted the need for further research to improve the understanding and management of lean NAFLD. Recognizing and addressing this condition is essential for mitigating its long-term health impacts and improving patient outcomes.

REFERENCES

1. Chalasani N, Younossi Z, Lavine JE, Diehl AM, Brunt EM, Cusi K, et al. The Diagnosis and Management of Non-Alcoholic Fatty Liver Disease: Practice Guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association. Hepatology. 2012 Jun;55:2005-23.
2. Matteoni CA, Younossi ZM, Gramlich T, Boparai N, Liu YC, McCullough AJ. Nonalcoholic Fatty Liver Disease: A Spectrum of Clinical and Pathological Severity. Gastroenterology. 1999 Jun 1;116:1413-9.
3. Farrell GC, Wong VW, Chitturi S. NAFLD in Asia- As Common and Important as in the West. Nat Rev Gastroenterol Hepatol. 2013 May;10:307-18.
4. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global Epidemiology of Non-Alcoholic Fatty Liver Disease - Meta-Analytic Assessment of Prevalence, Incidence and Outcomes. Hepatology. 2016 Jul 1;64:73-84.
5. Abbas ZA, Zaheer R. Non-Alcoholic Fatty Liver Disease a Real Threat in Pakistan. J Pak Med Assoc. 2020 Dec 1;70(12(B)):2437-40.
6. Onitsuka Y, Takeshima F, Ichikawa T, Kohno S, Nakao K. Estimation of Visceral Fat and Fatty Liver Disease Using Ultrasound in Patients with Diabetes. Intern Med. 2014;53(6):545-53.
7. Pan WH, Yeh WT. How to Define Obesity? Evidence-Based Multiple Action Points for Public Awareness, Screening, and Treatment: An Extension of Asian-Pacific Recommendations. Asia Pac J Clin Nutr. 2008;17(3):370-4.
8. Diagnosis and Classification of Diabetes Mellitus. Diabetes Care. 2005 Jan 1;28(S37)
.
9. Milić S, Lulić D, Štimac D. Non-Alcoholic Fatty Liver Disease and Obesity: Biochemical, Metabolic and Clinical Presentations. World J Gastroenterol. 2014 Jul 28;20(28):9330.
10. Ha Y, Seo N, Shim JH, Kim SY, Park JA, Han S, et al. Intimate Association of Visceral Obesity with Non-Alcoholic Fatty Liver Disease in Healthy Asians: A Case-Control Study. J Gastroenterol Hepatol. 2015 Nov;30:1666-72.
11. Wang L, Guo J, Lu J. Risk Factor Compositions of Nonalcoholic Fatty Liver Disease Change with Body Mass Index in Males and Females. Oncotarget. 2016 Jun 14;7(24):35632.
12. Rush E, Plank L, Chandu V, Laulu M, Simmons D, Swinburn B, et al. Body Size, Body Composition, and Fat Distribution: A Comparison of Young New Zealand Men of European, Pacific Island, and Asian Indian Ethnicities. N Z Med J. 2004;117(1207):1-9.
13. Deurenberg-Yap M, Chew SK, Deurenberg P. Elevated Body Fat Percentage and Cardiovascular Risks at Low Body Mass Index Levels Among Singaporean Chinese, Malays and Indians. Obes Rev. 2002 Aug;3(3):209-15.

14. Wang J, Thornton JC, Russell M, Burastero S, Heymsfield SB, Pierson RN. Asians Have Lower Body Mass Index but Higher Percent Body Fat Than Do Whites: Comparisons of Anthropometric Measurements. Am J Clin Nutr. 1994 Jul 1;60:23-8.
15. Deurenberg-Yap M, Schmidt G, Staveren van WA, Deurenberg P. The Paradox of Low Body Mass Index and High Body Fat Percent Among Chinese, Malays and Indians in Singapore. Int J Obes. 2000 Aug;24:1011-7.
16. Grasgruber P, Sebera M, Hrazdíra E, Cacek J, Kalina T. Major Correlates of Male Height: A Study of 105 Countries. Econ Hum Biol. 2016 May 1;21:172-95.
17. Das K, Mukherjee PS, Ghosh A, Ghosh S, Mridha AR, Mukhopadhyay P, et al. Nonobese Population in a Developing Country Has a High Prevalence of Nonalcoholic Fatty Liver and Significant Liver Disease. Hepatology. 2010 May;51(5):1593-602.
18. Khan RTY, Hussain SZ, Shahzad S, et al. Frequency of Non-Alcoholic Fatty Liver Disease Among the Non-Obese Population Presenting to the Gastrointestinal Outpatient Clinic. J Liaquat Natl Hosp. 2024;2(1):117-121.
19. Wong RJ, Liu B, Bhuket T. Significant Burden of Nonalcoholic Fatty Liver Disease with Advanced Fibrosis in the US: A Cross-Sectional Analysis of 2011-2014 National Health and Nutrition Examination Survey. Aliment Pharmacol Ther. 2017 Nov;46(10):974-80.
20. Kwon YM, Oh SW, Hwang SS, Lee C, Kwon H, Chung GE. Association of Nonalcoholic Fatty Liver Disease with Components of Metabolic Syndrome According to Body Mass Index in Korean Adults. Am J Gastroenterol. 2012;107:1852–8.
21. Lee CM, Huxley RR, Wildman RP, Woodward M. Indices of Abdominal Obesity Are Better Discriminators of Cardiovascular Risk Factors Than BMI: A Meta-Analysis. J Clin Epidemiol. 2008 Jul;61(7):646-53.
22. Xu C, Yu C, Ma H, Xu L, Miao M, Li Y. Prevalence and Risk Factors for the Development of Nonalcoholic Fatty Liver Disease in a Nonobese Chinese Population: The Zhejiang Zhenhai Study. Am J Gastroenterol. 2013;108:1299–304.
23. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global Epidemiology of Non-Alcoholic Fatty Liver Disease: Meta-Analytic Assessment of Prevalence, Incidence, and Outcomes. Hepatology. 2016;64:73–84.
24. Zheng RD, Chen ZR, Chen JN, Lu YH, Chen J. Role of Body Mass Index, Waist-To-Height and Waist-To-Hip Ratio in Prediction of Nonalcoholic Fatty Liver Disease. Gastroenterol Res Pract. 2012;2012:1-8.
25. WHO Expert Consultation. Appropriate Body-Mass Index for Policy and Intervention Strategies. Lancet. 2004;363:157–63.
26. Park YW, Allison DB, Heymsfield SB, Gallagher D. Larger Amounts of Visceral Adipose Tissue in Asian Americans. Obes Res. 2001;9:381–7.
27. Younossi ZM, Stepanova M, Negro F, et al. Nonalcoholic Fatty Liver Disease in Lean Individuals in the United States. Medicine (Baltimore). 2012;91:319–27.
28. Donati G, Stagni B, Piscaglia F, Venturoli N, Morselli-Labate AM, Rasciti L, et al. Increased Prevalence of Fatty Liver in Arterial Hypertensive Patients with Normal Liver Enzymes: Role of Insulin Resistance. Gut. 2004;53:1020-3.
29. Lankarani KB, Ghaffarpasand F, Mahmoodi M, Lotfi M, Zamiri N, Hyderi ST, et al. Non Alcoholic Fatty Liver Disease in Shiraz. Hepat Mon. 2013;13
.
30. Okamoto M, Miyake T, Kitai K, Furukawa S, Yamamoto S, Senba H, et al. Cigarette Smoking Is a Risk Factor for the Onset of Fatty Liver Disease in Nondrinkers: A Longitudinal Cohort Study. PLoS One. 2018;13
.
31. Hamabe A, Uto H, Imamura Y, Kusano K, Mawatari S, Kumagai K, et al. Impact of Cigarette Smoking on Onset of Nonalcoholic Fatty Liver Disease Over a 10-Year Period. J Gastroenterol. 2011;46:769–78.
32. Liu Y, Dai M, Bi Y, Xu M, Xu Y, Li M, et al. Active Smoking, Passive Smoking, and Risk of Nonalcoholic Fatty Liver Disease: A Population-Based Study in China. J Epidemiol. 2013;23:115–21.
33. Chen Z, Qin H, Qiu S, Chen G, Chen Y. Correlation of Triglyceride to High-Density Lipoprotein Cholesterol Ratio with Nonalcoholic Fatty Liver Disease Among the Non-Obese Chinese Population with Normal Blood Lipid Levels: A Retrospective Cohort Research. Lipids Health Dis. 2019 Aug 9;18(1):162.
34. Zhang YN, Wang QQ, Chen YS, Shen C, Xu CF. Association Between Serum Uric Acid to HDL-Cholesterol Ratio and Nonalcoholic Fatty Liver Disease in Lean Chinese Adults. Int J Endocrinol. 2020 Mar 23;2020:5953461.
35. Mathiesen U, Franzén L, Aselius H, Resjö M, Jacobsson L, Foberg U, et al. Increased Liver Echogenicity at Ultrasound Examination Reflects Degree of Steatosis but Not of Fibrosis in Asymptomatic Patients with Mild/Moderate Abnormalities of Liver Transaminases. Dig Liver Dis. 2002;34:516-22.
36. Joseph AE, Saverymuttu SH, al-Sam S, Cook MG, Maxwell JD. Comparison of Liver Histology with Ultrasonography in Assessing Diffuse Parenchymal Liver Disease. Clin Radiol. 1991;43:26-31.

Journal of Health and Rehabilitation Research 2791-156X JHRR

37. Palmentieri B, de Sio I, La Mura V, Masarone M, Vecchione R, Bruno S, et al. The Role of Bright Liver Echo Pattern on Ultrasound B-Mode Examination in the Diagnosis of Liver Steatosis. Dig Liver Dis. 2006;38:485-9.