Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 2; P263

Fatty Liver Infiltration on Executive Health Screen

C. Frengopoulos[1], F. Azadian[1], M. Ryan[1,2]

1. School of Medicine, University of Limerick, Limerick, Ireland.
2. Consultant Endocrinologist, Bon Secours at Barringtons, Limerick, Ireland.

Abstract

Aim

To describe the relationship between level of fatty infiltration in non-alcoholic fatty liver disease (NAFLD) and known risk factors in a population with incidentally discovered findings.

Methods

This was a retrospective cohort study through chart audit of asymptomatic patients attending an executive health screen. Pearson correlation coefficients (r) were calculated between degree of fatty liver infiltration and known risk factors of fatty liver disease.

Results

Thirty-six individuals were included. Participants tended to be male (n=27,75.0%) with high BMI (30.59±3.66 kg/m^2). Nearly half of patients (n=15, 41.7%) had a moderate degree of fatty infiltration. The degree of infiltration was positively correlated with BMI, total cholesterol, LDL and triglycerides and negatively correlated with weekly alcohol consumption and presence of metabolic syndrome. None of these relationships were statistically significant.

Discussion

The current study investigates the relationship between level of fatty liver infiltration and known pathogenic risk factors previously described in the literature. No relationship was found between level of fatty liver infiltration and metabolic syndrome, BMI, lipid levels, or alcohol consumption in our population of asymptomatic individuals. This study further highlights the need to better identification and management of NAFLD to optimize risk factors and decrease risk of complications.

Introduction

The histological representation of hepatic steatosis has been known for centuries. Initial descriptions were used in the setting of alcoholic liver disease, however in 1980, a non-alcoholic steatosis was described.[1] This Non-Alcoholic Fatty Liver Disease (NAFLD) was noted in biopsy samples of patients without a history of alcohol abuse or a significant history of alcohol intake.[1]

Other distinguishing features are the biochemical patterns: NAFLD is described as having alanine aminotransferase (ALT) levels exceeding those of aspartate aminotransferase (AST), while alcoholic liver injury is characterized by a high AST:ALT ratio.[2]

NAFLD is currently defined as macrovesicular steatosis in ≥5% hepatocytes, with the absence of secondary causes, such as alcohol or drugs.[3,4] It refers to a spectrum of disease from non-alcoholic fatty liver (NAFL) and non-alcoholic steatohepatitis (NASH) to fibrosis and cirrhosis.[2–4] The global prevalence is estimated to be around 25%, with a rising incidence due to increasing levels of obesity, Type 2 Diabetes Mellitus (T2DM) and metabolic syndrome.[2,3,5,6] This prevalence may be underestimated due to the asymptomatic nature and prolonged period before progression. NAFLD may be initially identified due to derangement of liver function tests or evidence of hepatic steatosis on abdominal ultrasound, with the gold standard for diagnosis being liver biopsy.[2,4,7]

The pathogenesis of NAFLD is related to a decrease in insulin sensitivity and hyperinsulinemia.[8] This insensitivity results in decreased effects of insulin on the metabolism of both lipids and glucose.[9] The literature indicates that this effect is not only found in patients with abnormal glucose regulation or obesity, but is also observed in some individuals with normal weight and normal glucose tolerance.[8,9] Research supports the connection between metabolic syndrome and NAFLD, with some suggesting that the two are merely different facets of the same pathophysiologic mechanism.[5] Other proposed risk factors for the development of NAFLD include diet high in fats and cigarette smoking.[10] However, there are still gaps in the literature with regards to the lifestyle factors that predispose individuals to developing NAFLD, especially in asymptomatic patients.

The objective of the current study is to describe the relationship between level of fatty infiltration in hepatic steatosis and known risk factors in a population with incidentally discovered fatty liver disease.

Methods

This was a retrospective cohort study through chart audit on individuals attending Bon Secours Hospital in Limerick, Ireland for Executive Health Screen between 2011-2018. Data were abstracted for individuals with incidental findings of fatty liver on abdominal ultrasound.

The following information was collected from patient charts: age, sex, height, weight, blood pressure, total cholesterol, HDL, LDL, triglycerides, fasting glucose, ALT, GGT, smoking status, alcohol consumption, and extent of fatty liver infiltration.
Presence of metabolic syndrome was identified by the presence of three or more of the following: abdominal obesity (waist circumference >102 cm in men, >88 cm in women), elevated triglycerides (>150 mg/dl or on drug treatment for elevated triglycerides), reduced HDL-C level (<40 mg/dl in men, <50 mg/ dl in women or on drug treatment for reduced HDL-C), hypertension (systolic blood pressure >130 mmHg or diastolic blood pressure >85 mm Hg or on antihypertensive drug treatment) and impaired fasting glucose (100 - 125 mg/dl or on antidiabetic drug treatment).[5]

Level of fatty infiltration was graded as mild, moderate or severe. Above information was collected as part of the Executive Health Screen. Individuals were asymptomatic at the time of screening.

Pearson correlation coefficients (r) were calculated between degree of fatty liver infiltration and the following: BMI, presence of metabolic syndrome, total cholesterol, LDL, triglycerides, alcohol consumption per week. No patients in the current study met criteria for alcoholic fatty liver disease. We hypothesized that level of fatty liver infiltration would be positively correlated with all above-mentioned variables.

Variables were calculated as means and SDs or frequencies and percentages as appropriate. Significance level was set to $p<0.05$. Statistical analysis was performed using the IBM SPSS Statistics version 24.0 (IBM Corporation, Armonk, NY).

Results

Demographic data are summarized in Table 1. Thirty-six participants were included in the study. Participants in the analysis tended to be male (n=27, 75.0%) with BMI in the class I obesity range (BMI=30.59±3.66). A number of participants reported having comorbid conditions (n=19, 52.8%). The most commonly reported conditions were dyslipidemia (n=6, 16.7%), hypertension (n=6, 16.7%), respiratory conditions (n=3, 8.3%) and thyroid conditions (n=3, 8.3%). Just under half of participants (n=17, 47.2%) were not taking any medication. Of participants taking medications, four (11.1%) were taking lipid lowering medications, four (11.1%) were on antihypertensive medications and two (5.5%) were taking both lipid lowering medications and antihypertensives. Nearly half of patients (n=15, 41.7%) had a moderate degree of fatty liver infiltration based on ultrasound reports.

Table 1. Descriptive statistics for n=36 patients included in study.

Characteristic	**Values**
Age (years)	59.89 ± 10.29
Sex (n, % males)	27 (75.0%)
Body Mass Index (kg/m^2)	30.59 ± 3.66
Blood Pressure (mmHg)	135.31 ± 12.13 / 73.17 ± 6.91
Alcohol Consumption (units/week)	6.77 ± 8.53
Metabolic Syndrome (n, % yes)	7 (19.4%)
Number of Medications	1.89 ± 2.63
Total Cholesterol	5.19 ± 1.19
HDL	1.26 ± 0.32
LDL	3.15 ± 1.06
Triglycerides	1.68 ± 0.83
Glucose	5.52 ± 0.54
ALT	40.72 ± 17.45

GGT	44.72 ± 55.50
Level of Fatty Infiltration	
Minor	9 (25.0%)
Minor to moderate	3 (8.3%)
Moderate	15 (41.7%)
Moderate to severe	1 (2.7%)
Severe	8 (22.2%)

Note: Values are mean ± SD, n (%), or as otherwise indicated

Level of fatty liver infiltration was negatively correlated with weekly alcohol consumption and presence of metabolic syndrome, but positively correlated with BMI, total cholesterol, LDL and triglycerides. None of these relationships were statistically significant. Unsurprisingly, presence of metabolic syndrome was positively correlated with BMI, $r(36)=0.432$, $p=0.015$ and total cholesterol was correlated with LDL $r(36)=0.797$, $p<0.001$. Complete results for the correlation analysis are found in Table 2.

Table 2. Correlation analysis of relationships between fatty liver infiltration and other variables.

	Fatty Liver Infiltration	**Body Mass Index**	**Metabolic Syndrome**	**Total Cholesterol**	**LDL**	**Triglycerides**	**Alcohol Consumption per week**
Fatty Liver Infiltration		0.213 0.250 36	-0.065 0.728 36	0.142 0.447 36	0.280 0.127 36	0.339 0.062 36	-0.084 0.654 36
Body Mass Index			**0.432*** **0.015** **36**	-0.158 0.397 36	-0.044 0.815 36	0.067 0.721 36	0.077 0.682 36
Metabolic Syndrome				0.020 0.916 36	-0.110 0.557 36	0.182 0.328 36	0.090 0.630 36
Total Cholesterol					**0.797**** **0.000** **36**	0.300 0.101 36	-0.112 0.547 36
LDL		Pearson *r* Sig (2 tailed) N				0.004 0.984 36	-0.192 0.302 36
Triglycerides							0.075 0.688 36
Alcohol Consumption per week							

*Note: *Correlation significant at p<0.05; **Correlation significant at p<0.001*

Discussion

The current study was a retrospective chart audit of patients with incidental finding of fatty liver disease on Executive Health Screen. It demonstrates that level of fatty liver infiltration is not related to metabolic syndrome, BMI, lipid levels, or alcohol consumption.

Participants in the current study were demonstrated to have significant levels of fatty liver infiltration while being asymptomatic for any liver pathology. This is similar to reports in the literature, where hepatic steatosis was detected incidentally during investigation of other complaints.[2,3] While in NAFLD there are described patterns of liver biochemical tests,[2] there is also evidence that many patients will have normal liver function tests.[3] This has been a limitation with regards to screening for NAFLD in the general population.[5] Other limitations have include the low accuracy of non-invasive tools and inconsistency of self-reported ethanol ingestion histories.[2,5,8]

Interestingly, level of fatty liver infiltration in the current study was not found to be related to metabolic syndrome. However, these results may be limited by the small sample size of the current study. Metabolic syndrome refers to a cluster of risk factors that lead to an increased risk for atherosclerotic cardiovascular disease, type 2 diabetes mellitus and chronic kidney disease.[5,11] The etiology of both metabolic syndrome and NAFLD have been linked to insulin resistance and compensatory hyperinsulinemia in patients with obesity and normal body weight.[5,8,9,11,12]

The results from this study demonstrate a relatively healthy overweight population, with many reporting one or no comorbidities. The BMI of the participants reported in the current study is similar to the average BMI of those presenting for Executive Health Screen at this institution over the study period. The high BMI found in study participants is not surprising as the prevalence of obesity has been increasing in Ireland over the last two decades.[13] The 2017 Healthy Ireland Survey reported that 39% of Irish adults were overweight and 23% were obese.[14] These numbers increase to 44% in the overweight category and 32% in the obese category for adults between the ages of 55-64 years, which is the age group captured by the current study.[14] Therefore, the population captured by the current study may be comparable to the larger population, although further research is needed to confirm whether the findings of the current study are generalizable. Other considerations when interpreting the results from the current study are recall bias and possible under-reporting of alcohol consumption.

Although the initial stages NAFLD are asymptomatic, there are several serious complications that must be considered. In some patients with NAFLD, isolated steatosis can progress to advanced stages with non-alcoholic steatohepatitis (NASH) and fibrosis, increasing the risk of cirrhosis and hepatocellular carcinoma,[12] although only a minority of patients will develop these complications of chronic liver disease.[3] The most commonly described complications and cause of death in patients with NAFLD is cardiovascular disease.[5,9,15] A large cohort trial has demonstrated a higher 5-year health care cost in individuals with NAFLD due to the cardiovascular burden in these individuals.[16]

Management of NAFLD is crucial in order to minimize complications. Current options depend on severity of disease but includes lifestyle modifications and pharmacological treatment.

Drug treatments assessed in NAFLD seem to differ with respect to cardiometabolic and antifibrotic efficacy, suggesting the need to better identify and tailor the most appropriate treatment approach, or to use a combination of approaches.[12] The assessment and management of blood pressure, lipids, weight, smoking status and diabetes control are therefore the basis of management in NAFLD, especially in the early stages.[3,6] Further longitudinal research is required to better characterize the risk profile and impact of treatment in individuals with NAFLD.

To conclude, the current study investigates the relationship between level of fatty liver infiltration and known pathogenic risk factors previously described in the literature. No relationship was found between level of fatty liver infiltration and metabolic syndrome, BMI, lipid levels, or alcohol consumption in our population of asymptomatic individuals. This study further highlights the need to better identification and management of NAFLD.

Declaration of Conflicts of Interest:
The authors have no conflicts of interest to declare.

Corresponding Author:
Dr. Mary Ryan
Consultant Endocrinologist
Bon Secours at Barrington's,
George's Quay,
Limerick,
County Limerick,
Ireland.
E-mail: docmaryryan@gmail.com

References:

1. Ludwig J, Viggiano TR, McGill DB, Ott BJ. Nonalcoholic steatohepatitis. Mayo Clinic experiences with a hitherto unnamed disease. Mayo Clin Proc. 1980;55(7):434-438. doi:10.1111/j.1572-0241.2002.07069.x
2. Sattar N, Forrest E, Preiss D. Non-alcoholic fatty liver disease. Br Med J. 2014;349. doi:10.2307/26516755
3. Maurice J, Manousou P. Non-alcoholic fatty liver disease. C Gastroenterol. 2018;18:245-250.
4. Neuschwander-Tetri B. Nonalcoholic steatohepatitis: Summary of an AASLD Single Topic Conference. Hepatology. 2003;37(5):1202-1219. doi:10.1053/jhep.2003.50193
5. Paschos P, Paletas K. Non alcoholic fatty liver disease and metabolic syndrome. Hippokratia. 2009;13(1):9-19.
6. Jepsen P, Grønbaek H. Prognosis and staging of non-alcoholic fatty liver disease: Impact of staging on mortality is unclear, and liver biopsy remains the definitive method. Br Med J. 2011;343(7836):1236.

7. George ES, Roberts SK, Nicoll AJ, et al. Non Alcoholic Fatty Liver Disease Patients Attending Two Metropolitan Hospitals in Melbourne, Australia; High Risk Status and Low Prevalence. Intern Med J. 2018;48(11):1369-1376. doi:10.1111/imj.13973
8. Lee JH, Rhee PL, Lee JK, et al. Role of Hyperinsulinemia and Glucose Intolerance in the Pathogenesis of Nonalcoholic Fatty Liver in Patients with Normal Body Weight. Korean J Intern Med. 1998;13(1):10-14. doi:10.3904/kjim.1998.13.1.10
9. Marchesini G, Brizi M, Bianchi G, et al. Nonalcoholic Fatty Liver Disease A Feature of the Metabolic Syndrome. Diabetes. 2001;50:1844-1850.
10. Benedict M, Zhang X. Non-alcoholic fatty liver disease: An expanded review. World J Hepatol. 2017;9(16):715-732. doi:10.4254/wjh.v9.i16.715
11. Defronzo RA, Ferrannini E. Insulin Resistance: A Multifaceted Syndrome Responsible for NIDDM, Obesity, Hypertension, Dyslipidemia, and Atherosclerotic Cardiovascular Disease. Vol 14.; 1991.
12. Stefan N, Häring HU, Cusi K. Non-alcoholic fatty liver disease: causes, diagnosis, cardiometabolic consequences, and treatment strategies. Lancet Diabetes Endocrinol. 2019;7(4):313-324. doi:10.1016/S2213-8587(18)30154-2
13. Irish Heart Foundation and Social Justice Ireland. Reducing Obesity and Future Health Costs. Dublin, Ireland; 2015.
14. Healthy Ireland. Healthy Ireland Survey: Summary of Findings. Dublin, Ireland; 2017.
15. Lazo M, Hernaez R, Bonekamp S, et al. Non-alcoholic fatty liver disease and mortality among US adults: prospective cohort study. Br Med J. 2011;343(7836):1245. doi:10.1136/bmj.d6891
16. Baumeister SE, Völzke H, Marschall P, et al. Impact of Fatty Liver Disease on Health Care Utilization and Costs in a General Population: A 5-Year Observation. Gastroenterology. 2008;134(1):85-94. doi:10.1053/j.gastro.2007.10.024