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ORIGINAL ARTICLE

Prevalence of hepatic steatosis and its relation to liver function tests and lipid profile in patients at medical check-up☆

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KEYWORDS
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Abstract
Introduction and aims: Nonalcoholic fatty liver disease has now become a worldwide health problem, and its dramatic increase is due to the prevalence of diseases such as obesity, type 2 diabetes mellitus, and metabolic syndrome. The aim of our study was to publish the current prevalence of hepatic steatosis in a Mexican population undergoing routine medical check-up, as well as to analyze its relation to BMI, liver function tests, and lipid profile.
Materials and methods: An observational, retrospective, cross-sectional study was conducted on patients that underwent medical check-up within the time frame of January 2011 and December 2015 at the *Hospital San Javier*. Patients included in the study were those with somatometry measurements (BMI), lipid profile, liver function tests, and abdominal ultrasound with a multi-frequency convex transducer.
Results: We found that 65% of the patients presented with overweight or obesity and there was a 49.19% prevalence of hepatic steatosis in the study population. That prevalence was more frequent in men and hepatic steatosis was strongly linked to an increase in triglycerides, AST, and GGT and a decrease in HDL.
Conclusions: Establishing the technical aspects of the study was an important aid to having better correlation with and standardization of the accepted definitions, given that ultrasound is an adequate screening technique for an open population. Our results clearly showed a direct relation between hepatic steatosis and alterations in BMI, triglycerides, HDL, ALT, and GGT.

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PALABRAS CLAVE
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Pruebas de función hepática;
Dislipidemia

Prevalencia y relación de esteatosis hepática con perfil lipídico y hepático en pacientes de chequeo médico

Resumen

Introducción y objetivos: En la actualidad el hígado graso no alcohólico se ha convertido en un problema de salud a nivel mundial ya que con la prevalencia de enfermedades como la obesidad, la diabetes mellitus tipo 2 y el síndrome metabólico existe un dramático incremento de la enfermedad. Nuestro objetivo es dar a conocer la prevalencia actual de esteatosis hepática en la población mexicana que se realiza chequeo médico de rutina, así como analizar su relación con el IMC, perfil lipídico y hepático.

Material y métodos: Se llevó a cabo un estudio observacional, retrospectivo, transversal, de enero de 2011 a diciembre de 2015 en pacientes de chequeo médico de Hospital San Javier. Se incluyeron pacientes con somatometría (IMC), perfil lipídico, hepático y ultrasonido abdominal con transductor convexo multifrecuencia.

Resultados: Encontramos que el 65% de los pacientes presentan sobrepeso u obesidad, una prevalencia de esteatosis hepática del 49.19%; esta se presenta con mayor frecuencia en pacientes del sexo masculino y se encuentra fuertemente ligada al aumento de triglicéridos, AST, GGT; y disminución de HDL.

Conclusiones: Es importante establecer los aspectos técnicos de la realización del estudio, lo cual ayuda a hacer una mejor correlación y estandarización con las definiciones ya establecidas, ya que el ultrasonido es una técnica adecuada para el tamizaje en la población abierta. Queda claro que la esteatosis hepática tiene una relación directa con el aumento del IMC, triglicéridos, HDL, ALT y GGT.

Introduction and aims

Nonalcoholic fatty liver disease (NAFLD) is a condition defined by significant lipid accumulation (5-10%) in hepatic tissue in the absence of significant chronic alcohol consumption, viral infection, or any other specific cause of liver disease. The majority of patients with NAFLD have an increase in hepatic fat, defined as non-alcoholic steatohepatitis, and up to 20% of patients present with progressive liver fibrosis, which can lead to the development of cirrhosis of the liver and hepatocellular carcinoma.[1,2] The 2 most common conditions associated with fatty liver are alcoholic liver disease and NAFLD. Alcoholic liver disease, as its name implies, is caused by excessive alcohol consumption, whereas the non-alcoholic variant is related to insulin resistance, metabolic syndrome, obesity, high blood pressure, and dyslipidemia.[3–6]

Nonalcoholic steatohepatitis (NASH) presents in subjects that do not drink alcohol, or do so moderately (< 20 g/day).[7]

Obesity has become a worldwide epidemic. According to data from the WHO, 150 million adults are overweight, 15 million of whom will die prematurely due to obesity-related diseases. NASH is currently the third most common cause of liver transplantation and it is projected to be the main cause by 2020.[8]

At present, the prevalence of NAFLD is 28-46% in the United States and 6-35% in the rest of the world. The precise prevalence of the disease in Mexico is not known, but the overall average of overweight is 38% and it is 21% for obesity in the population in general. There are 2 Mexican studies, one of which reported a prevalence of 17.4%,[9] and the other reported a prevalence of NAFLD of 82.9% in patients with metabolic syndrome.[10]

Therefore, we conducted a study to find out the prevalence of hepatic steatosis in the Mexican population, in asymptomatic patients that came for a routine medical check-up, identifying the grade of steatosis, its relation to body mass index, and analyzing its relation to liver function tests and lipid profile, as well as the presence of the disease between men and women.

Materials and methods

A retrospective, observational, cross-sectional study was conducted. The sample was made up of patients that had their medical check-up at the *Hospital San Javier*, in Guadalajara, Jalisco, Mexico, within the time frame of January 2011 to December 2015.

Inclusion criteria were patients above 18 years of age, whose case records included complete somatometry, body mass index (BMI), liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], gamma-glutamyl transferase [GGT]), lipid profile (cholesterol, high-density lipoprotein [HDL], low-density lipoprotein [LDL], and triglycerides), and abdominal ultrasound.

The exclusion criteria were non-Mexican patients, patients with more than 2 medical check-ups, patients with no laboratory studies or abdominal ultrasound, patients with findings suggestive of cirrhosis of the liver or with a known liver disease, patients on medications that produce steatosis (amiodarone, tetracyclines, methotrexate, valproic acid, tamoxifen, inverse transcriptase inhibitors, estrogens, and corticosteroids), and patients with weight loss > 10 kg within the last 6 months. In addition, patients were excluded that had daily alcohol ingestion > 20 g for women and 30 g for men, based on the standard drink unit (SDU), in which 1 SDU corresponds to 10 g. Consequently, 1 glass of wine (100 ml) is 1 SDU, 200 ml of beer are 1 SDU, and 50 ml of distilled alcohol are 2 SDUs.

BMI was calculated as weight (kg)/height (m^2) and malnourished was defined as < 18.4 kg/m^2, normal weight 18.5-24.9 kg/m^2, overweight 25-29.9 kg/m^2, grade 1 obesity 30-34.9 kg/m^2, grade 2 obesity 35-39.5 kg/m^2, and grade 3 obesity > 40 kg/m^2.

The grade of hepatic steatosis was defined as: grade 1 or mild, a slight diffuse increase in the echogenicity of the liver with clear visualization of the intrahepatic vessel membranes and walls; grade 2 or moderate, a diffuse increase in the echogenicity of the liver and a darkening of the intrahepatic vessel walls and the diaphragm; grade 3 or severe, an important increase in the echogenicity of the liver with poor or null visualization of the hepatic vessels and diaphragm.

Laboratory variables outside of the normal parameters were defined as: total cholesterol (> 200 mg/dl), HDL cholesterol (< 40 mg/dl), LDL cholesterol (> 130 mg/dl), triglycerides (> 150 mg/dl), AST (> 72 U/L), ALT (> 72 U/L), and GGT (> 43 U/L).

The ultrasound studies were carried out with the following equipment: Philips IU22 with a 2-5 MHz convex transducer, Philips Epic 7 with a 1-5 MHz convex transducer, and Aloka Prosound α7 with a 2-6 MHz multifrequency convex transducer. The ultrasound images were evaluated by a radiology and imaging specialist with more than 25 years of experience in abdominal radiology, through the Synapse system database, without the specialist's knowing the age, sex, BMI, or any other patient data. Furthermore, agreement between the radiologists that performed the study and the liver imaging specialist was also carried out.

Statistical analysis

The variables were entered into an Excel database and once the information was obtained, the statistical analysis was carried out using the SPSS program. The numerical variables were described through mean and standard deviation and the categorical and continuous variables were described through frequencies and percentages. The statistical analysis was done using the Student's t test, utilizing association and the Pearson's correlation coefficient, with significance set at a $p < 0.01$. The Kappa index was used for the concordance analysis.

The study was approved by the Research Ethics Committee of the *Hospital San Javier* and its publication was authorized.

Results

A total of 711 case records were evaluated, and 431 patients met the inclusion criteria. Two hundred and eighty patients were excluded. The mean patient age was 47.71 years, with a range of 20 to 80 years, a standard deviation of 11.78, and a median of 47 years. Mean BMI was 26.97 kg/m^2. Four patients (0.93%) were malnourished (0.93%), 145 patients (33.64%) had normal weight, and a total of 65.43% had overweight and obesity. Of those patients, 184 patients (42.69%) presented with overweight and 22.74% with obesity. Of the obese patients, 76 patients (17.63%) had grade 1 obesity, 14 patients (3.25%) had grade 2, and 8 patients (1.86%) had grade 3 (Table 1).

The prevalence of fatty liver found in our Mexican study population was high, reaching 49.19%.

In the correlation of BMI with the grade of hepatic steatosis, we found a correlation coefficient of 0.458 ($p > 0.01$), which supposes a greater probability of presenting with non-alcoholic steatohepatitis, the higher the grade of overweight or obesity (Table 2).

The relation between sex and grade of hepatic steatosis was as follows: of the 128 female patients, only 30 (23.61%) presented with a grade of steatosis, whereas of the 303 male patients, 182 (59.86%) presented with a grade of fatty liver. There was a greater prevalence of the disease in males in our study (Table 3).

Serum levels of cholesterol, triglycerides, LDL, HDL, ALT, AST, and GGT were determined. Table 4 describes the percentage of abnormal values. The Spearman correlation coefficient between the appearance of the liver in the ultrasound study and the lipid and liver profile results were statistically significant: cholesterol 0.152, triglycerides 0.355, AST 0.310, ALT 0.329, GGT 0.351, and HDL -0.348, all with a $p < 0.01$. Triglycerides and GGT had the highest coefficient, making it clear that there is a greater risk for presenting with hepatic steatosis, the higher the triglyceride concentration. The results also showed that there is a greater likelihood of presenting with fatty liver, the lower the HDL concentration.

In relation to interobserver variability, the concordance analysis produced a Kappa coefficient of 0.28, signifying an acceptable degree of agreement.

Discussion

Non-alcoholic steatohepatitis is a chronic inflammatory liver disease that presently has great clinical, laboratory, and imaging relevance. The natural history of the disease can be associated with other types of diseases, without forgetting that it can progress to cirrhosis of the liver on its own.

We evaluated the prevalence of fatty liver in patients having a medical check-up and excluded individuals with possible causes of secondary hepatic steatosis. We also examined the correlations between ultrasound-diagnosed NAFLD, BMI, and liver and lipid profiles, finding a prevalence of 49.19%. The German study by Kirovski et al. reported a prevalence of 40%,[11] an ultrasound-based Italian study on the general population reported a prevalence of 20%,[12] studies from Israel,[13] Taiwan,[14] China,[15] and Sri Lanka[16] reported a prevalence of 30.5, 11.5, 17.2, and 32.6%, respectively.

Table 1 Sociodemographics.

Patient total = 431				
	Minimum	Maximum	Mean	Standard deviation
Age	20	88	47.71	11.78
BMI	16.26	49.47	26.97	4.5
	Nutritional status		Patients	Percentage
	Malnourished		4	0.93%
	Normal		145	33.64%
	Overweight		184	42.69%
	G1 obesity		76	17.63%
	G2 obesity		14	3.25%
	G3 obesity		8	1.86%
Sex	Total		Percentage	
Men	303		70.31%	
Women	128		29.69%	
	Minimum	Maximum	Mean	Standard deviation
Cholesterol	91	367	196.39	39.90
Triglycerides	30	657	160.42	90.49
HDL	17	160	47.09	16.55
LDL	23	644	116.40	43.16
AST	10	396	29.44	24.04
ALT	3	317	39.52	26.27
GGT	8	391	35.14	28.33

Table 2 Results of the correlation of BMI with hepatic steatosis grade.

	Without steatosis	Percentage	G1 steatosis	Percentage	G2 steatosis	Percentage	G3 steatosis	Percentage	Total
Malnutrition	3	0.69%	1	0.23%	0	0	0	0	4
Normal	113	26.21%	27	6.26%	5	1.16%	0	0	145
Overweight	76	17.63%	71	16.47%	28	6.49%	9	2.09%	184
G1 obesity	26	6.03%	31	7.19%	13	3.01%	6	1.39%	76
G2 obesity	1	0.23%	3	0.69%	7	1.62%	3	0.69%	14
G3 obesity	0	0	3	0.69%	1	0.23%	4	0.93%	8
Total	219	50.82%	136	31.57%	54	12.51%	22	5.10%	431

G1: Grade 1; G2: Grade 2; G3: Grade 3

Table 3 Relation between sex and hepatic steatosis grade.

	Female	Percentage	Male	Percentage	Total	Percentage
Normal	97	76.37%	122	40.13%	219	50.81%
G1 steatosis	21	15.74%	116	38.15%	136	31.55%
G2 steatosis	7	5.51%	47	15.46%	54	1.52%
G3 steatosis	3	2.36%	19	6.25%	22	5.19%
Total	128	29.69%	303	70.31%	431	100%

G1: Grade 1; G2: Grade 2; G3: Grade 3

Table 4 Relation between abnormal lipid and liver profile values and hepatic steatosis grade.

	Normal liver	Grade 1 steatosis	Grade 2 steatosis	Grade 3 steatosis	Spearman	Significance
Cholesterol	36.98%	50%	61.11%	31%	0.152	$p = 0.01$
Triglycerides	28.76%	53.67%	61.11%	77.27%	0.355	$p = 0.01$
HDL	27.74%	47.05%	48.14%	81.81%	0.348	$p = 0.01$
LDL	26.48%	37.5%	40.74%	31.81%	0.088	$p = 0.01$
AST	1.36%	2.20%	1.85%	4.54%	0.310	$p = 0.01$
ALT	1.82%	3.67%	9.25%	36.36%	0.329	$p = 0.01$
GGT	13.24%	25%%	33.33%	40.90%	0.351	$p = 0.01$

We also found that the majority of studies in the medical literature evaluate the presence of fatty liver associated with metabolic syndrome or the cardiovascular risk factor,[17] describing a prevalence of steatosis of up to 72%, of which 34% of the cases presented with a grade of obesity. A study conducted in the United States evaluated the presence of steatosis by ethnic groups, finding 45% of cases in Hispanics, 33% in Caucasians, and 24% in the black race.[18]

There is conflicting evidence regarding sex as a risk factor for NAFLD. Our study clearly showed a sex-related prevalence. Of the 303 men in the study, 59.86% presented with fatty liver and of the 128 women, 23.61% had fatty liver. We found a study in the literature that reported a greater prevalence of NAFLD in women,[19] as well as studies in Caucasian populations describing a greater prevalence in men. An Italian study[12] showed no significant difference in relation to sex, and a Mexican study reported an 86.9% prevalence of NAFLD in men.[10]

The results of our study confirm the important correlation between NAFLD and BMI. We found that of the 212 patients that presented with NAFLD, only 32 (7.42%) had a BMI within normal limits, telling us that overweight and obesity are strongly linked to NAFLD.

It is widely accepted that serum lipid profile and transaminase levels are neither sufficiently specific nor sensitive for detecting NAFLD.[18,20,21] However, in our study, we found elevated cholesterol and triglyceride levels and reduced HDL levels in over 50% of the patients assessed. Up to 81.81% of the patients with grade 3 hepatic steatosis had abnormal HDL values, signifying that a higher grade of steatosis increases the likelihood of presenting with hyperlipidemia. In the liver function test correlations, we found that a higher grade of steatosis increased the probability of abnormal GGT levels. ALT values were altered in 36.36% of the patients with grade 3 hepatic steatosis and in less than 10% of the patients with grades 1 and 2.

With respect to the acceptable agreement found in our study, it is important to emphasize adequate imaging evaluation when performing the study, based on the grades of steatosis described above.

Ultrasound has become a fast, high-yield, efficacious, and low-cost screening method in the open population. It has reasonable sensitivity and specificity in the detection of fatty liver, especially in the moderate and severe grades, but limited accuracy for mild hepatic steatosis. Another limitation is the fact that it is an operator-dependent method.

To aid in the future research on NAFLD, it is important to establish the technical aspects for conducting the study, providing better correlation with and standardization of the definitions that are already established.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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