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ORIGINAL

Variables that influence the values of 7 scales that determine the risk of nonalcoholic fatty liver disease and liver fibrosis in 219,477 spanish workers

Variables que influyen en los valores de 7 escalas que determinan el riesgo de hígado graso no alcohólico y fibrosis hepática en 219.477 Trabajadores españoles

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Abstract

Introduction: Non-alcoholic fatty liver disease (NAFLD) is a very frequent and multifactorial pathology that can lead to liver fibrosis (LF). The aim of the present study was to assess the influence of sociodemographic variables such as age, sex, social class and tobacco consumption on the increased risk of NASFLD and HF.

Material and methods: Descriptive and cross-sectional study in 219.477 Spanish workers in which the influence of age, sex, social class and tobacco consumption on the increased risk of presenting NASH and FH determined with 7 different scales was assessed. We also assessed the concordance and correlation between the different scales using Pearson's and Cohen's kappa indices, respectively.

Results: All the EHGNA and FH risk scales have increased values as age increases and as one moves down the social scale. These values are also higher in men. Smoking does not seem to show any effect on the risk of NASH and FH. The degree of correlation of the different scales is high.

Conclusions: Age, sex and social class all have an influence on the increased risk of NASH and FH, while smoking has no effect.

Keywords: non-alcoholic fatty liver disease (NAFLD), sociodemographic variables, tobacco consumption, social class.

Resumen

Introducción: La enfermedad del hígado graso no alcohólico (EHGNA) es una patología muy frecuente y multifactorial que puede terminar en fibrosis hepática (FH). El presente estudio tiene como objetivo valorar la influencia de variables sociodemográficas como edad, sexo y clase social y el consumo de tabaco en el incremento del riesgo de presentar EHGNA y FH.

Material y métodos: Estudio descriptivo y transversal en 219.477 trabajadores españoles en los que se valora la influencia de la edad, el sexo, la clase social y el consumo de tabaco en el incremento del riesgo de presentar EHGNA y FH determinadas con 7 escalas diferentes. También se valora la concordancia y correlación entre las diferentes escalas empleando los índices de Pearson y kappa Cohen respectivamente.

Resultados: Todas las escalas de riesgo de EHGNA y FH ven incrementados sus valores a medida que aumenta la edad y a medida que se desciende en la escala social. Estos valores también son más elevados en los hombres. El tabaco no parece mostrar ningún efecto en el riesgo de EHGNA y la FH. El grado de correlación de las diferentes escalas es alto.

Conclusiones: Tanto la edad como el sexo y la clase social influyen en el incremento del riesgo de presentar EHGNA y FH mientras el consumo de tabaco no afecta.

Palabras clave: Enfermedad del hígado graso no alcohólico (EHGNA), variables sociodemográficas, consumo de tabaco, clase social.

Introduction

Non-alcoholic fatty liver disease (NAFLD) is a clinical disease that encompasses different liver conditions in people who consume little or no alcohol[1]. The defining characteristic of this pathology is the excess fat stored in liver cells[2].

NASH is increasing in prevalence worldwide, but especially in more developed countries[3] and in the United States it is considered the most common form of chronic liver disease, affecting almost 25% of the population[4].

Some people with NASH may eventually develop non-alcoholic steatohepatitis, which is one of the most aggressive forms of the disease and is characterized by liver inflammation that can progress to severe scarring (cirrhosis) and liver failure. This pathologic picture is very similar to that caused by excessive alcohol consumption[5].

There are many known risk factors for NASH, including dyslipidemia[6], obesity[7], especially abdominal obesity[8], polycystic ovary syndrome[9], type 2 diabetes[10], hypothyroidism[11], hypopituitarism[12] and advanced age[13].

There are not too many studies that assess the effect of sociodemographic variables and tobacco consumption on the appearance of NASH, so the aim of this study is precisely to assess this association.

Material and methods

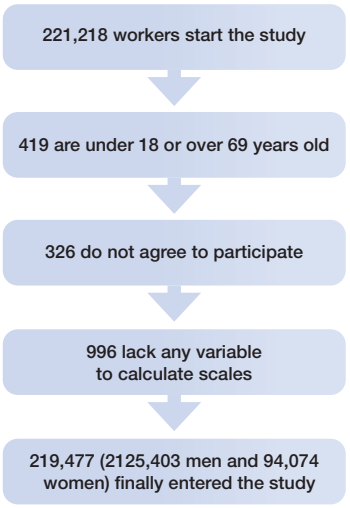
Descriptive and cross-sectional study in 219,477 Spanish workers from different Spanish regions (Balearic Islands, Canary Islands, Andalusia, Valencian Community, Madrid, Catalonia, Castile and Leon, Castile La Mancha, and Basque Country) and belonging mainly to labor sectors of public administration, health, construction, and commerce. Participants were selected from occupational medical examinations between the months of January 2017 and December 2019 from the different companies that participated in the study. Participants were recruited when they met the following inclusion criteria: age between 18 and 69 years, belonging to one of the companies included in the study, not being on temporary disability, giving written consent to participate in the study and to use their data for epidemiological purposes.

Figure 1 shows the flow diagram of the study participants.

Measurements and data collection

Anthropometric measurements and the determination of different analytical parameters were performed on all the workers who attended the occupational health check-ups.

Figure 1: flow chart of the participants in the study.



The anthropometric (height and weight), clinical and analytical measurements were taken by health professionals from the different occupational health units participating in the study, after standardization of the measurement techniques.

Weight (in kg) and height (in cm) were determined using a SECA 700 scale with an attached SECA 220 telescopic measuring rod. Waist circumference (WC) was measured with a SECA measuring tape with the person in a standing position, feet together, trunk straight and abdomen relaxed. The tape was placed parallel to the ground at the level of the last floating rib.

Blood pressure was determined with the person in a seated position and after 10 minutes of rest. A calibrated OMRON M3 automatic sphygmomanometer was used. Three determinations were made at one-minute intervals and the mean of the three was obtained. Blood was obtained after 12h of fasting. Samples were sent to reference laboratories and processed within 2-3 days. Automated enzymatic methods were used to determine glucose, total cholesterol and TG. HDL-c was determined by precipitation with dextran sulfate-MgCl2. LDL-c was calculated using the Friedewald formula (provided that TG was less than 400 mg/dL). The values of all these parameters are expressed in mg/dL.Friedewald formula:

LDL = colesterol – HDL – tryglicerides/5

The risk of NAFLD and liver fibrosis were determined by applying different scales:

- Fatty liver index (FLI)[14]

$$FLI = (e^{0.953*\log_e(\text{triglycerides}) + 0.139*BMI + 0.718*\log_e(GGT) + 0.053*\text{waist circumference} - 15.745}) / (1 + e^{0.953*\log_e(\text{triglycerides}) + 0.139*BMI + 0.718*\log_e(GGT) + 0.053*\text{waist circumference} - 15.745}) \times 100$$

FLI values above 60 are considered high risk.

• Hepatic steatosis index (HSI)[15]

HSI= 8 × AST/ALT + BMI + 2 if diabetes + 2 if female
Values above 36 are considered high risk.

• Zhejian University index (ZJU index)[16]

ZJU= BMI + glycaemia (mmol L) + tryglicerides (mmol L) + 3 AST/ALT + + 2 if female
Values above 38 are considered high risk.

• Fatty liver disease index (FLD)[17]

FLD = BMI + tryglicerides + 3 × (AST/ALT) + 2 × hyperglicaemia (present = 1; absent = 0).
Values above 37 are considered high risk.

• Framingham steatosis index (FSI)[18]

FSI = −7.981 + 0.011 × age (years) − 0.146 × sex (woman = 1; man = 0) + 0.173 × BMI (kg/m^2) + 0.007 × tryglicerides (mg/dL) + 0.593 × hypertension (yes = 1; no = 0) + 0.789 × diabetes (yes= 1; no = 0) + 1.1 × AST/ALT ratio ≥ 1.33 (yes= 1; no = 0)

• Lipid accumulation product (LAP)[19]

Men. (waist (cm) − 65) × (tryglicerides (mMol))
Women: (waist (cm) − 58) × (tryglicerides (mMol))
Values above 42,7 are considered high risk.

• BARD score. This is a scale that evaluates the risk of hepatic fibrosis in patients with NAFLD[20].

The presence of a BMI greater than 28 is scored with 1 point, an AST/ALT ratio greater than 0.8 is scored with 2 points and the presence of diabetes mellitus is also scored with 2 points. Values between 2 and 4 points indicate a high risk of liver fibrosis.

A person was considered a smoker if he/she had smoked at least one cigarette/day (or its equivalent in other types of consumption) in the last 30 days, or had quit smoking less than 12 months ago. A person who had not smoked in the last year or who had never smoked was considered a nonsmoker.

Social class was determined from the National Classification of Occupations 2011 (CNO-11) according to the proposal of the social determinants group of the Spanish Society of Epidemiology[21]. Three categories were established:

Class I: directors/managers, university professionals, sportsmen and artists; Class II: intermediate occupations and skilled self-employed workers; Class III: unskilled workers.

Statistical analysis

A descriptive analysis of the categorical variables was performed, calculating the frequency and distribution of the responses for each of them. For quantitative variables, the mean and standard deviation were calculated following a normal distribution.

Bivariate association analysis was performed using the chi2 test (with correction for Fisher's exact statistic when conditions required it) and Student's t test for independent samples (for comparison of means). Multivariate techniques were used to establish the variables associated with the most significant risk factors. Logistic regression was used for multivariate analysis, with calculation of the odds ratio and the Hosmer-Lemeshow goodness-of-fit test. The degree of correlation and concordance of the different variables studied was determined by applying Pearson's and Cohen's kappa tests, respectively. Statistical analysis was performed with the Statistical Package for the Social Sciences (SPSS) version 28.0 (IBM Company, New York, NY, USA) for Windows, with an accepted level of statistical significance of 0.05.

Ethical considerations and/or aspects

The research team undertook at all times to follow the ethical principles of health sciences research established nationally and internationally (Declaration of Helsinki), paying special attention to the anonymity of the participants and the confidentiality of the data collected. Approval was requested from the Ethics and Research Committee of the Balearic Islands (CEI-IB), which was obtained with indicator IB 4383/20. Participation in the study was voluntary, so the participants gave their written and oral consent to participate in the study after receiving sufficient information about the nature of the study. To this end, they were given an informed consent form, as well as an information sheet explaining the objective of the study.

The data collected for the study were identified by a code and only the person responsible for the study can relate these data to the participants. The identity of the participants will not be disclosed in any report of this study. The investigators will not disseminate any information that could identify them. In any case, the research team undertakes to strictly comply with the Organic Law 3/2018, of December 5, on the protection of personal data and guarantee of digital rights, guaranteeing the participant in this study that he/she may exercise his/her rights of access, rectification, cancellation and opposition of the data collected

Table I: Characteristics of the population.

	Men n=125,403 Mean (SD)	Women n=94,074 Mean (SD)	p
Age	41.8 (10.5)	39.9 (10.5)	<0.0001
Height	175.2 (6.8)	162.3 (6.3)	<0.0001
Weight	82.6 (15.0)	68.0 (14.7)	<0.0001
SBP	126.1 (15.6)	115.4 (15.5)	<0.0001
DBP	77.3 (11.1)	72.3 (10.5)	<0.0001
Cholesterol	195.6 (37.9)	192.1 (35.5)	<0.001
HDL-c	52.1 (9.8)	57.2 (10.3)	<0.0001
LDL-c	118.4 (35.1)	116.3 (33.5)	<0.001
Tryglicerides	125.7 (76.0)	93.1 (45.6)	<0.0001
Glycaemia	93.4 (21.5)	88.3 (16.0)	<0.0001
AST	29.0 (17.5)	18.7 (11.6)	<0.0001
ALT	24.4 (13.3)	18.2 (7.9)	<0.0001
GGT	32.7 (31.8)	18.8 (16.3)	<0.0001
Creatinine	0.86 (0.17)	0.68 (0.14)	<0.0001
	%	**%**	**p**
18-29 years	14.4	19.4	<0.0001
30-39 years	26.6	28.9	
40-49 years	33.6	32.0	
50-59 years	21.5	16.8	
60-69 years	3.9	2.9	
Social class I	6.1	7.5	<0.0001
Social class II	14.5	20.5	
Social class III	79.4	72.0	
Non smokers	67.5	66.7	<0.001
Smokers	32.5	33.3	

SBP systolic blood pressure. DBP diastolic blood pressure. HDL High density lipoprotein. LDL Low density lipoprotein. AST aspartate transaminase. ALT alanine transaminase. GGT gamma-glutamyl transferase.

Table II: Mean values of different risk scales for nonalcoholic fatty liver disease and liver fibrosis according to sociodemographic variables and tobacco consumption.

		FLI	HSI	ZJU	FLD	FSI	LAP	BARD
Men	**n**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**
18-29 years	18006	26.9 (24.2)	34.5 (6.7)	34.6 (5.3)	29.8 (5.2)	0.12 (0.13)	23.8 (21.2)	0.56 (0.79)
30-39 years	33411	36.4 (26.4)	36.4 (6.8)	36.5 (5.5)	31.6 (5.3)	0.17 (0.17)	32.0 (29.4)	0.79 (0.90)
40-49 years	42192	43.3 (26.7)	37.4 (6.8)	37.8 (5.6)	32.6 (5.3)	0.22 (0.19)	36.7 (31.0)	0.98 (0.95)
50-59 years	26955	45.5 (25.9)	37.6 (6.3)	38.3 (5.6)	32.9 (5.2)	0.26 (0.20)	37.1 (28.9)	2.02 (0.93)
60-69 years	4839	46.0 (25.2)	37.7 (6.1)	38.8 (5.3)	33.2 (4.9)	0.30 (0.20)	36.4 (26.2)	1.99 (0.89)
Social class I	7623	38.1 (25.5)	36.6 (6.6)	36.8 (5.2)	31.7 (4.9)	0.20 (0.17)	32.4 (28.0)	1.10 (1.06)
Social class II	18237	39.7 (25.5)	37.1 (6.4)	37.3 (5.3)	32.2 (5.0)	0.20 (0.18)	33.3 (27.2)	1.15 (1.05)
Social class III	99543	39.8 (27.1)	36.7 (6.8)	37.1 (5.8)	32.0 (5.5)	0.21 (0.19)	33.8 (29.4)	1.13 (1.05)
Non smokers*	84642	39.8 (26.8)	36.8 (6.7)	37.2 (5.7)	32.1 (5.4)	0.21 (0.19)	33.8 (28.9)	1.14 (1.05)
Smokers	40761	39.5 (26.7)	36.7 (6.9)	37.1 (5.7)	32.0 (5.3)	0.20 (0.18)	33.4 (29.3)	1.12 (1.06)
Women	**n**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**
18-29 years	18270	14.3 (19.7)	34.4 (6.5)	35.1 (5.8)	28.4 (5.7)	0.10 (0.12)	15.9 (15.9)	0.29 (0.53)
30-39 years	27189	18.0 (22.5)	35.9 (7.1)	36.5 (6.3)	29.7 (6.2)	0.13 (0.15)	18.2 (17.8)	0.39 (0.61)
40-49 years	30123	20.1 (22.2)	36.7 (6.6)	37.2 (5.8)	30.4 (5.6)	0.15 (0.16)	19.7 (18.1)	0.45 (0.65)
50-59 years	15774	25.3 (24.1)	38.0 (6.8)	38.7 (6.1)	31.6 (5.7)	0.20 (0.18)	23.5 (20.6)	1.65 (0.78)
60-69 years	2718	26.9 (23.7)	38.6 (6.6)	39.4 (5.9)	32.1 (5.5)	0.23 (0.19)	24.2 (19.2)	1.69 (0.77)
Social class I	7044	13.0 (17.4)	34.2 (5.6)	34.9 (5.0)	28.2 (4.8)	0.11 (0.13)	14.5 (15.8)	0.43 (0.70)
Social class II	19284	17.0 (20.9)	35.7 (6.6)	36.2 (5.7)	29.4 (5.5)	0.13 (0.14)	17.2 (16.9)	0.55 (0.78)
Social class III	67746	20.8 (23.2)	36.7 (7.0)	37.3 (6.3)	30.4 (6.1)	0.15 (0.17)	20.4 (18.7)	0.68 (0.84)
Non smokers*	62706	19.6 (22.5)	36.4 (6.9)	37.0 (6.2)	30.1 (5.9)	0.15 (0.16)	19.4 (18.2)	0.64 (0.82)
Smokers	31368	19.2 (22.4)	36.2 (6.8)	36.8 (6.1)	29.9 (5.9)	0.14 (0.16)	19.1 (18.3)	0.63 (0.82)

FLI Fatty liver index. HSI Hepatic steatosis index. ZJU Zhejiang University index. FLD Fatty liver disease. FSI Framingham Steatosis index. LAP Lipid accumulation product. (*) No statistically significant differences between smokers and non-smokers on all scales. Age and social class show statistically significant differences in all scales.

Results

Table I shows the anthropometric and clinical characteristics of the workers included in the study. A total of 125,403 men (57.14%) and 94,074 women (42.86%) were included in the analyses. The mean age of the sample was 40.5 ± 10.5 years, and the majority group was between 30 and 49 years. Anthropometric, clinical and analytical values were higher among men. The highest percentage of workers (75.5%) belonged to social class III. A total of 33.3% of the women and 32.5% of the men were smokers. The percentage of patients with obesity I was 14.2%, 4.2% of the total sample had obesity II, and 1.5% of the population was classified in obesity category III.

Table II shows the mean values of different scales of nonalcoholic fatty liver disease and liver fibrosis according

to sociodemographic variables, such as age, sex, social class and tobacco consumption. The mean values of all the aforementioned risk scales increase with increasing age in both sexes. The lowest values in all the scales are observed in people belonging to the most favored social class (class I). Smokers present slightly lower values than non-smokers in both sexes, although the differences are not statistically significant. The mean values in all cases are lower in women.

Table III shows the prevalence of elevated values of different risk scales for nonalcoholic fatty liver disease and liver fibrosis according to sociodemographic variables such as age, sex and Social class, and tobacco consumption. A trend similar to that already discussed with the mean values is observed, i.e. an increase in prevalences as age increases and as one descends in the Social class. In general, prevalences are higher in non-smokers, although without statistical significance. Prevalences are higher in males.

Table III: Prevalence of high values of different risk scales for nonalcoholic fatty liver disease and liver fibrosis according to sociodemographic variables and tobacco consumption.

		FLI high	HSI high	ZJU high	FLD high	LAP high	BARD high
Men	**n**	**%**	**%**	**%**	**%**	**%**	**%**
18-29 years	18006	12.9	33.9	21.9	48.5	24.3	13.6
30-39 years	33411	21.5	45.8	32.3	59.9	37.5	21.0
40-49 years	42192	29.0	53.6	42.7	64.6	45.6	28.9
50-59 years	26955	31.6	56.3	47.2	65.1	49.2	65.1
60-69 years	4839	31.4	59.1	52.4	67.3	49.5	65.7
Social class I	7623	22.3	49.4	35.9	64.9	38.0	32.4
Social class II	18237	23.8	51.2	38.3	66.3	41.9	34.7
Social class III	99543	25.8	49.2	38.4	60.1	41.5	33.7
Non smokers	84642	25.4*	49.6*	38.2*	61.5*	41.6	33.8*
Smokers	40761	25.1	49.3	38.3	60.9	40.8	33.7
Women	**n**	**%**	**%**	**%**	**%**	**%**	**%**
18-29 years	18270	5.6	32.5	23.9	34.7	20.1	3.4
30-39 years	27189	8.3	40.6	31.6	39.9	25.6	5.7
40-49 years	30123	8.7	47.5	37.8	48.2	29.4	7.5
50-59 years	15774	11.8	57.4	48.0	54.0	37.9	48.6
60-69 years	2718	12.0	62.9	54.4	60.7	39.8	52.2
Social class I	7044	4.1	30.2	21.3	37.2	16.1	7.7
Social class II	19284	6.7	40.7	30.2	42.5	23.1	11.8
Social class III	67746	9.6	47.4	38.5	45.8	30.9	15.8
Non smokers	62706	8.6*	45.1	35.8	44.5*	28.4*	14.7
Smokers	31368	8.6	43.9	34.8	44.5	27.8	13.7

FLI Fatty liver index. HSI Hepatic steatosis index. ZJU Zhejiang University index. FLD Fatty liver disease. LAP Lipid accumulation product. (*) No statistically significant differences.

Table IV shows the results of the multivariate analysis using multinomial logistic regression. The risk of presenting elevated values for all the nonalcoholic fatty liver disease and liver fibrosis scales is higher in men, with odds ratios ranging from 1.03 (95% CI 1.02-1.05) for ZJU and 3.41 (95% CI 3.32-3.50) for FLI. The risk increases with age in all the scales, with the highest values for the BARD score. The level of risk increased as we descended in the Social class with similar odds ratios for all scales. Tobacco consumption in all scales does not show any influence in any case.

Table IV: Multinomial logistic regression.

	FLI high OR (95% CI)	HSI high OR (95% CI)	ZJU high OR (95% CI)	FLD high OR (95% CI)	LAP high OR (95% CI)	BARD high OR (95% CI)
Woman	1	1	1	1	1	1
Man	3.41 (3.32-3.50)	1.13 (1.11-1.15)	1.03 (1.02-1.05)	1.91 (1.87-1.94)	1.68 (1.65-1.71)	3.18 (3.11-3.26)
18-29 years	1	1	1	1	1	1
30-39 years	ns	1.17 (1.11-1.23)	1.26 (1.20-1.32)	1.18 (1.12-1.25)	ns	1.08 (1.02-1.13)
40-49 years	1.18 (1.11-1.25)	1.45 (1.38-1.52)	1.64 (1.56-1.72)	1.32 (1.25-1.38)	1.30 (1.24-1.36)	6.59 (6.26-6.94)
50-59 years	1.64 (1.55-1.74)	1.97 (1.88-2.07)	2.42 (2.30-2.54)	1.71 (1.62-1.80)	1.74 (1.66-1.83)	9.93 (9.41-10.48)
60-69 years	2.93 (2.75-3.13)	3.10 (2.95-3.27)	3.93 (3.74-4.14)	2.43 (2.31-2.56)	2.91 (2.77-3.07)	17.31 (16.28-18.40)
Social class I	1	1	1	1	1	1
Social class II	1.30 (1.26-1.35)	1.18 (1.15-1.21)	1.30 (1.27-1.33)	ns	1.27 (1.24-1.30)	1.21 (1.18-1.25)
Social class III	1.52 (1.44-1.59)	1.46 (1.41-1.52)	1.63 (1.57-1.69)	1.11 (1.07-1.14)	1.60 (1.54-1.67)	1.50 (1.43-1.58)
Non smokers	1	1	1	1	1	1
Smokers	ns	ns	ns	ns	ns	ns

FLI Fatty liver index. HSI Hepatic steatosis index. ZJU Zhejiang University index. FLD Fatty liver disease. LAP Lipid accumulation product.

Table V presents the results of the Pearson correlation coefficient between the different scales, showing a higher correlation between FLD with ZJU (0.978) and HSI (0.928) and between ZJU and HSI (0.923).

Table VI shows the results of Cohen's Kappa concordance index, whose highest value corresponds to ZJU and HSI (0.731).

Table V: Pearson correlation coefficient of the seven scales.

	FLI	HSI	ZJU	FLD	FSI	LAP	BARD score
FLI	1	0,712	0,813	0,864	0,809	0,809	0,731
HSI		1	0,923	0,928	0,590	0,513	0,587
ZJU			1	0,978	0,768	0,649	0,647
FLD				1	0,781	0,681	0,669
FSI					1	0,774	0,649
LAP						1	0,617
BARD score							1

FLI Fatty liver index. HSI Hepatic steatosis index. ZJU Zhejiang University index. FLD Fatty liver disease. FSI Framingham steatosis index. LAP Lipid accumulation product.

Table VI: Cohen's Kappa concordance index of the seven scales.

	FLI	HSI	ZJU	FLD	LAP	BARD score
FLI	1	0,350	0,504	0,130	0,532	0,524
HSI		1	0,731	0,273	0,458	0,401
ZJU			1	0,098	0,585	0,530
FLD				1	0,086	0,025
LAP					1	0,471
BARD score						1

FLI Fatty liver index. HSI Hepatic steatosis index. ZJU Zhejiang University index. FLD Fatty liver disease. LAP Lipid accumulation product.

Discussion

Both the mean values and the prevalence of high values of the nonalcoholic fatty liver disease and liver fibrosis risk scales are higher as age increases and as we descend in the Social class, and they are also lower in women.

In the multivariate analysis, it can be seen that the variable that most increases the risk of presenting highs of the different risk scales for nonalcoholic fatty liver disease and liver fibrosis is age, followed by sex and social class, without finding any influence of tobacco consumption.

The Pearson correlation index of the different scales is, in general, high, especially highlighting the relationship between FLD with ZJU and HSI and between ZJU and HSI. The degree of agreement using Cohen's kappa found in our study is moderate to insignificant among the scales evaluated, with the exception of ZJU and HSI in which there is good (substantial) agreement.

Different studies have assessed the prevalence of NASH according to age, with the conclusion that as age increases the prevalence of NASH also increases, a result that agrees with that obtained by us in this study. Data from the Third National Health and Nutrition Examination Survey (NHANES III) carried out in the United States in 3,270 persons showed very high rates of NASH, especially in older persons, even exceeding 40%[22] as in our study. Similar data are found in the studies by Alqahtani et al[23] and Bertolotti et al[24], the latter also showing a greater number of complications derived from NASH in older persons. A study carried out in a Spanish working population of more than 30,000 workers also found an increase in the prevalence of a risk scale, in this case FLI, with age[25]. The study by Abeysekera et al[26] conducted in more than 10,000 people in Bristol showed a higher prevalence of liver fibrosis determined by FibroScan in older people.

The work of Fresneda et al[25] found, as we did, a higher prevalence of elevated FLI values in males and in people from the most disadvantaged social classes. Data from 5,272 middle-aged adults who participated in the 2014-2018 Korean National Health and Nutrition Examination Surveys (KNHANES)[27] also showed a higher prevalence of elevated values of an EHGNA risk scale, in this case HSI, in people with lower socioeconomic status. A paper by Ramirez-Manent et al[28] in 15,057 Spanish workers showed that the risk of developing nonalcoholic fatty liver disease and liver fibrosis was much higher in men than in women.

The role of smoking in the development of NASH remains controversial, some authors such as Jung et al[29] found an increased prevalence in smokers. Other authors such as Zein et al[30] observed an increased likelihood of smoking-associated liver fibrosis. A cross-sectional study in 160,862 persons showed that smoking was associated with an increased risk

of NAFLD (adjusted odds ratio 1.10; 95% confidence interval, 1.06-1.14). Furthermore, among Smokers, the risk of NASH increased with the number of cigarettes (<10 and ≥10 pack-years vs. never Smokers; odds ratios 1.04 and 1.11; 95% CI, 1.01-1.08 and 1.05-1.16, respectively.

Strengths and limitations

As strengths of the study, we can highlight the large sample size (more than 200,000 people) and the large number of NASH and liver fibrosis risk scales used. The main limitation is that diagnostic techniques for NASH or liver fibrosis other than the risk scales were not performed.

Conclusions

Taking into account the results obtained in our study, we can conclude that in this Spanish working population there is a direct relationship between the values of the different NASH risk scales and liver fibrosis when considering different sociodemographic variables such as age, sex and social class, and we found no relationship with tobacco consumption. The degree of correlation of the different scales is good, especially between FLD with ZJU and HSI and between ZJU and HSI. The degree of concordance however is not as good except between ZJU and HSI.

Conflict of Interest

The authors declare that no competing interests exist.

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