Diabetes as a risk factor of liver fibrosis in patients with non-alcoholic fatty liver disease.

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Introduction

Non-alcoholic liver disease (NAFLD) ranks first in the prevalence among liver diseases, affecting 20-30% of the population worldwide.

Type 2 diabetes mellitus (T2DM) commonly co-exists with NAFLD and may act synergically to drive adverse outcomes.

We aimed to compare the characteristics and severity of liver disease between diabetic and non-diabetic patients with NAFLD, in a tertiary referral center in Greece.

Methods and Materials

Data from patients with NAFLD that presented to the outpatient clinic from 1/2015 up to1/2021.

Data collection
Demographics
Blood results
Liver stiffness measurements (LSM)

FIB-4 score was afterwards calculated aiming to non-invasively assess the severity of NAFLD .

FIB-4 score includes age, AST, PLT and ALT
< 1.3: rules out fibrosis
>3.23 : predicts fibrosis

Table 1. Baseline characteristics of diabetic and non-diabetic patients.

	Diabetics	Non-diabetics	P-value
Female (%)	67.2%	46.2%	0.05
Age (yrs)	65.8	54.6	0.005
BMI	35.6	34.6	0.76
ALT	25.2	60.2	0.04
AST	39.6	51	0.26
GGT	99.3	102.1	0.95
LSM (kPa)	21.9	11.9	0.01
Cirrhosis (>11.5 kPa)	75%	41.3%	0.01
FIB-4 score	4.1	2.2	0.01

Table 2. Univariate and multivariate analysis

Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Male	1.49 (0.7-3.85)	0.41	-	-
Age	1.05 (1.01-1.09)	0.003	1.04 (1.00-1.08)	0.03
BMI	1.03 (0.95-1.10)	0.49	-	-
Diabetes Mellitus	8.52 (2.49-29.16)	0.001	6.45(1.80-23.03)	0.004
Moderate alcohol consumption	1.09 (0.46- 2.60)	0.84	-	-
Hypertension	4.28 (0.96-18.97)	0.06	-	-
ALT	0.99 (0.98-1.00)	0.43	-	-
AST	0.99 (0.97-1.00)	0.32	-	-
gGT	1.00 (0.99-1.00)	0.77	-	-

$$\text{FIB-4} = \text{Age (years)} \times \text{AST (U/L)} / [\text{PLT}(10^9/\text{L}) \times \text{ALT}^{1/2} \text{ (U/L)}]$$

Results

98 patients (54.3% females)
- 64 patients (65.3%) were non-diabetics
- 34 patients (34.6%) were diabetics

Mean age 60.4 ± 15 years
Presence of cirrhosis: 51.8% of patients

Diabetic patients were more frequently **(Table 1)**
-females
-older
-lower ALT levels

The two groups had similar
- AST levels
- GGT levels
- BMI

Severity of NAFLD
Diabetic patients had:
-higher mean LSM
- higher FIB-4 values
- higher prevalence of cirrhosis (>11.5kPa by LSM)

Multivariate Analysis **(Table 2)**
Advanced age
T2DM
were independently associated with cirrhosis

Age : OR 1.04 (1.00-1.08), p=0.03
T2DM: OR 6.45 (1.8-23.03), p=0.004

Discussion

Females and older patients were more frequently diabetic

Regarding to severity of NAFLD, diabetic patients exhibited more advanced fibrosis than non-diabetic patients.

The prevalence of cirrhosis (>11.5kPa by LSM) was significantly higher in diabetic compared to non-diabetic patients, when accessed with non-invasive modalities.

History of T2DM and advanced age were independently associated with cirrhosis.

FIB-4 score may serve as a useful non- invasive modality when evaluating disease severity

Conclusions

Our findings underline the importance of T2DM as a predisposing factor correlating with the severity of liver fibrosis in patients with NAFLD.

Contact

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References

European Association for the Study of the Liver (EASL); European Association for the Study of Diabetes (EASD); European Association for the Study of Obesity (EASO). EASL-EASD-EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. J Hepatol. 2016 Jun;64(6):1388-402. doi: 10.1016/j.jhep.2015.11.004. Epub 2016 Apr 7. PMID: 27062661.

Siddiqui MS, Yamada G, Vuppalanchi R, Van Natta M, Loomba R, Guy C, Brandman D, Tonascia J, Chalasani N, Neuschwander-Tetri B, Sanyal AJ; NASH Clinical Research Network. Diagnostic Accuracy of Noninvasive Fibrosis Models to Detect Change in Fibrosis Stage. Clin Gastroenterol Hepatol. 2019 Aug;17(9):1877-1885.e5. doi: 10.1016/j.cgh.2018.12.031. Epub 2019 Jan 4. PMID: 30616027; PMCID: PMC6609497.

Targher G, Corey KE, Byrne CD, Roden M. The complex link between NAFLD and type 2 diabetes mellitus - mechanisms and treatments. Nat Rev Gastroenterol Hepatol. 2021 Sep;18(9):599-612. doi: 10.1038/s41575-021-00448-y. Epub 2021 May 10. PMID: 33972770.