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Cross-sectional pilot study about the liver enzymes profile in type 2 diabetic patients from an Algerian west region: Wilaya of Mostaganem

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ABSTRACT

Aims: The magnitude of abnormal liver enzymes profile in type 2 diabetic patients is unknown in Algerian west region even though it counts among liver diseases considered as an important cause of death in type 2 diabetes. The main objective is to assess the prevalence of elevated liver enzymes levels among patients with type 2 diabetes from Algerian west region and to determine associated risk factors.
Materials and methods: A descriptive cross sectional study was performed on 180 type 2 diabetic patients in whom anthropometric and biochemical parameters were determined.
Results: Twenty-five patients had abnormal elevated alanine transaminase (ALT) (13.9%) with the gender-wise prevalence being 15.9% ($n = 17$) in women and 10.9% ($n = 8$) in men. The prevalence of abnormal elevated aspartate transaminase (AST), gamma glutamyl transferase and alkaline phosphatase level was respectively 10% ($n = 18$), 6.1% ($n = 11$) and 8.9% (16). High waist circumference (OR: 5, CI: 1.04–24.04) and high blood pressure (OR: 4.86, CI: 0.94–25.12) were only associated with elevated AST. Fasting glucose >1.4 g/l were associated both with elevated ALT (OR: 3.03, CI: 0.86–10.67) and AST (OR: 5.7, CI: 1.09–29.8).
Conclusion: A relatively high prevalence of elevated liver enzymes was found in diabetic patients from west Algeria, especially in female patients.

1. Introduction

In addition of being associated with micro and macrovascular complications, diabetes mellitus type 2 has been recently associated with different hepatic diseases including abnormal liver enzymes, non-alcoholic fatty liver disease, cirrhosis, hepatocellular carcinoma and hepatitis C. These liver diseases are an important cause of death in type 2 diabetes [1]. Therefore, it is important to screen liver diseases since they are considered as potential complications of type 2 diabetes [2].

Altered portal insulin levels and the insulin/glucagon ratio may influence hepatocyte function and integrity in diabetic patients [3]. Moreover, insulin-resistance induces an excessive production of free fatty acids which are known to be directly toxic to hepatocytes [4]. Hepatocellular injury is reflected by alanine transaminase (ALT) and aspartate transaminase (AST) release from damaged hepatocytes into the blood [5]. In fact, during hepatocellular injury, ALT and AST levels increase primarily, cholestasis parameters levels remain normal or slightly elevated [6].

Several epidemiological studies reported elevated transaminase levels in patients with type 2 diabetes compared with the general population [1,7–11].

The epidemiological data concerning the extent of elevated transaminases in Algerian patients type 2 diabetic are very rare, and to our knowledge only one study was published in this regard [12]. This study aims to assess prevalence of elevated transaminases, gamma glutamyl transferase (γGT) and alkaline phosphatase (ALP) among patients with type 2 diabetes in the west region of Algeria, and to determine associated risk factors.

2. Methods

2.1. Subjects

A descriptive cross-sectional study was performed between March 2014 and October 2014 on 180 patients with type 2 diabetes.

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The participants were admitted to biochemical laboratory unit of Ain Tedless Hospital of Mostaganem wilaya (west of Algeria). After giving their oral consent, patients were questioned about their age, duration of diabetes, hypertension, presence or absence of micro vascular and/or macro vascular complications, treatments for diabetes and other diseases. Hepatitis B and C screening, performed by blood transfusion center of the same hospital, confirmed their absence in the 180 patients. On the other hand, no patient drank alcohol or was treated with a drug that increased levels of liver enzymes.

2.2. Biochemical measurements

Plasma parameters were determined from centrifuged blood, drawn in morning after 12 h of overnight fast. Fasting glucose level (GODPOD method), total cholesterol (CHOD-PAP method), triglycerides (GPO—PAP) HDL-c (phosphotungstic precipitation method) were determined by using Biomaghreb kits (Tunisia). Activities of ALT, AST, γGT and ALP were measured using COBAS systems supplied by Roche Diagnostic (Germany). Elevated ALT and AST levels were defined as enzyme activity >40 U/L and 41 U/L in men respectively and >32 U/L and 33 U/L in women according to the clinical assay adopted by the center's laboratory. γGT and ALP are considered abnormally elevated when they exceed respectively 60 U/L and 130 U/L in men, and 40 U/L and 105 U/L in women.

2.3. Anthropometric parameters

Weight and height of each participant were measured to calculate body mass index (BMI) (kg/m^2) which was calculated as the ratio of weight (kilograms) to the square of height (meters). Patients' BMI was classified according to WHO classification, as being normal (BMI; 18.5 to 24.9 kg/m^2), overweight (BMI; 25 to 29.9 kg/m^2) or obese (BMI>30 kg/m^2) [13]. Waist and hip circumference were also measured to calculate the waist hip ratio (WHR). The WHR is considered abnormal if it exceeded 0.9 in men, and 0.85 in women [14].

3. Statistical analysis

Data were analyzed using SPSS software 20.0. Descriptive statistics were expressed as frequencies and percentages for categorical variables. Continuous variables were expressed as means ± standard deviation for normally distributed variables (age, Chol-c, LDL-c and WHR) and as median for non-normally distributed ones. Multivariate analysis using logistic regression analysis was performed to determine risk factors associated to elevated liver enzymes. The association of a particular variable was expressed as odds ratio (OR) with a 95% confidence interval (CI). A two-tailed *P* value of less than 0.05 was considered to be statistically significant.

4. Results

4.1. Sociodemographic, clinical and anthropometric characteristics

Sociodemographic, clinical and anthropometric characteristics of the participants have been displayed in Table 1. Among the 180 type 2 diabetics enrolled in this study, 59.4% ($n = 107$) were females and 40.6% ($n = 73$) were males. The mean age was 62.56 ± 8.1 years, ranged between 41 and 87 years. In sixty-six patients (36.7%), diabetes was diagnosed during the 5 last years. The 180 diabetic patients were either treated with metformin (42.8%, $n = 77$), sulfonylureas (16.7%, $n = 30$) and insulin alone (36.7%, $n = 66$) or associated to oral antidiabetic (3.9%, $n = 7$). Eighty-seven patients (48.3%) have declared being treated for hypertension.

Table 1
Sociodemographic, clinical and anthropometric characteristics of the 180 patients with type 2 diabetes.

Variables	*N* (%)/Means (median)
Sex	
Women	107 (59.4%)
Age (years)	62.56 ± 8.1
40–49	24 (13.3%)
50–59	60 (33.3%)
60–69	66 (36.7%)
>70	30 (16.7%)
Diabetes duration (years)	5
<5	66 (36.7%)
5–10	69 (38.3%)
11–15	22 (12.2%)
>15	23 (12.7%)
BMI (kg/m^2)	27.15
Normal (18.5–24.9)	70 (38.9%)
Overweighed (25–29.9)	77 (42.8%)
Obese (>30)	33 (18.3%)
WHR ratio	0.94 ± 0.04
Elevated	150 (83.3%)
Treatment	
Metformin	77 (42.8%)
Sulfonylureas	30 (16.7%)
Insulin	66 (36.7%)
Insulin + OAD	7 (3.9%)
Arterial hypertension	87 (48.3%)
Metabolic syndrome[a]	111 (61.7%)
Fasting glucose (g/L)	1.29
Total cholesterol (g/L)	1.58 ± 0.37
Triglycerides (g/L)	1.31
HDL-c (g/L)	0.43
LDL-c (g/L)	1.05 ± 0.2
ALT (U/L)	20
Elevated	25 (13.9%)
AST (U/L)	23
Elevated	18 (10%)
Elevated ALT and AST	11 (44%)
γGT (U/L)	18.8
Elevated	11 (6.1%)
PAL (U/L)	58
Elevated	16 (8.9%)

OAD: oral antidiabetic drug.
[a] According to WHO (1999).

Concerning anthropometric characteristics of the 180 diabetic patients, 18.3% ($n = 33$) were obese with abdominal obesity. However, normal (38.9%, $n = 70$) and overweighed patients (42.8%, $n = 77$) have elevated WHR in 71.4% ($n = 50$) and 80.5% ($n = 62$) of cases respectively. Finally, 111patients (61.7%) gathered metabolic syndrome criteria.

4.2. Biochemical data

The fasting glucose values recorded in the 180 patients vary between 0.56 and 5.2 g/l (median: 1.29 g/l) (Table 1). Concerning lipid parameters, the means values for total cholesterol and triglycerides averaged respectively 1.58 ± 0.37 g/l and 1.51 g/l (median: 1.31 g/l). The means values of HDL-c and LDL-c averaged respectively 0.56 g/l (median: 0.43 g/l) and 1.05 ± 0.2 g/l (Table 1).

Finally, ALT, AST, γGT and PAL median averaged respectively 20 U/L, 23 U/L, 18.8 U/L and 58 U/L (Table 1).

4.3. Prevalence of elevated transaminases, γ glutamyl transferase and alkaline phosphatase

The prevalence of elevated ALT was 13.9% ($n = 25$) with gender-wise prevalence of 15.9% ($n = 17$) in women and 10.9% ($n = 8$) in men (Table 2). The prevalence of elevated AST was 10% ($n = 18$) with gender-wise prevalence of 13.1% ($n = 14$) in women and 5.5%

Table 2
Multivariate analysis of factors associated with elevated ALT and AST.

Variables	Total	High ALT				High AST			
		n (%)	OR (CI 95%)	χ^2	*p*	*n* (%)	OR (CI 95%)	χ^2	*p*
Sex									
Men	73	8 (10.9%)	1	0.68	0.44	4 (5.5%)	1	2.28	0.141
Women	107	17 (15.9%)	1.72 (0.52–5.68)			14 (13.1%)	2.98 (0.59–15.05)		
Age									
40–49	24	6 (25%)	4.78 (0.41–55.72)	2.25	0.491	4 (16.7%)	3.1 (0.26–36.96)	0.94	0.791
50–59	60	10 (16.7%)	3.28 (0.35–30.74)			6 (10%)	1.66 (0.14–19.68)		
60–69	66	8 (12.1%)	2 (0.19–21.05)			6 (9.1%)	2.2 (0.23–21.04)		
>70	30	1 (3.3%)	1			2 (6.7%)	1		
BMI									
Normal	70	6 (8.6%)	1	0.4	0.74	4 (5.7%)	1	2.39	0.25
Overweighed	77	13 (16.9%)	1.48 (0.37–5.92)			6 (7.8%)	0.86 (0.16–4.62)		
Obese	33	6 (18.2%)	1.52 (0.32–7.22)			8 (24.2%)	2.87 (0.56–14.71)		
WHR ratio									
Normal	30	6 (20%)	1	1.2	0.336	7 (23.3%)	1	5.58	0.01
Elevated	150	19 (12.7%)	0.38 (0.07–2.06)			11(7.3%)	5 (1.04–24.04)		
Diabetes duration									
<5	66	10 (15.1%)	1	1.09	0.81	3 (4.5%)	1	5.71	0.13
5–10	69	7 (10.1%)	0.69 (0.15–3.17)			4 (5.8%)	0.58 (0.08–4.2)		
11–15	23	4 (17.4%)	1.64 (0.25–10.76)			6 (26.1%)	5.4 (0.9–32.4)		
>15	22	4 (18.2%)	1.65 (0.24–11.34)			5 (22.7%)	2.84 (0.39–20.68)		
HTA									
Absent	93	10 (10.7%)	1	2.94	0.07	4 (4.3%)	1	4.83	0.03
Present	87	15 (17.2%)	2.91 (0.87–9.73)			14 (16.1%)	4.86 (0.94–25.12)		
Fasting glucose									
<1.4 g/l	95	8 (8.4%)	1	3.33	0.04	4 (4.2%)	1	5.5	0.02
>1.4 g/l	85	17 (20%)	3.03 (0.86–10.67)			14 (16.5%)	5.7 (1.09–29.8)		
Triglycerides									
Normal	112	12 (10.7%)	1	0.61	0.52	8 (7.1%)	1	0.84	0.43
Elevated	68	13 (19.1%)	1.5 (0.4–5.62)			10 (14.7%)	1.82 (0.47–7.05)		

CI: confidence interval; OR: Odd ratio; χ^2: Chi^2; BMI: body mass index; WHR: waist hip ratio.

($n = 4$) in men (Table 2). Eleven patients (6.1%) and sixteen patients (8.9%) have elevated γGT and ALP respectively (Table 1).

The prevalence of elevated ALT seems to increase with BMI (OR: 1.48 for overweighed patients and 1.52 for obese ones). Moreover, Spearman correlation revealed a significant correlation between ALT and BMI ($r = 0.29$, $p = 0.01$) and even between AST and BMI ($r = 0.25$, $p = 0.02$).

Multivariate analysis has revealed a significant association between WHR ratio and AST (OR: 5, CI: 1.04–24.04) and arterial hypertension and AST (OR: 4.86, CI: 0.94–25.12). However, fasting glucose >1.4 g/l was significantly associated with both ALT (OR: 3.03, CI: 0.86–10.67) and AST (OR: 5.7, CI: 1.09–29.8) (Table 2).

Finally, patients with elevated ALT level had high predisposition to have elevated γGT levels (OR: 11.46, CI: 1.7–77.25, $p = 0.01$), and those with elevated AST levels are more likely to have elevated γGT (OR: 17.1, CI: 2.42–120.83, $p = 0.004$).

5. Discussion

The prevalence of elevated transaminases, γGT and ALP level, is not well known in Algerian type 2 diabetic patients, especially in western region of Algeria. In this study, the prevalence of elevated ALT and AST levels (respectively 13.9% and 10%) is higher to those reported by Gouri et al. who studied transaminases prevalence in type 2 diabetic patients from eastern of Algeria [12]. In the other hand, the same author [12] and others [8,9,15,16] reported a higher prevalence of elevated transaminases in men than in women whereas, in the present study, women had a higher tendency to have elevated transaminases compared to men.

Alanine and aspartate transaminases elevation could be due to the presence of nonalcoholic fatty liver (NAFLD). In fact, several authors report that NAFLD is the potential cause of aminotransferases elevation once other causes of liver disease are excluded [17–19]. A high BMI represent an important risk factor for NAFLD and even for nonalcoholic steatohepatitis [20]. Moreover, prevalence of elevated ALT and AST levels was higher in obese and overweighed patients. Besides, Spearman correlation revealed a positive correlation between BMI and ALT ($r = 0.29$, $p = 0.01$), and BMI and AST ($r = 0.25$, $p = 0.02$). This correlation was also found in others studies [8,21]. In other part, WHR, indicating the presence of abdominal obesity, was found as a significant risk factor for elevated AST (OR: 5, IC: 1.04–24.04, $p = 0.01$). Among the twenty-five patients having elevated ALT, 12 patients (48%) had an ALT/AST ratio greater than 1, which could confirm the presence of nonalcoholic hepatic steatosis in these patients [2,6]. In the Fenoli et al. study, the ALT/AST ratio superior than 1 was much more greater (91.1%) probably due to the fact that the patients consuming alcohol were not excluded [22]. Finally, in the remaining thirteen patients, the ALT/AST ratio was less than 1. This is considered as an independent risk factor for an advanced fibrosis [8,23] especially as 17–25% of cases of NAFLD progressed in NASH [24]. In addition to elevated transaminases levels, those of γGT were abnormally elevated in eleven patients (6.1%) whose 9 had elevated levels of ALT and/or AST. This prevalence is found more elevated in others studies (12% [10], 15.6% [25], 23.7% [3]); whereas, no abnormality in γGT level was found in Ni et al. study [21]. The γGT, considered most of the time as a cholestasis markers [4,5,26], are also used as markers of NAFLD [17,27]. Bedogni et al. have even considered γGT as the only independent predictor of fatty liver [28]. This enzyme is equally considered as a risk factor of cardiovascular disease, especially in type 2 diabetic patients [29]. Finally, the prevalence of elevated ALP was 8.9%. According to

some authors, γGT and ALP levels were either elevated or mildly elevated in the presence of fatty liver [1,30,31].

Finally, the normal levels of transaminases in the remaining patients do not exclude the presence of NAFLD and even liver fibrosis especially since most patients even in the presence of hepatic fibrosis remains asymptomatic [32]. Hepatic biopsy remains "the Gold standard" to diagnostic NAFLD, steatohepatitis or cirrhosis [1], or an ultrasound examination which gives a qualitative evaluation which is not well correlated to histologic observations [30]. The absence of common standard levels of ALT, AST, γGT elevation that is considered abnormal, could underestimate the burden of NAFLD [7].

In conclusion, this finding is important since the prevalence of elevated transaminases was higher in type 2 diabetic women than in men from western of Algeria, which is different from diabetic patients in the eastern of Algeria. It will be interesting to perform the same study on a large population from different region of the western of Algeria and others region to confirm our finding, especially that several authors report that lifestyle particularly eating habits could influence transaminases and γGT levels. This could contribute to a better knowledge about prevalence of different liver enzymes in Algerian type 2 diabetic patients which could help to prevent liver complications related to diabetes.

Conflicts of interest

The authors have none to declare.

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