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A RESEARCH ARTICLE

Study of Liver Function Tests in Newly Diagnosed Type II Diabetic Patients and Its Relation with Smoking as a Risk Factor

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Abstract

Diabetes mellitus (DM) stay as disease that can affect function of many organs and body's systems. The liver is one of the organs that are adversely influenced by diabetes mellitus, so the current research aimed to study some liver enzymes which correlated to liver functions in newly diagnosed type II diabetes patients compared with healthy adults and its relation with smoking as a risk factor. In the present study the tests of liver function were represented as (Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Alkaline phosphatase (ALP) in addition to De Ritis Ratio) measured in blood samples of 45 newly diagnosed type II diabetic patients (24males&21females) which divided into two subgroups according to smoking habit; the first include 17 smoker diabetic patients, the second include 28 nonsmoker diabetic patients. The control group included 42 healthy nonsmoker volunteers, to assess the association between some liver function biochemical parameters such as ALT, AST, ALP and De Ritis Ratio in newly diagnosed type II diabetes in a Mosul population; in addition to finding the gender & smoking effects on these hepatic enzymes. According to measured results in this current research, a major elevation in enzyme activity of (ALT, AST, in addition to ALP) was noticed in diabetic patients in comparison with non-diabetic control, as well as, there is a significant effect of smoking in smokers group of patients in comparison with non- smokers diabetic group and control group. While non-significant effect noticed in the sera hepatic enzymes mean (ALT&AST) and (ALP) activity of male & female diabetics. Lastly, the outcomes of the De Ritis Ratio established that non-significant alteration in every one comparison in this study.

1. Introduction

Diabetes mellitus disorder (DM) is a metabolic abnormality effecting the carbohydrate , lipid and protein, mainly recognized as a chronic elevation in glucose of blood which as result from deficient insulin secretion, insulin résistance (IR) or together [1,2]. All systems in the body are affected by this medical condition; including the liver [3].

Two main kinds of DM: 1. Type I (Insulin - Dependent Diabetes Mellitus ; IDDM), 2. Type II (Non-Insulin Dependent Diabetes Mellitus ; NIDDM) [4]. Type I Diabetes Mellitus (T1DM) resulted from autoimmune damage of insulin forming pancreatic β- cells, caused by insulin absolute deficiency [5]. Type II of diabetes mellitus (T2DM) is a major health problem affecting a lot of people all over the world [6].

It is a metabolic disorder which is described by elevation of blood glucose level due to defective insulin function or secretion [7]. Insulin is the hormone that is responsible for the regulation of glucose uptake from the circulation into the insulin sensitive cells; including adipocytes and skeletal muscle cells [8,9]. The liver is crucial in the control of metabolism of carbohydrates and lipids. Any changes in liver function may lead to alteration in the metabolism of both glucose and lipids [10,11]. This crucial control of liver makes abnormality more prone to in persons with a metabolic disease, specifically for (DM) [3]. The most important parameters in the evaluation of hepatic damage are plasma concentration of alanine and aspartate aminotransferases (ALT& AST), alkaline phosphatase enzyme (ALP) and γ- glutamyl transpeptidase (GGT) [12,13]. Liver function tests (LFTs) are routinely used for

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screening, finding, evaluation of disease developing, severity and management of hepatic diseases in addition, adverse effect of hepatotoxic drugs [14,15]. Deterioration in LFTs are found, elevated hepatic enzymes in type 2 diabetes mellitus cases than non diabetics [13,16]. De Ritis Ratio, well-defined as the sera activity AST to ALT ratio, is generally recognized biological indicator with the important applications in diagnosed and dealing with various diseases, mainly liver disorders [17]. It was regarded as one of the best surrogate indicators for non-alcoholic fatty liver disease (NAFLD) which association with the risk of developing T2DM [18].

2. Subjects, Materials and Methods

2.1. Materials and Methods

The study was conducted by 45 newly diagnosed diabetic patients with type II which included (24 males& 21 females) the age ranging from (41-60) years with a mean of age (51) year. The control group was 42 healthy nonsmokers with range of age (40-62) years with a mean of age (49) year. The diabetic group was divided into two subgroups depending on smoking intake. The first subgroup (diabetic smokers) included 17 individuals. The second diabetic subgroup (diabetic nonsmokers) included 28 individuals. The full history from each case was taken: name, age, gender, weight, height, job, smoking and alcohol consumption, personal history and any medicine history. Cases with past hepatic diseases, obesity, and alcohol intake were excluded from the study. Blood samples (5mL) were drawn from each case in this research by anticubital puncture, stressful puncture not included. The samples were directly transported into non heparinized test tubes and incubated at 37 ºC about 10 minutes, then make centrifugation for 15 minutes at 3 thousand rpm to make sure that the sera is completely separated. Separated sera sample was used to measure the activity of sera enzymes (AST, ALT, and ALP). The activity of aminotransferase enzymes (ALT&AST) was estimated colorimetrically regarding the technique Reitman and Frankel; 1957 [19]; using a kit supplied by (Randox / UK). The estimation of alkaline phosphatase activity depends upon the colorimetric analysis [20]; using a kit supplied by (biolabo / France). Lastly, De Ritis Ratio calculates from divided of AST above ALT level [21].

2.2. Statistical analysis

The results in the current study were statistically analysed by the usage of an unpaired t-test. Data is presented as mean ± standard deviation (S.D). Significant changes was regarded at p values was ≤ 0.05 [22].

3. Results

The contrast was done between the results of liver enzymes alanine and aspartate aminotransferases & alkaline phosphatase in diabetics and control cases; as understood in Table 1, conclude that a significant increase was noticed in activity of (ALT & AST) besides ALP in diabetic patients (12.11±3.22), (11.56±2.57) and (56.5±10.7) respectively in comparison with non-diabetic subjects (9.71±3.09), (9.45±3.11) and (49.1±10.6) respectively.

According to the gender effect on some liver function tests; the current research shows the differences of sera these hepatic enzymes between both gender of diabetics; as seen in Table 2, a slight rises was noticed in the mean activity of amino transferases & ALP enzymes in male diabetics (12.25±3.52), (12.13±2.58) and (57.5±10.5) respectively in comparable` with female diabetics (11.95±2.92), (10.90±2.47) and (55.4±11.0) respectively but its statistically not significant.

The smoking impact on sera liver enzymes (ALT & AST) and ALP within diabetic groups; as seen in Table 3, there was a significant elevation of sera (ALT&AST) and ALP in diabetic smokers (13.35±2.29), (12.88±2.23) and (60.76±7.96) respectively in comparison with diabetic nonsmokers (11.36±3.50), (10.75±2.46) and (53.9±11.4) respectively. Also the comparison of sera liver enzymes between diabetic cigarette smokers and healthy nonsmokers controls; as shown in Table 4, the results show a significant rise of (ALT& AST) and ALP in diabetic smokers (13.35±2.29), (12.88±2.23) and (60.76±7.96) respectively in contrast with the control group (9.71±3.09), (9.45±3.11) and (49.1±10.6) respectively.

Finally, the finding of De Ritis Ratio show there is no significant alteration in all comparison measured in this study.

Table 1. Liver Function Tests in diabetics and control groups

Parameters	Mean ± S.D		T-value	
	Control group (No.=42)	Diabetic group (No.=45)		
Sera ALT (U/L)	9.71±3.09	12.11±3.22	-3.54	0.0007**
Sera AST (U/L)	9.45±3.11	11.56±2.57	-3.45	0.0009**
Sera ALP (U/L)	49.1±10.6	56.5±10.7	-3.25	0.0016*
De Ritis Ratio	1.058±0.516	1.023±0.343	0.37	0.71

*Significant at (p≤0.05), ** Significant at (p≤0.001).

Table 2. Effect of gender on liver function tests within the diabetics group

Parameters	Mean ± S.D		T-value	P-value
	Diabetic males group (No.=24)	Diabetic females group (No.=21)		
Sera ALT (U/L)	12.25±3.52	11.95±2.92	0.31	0.76
Sera AST (U/L)	12.13±2.58	10.90±2.47	1.62	0.11
Sera ALP (U/L)	57.5±10.5	55.4±11.0	0.65	0.52
De Ritis Ratio	1.047±0.294	0.996±0.397	0.49	0.62

Table 3. Effect of smoking on liver function tests within the diabetic group

Parameters	Mean±S.D		T-value	P-value
	Diabetic nonsmokers group (No.=28)	Diabetic smokers group (No.=17)		
Sera ALT (U/L)	11.36±3.50	13.35±2.29	-2.09	0.042*
Sera AST (U/L)	10.75±2.46	12.88±2.23	-2.92	0.0056*
Sera ALP (U/L)	53.9±11.4	60.76±7.96	-2.18	0.035*
De Ritis Ratio	1.028±0.354	0.996±0.265	0.32	0.75

*Significant at (p≤0.05).

Table 4. Liver function tests in diabetic smokers and control groups

Parameters	Mean±S.D		T-value	P-value
	Control group (No.=42)	Diabetic smokers (No.=17)		
Sera ALT (U/L)	9.71±3.09	13.35±2.29	-4.39	0.0001***
Sera AST (U/L)	9.45±3.11	12.88±2.23	-4.13	0.0001***
Sera ALP (U/L)	49.1±10.6	60.76±7.96	-4.11	0.0001***
De Ritis Ratio	1.058±0.516	0.996±0.265	0.47	0.64

*** Significant at (p≤0.0001).

4. Discussion

According to the impact DM on sera alanine and aspartate aminotransferases & alkaline phosphatase activity in this investigation, a markedly significant elevation of both aminotransferase enzymes activity (ALT&AST), and ALP in diabetic patients when compared to non-diabetic individuals was noticed; as seen in Table 1. These results of the current study are in agreement with Mathur S *et al*. [23] and Vozarova *et al*. [24], Harris *et al*. [25].

Elevations in sera aminotransferases activity are frequently seen in patients with DM and these changes are mostly related to fatty infiltration of the liver [26,27]. ALP enzyme is usually a measured as indicator for many hepatic and bile duct disease [28]. Alanine and aspartate aminotransferase enzymes give the idea in the sera following hepatic cellular damage [29]. Elevated hepatic enzymes can be due to inflammation or damage to the cells in the liver [30]. The comparing mean values of these hepatic enzymes activities among males and females within the diabetic group, statistically not significant differences is found in mean activities of sera alanine and aspartate aminotransferases as well as, alkaline phosphatase was noticed; as seen in (Table 2).

Also, the current study showed that cigarette smoking caused a considerable rise of sera enzymes ((ALT& AST) and ALP) has been discovered in cigarette cigarette smoker diabetics in comparable with nonsmokers diabetics and non-diabetics controls; as in Table (3,4). The human body systems affected by cigarette smoking [31].

An acceptable explanation for rising aminotransferases levels in smoker persons is the side by side effects between both smoking, and oxidative stress [32]. One of the reasons that might induce alterations in liver enzymes (AST&ALT) and ALP is oxidative stress [23]. The alteration in the activity of ALP can reflect an elevated insulin resistance / or oxidative stress [33]. As well as the accumulative effect of toxic metals and substances resulting from smoking habit are responsible for occurrence of oxidative stress and liver function disturbances [34,35]. Oxidative stress well defined as loss of system balance between the development of oxidants and the antioxidant protection system and related with many human disorder that contain hypertension, inflammation, atherosclerosis, Alzheimer's disease, Parkinson's disease, and diseases of female reproductive system including pregnancy related disorders [36,37].

Conclusion

The current study concludes that liver enzymes (ALT&AST) and ALP can be associated with increased activity in newly diagnosed type II diabetes mellitus patients than cases who do not have diabetes mellitus, in addition to the smoking habit has a relative risk on liver diseases.

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Conflict of Interest

The researcher ensures there is no conflict of interest.

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دراسة اختبارات وظائف الكبد لدى مرضى السكري من النوع الثاني حديثي التشخيص وعلاقتها بالتدخين كعامل خطر

الملخص

يُعدّ داء السكري مرضًا يؤثر على وظائف العديد من أعضاء الجسم وأجهزته. ويُعتبر الكبد أحد الأعضاء الأكثر تأثرًا سلبًا بهذا المرض، لذا هدفت هذه الدراسة إلى بحث بعض إنزيمات الكبد المرتبطة بوظائف الكبد لدى مرضى السكري من النوع الثاني حديثي التشخيص، مقارنةً بالبالغين الأصحاء، وعلاقتها بالتدخين كعامل خطر. في هذه الدراسة، تم قياس وظائف الكبد (ناقلة أمين الأسبارتات(AST) ، وناقلة أمين الألانين(ALT) ، والفوسفاتاز القلوي(ALP) ، بالإضافة إلى نسبة دي رايت) في عينات دم مأخوذة من 45 مريضًا بالسكري من النوع الثاني حديثي التشخيص (24 ذكرًا و21 أنثى)، تم تقسيمهم إلى مجموعتين فرعيتين وفقًا لعادات التدخين؛ ضمت المجموعة الأولى 17 مريضًا مدخنًا، بينما ضمت المجموعة الثانية 28 مريضًا غير مدخن. شملت المجموعة الضابطة 42 متطوعًا سليمًا غير مدخن، لتقييم العلاقة بين بعض المؤشرات الكيميائية الحيوية لوظائف الكبد، مثل ALT و ASTو ALPونسبة دي ريتيس، لدى مرضى السكري من النوع الثاني الذين تم تشخيصهم حديثًا في مدينة الموصل؛ بالإضافة إلى تحديد تأثير الجنس والتدخين على هذه الإنزيمات الكبدية. وفقًا للنتائج المقاسة في هذا البحث، لوحظ ارتفاع ملحوظ في نشاط إنزيمات ALT) و ASTو (ALPلدى مرضى السكري مقارنةً بالمجموعة الضابطة غير المصابة بالسكري، كما لوحظ تأثير معنوي للتدخين على مجموعة المدخنين من المرضى مقارنةً بمجموعة مرضى السكري غير المدخنين والمجموعة الضابطة. في حين لم يُلاحظ تأثير معنوي على متوسط نشاط إنزيمات الكبد ALT) و (ASTو (ALP)في مصل الدم لدى مرضى السكري من الذكور والإناث. أخيرًا، أظهرت نتائج نسبة دي ريتيس عدم وجود تغيير معنوي في جميع المقارنات في هذه الدراسة.

الكلمات المفتاحية: داء السكري، اختبارات وظائف الكبد، التدخين، AST، ALT، ALP، نسبة دي ريتيس.