Association between Cardiac Enzymes Level in Type 2 Diabetes Mellitus from Jazan Region, Saudi Arabia

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ABSTRACT
Diabetes mellitus is characterized by deficiencies in insulin secretion and action, often leading to complications such as cardiac dysfunction associated with insulin-resistance syndrome. This study aimed to investigate the associations between serum cardiac enzyme levels (lactate dehydrogenase [LDH] and creatine kinase-MB [CK-MB]) and the incidence of type 2 diabetes mellitus in the Jazan population. Conducted at the MLT-Biochemistry laboratory of the College of Applied Medical Sciences, Jazan University, Saudi Arabia, the study involved the collection of 5 ml blood samples from 55 patients with type 2 diabetes and 35 control subjects. The mean (±S.D.) levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) in the control group were found to be 12.13±0.70 and 17.47±0.70 U/L, respectively, while in diabetic patients, the levels were significantly elevated at 20.55±1.90 and 24.15±2.10 U/L. Statistical analysis revealed significant differences in the means of ALT and AST levels between the two groups. The findings indicate that individuals with type 2 diabetes exhibit markedly higher serum liver enzyme levels compared to non-diabetic individuals, highlighting a greater incidence of liver function test (LFT) abnormalities in diabetic subjects. This study underscores the need for monitoring liver enzyme levels in patients with type 2 diabetes to better understand the associated risks and complications.

INTRODUCTION: Rewriten:

Diabetes mellitus is characterized by inadequate insulin secretion, insulin action, or a combination of both, leading to chronic hyperglycemia and disturbances in carbohydrate, lipid, and protein metabolism [1,4]. In Saudi Arabia, diabetes is rapidly becoming an epidemic, with over 3.4 million individuals diagnosed in 2015, representing approximately 32.8% of the population [2,3]. This common metabolic disorder can result in various microvascular and macrovascular complications, including cardiovascular disease (CVD), retinopathy,

nephropathy, and neuropathy, primarily as a consequence of uncontrolled hyperglycemia [5,6]. The heart plays a crucial role in maintaining normal glucose levels during fasting and postprandial states, and cardiac dysfunction stemming from insulin-resistance syndrome may contribute to the development of type 2 diabetes [7,8].

Cardiac enzymes such as lactate dehydrogenase (LDH), creatine kinase-MB (CK-MB), and troponin are routinely assessed to evaluate cardiac function, with LDH and CK-MB serving as markers of cardiac health [9,10]. Numerous studies have established a correlation between elevated levels of these enzymes and the incidence of type 2 diabetes. This study aimed to explore the relationship between serum cardiac enzyme levels (LDH and CK-MB) and the incidence of type 2 diabetes within the Jazan population, focusing on differences in serum glucose levels between diabetic and non-diabetic subjects.

Globally, diabetes affects an estimated 422 million adults, with prevalence rates projected to nearly double by 2030 [11]. Diabetes is one of the top ten causes of disability, leading to severe complications such as heart disease, stroke, lower limb amputations, and blindness, with approximately 50% of individuals remaining undiagnosed [12]. Type 2 diabetes accounts for 85-90% of all diabetes cases, and its prevalence in Saudi Arabia is escalating rapidly, with forecasts suggesting rates will reach 35.37% in 2020, 40.8% in 2025, and 45.8% by 2030 [13,14]. This alarming trend presents significant challenges for healthcare providers, with the country reportedly spending around SR 30 billion annually on diabetes-related healthcare. Consequently, it is imperative for Saudi Arabia to implement comprehensive diabetes prevention strategies as part of its national health policy [15].

Diabetes mellitus is classified into two primary types: type 1 diabetes, characterized by complete or near-total insulin deficiency, and type 2 diabetes, which results from insulin resistance and defects in insulin secretion [16,17,18]. Type 1 diabetes accounts for about 10% of all cases [19,20,21], while type 2 diabetes is the most prevalent form, comprising nearly 90% [22]. The progression of type 2 diabetes is influenced by a complex interplay of genetic predisposition, obesity, and sedentary lifestyle factors, leading to insulin resistance and subsequent β-cell dysfunction.

Individuals with diabetes face a heightened risk of serious health complications, including diabetic retinopathy [23,24], which can cause blindness, and diabetic neuropathy, which can affect both somatic and autonomic functions [25,26]. Cardiovascular disease is a major contributor to mortality among diabetic patients, accounting for over half of all deaths in this population [27,28]. Dyslipidemia, characterized by abnormal lipid levels, is a common metabolic disorder associated with diabetes [29]. Diabetic nephropathy, resulting from prolonged hyperglycemia, affects approximately 30% of diabetics and can lead to end-stage renal disease [30,31].

LDH is an enzyme found in nearly all body tissues, playing a vital role in energy production. Elevated serum LDH levels are often indicative of cardiac dysfunction [32,33]. Similarly, increased creatine kinase levels, particularly CK-MB, suggest damage to heart muscle. The heart's role in regulating blood glucose levels is significant; disruptions in insulin signaling can lead to increased cardiac glucose production and triglyceride abnormalities, which are early indicators of insulin resistance [34].

Research indicates that higher levels of LDH and CK-MB may be linked to the development of type 2 diabetes. Studies have shown that elevated LDH levels in non-diabetic individuals can serve as a risk factor for developing diabetes, suggesting a potential connection between cardiac injury, inflammation, and diabetes pathogenesis [35,36,37]. Furthermore, type 2 diabetic patients

frequently exhibit elevated LDH and CK-MB levels, correlating with abnormal lipid profiles, which indicate an increased risk of cardiovascular disease.
In summary, the rising prevalence of type 2 diabetes, coupled with its associated complications, underscores the need for vigilant monitoring of cardiac health markers, such as LDH and CK-MB, as part of comprehensive diabetes management and prevention strategies.

METHODOLOGY

The study necessitated the use of a cardiac enzyme analysis kit, a UV-Visible spectrophotometer, cuvettes, pipettes, 1 ml and 100 µl tips, urine collection tubes, and all chemicals of analytical grade. It was conducted at the MLT-Biochemistry laboratory of the College of Applied Medical Sciences, Jazan University, in Jazan, Saudi Arabia. Blood samples were collected from participants at the Diabetes Institute in Jazan, where informed written consent was obtained from each individual. The Institute serves the local community in the Jazan region.
Prior to commencement, the study received approval from the Department of Laboratory Technology at the University of Jazan. A total of 5 ml of blood samples were collected from 55 patients diagnosed with type 2 diabetes and 35 control subjects. Serum was separated immediately after blood collection, which was performed after an overnight fast, using centrifugation for 10 minutes. Fasting blood glucose levels and cardiac enzyme concentrations (LDH and CK-MB) were analyzed using appropriate human reagent testing kits. Data were presented as mean ± standard deviation (SD), and statistical significance was assessed using Student's t-test via SPSS version 16 software, with a p-value of <0.05 considered statistically significant.

RESULTS

Among the 35 control subjects, all exhibited normal serum levels of lactate dehydrogenase (LDH) and creatine kinase-MB (CK-MB), with only 2 individuals (5.71%) presenting abnormal serum levels. Table 1 summarizes the activity of serum marker enzymes (LDH and CK-MB) in both diabetic and non-diabetic individuals. Of the 55 diabetic subjects, 18 (32.72%) demonstrated elevated serum levels of LDH and CK-MB. A statistically significant increase in both LDH and CK-MB levels was observed in diabetic patients compared to their non-diabetic counterparts.

Table 1: Frequency occurrence of CK-MB and LDH level in diabetic and normal subjects.

Parameter	Control Subject	Diabetic Subjects
Cardiac Enzymes		
LDH	5.71% (2)/35	32.72% (18)/55
CK-MB	5.71%(2)/ 35	30.90%(17)/55

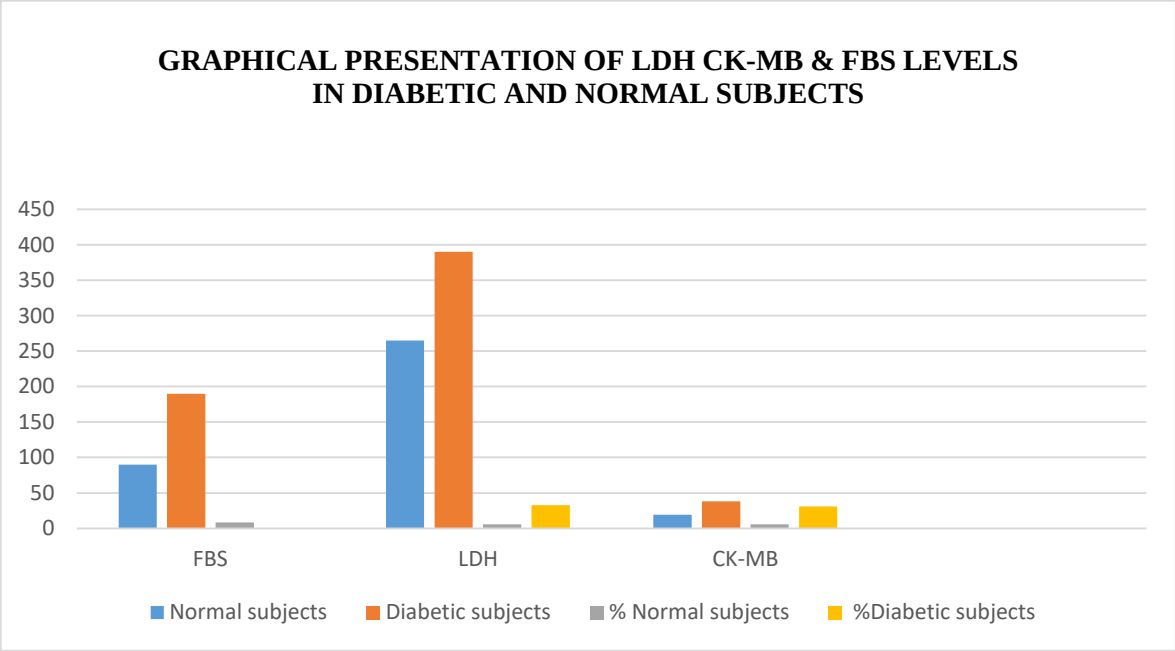

Figure-1 Graphic presentation is showing the comparison between normal and diabetic subjects' level of FBS, LDH and CK-MB.

The mean fasting blood glucose level in the control group was measured at 91.61 ± 5.12 mg/dl, indicating normal glucose metabolism. In contrast, diabetic participants had a significantly higher mean fasting blood glucose level of 166.83 ± 7.59 mg/dl, confirming the presence of hyperglycemia associated with diabetes.

Additionally, the mean serum levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were assessed. In the control group, the mean AST and ALT levels were recorded at 12.13 ± 0.70 U/L and 17.47 ± 0.70 U/L, respectively. Conversely, diabetic subjects exhibited markedly elevated mean levels of AST at 20.55 ± 1.90 U/L and ALT at 24.15 ± 2.10 U/L. These findings, presented in Table 2, highlight that serum AST and ALT levels are significantly higher in diabetic patients compared to the non-diabetic control group, suggesting potential liver function abnormalities associated with diabetes. Overall, the results of this study underscore the metabolic disturbances present in individuals with type 2 diabetes, as evidenced by elevated cardiac and liver enzyme levels.

Table 2: Mean Serum sugar and enzymes (LDH and CK-MB) in diabetic subjects and control subjects

Sample	N	LDH (U/ L)	CK-M B (U/ L)	Fasting Blood Sugar (mg/dl)
Control Subjects	35	12.13±0.70	17.47±0.70	91.61 ± 5.12
Diabetic Subjects	55	20.55±1.90	24.15±2.10	166.83 ± 7.59

DISCUSSION

The differences in mean levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) between diabetic patients and the control group were statistically significant. This finding is consistent with previous research, including a study in which 57% of 175 diabetic outpatients exhibited at least two abnormal test results [38]. Similarly, another investigation reported significant elevations in cardiac function tests, specifically lactate dehydrogenase (LDH) and creatine kinase-MB (CK-MB), among Sudanese patients with type 2 diabetes compared to control subjects [39].

Several researchers have proposed that elevated liver enzyme levels in individuals with diabetes mellitus may be linked to the effects of insulin on liver and muscle tissues [40]. It has been suggested that increased LDH levels reflect fatty changes in the heart, an abnormality that can manifest prior to the clinical onset of type 2 diabetes [41]. These biochemical alterations are particularly pertinent for patients with a prolonged history of diabetes, where a repression of glycolytic enzymes and a decrease in gluconeogenic enzymes are observed. This imbalance leads to increased gluconeogenesis in the liver, thereby contributing to the persistence of hyperglycemia.

The interplay between insulin resistance and the metabolic dysregulation of liver enzymes underscores the complexity of diabetes and its complications. As insulin sensitivity diminishes, the liver's capacity to regulate glucose production becomes impaired, further exacerbating hyperglycemic conditions [42]. These findings highlight the need for ongoing monitoring of liver and cardiac enzyme levels in diabetic patients to better understand the underlying mechanisms and potential complications associated with the disease.

CONCLUSION

The current study demonstrates that serum liver enzyme levels are significantly elevated in individuals with type 2 diabetes compared to non-diabetic subjects. This indicates that individuals with type 2 diabetes have a higher incidence of liver function test (LFT) abnormalities. Elevated serum liver enzymes may serve as early risk markers for the development of chronic diseases, including type 2 diabetes and cardiovascular disease (CVD), suggesting their potential utility in preventive strategies for these conditions.

While the underlying mechanisms driving these associations warrant further investigation, the findings support the notion that the liver plays a critical role in the pathogenesis of type 2 diabetes. Furthermore, hepatic enzymes may serve as valuable additional markers to identify individuals at high risk for developing diabetes.

Additionally, physical activity has been shown to have an inverse association with LDH and CK-MB levels, underscoring the importance of promoting regular exercise as a preventive measure. Encouraging physical activity could be an effective strategy to mitigate the risk of developing diabetes and its associated complications.

REFERENCE

[1] Amos AF, McCarty DJ, Zimmet P (1997) The rising global burden of diabetes and its complications Diabetic Med 14,1-85.
[2] http://www.diabetesatlas.org/
[3] http://www.diabetesatlas.org/

[4] Abou-Seif MA, Youssef AA (2004) Evaluation of some biochemical changes in diabetic patients. Clin Chim Acta 346,161–170.
[5] Taskinen MR (2002) Diabetic dyslipidemia. AtherosclerSuppl 3, 47–51.
[6] Folli F, Corradi D, Fanti P, Davalli A, Paez A, Giaccari A, Perego C, Muscogiuri G (2011) The role of oxidative stress in the pathogenesis of type 2 diabetes mellitus micro- and macrovascular complications: avenues for a mechanistic-based therapeutic approach. Curr Diabetes Rev 7, 313–324.
[7] Duckworth WC, Hamel FG, Peavy DE (1988) Hepatic metabolism of insulin. Am J Med 85, 71–76.
[8] Marchesini G, Brizi M, Bianchi G, Tomassetti S, Bugianesi E, Lenzi M, McCullough AJ, Natale S, Forlani G, Melchionda N (2001,) Non-alcoholic fatty liver disease: a feature of the metabolic syndrome. Diabetes 50, 1844–1850.
[9] Hanley AJ, Williams K, Festa A, Wagenknecht LE, D'Agostino RB Jr, Kempf J, Zinman B, Haffner SM (2004) Elevations in markers of liver injury and risk of type 2 diabetes - The insulin resistance atherosclerosis study. Diabetes 53, 2623–2632.
[10] Sato KK, Hayashi T, Nadamura Y (2008) Liver enzymes compared with alcohol consumption in predicting the risk of type 2 diabetes. Diabetes Care 31, 1230–1236.
[11] Nakanishi N, Suzuki K, Tatara K (2004) Serum gamma-glutamyltransferase and risk of metabolic syndrome and type 2 diabetes in middle-aged Japanese men. Diabetes Care 27, 1427–1432.
[12]World Health Organization, Global Report on Diabetes (2016)(http://www.who.int/diabetes/global-report/en/) Geneva.
[13] Wild S, Roglic G, Green A, Sicree R, King H (2004) Diabetes Care 27, 1047–1053.
[14] Williams textbook of endocrinology (12th ed.)Philadelphia: Elsevier/Saunders. pp. 1371–1435.
[15] Australian Indigenous Health Info Net, Chronic conditions: (2016) Diabetes (http://www.healthinfonet.ecu.edu.au/chronic-conditions/diabetes/plain-language/our-review).
[16] Meo SA (2016) J Pak Med Assoc 66, 722-725.
[17] WHO Consultation Report, Geneva, 1999.
[18] Zimmet PZ, McCarty DJ and de Courten MP (1997) J Diabetes Compli11, 60–68.
[19] Kasper DL, Fauci, AS, Longo DL, Braunwald E, Hauser SL and Jameson JL (2005) Harrison's Principles of Internal Medicine 16th edition: Vol 2, pp. 2152–2180.
[20] Cecil RL, Bennett JC and Plum F (1996) Cecil textbook of medicine. Saunders, Philadelphia.
[21] Eisenbarth GS (1986) New Engl J Med 314, 1360–1368.
[22] Alberti KG and Zimmet PZ (1998) Diabetes Med 15, 539–553.
[23] Eriksson J, Franssila-Kallunki A, Ekstrand A, Saloranta C, Widén, E, Schalin C and Groop L (1989) New Engl J Med 321, 337–343.
[24] Frank RN (2004) New Engl J Med 350, 48–58.
[25] Hirai FE, Tielsch JM, Klein BE and Klein R (2011) Ophthalmology 118, 353–358.
[26] Selvarajah D, Wilkinson ID, Emery CJ, Harris ND, Shaw PJ, Witte DR, Griffiths PD and Tesfaye S (2006) Diabetes Care 29, 2664–2669.
[27] Wessels AM, Rombouts SA, Simsek S, Kuijer JP, Kostense PJ, Barkhof F, Scheltens P, Snoek FJ and Heine RJ (2006) Diabetes 55, 334–340.

[28] Haffner SM, Lehto S, Ronnemaa T, Pyorala K and Laakso M (1998) New Engl J Med 339, 229–234.
[29] Laing SP, Swerdlow AJ, Slater SD, Burden AC, Morris A, Waugh NR, Gatling W, Bingley PJ and Patterson CC (2003) Diabetologia46, 760–765.
[30] Arca M, Pigna G, Favoccia C. (2012) Mechanisms of diabetic dyslipidemia: relevance for atherogenesis. CurrVascPharmacol 10, 684–686.
[31] Shlomo M, Polonsky KS, Larsen PR, Kronenberg HM (2011). Diabetes Mellitus. Willams textbook of endocrinology, 12th Ed. Philadelphia: Elsevier/Saunders; p.1371-1435.
[32] Zimmet P, Alberti KG, Shaw J (2001) Global and societal implications of the diabetes epidemic. Nature 414, 782-787.
[33] Giannini EG, Testa R, Savarino V (2005) Liver enzyme alteration: a guide for clinicians. CMAJ 172, 367-379.
[34] Whitfield JB (2001) Gamma glutamyl transferase. Crit Rev Clin Lab Sci 38, 263-355.
[35] Lewis GF, Carpentier A, Khosrow A, Giacca A (2002) Disordered fat storage and mobilization in the pathogenesis of insulin resistance and type 2 diabetes. Endocr Rev 23, 201–229.
[36] Perry IJ,Wannamethee SG, Shaper AG (1998) Prospective study of serum gamma-glutamyltransferase and risk of NIDDM. Diabetes Care 21, 732–737.
[37] Ohlson LO, Larsson B, Bjorntorp P, Erksson H, SvardsuddK,Welin L, TibblinG,Wilhelmsen L (1988) Risk factors for type 2 diabetes mellitus: thirteen and one-half years of follow-up of the participants in a study of Swedish men born in 1913. Diabetologia 31, 798–305.
[38] Vozarova B, Stefan N, Lindsay RS, Saremi A, Pratley RE, Bogardus C, Tataranni PA (2002) High alanine aminotransferases is associated with decreased hepatic insulin sensitivity and predicts the development of type 2 diabetes. Diabetes 51, 1889–1895.
[39] Salmel PI, Sotaniemi EA, Niemi M, Maentausta O (1984) Liver function tests in diabetic patients. Diabetes Care, 7, 248 -254.
[40] Idris A, Mekky KFH, Abdalla BEE, Ali KA (2011) Liver function tests in type 2 Sudanese diabetic patients. Inter J Nut Met 3, 17-21.
[41] Clore JN, Post EP, Baily D., Nester JF, Blackard WG (1992) Evidence for increased liver glycogen in patients with Non-insulin dependent diabetes mellitus after a 3-day fast. J Clin EndocrMetab 74, 660-666.
[42] Wun YT, Chan CS, Lui CS (2008) Hyperuricemia in type 2 diabetes mellitus I Bangladesh. Med Res Counce Bull 4, 84-89.