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A case-control study evaluating the predictive role of creatine kinase and lactate dehydrogenase in type 2 diabetes mellitus

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Abstract

Diabetes mellitus (DM) is a global epidemic affecting millions of people, often accompanied by inflammatory diseases. It is a significant risk factor for cardiovascular disorders, particularly in India. A study was conducted to explore the role of inflammatory markers like lactate dehydrogenase and creatine kinase in diabetes. The study involved 100 subjects, including 50 cases with type 2 diabetes mellitus and 50 healthy controls. The results showed reduced activity of lactate dehydrogenase and creatine kinase in cases compared to controls. No significant changes in BMI were found in both groups. A positive correlation was found between creatine kinase and lactate dehydrogenase in diabetics. Regression analysis showed that serum lactate dehydrogenase (LDH) accounts for 20% of the variance in serum creatine kinase, while serum creatine kinase accounts for 16.3%. The study suggests testing for inflammatory markers may help to monitor disease progression and provide a theoretical basis for understanding the disease's pathogenesis.

Keywords: Creatine kinase, Diabetes mellitus, Lactate dehydrogenase.

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1. Introduction

Diabetes is a chronic disorder that is caused by hyperglycemia and changes in carbohydrate, lipid, and protein metabolism [1]. It is a major public health concern on a global scale, with type 2 diabetes ranking as the ninth-leading cause of death [2]. The global diabetes prevalence is expected to rise from 171 million in 2000 to 366 million by 2030, with India leading with a lead of 79.4 million [3]. Diabetes type 2 is becoming more common due to a variety of causes, including an aging population, sedentary lifestyles, and poor dietary habits [4]. Early diagnosis, followed by glycaemic management, is the starting point for living well with diabetes [5]. LDH is an enzyme that catalyses the conversion of pyruvate to lactic acid via glycolysis. It is mostly found in the cytoplasm of the cell and becomes extracellular when the cell dies [6]. It has been proposed that LDH concentrations vary according to the energy requirements of various tissues [7]. There are several LDH isoenzymes with varying activity in saliva and blood. LDH1 and LDH2 are found mostly in the blood, whereas LDH4 and LDH5 are found primarily in the saliva [8-9]. LDH activity helps in the detection of disease development, including malignancy and myocardial infarction [9-10]. Insulin is produced in response to glucose levels and regulates sugar metabolism via glycolysis and pyruvate oxidation in the mitochondria [11-15]. This is consistent with the fact that mitochondria create more ATP than glycolysis, which is known to stimulate insulin secretion [16]. Creatine kinase is an inflammatory enzyme that needs to be assessed in type 2 diabetes mellitus patients. It is a cytosolic compound that helps mitochondria exchange phosphate through the cytoplasm as a source of high energy. It has three isoenzymes, CK-MM, CK-MB, and CK-BB, which are found in muscles and are considered muscle damage biomarkers. In diabetic patients, the dimension of creatine kinase increases due to a rise in the isoenzyme, and the source of this expansion is destruction in skeletal muscle caused by a decrease in vitality. CK-MB and CK-BB are common isoenzymes [17]. The main cause of elevated CK in diabetics is skeletal muscle damage, specifically the CK-MM isoenzyme [17]. There has been no well-documented investigation to investigate the amount of compliance and adherence to serum CK and LDH level advancement among T2DM patients. Serum CK measurement is an important aspect of evaluating individuals with muscular weakness or myalgia, as well as patients with myopathies or muscle injuries [18]. Similarly, serum LDH or LDH isoenzyme levels play a role in the diagnosis, prognosis, and monitoring of conditions such as myocardial infarction,

haemolytic anaemia, hepatocellular cancer, ovarian dysgerminoma, and testicular germ cell tumour [10]. Therefore, the present study was conducted to evaluate and compare the serum LDH and CK levels in diabetes mellitus cases and healthy controls.

2. Materials & Methods

The present case-control study was carried out at the Integral Institute of Medical Sciences & Research's Department of Biochemistry in Lucknow, Uttar Pradesh. With written informed consent, 100 subjects (50 diabetic cases and 50 healthy controls) between the age group of 18 - 70 were selected for the study. Diabetic cases were selected from patients attending the IIMS&R medical OPD. Patients were diagnosed per the American Diabetes Association's criteria (2021). Patients with thyroid and liver diseases, as well as pregnant women, were excluded from the study. BMI was calculated as body weight (kg) divided by height (m^2). For the estimation of BMI, a stepwise approach to NCD Risk Factor Surveillance (STEPS) recommendations was used for the assessment of weight and height. A data collection form was used to collect demographic, anthropometric, and clinical information from each study subject.

2.1. Ethical Approval

The Institutional Ethics Committee of the Integral Institute of Medical Sciences and Research, Lucknow, Uttar Pradesh, has approved human participant enrolment and blood sample collection. [IEC NO.IEC/IIMS&R/2022/11].

2.2. Sample collection, storage, and Processing of Samples

Under aseptic conditions, 3ml venous blood was collected in plain and EDTA vials from each individual. The blood samples were allowed to coagulate at room temperature for 15 minutes. The serum was then separated by centrifuging the sample at 2500 rpm for 5 minutes.

2.3. Laboratory investigations

Estimation of HbA1c was done by the High-performance liquid chromatography (HPLC) method. Estimation of serum creatine kinase was done by the IFCC method, and lactate dehydrogenase was estimated by the Deutsche Gesellschaft Fur Klinische Chemie (DGKC) method using the ERBA Chem 7 semi-autoanalyzer machine.

2.4. Statistical analysis

IBM SPSS Statistics software, version 20, was used for statistical analysis. All data were presented as mean ± standard deviation. To compare the study parameters between cases and controls, an unpaired t-test was used. To determine the relationship between variables, Pearson's correlation coefficient. Regression analysis was done to find independent forecasters for creatine kinase and lactate dehydrogenase in diabetes mellitus cases. P-values less than 0.05 were deemed statistically significant.

3. Results

Creatine kinase and lactate dehydrogenase activity were reduced in type 2 diabetes mellitus cases compared to healthy controls; no significant difference was observed in BMI in both groups as shown in Table 1. The Pearson coefficient was calculated and analysed separately for both groups to determine how the measured parameters correlate with one another, as shown in Table 2. Lactate dehydrogenase and creatine kinase were found to be significantly co-related in diabetes cases, as shown in Figure 1. Table 3 shows the linear regression among dependent and predictor variables in different models. In Model 1 the predictor variables, including HbA1c, BMI, and Serum LDH, account for 20% of the variance in Serum CK. In Model 2, the predictor variables account for 16.3% of the variance in Serum LDH indicating that the models as a whole may not be statistically significant.

4. Discussion

Traditional diabetic complications are widely documented and continue to place a significant burden on millions of people living with diabetes. However, advances in diabetes management and, as a result, increased life expectancy have resulted in the development of evidence indicating the presence of a separate category of diabetes mellitus complications. With vascular disease mortality declining, the primary cause of death in many countries is diabetes mellitus [19]. In our study, the activity of serum lactate dehydrogenase and creatine kinase were estimated in diabetic cases and healthy controls. The mean value of lactate dehydrogenase was (278.63±46.87) in diabetes cases, whereas in controls, the mean value was (316.51±71.21). In diabetes cases, the mean value of creatine kinase was (35.7±16.86), whereas in controls, the mean value was (39.63±22.07). However, no significant difference was found in BMI among diabetic cases and healthy controls.

The study also reported a significant positive correlation between lactate dehydrogenase and creatine kinase among diabetic cases (p-value =.403*) and a negative correlation between lactate dehydrogenase and creatine kinase with HbA1c but was not significant. The results of the study were following previously conducted studies that have reported a significant variation in LDH activity and have also reported that LDH activity is significantly associated with diabetes [20]. This association is explained by the direct measure of diabetes (glucose) and the indirect effect of diabetes (LDH) [21-22]. Several studies considered creatine kinase as a biomarker for the risk factor for cardiovascular issues in people with diabetes. Evliyaolu et al., discovered that blood creatine kinase activity was significantly connected with type 2 diabetes patients' glucose management when compared to healthy controls [23]. Diabetes patients with uncontrolled glucose levels exhibited considerably higher CKMB and CK activity. According to Mohamed et al., blood creatine kinase levels increased in diabetes mellitus patients with type 1 or type 2 diabetes when compared to control groups [17]. This discovery supports a previous study by Arkkila et al., who discovered that T1DM and T2DM patients had higher blood creatine kinase levels [24]. The findings support the hypothesis that both the microvascular and macrovascular problems of diabetes can cause cardiovascular disease, resulting in mortality and morbidity. In addition, we observed a significant decrease in lactate dehydrogenase activity in diabetes patients compared to healthy controls in our study.

Table 1: Comparison of Anthropometric and Biochemical Parameters between Type 2 diabetes mellitus cases and healthy controls.

Anthropometric and Biochemical Profile	Cases (Mean±SD) N=50	Controls (Mean±SD) N=50	p-value (<0.05)
BMI(Kg/m2)	22.96±2.39	22.69±3.87	0 .676
HBA1c (%)	7.74±1.17	4.54±0.82	0.000*
CK(U/L)	35.7±16.86	39.63±22.07	0.320
LDH(U/L)	278.63±46.87	316.51±71.21	0.002*
BMI: Body Mass Index, HBA1c: Glycated haemoglobin, CK: Creatine Kinase, LDH: Lactate Dehydrogenase *p<0.05 is considered statistically significant			

Table 2: Correlation between variables in Type 2 diabetes mellitus Cases

Parameters	CK	LDH	BMI	HbA1C
CK	1	.403*	-.102	-.209
LDH	-	1	-.048	-.081
BMI	-	-	1	.024
HbA1c	-	-	-	1
*p<0.05 is considered statistically significant BMI: Body Mass Index, HBA1c: Glycated haemoglobin, CK: Creatine Kinase, LDH: Lactate Dehydrogenase.				

Table 3: Model Summary of Regression analysis between anthropometric and biochemical parameters in type 2 diabetes mellitus cases

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics				
					R Square Change	F Change	df1	df2	Sig. Change
1.	.448[a]	.200	.123	15.788	.200	2.588	3	31	.071
2.	.403[b]	.163	.082	44.921	.163	2.007	3	31	.133
(Model 1): [a] Dependent Variable: Serum CK Predictors: (Constant), HbA1c, BMI, Serum LDH (Model 2): b Dependent Variable: Serum LDH Predictors: (Constant), HbA1c, BMI, Serum CK *p<0.05 considered statistically significant BMI: Body mass index, HbA1c: Glycated Haemoglobin, CK: Creatine kinase, LDH: Lactate dehydrogenase									

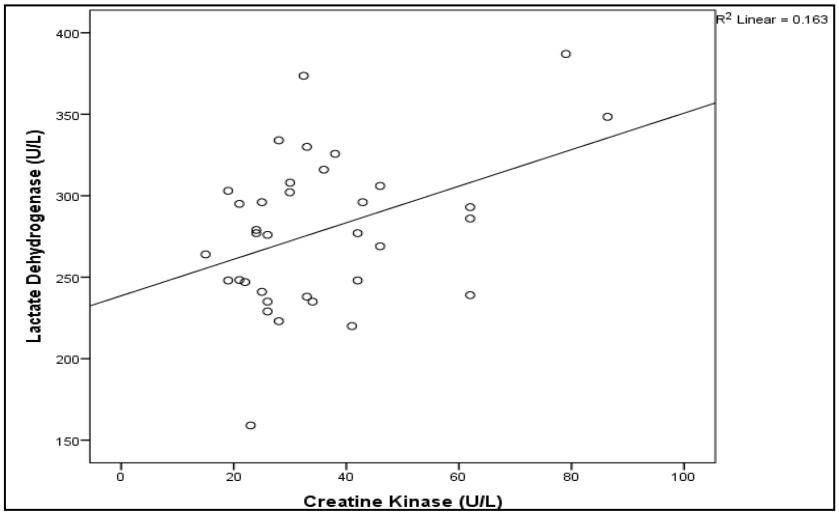

Fig 1: Scatter diagram showing a correlation between Creatine Kinase and Lactate Dehydrogenase among Type 2 diabetes mellitus cases

However, a study conducted by Oliver et al. found no difference in serum LDH levels between diabetics and healthy controls [25]. These findings support Kamble et al.'s findings that moderate diabetes mellitus did not affect LDH, whereas elevated levels of LDH were extremely significant in severe diabetes mellitus patients.

5. Conclusion

Diabetes is a chronic condition that is often associated with inflammatory diseases. Lactate dehydrogenase and creatine kinase activities were shown to be lower in the study. Testing for inflammatory markers such as lactate dehydrogenase (LDH) and creatine kinase (CK) may help monitor the progression of the disease. Moreover, identifying the role of lactate dehydrogenase in diabetes mellitus will provide a theoretical basis for a better understanding of the disease's pathogenesis.

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Conflicts of interest

No conflicts of interest exist.

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