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# CK-MB serum as indicator of silent cardiac damage in type -2 diabetic patients

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**Abstract**
**Background:** Type 2 diabetes mellitus (T2DM) is a common metabolic disorder, leading to cardiovascular disease (CVD), such as ischemic heart disease (IHD). The interaction between T2DM and heart disease is bi-directional and is reflected in mechanisms such as oxidative stress, endothelial dysfunction, and insulin resistance. The objective of this study was to assess the biochemical and cardiac markers among diabetic heart patients in comparison with healthy control group.
**Methodology:** Case-control study was conducted in 140 subjects (70 diabetic patients with hearts disease and 70 normal individuals), aged 41–76 years, the sample collected from Al-Fayhaa Teaching Hospital, Basrah, Iraq. From each participant, the blood samples were obtained and centrifuged to assay for fasting blood glucose (FBS), HbA1c, insulin & CK-MB Automated systems targeted for analytical procedures were Cobas c111, Cobas E411 and Bio-Rad D-10 for standardized enzymatic and immunoassay methods
**Results:** Showed FBS, HbA1c and insulin levels of diabetic subjects significantly higher ($p$<0.001) as compared to non-diabetics suggested poor glycemic control consistent with the results. In addition, the diabetic group had significantly higher cardiac biomarkers CK-MB ($p$<0.001) suggestive of myocardial stretch/damage.
**Conclusions** The study concluded underscores the relevant metabolic and cardiac changes in diabetic patients with CVD, suggesting the timely biomarker-based follow-up in order to avoid CVD complications.

**Keywords:** Diabetes mellitus, Cardiac parameters, CK-MB, Silent cardiac damage

## Introduction
Increased blood glucose levels (i.e. hyperglycemia) characterized by deficiencies in the insulin actions, insulin secretion, or both are a hallmark of the metabolic disease DM, the pancreas's beta cells produce the hormone insulin, which the body needs to use the glucose from digested meals as an energy source (Ubeid *et al*., 2020) [18].
Diabetes mellitus, particularly type 2 diabetes (T2DM), is characterized by chronic hyperglycemia resulting from insulin resistance or impaired insulin secretion. Endothelial dysfunction, chronic inflammation, oxidative stress, and dyslipidaemia are some of the ways that this metabolic disease greatly raises the chance of heart problems (American Diabetes Association, 2021). There is a strong link between diabetes and heart disease. Diabetes speeds up atherosclerosis and raises the risk of myocardial infarction, and heart disease can make glucose metabolism even worse, creating a circle of harm (Camm *et al*., 2022) [7].
Prevalence of DM recent findings suggest that the burden of DM has risen significantly over the past decade and may be considered a growing epidemic (Lovic *et al*., 2020) [10]. According to the 2021 International Diabetes Federation (IDF) report, the prevalence of T2DM in people aged 20 79 years is 537 million (10.5%) and is projected to reach 783 million (12%) by 2045 (Adamu *et al*., 2023) [1].
Heart diseases are a major public health concern worldwide, contributing significantly to morbidity and mortality. According to the World Health Organization (WHO), noncommunicable diseases (NCDs), including cardiovascular diseases (CVDs), account for 27% of all deaths in Iraq, with heart diseases being the leading cause (WHO, 2021).
Creatine kinase (CK) is a dimeric enzyme that catalyzes the reversible phosphorylation of creatine using ATP. In 1966, CK isoenzymes were identified in various tissues, the isoenzymes of CK are dimers of either type B or M polypeptide chains. The BB isoenzyme is

found in the central nervous system, whereas the MM isoenzyme is a principal component in adult skeletal muscles, The myocardium has 15% CK-MB isoenzyme and 85% CK-MM. Skeletal muscles contain about 1% to 3% of CK-MB (Moghadam *et al*., 2016) [13].

Creatine kinase-MB (CK-MB) is a clinically recognised biomarker for detecting myocardial injury. It is mainly present in myocardial tissue; when myocardial cells experience ischemia or necrosis, CK-MB is released into the blood, resulting in an elevated CK-MB index in the serum (Liu *et al*., 2014) [9].

## Methodology

A case-control study was conducted between November 2024 and April 2025, involving a total of 140 participants. The study group comprised 70 individuals with diabetes mellitus (35 males and 35 females) who had clinical history of cardiovascular disease. they were diagnosed by a specialist physician at Al-Fayhaa Teaching Hospital, located in Basrah Governorate, Iraq. The control group consisted of 70 healthy individuals (34 males and 36 females), matched for age and sex. Demographic and clinical data, including age, sex, and relevant clinical information, were obtained from all participants using a standardized questionnaire. Venous blood samples (10 mL) were collected from each participant. Whole blood was used to determine glycated hemoglobin (HbA1c), while serum was separated by centrifugation for the assessment of fasting blood glucose, insulin, and creatine kinase-MB (CK-MB). Biochemical analyses were performed using the Cobas e411 automated immunoassay analyzer (Roche Diagnostics, Germany).

## Statistical Analysis

All data were analyses using the Statistical Package for the Social Sciences (SPSS) version 26. The study employed an independent sample t-test. The outcome was deemed statistically significant based on a p-value of less than or equal to 0.05.

## Results

Socio-demographic characteristics of the studied groups show that a non-significant difference in age distribution (P=0.12) between control and diabetic patients groups. As well as the sex distribution among the study groups which was not significant (p>0.5). For the Residence among the groups no statistical significance was shown (P=0.73) (Table 1).

**Table 1:** Socio-demographic characteristics among the study groups

| Characteristic | | Patients group (n=70) | Control group (n=70) | P. value |
|---|---|---|---|---|
| Age (year) | | 56.66 ± 7.90 | 54.61 ± 7.54 | 0.12 NS* |
| Sex | Male | 35 (50.0%) | 34 (48.6%) | 0.96 NS ** |
| | Female | 35 (50.0%) | 36 (51.4%) | |
| Residence | Urban | 37 (52.9%) | 35 (50.0%) | 0.73 NS ** |
| | Rural | 33 (47.1%) | 35 (50.0%) | |

NS: Non-significant, *t-test, **Chi-square test

The results show a significantly increased ($p$< 0.001) in FBS, HbA1c and fasting insulin values in diabetic group comparing with that in the control group (Table 2).

**Table 2:** Diabetic biomarkers levels between patients and control groups

| Parameters | Patient group (n=70) Mean ±SD | Control group (n=70) Mean ±SD | P. value |
|---|---|---|---|
| FBS (mg/dl) | 258.07 ± 96.11 | 97.13 ± 13.66 | <0.001 |
| HbA1c (%) | 10.26 ± 1.97 | 5.14 ± 0.50 | <0.001 |
| Insulin | 23.36 ± 12.24 | 5.21 ± 1.16 | <0.001 |

As comparison in diabetic parameters levels between males and females in patients' group, The results showed non-significant difference in the levels of FBS, HbA1c and insulin between the two groups (Table 3).

**Table 3:** Diabetic biomarkers levels between males and females in patients group

| Parameters | Male group (n=35) Mean ±SD | Female group (n=35) Mean ±SD | P. value |
|---|---|---|---|
| FBS (mg/dl) | 239.74 ± 85.55 | 276.40 ± 103.62 | 0.11 NS |
| HbA1c (%) | 10.06 ± 2.07 | 10.46 ± 1.87 | 0.39 NS |
| Insulin | 20.83 ± 11.91 | 25.71 ± 12.30 | 0.15 NS |

As comparison in cardiac parameters between the healthy and patients group, The results showed a significant increase in the levels of CK-MB ($p$<0.001) among patients' group (Table 4).

**Table 4:** Cardiac biomarkers levels between patients and control groups

| Parameters | Patient group (n=70) Mean ±SD | Control group (n=70) Mean ±SD | P. value |
|---|---|---|---|
| CK-MB | 3.85 ± 2.78 | 2.08 ± 0.94 | <0.001 |

Also there is a non-significant difference in the levels of CK-MB among males and females in patients group (Table 5).

**Table 5:** Cardiac biomarkers values between males and females in patients group

| Parameters | Male group (n=35) Mean ±SD | Female group (n=35) Mean ±SD | P. value |
|---|---|---|---|
| CK-MB | 4.06 ± 2.88 | 3.66 ± 3.74 | 0.63 NS |

## Discussion

There is evidence that fasting blood glucose, HbA1c and fasting insulin were increased in diabetic patients with heart disease as the present study detected which is accordance with those of Mohamed *et al*. (2022) [14] and Bhowmik *et al*. (2018) [5]. and Artha *et al*. (2019) [3].

These metabolic markers are particularly important as they offer insights into the pathophysiological interrelationship between type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD)—two conditions that frequently co-occur and together amplify the progression of each other.

Elevated fasting glucose and HbA1c are indicators of poor glucose control in diabetic patients, and they are a diagnostic and prognostic measures of cardiovascular risk. Endothelial system damage, oxidant stress and sub-clinical inflammation are the main actors in the atherogenesis, as all are promoted by chronic hyperglycaemia (Maranta *et al*., 2021) [12]. HbA1c, which reflect control state of blood glucose for 2 to 3 months, has also been reported closely associated with arterial stiffness and subclinical

atherosclerosis in those without apparent CVD (Bae *et al*., 2020) [4].

The increase in HbA1c is an independent risk factor of coronary heart disease (Madsen *et al*. 2015) [11]. Conversely, another trial demonstrated that the greater the baseline HbA1c level of patients, the higher their CV death risk was; thus clearly demonstrating that the long-term effects of hyperglycemia are negative for CV outcomes (Zinman *et al*., 2015) [22]. Similarly, Rawshani *et al*. (2018) [16] reported duration of diabetes and HbA1c levels were related to the risk of developing heart failure and cardiovascular death, especially in young individuals.

Plasma fasting insulin was also higher due to harmony with the premises that hyperinsulinemia and insulin resistance are pinpointed, not only in the etiology of diabetes but systemic atherosclerotic mass as well, Reduced peripheral glucose clearance is involved in the compensatory increase in insulin secretion. Elevated levels of insulin in the long term also cause hypertension, dyslipidaemia, endothelial dysregulation and increased sympathetic outflow, risk factors in the pathology of CVD (Rochlani *et al*., 2017; Borné *et al*., 2017) [17, 6].

In contrast, healthy individuals maintain normal glucose and insulin homeostasis through intact β-cell function and insulin sensitivity. Their lower HbA1c and fasting insulin levels reflect efficient glucose metabolism and the absence of chronic metabolic stress and inflammation. These physiological differences highlight the profound impact of disrupted glucose-insulin dynamics in patients with coexisting diabetes and CVD.

In the present study, diabetic patients with heart disease demonstrated significantly elevated levels of creatine kinase-MB compared to healthy controls. These results agree with Montaser *et al*. (2016) [15] who showed that CK-MB median in the MI group were significantly higher 6.5 ng/L than the respective concentrations in the control group 1.4 ng/L ($p< 0.001$).

A modern study by Wu *et al*. (2020) [20] confirms that stable CHD patients with a higher serum CK-MB level (≥4.730 ng/mL) have a higher risk of all-cause mortality.

These findings reflect the cardiac stress and subclinical myocardial injury commonly present in diabetic individuals with coexisting cardiovascular disease (CVD), despite the absence of acute myocardial infarction.

CK-MB is a well-established biomarker of myocardial cell injury, traditionally used to diagnose myocardial infarction (MI) (Khalid *et al*., 2022) [8].

This observation also provides support for a concept in diabetic patients with Coronary Heart Disease that is characterized by chronic myocardial stress hemodynamically and not "Overt Myocardial Infarction" as such, Sensitive Cardiac Biomarkers such as this need to be used for early risk stratification which is consistent with Xie *et al*. (2019) [21] study.

## Conclusion

The findings emphasize the utility of CK-MB as a potential early biomarker for subclinical myocardial injury in T2DM, advocating for its incorporation in routine screening protocols for diabetic patients. Early detection of cardiac involvement through biochemical markers can facilitate timely interventions, potentially reducing the burden of cardiovascular disease in this high-risk population. These results support the need for comprehensive metabolic and cardiac monitoring in diabetic care, even in the absence of clinical signs of heart disease.

## Conflict of Interest

Not available

## Financial Support

Not available

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