

Study of Total Creatine Kinase Creatine Kinase-MB and CK-MB Relative Index and Correlation with Some Modifiable Factors in Cardiovascular Diseases in Thi Qar Province

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Abstract: The current study follows the role of some adjustable factors, and this includes High percentage of Glycated hemoglobin (HbA1C), Hypertension, obesity(BMI), vitamin D levels and the competitive with total CK and CK-MB in progression and worsening with cardio-vascular disease (CVD). It was aimed to determine levels total CK, CK-MB and verifying their relationship with some modifiable risk factors and follow-up of condition myocardial throughout the measurements of CK-MB relative index in CVD patients. The study included 60 subject divided into two groups, 30 healthy individuals as a control group, 30 patients with cardiovascular disease(CVD) which were previously diagnosed. Samples were collected from patients at Heart Center and Private Clinics in Thi-Qar City, during June 2024 to November 2024. Blood samples were collected from patients and healthy after fasting for at least 8 hours. Vitamin D, glycated hemoglobin (HbA1c), the total CK- enzyme and the enzyme isoenzyme CK-MB were determined using ELISA.

Keywords— CK, CK-MB, vitamin D, HbA1c, obesity

I. INTRODUCTION

Cardiovascular diseases are responsible for a high number of deaths world-wide, year 2022, which amounted to approx. 19.8 M people of all ages died from cardiovascular diseases, cause 32% of all deaths globally. 85% most deaths were caused by heart attacks and strokes. Cardiovascular diseases are responsible for highest mortality rate in low-, middle-income areas [1]. The heart is a muscular organ that pumps blood to all tissues of the body through the circulatory system muscle can be affected by several diseases known as cardiovascular diseases, among them Coronary artery. Ischemic heart disease, it is also called coronary artery disease (ischemic heart), it is one of the most common heart diseases. This disease refers to heart disorders due to narrowing of the coronary arteries that supply the heart muscle. blood, Heart attack, other conditions, Arrhythmia, Aortic disease Cardiomyopathy, Heart failure, heart valve disease, pericarditis, rheumatic heart disease, blood vessel problems, Peripheral vascular disease, congenital heart disease, and cerebrovascular disease [2-4]. Cardiomyopathy is characterized by left ventricular dysfunction, usually affects individuals in their thirties or forties and it is a significant cause of heart failure [5]. There are several factors known as cardiovascular risk factors. The presence of these factors increases a person's likelihood from contracting

disease-or its complications. Unchangeable risk indicators such as age, sex, menopause in women, history of family, and LDL cholesterol, factors such as smoke, hypertension, HbA1c, elevated LD.L and cholesterol, and lack physical activity [6]. Creatine kinase (CK) is an essential enzyme for cellular energy transport. It regenerates adenosine triphosphate (ATP) via the phospho creatine transporter and supports ATP-dependent processes essential for cardiovascular function (such as vascular smooth muscle contraction and ion transport). Clinical studies indicated correlations between total CK levels and the circulating CK-MB enzyme isoform and their relationship to cardiomyopathy and modifiable chloride factors like B.P, HbA1c, B.M.I, and vitamin D levels. These levels vary depending on sex and body characteristics, likely reflecting differences in skeletal muscle mass [7-8]. Creatine kinase (CK) is a binary molecule composed. The Ck_MM, Ck_MB, and Ck_BB homologs are created by combination of these two sub-units. Creatine kinase-MB is a key cardiac biomarker used in the diagnosis and prediction of myocardial damage and the course of acute myocardial infarction [9]. sub-units M and B. Vitamin -D is a steroidal compound that is fat-soluble, and it is obtained from food, dietary supplements, and also from exposure to sunlight.(10) Vit-D is important to Ca-metabolism, essential for Bone Marrow and muscle health. It plays a key role in reducing insulin resistance, mitigating oxidative stress, and decreasing the risk of metabolic syndrome [11]. Vitamin D plays a crucial role in many body systems, including the immune system, the cardiovascular system, and hypertension [12], and in bone diseases and disorders such as rickets in children [13-14]. The relationship between vitamin D and cardiovascular disease remains unclear. When interpreting studies related to hypertension, cardiovascular disease prevention, and their relationship to vitamin D, some research findings suggested its importance in reducing the risk of developing a variety. The results of the study by Giovannucci et al. [15] showed that the risk of myocardial infarction is approximately two and a half times higher in patients with vitamin D deficiency. In the study by Acharya et al. it was concluded that patients who were not deficient in vitamin D and no history of myocardial infarction or atrial fibrillation, and treated with concentrations higher than 20 ng/ml and 30 ng/ml of (25-OH)D, the results showed a significant reduction in the risk of death and the risk of developing atrial fibrillation [16-18].



The results of Mirhossein, Raynsbury, and Kim-ball [19] demonstrated that taking vitamin D supplements have a clear with-link a reduction in B.P. Mirhosseini, Fatnparast, and Kim-ball [20]. Showed low Vit.D3 levels are associated with both SBP and DBP. Mortality rates from cardiovascular diseases are attributed to Pre-existing Daily (behavioral) risk factors include an unhealthy diet, lack of physical activity, and alcohol consumption, cigarette, e-cigarette, and hookah use. Biological risk factors include obesity, high blood pressure, all types of diabetes, and dyslipidemia [21]. This study aims to follow up on myocardial damage in a sample of cardiovascular patients by Determining levels of total -CK and CK-MB, calculating CK-mass (CK-MB relative index) and its relationship to some variable factors risk factors in CVD patients like tobacco smoking and Hypertension, HbA1c, vitamin D levels. Furthermore, it aims to determine the prevalence of these factors in Rural-City (areas of residents in Thi-Qar province, southern Iraq).

II. METHODS AND MATERIALS

A. Study Design:

Our study was conducted in Nasiriya Heart Center and several private clinics. It included 60 samples 30 as a control group and 30 patients previously diagnosed by cardiologists with cardiovascular disease (CVD), ranging in age from 37 to 65 years. Serum total C K, CK_MB vitamin D, glycated hemoglobin (HbA1c) levels were determined using ELISA spectrophotometry.

B. Study Setting and Duration:

Thi Qar Province Iraq, from beginning June to November 2024.

C. Inclusion Criteria:

Pre-diagnosed cardiovascular disease patients, sample size(N) was 30 due to large of exclusion number of patients, study achieve resulting more impactful statistical, greater sample homogeneity and stronger statistical

D. Exclusion Criteria:

Cardiovascular patients with thyroid disorders, pregnant women, or cardiovascular patients undergoing surgical or catheterization interventions, cardiovascular patients with more than 120 minutes of exercise per week, cardiovascular patients with Rosuvastatin drug

E. Sample Collection:

Blood samples were drawn from all participants after an 8-hour overnight fast, 5ml of blood were collected in the morning using sterile, single-use syringes. The collected samples were placed in sterile, specially designed plastic tubes, then were separated by the centrifuge was used at a speed of 3000 rpm for 10 minutes, and stored at a temperature of -20 degrees Celsius.

F. Questionnaire:

The prepared questionnaire included several questions for participants Comprehensive social history of cardiovascular disease, medical history cigarette Smoking, physical activity (more than 120 min. of exercise in week), Age Sex family history of the disease, treatments type duration of illness, height, weight, residence (rural or urban)

G. Statistical analysis:

SPSS-23 software was used to analyze results (Means \pm S. D), chi-squared (X^2) test, t-test, statistical significance values P-value ($P \leq 0.05$) P-value ($P \leq 0.001$).

III. RESULTS AND DISCUSSION:

A. Clinical Characteristic Features of the Studied Groups:

This study included Sixty total subjects; 30 individuals were cardiovascular disease group compared with 30 Healthy as control. Average age of subjects 50.77 year, mean age healthy individuals 45.08 year,. Body mass index (BMI) is calculated by dividing weight in kilograms by the square of height in meters (Table 1)

TABLE 1. Descriptive data for all studied groups

Groups	No.	Sex (M//F)	Age (year) Mean \pm S.D	BMI (kg / m ²) Mean \pm S.D
CVD	30	17/13	50.77 \pm 10.33	21.59 \pm 5.21
Control	30	16/14	45.80 \pm 9.89	23.43 \pm 3.71
P-value			0.062 ^{Non. sig}	0.120 ^{Non. sig}

* P-value ≤ 0.05 consider sign. * Average difference is a significant at p-value 0.05

CVD: cardiovascular disease BMI: Body Mass Index, M: male, F:Female

The results of current study are consistent with those of Arif et al. (2024). The incidence of cardiovascular disease increases with increasing body mass index (BMI), particularly with age, as the inner lining of the artery walls widens. Most participants were overweight or obese [22]. These results are also consistent with previous studies conducted in Iraq (66.9%), Kuwait [23], and Iran [24]. Table 2 shows the frequency of several cardiovascular risk factors among the study participants, categorized by sex. Men with CVD constituted 56.7%, while women with CVD constituted 43.3% a statistically significant difference at $p \leq 0.05$

TABLE 2. Distribution of subjects according to Sex

Groups	No.	Sex					
		Male		Female		Total	
		No.	%	No.	%	No.	%
CVD	30	17	56.7%	13	43.3%	30	100%
Control	30	16	52.6%	14	47.4%	30	100%
Total	33	33	55%	27	45%	60	100%

X square = 0.157, d.f = 1, p_value = 0.692

Cardiovascular (CVD) affects both sexes and a leading cause of death. To reduce the impact of these diseases on society, risk assessment and management are essential. Multiple Global Systems for assessing and identifying anticipated time ahead risks cardiovascular disease precisely population groups. These systems consider both modifiable and non-modifiable risk factors like Age, Body Mass Index, Sex, Race, History of hypertension, diabetes and medication use [25-26].

B. The effect of risk factors

1) Smoking:

The results indicated that at p-value of 0.005 there a statistically significant difference. In CVD patient compared with control. Overall, 33% of the participants were smokers. The results showed no statistically significant relationship between the groups regarding smoking status, as the chi-squared value (X^2) was 0.415 (with one degree of freedom), not statistically significant (p-value = 0.519) (Table 3).

TABLE 3. Distribution of subjects according to Smoking

Groups	No.	Smoking					
		yes		No		Total	
		No	%	No.	%	No.	%
CVD	30	10	33.3%	20	66.7%	30	100%
Control	30	8	26.6%	22	73.4%	30	100%
Total		18	30%	42	70%	60	100%

$X^2=0.415$, $df=1$, $p\text{-value}=0.51$

2) Housing:

The chi-square test found that no statistically significant change in housing distribution in patient CVD compared with healthy ($X^2 = 0.000$, $d.f = 1$, $p\text{-value} = 1.000$). This means the results did not show a statistically significant relationship between housing and patient status (p value < 0.05) (Table 4)

Table 4. Tabulation of subjects according to Housing

Groups	No.	Housing					
		Urban		Rural		Total	
		No	%	No	%	No	%
CVD	30	20	66.7%	10	33.3%	30	100%
Cont.	30	20	66.7%	10	33.3%	30	100%
Total		40	66.7%	20	33.3%	60	100%

$X\text{-square} = 0.000$, $d.f=1$, $p\text{ value} = 1.000$

3) Systolic and Diastolic Blood Pressure

Hypertension or known High B.P poses a significant risk to individuals with cardiovascular disease. Statistical analysis revealed a significant increase at $p < 0.001$.in systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels (mmHg) in patients, reaching 136.60 and 84.13 mmHg, respectively, compared to the control group.

TABLE 5. Systolic and diastolic blood pressure status in cardiovascular disease Patients with control groups

Groups	No.	S.B.P (m mHg) Mean \pm S.D	D.B.P (m mHg) Mean \pm S.D
CVD	30	136.60 \pm 11.82	84.13 \pm 7.21
Control.	30	123.41 \pm 5.51	78.50 \pm 4.59
P.Value		< 0.001**	0.001**

4) Glycated hemoglobin (HbA1c%)

Elevated blood glucose levels, measured by the percentage of glycated hemoglobin (HbA1c), constitute a risk factor in patients with CVD. The study found a statistically significant increase in HbA1c levels (p-value < 0.003), as shown in Table 6.

TABLE 6. Glycated hemoglobin (HbA1c%) levels in cardiovascular patients with control groups

Groups	No.	HbA1c % Mean \pm SD
CVD	30	6.32 \pm 1.64
Control	30	5.28 \pm 0.88
P-value		< 0.003**

The study identified five easily assessable risk factors—high blood pressure, smoking, diabetes, BMI, and vitamin D levels. This represents more than ninety percent of the expected danger of developing heart disease in the future. Mainly, while the magnitude of CVD risk was similar between the sexes, the impact of modifying these danger factors is much clearer in patients. Numerous studies have shown that way of life changes and essential prohibition can lessen the incidence of cardiovascular disease and associated mortality in males and females.[27,28].

5) Vitamin -D

Results of statistical analysis (ANOVA) recorded a clear and significant difference in vitamin D levels between patients and healthy individuals ($P < 0.001$), with the average being significantly lower in CVD group compared to Cont. group (Table 7).

TABLE 7. Vitamin -D levels in cardiovascular patients with control groups

GROUPS	No.	D VIT. (NG/ML) MEAN \pm SD
CVD	30	13.30 \pm 4.61
CONT.	30	30.82 \pm 7.89
P. VALUE		< 0.001**

The current results record a strong association between vitamin D deficiency in serum and cardiovascular disease. It was found that there is a significant association between insufficient vitamin D in the blood and cardiovascular disease. Several studies mentioned that vitamin D is required for optimal health; its primary source—synthesis through skin exposure to sunlight— may not be enough to achieve ideal concentrations. Therefore vit D. is often prescribed as a dietary supplement. It is concerning that more than 20% of middle-aged and older adults have vitamin D [29] and dark-skinned individuals [30]. Data from the NHANES study showed that 75% of study participants who were vitamin D deficient suffered from heart disorders and diseases [31].

C. The effect of Creatine kinase Activity

1) Measurement of Total CK

Records of statistical analysis showed a high statistically significant relationship in Total CK levels between patients and healthy individuals ($P < 0.001$), with the average being significantly lower in CVD group compared to Cont. group (Table 8).

TABLE 8. Total CK levels in cardiovascular patients with control groups

Groups	No.	Total CK (U/L) Mean± SD
CVD	30	382.64 ± 150.87
Cont.	30	138.24 ± 52.91
P-value		< 0.001**

2) Measurement of CK-MB

The results noted a significant increase in CK-MB enzyme activity ($P < 0.01$) in cardiovascular patients by compared healthy group (Table 9 and Table 10).

TABLE 9. K-MB levels in cardiovascular patients with control groups

Groups	No.	CK-MB (ng/mL) Mean± SD
CVD	30	25.06 ± 10.40
Cont.	30	2.86 ± 1.39
P-value		< 0.001**

3) Measurement of CK-MB Relative Index

TABLE 10. CK-MB relative index Ratio in cardiovascular patients with control groups

Groups	No.	CK-MB Mass Mean± SD
CVD	30	7.36 ± 3.84
Cont.	30	2.37 ± 0.98
P-value		< 0.001**

- CK-mass for man with CVD 9.191765% : CK-mass for female with CVD 5.539231%
- CK-MB -Relative Index = CK-MB (n g/m L) × 100/C K (U / L)

Relative Index: A ratio of more than 5% strongly suggests a heart attack, while less than 5%. Studies indicated that elevated CK-MB enzyme levels are associated with patients in acute myocardial infarction and heart failure; the mortality rate was found to be significantly high in various other heart conditions. Elevated CK levels may also indicate skeletal muscle injury. Furthermore, persistently elevated CK-MB levels have been observed in patients undergoing percutaneous coronary intervention. This was related to an increased mortality rate at periods of 3, 6, and 1 year [32]. The study showed a statistical significance. At a P-value < 0.01, elevated isoenzyme CK-MB levels were observed in the cardiac patients included in the study compared to the control group. This finding is consistent with previous studies (Yang et al., 2020) [33], Insiardi et al. 2020 [34] and

Abu-Ghadir at.al. 2020) [35]. Since the chemical compounds secreted by the myocardium are first released into the cardiac blood and pericardial fluid, CK-MB enzyme levels in cardiac serum are higher than those in peripheral blood [36]. The muscle enzyme CK, or CPK, located in the cytoplasm of cardiomyocytes and largely secreted into the bloodstream from damaged myocardium, is the initial vital sign to show elevated levels, for the reason that it is more eclectic for myocardium, Recently,CK-MB has become the accepted biomarker instead of the total CK enzyme. Elevated total CK activity in serum without overt cell death in cardiomyocytes that appear to survive with limited ischemia [36].

4) Correlation Between Total CK,CK-MB and Studies risk factors

The current study recorded a statistically weak (+) correlation in glycated hemoglobin (HbA1c) with total-CK ($r = 0.16$). Also, a weak correlation was found between the duration of hyperglycemia and CK-MB levels (r -correlation = 0.13), Total creatine kinase and creatine kinase-MB are highly sensitive and qualitative vital signs for heart muscle damage and critical biomarkers for the diagnosis of myocardial infarction [37]. Moreover, current results are consistent with the findings of Odum and Young (2018). Researchers have reported noting many heart indicators were significantly elevated in diabetes mellitus patients compared to non-diabetic individuals and have observed chronically diabetic patients have elevated levels of T-CK enzyme, CK-MB, and myoglobin [38]. The current study demonstrates a moderate negative correlation between BMI and T-CK levels (r -correlation = -0.20) and a moderate negative correlation between BMI and CK-MB conc. (r -correlation = 0.34). This finding is consistent with those of Alberti et al. (2009), who demonstrated obesity is linked to an elevated danger of acute myocardial damage and heart failure [39]. Also, results of this study show a moderate positive- correlation between systolic and diastolic blood pressure and total -CK levels (r -correlation = 0.39, r -correlation = 0.27, r -correlation = 0.89, respectively), and CK-MB levels (r -correlation = 0.15 and r -correlation = 0.16), respectively in figures 1 and 2.

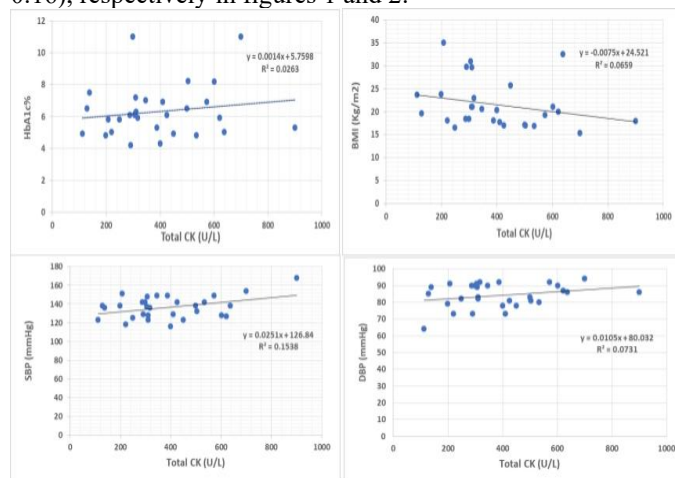


Fig. 1: Correlation between total CK With HbA1c, BMI,SBP and DBP in patient groups.

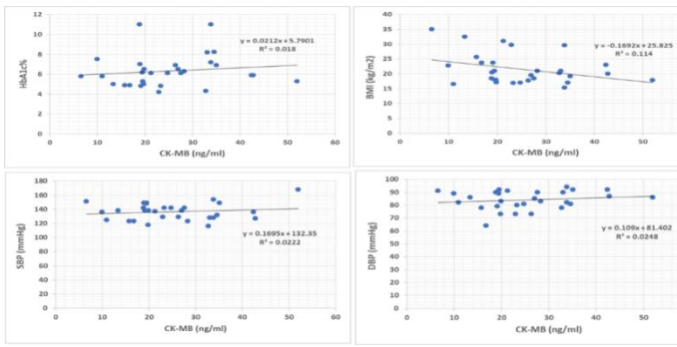


Fig. 2: Correlation between CK-MB With HbA1c, BMI, SBP and DBP in patient groups.

5) Correlation Vitamin- D and Risk Factors in Studies

The Results showed a moderate negative correlation between glycated hemoglobin (HbA1c) and vitamin D levels ($r = -0.24$). A strong, statistically significant (+) correlation was also recorded between vitamin D levels and BMI ($r = 0.76$). The results also indicated a weak positive correlation between vitamin D concentration and systolic P.B. ($r = 0.22$), and a very weak correlation with diastolic blood pressure ($r = 0.032$). Figure 3

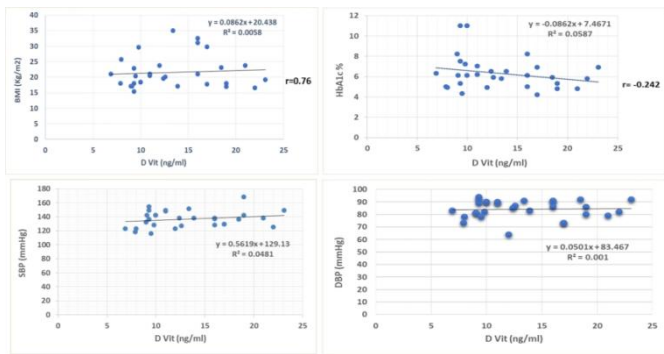


Fig. 3: Correlation between D-Vit. With HbA1c, BMI, SBP and DBP in patient groups.

Studies, such as Hung et al. 2023, indicated optimal levels of vitamin D in the body. Vitamin D is a biocompound important for heart muscle health and blood vessel elasticity. The study also indicated that vitamin D deficiency is strongly associated with an increased risk of CVD, including stroke, heart muscle disease, heart attack, and heart failure. Excessive vitamin D in the body was not linked with an increased danger of CVD [40].

IV. CONCLUSIONS

The present study concluded that there is a powerful correlation between risk factors under investigation and the development of cardiovascular diseases, particularly myocardial damage in the investigated patients. This correlation was demonstrated by elevated total and isoenzyme activity, as well as the calculation of the relationship index between total and cardiac creatine kinase. The increased enzyme activity is attributed to myocardial and vascular damage resulting from hypertension, elevated HbA1c levels, and low vitamin D levels.

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CONFLICT OF INTEREST

Authors declare that they have no conflict of interest.

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