How to Cite:
Singh, N., Aggarwal, J., Batra, J., & Srivastava, N. (2022). Biochemical cardiac markers: An index in the assessment/diagnosis of cardiovascular changes in type-2 diabetic patients. *International Journal of Health Sciences*, *6*(S2), 12979–12988. https://doi.org/10.53730/ijhs.v6nS2.8421

Biochemical cardiac markers: An index in the assessment/diagnosis of cardiovascular changes in type-2 diabetic patients

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***Abstract*---**Aim: The aim of this study is to estimate the changes in cardiac markers in type 2 diabetic patients with and without cardiovascular changes. Methods: In this cross -sectional study, 240 patients with diabetes mellitus type 2 were recruited. The biochemical marker of each patient is compared . Blood samples were gathered and processed for the estimation of CK-MB, LDH, trop-t ,uric acid, microalbuminuria and HbA1c. Results: Diabetic individuals had high levels CK-MB, LDH, trop-t and uric acid as compared with and without (CVS)cardiovascular changes in diabetic patients.. Study suggested that cardiac marker levels were significantly increased in hypertensive patients who's suffering from diabetes mellitus. Conclusion: There is a need for periodic assessment of the cardiac function and biochemical markers in diabetic patients so that patients can take early preventative measures. Early assessment of the cardiac function and biochemical markers provides early warning signals for patients to take additional precautions.

***Keywords*---**creatine kinase, lactate dehydrogenase, glycated hemoglobin.

Introduction

The diabetes epidemic has become one of the greatest health emergencies of this century, ranking among the top 10 leading causes of death along with cardiovascular disease (CVD), respiratory diseases, and cancer[1,2]. The World Health Organization (WHO) reports that noncommunicable diseases (NCDs) accounted for 74% of deaths globally in 2019, with diabetes contributing 1.6 million of them. Approximately 592 million people will die from diabetes by 2035. Uncontrolled diabetes leads to an increased risk of vascular disease; a large portion of diabetes[3] burden results from macrovascular (cardiovascular (CV), cerebrovascular, and peripheral artery disease) and microvascular (diabetic retinopathy, nephropathy, and neuropathy) complications[4]. According to a 2010 study, high blood pressure (BP) is the third most important risk factor for the attributable burden of disease in south Asia.[5] In India, hypertension has a significant impact on cardiovascular health and healthcare systems [6, 7]. 57% of all stroke deaths and 24% of coronary heart disease (CHD) deaths in India are directly caused by hypertension [8]. WHO considers HTN one of the major causes of premature death worldwide [9]. Global and Regional Burden of Disease and Risk Factors study (2001), which conducted a systematic analysis of population health data for attributable deaths and disease burden, has placed HTN in South Asia second only to child underweight for age [10]. An analysis of worldwide data for the global burden of HTN reports that 20.6% of Indian men and 20.9% of Indian women were suffering from HTN in 2005 [11]. The major cause of morbidity and mortality among diabetics is cardiovascular disease, accounting for 75% of hospitalizations and 70% to 80% of deaths[12,13] In fact, coronary heart disease (CHD) is the leading cause of death among diabetics, who have a 2 to 4-fold higher risk of death from CHD and incidence of nonfatal CHD events compared with those without diabetes.[14] The two diseases are interrelated, resulting in a predisposition to atherosclerotic cardio disease[15]. Diabetes mellitus is about twice as common as hypertension in individuals with diabetes.[16] As populations age, hypertension and noninsulin dependent diabetes mellitus incidence also increase with age . Indeed, it is estimated that 35-75% of diabetic cardiovascular and renal complications are related to hypertension. [15,16]

T2DM patients have decreased survival rates and quality of life due to conventional CV risk factors, and it has been suggested that cardiac biomarkers revealing pathophysiological stages of cardiac remodeling may affect those outcomes, Among the following factors, biomechanical stress, inflammation, necrosis/apoptosis, fibrosis, hypertrophy, and extracellular matrix remodeling have an incremental value for prediction of clinical outcomes (death, MACEs, hospital admissions, HF onset) in the patient population. Moreover, cardiac biomarkers, such as c-reactive protein, can provide new individual information that can have a great impact on predicting CV risk beyond conventional factors. However, each biomarker has its strengths and weaknesses, and each will affect cost, specificity, sensitivity, predictive value, as well as superiority in a face-to-face comparison.[17] Hyperglycemia, when prolonged, causes vascular damage [18] Chronic hyperglycemia is associated with cardiovascular complications, but this relationship is not well understood [19] HbA1c, a measure of blood glucose levels over the previous two to three months, is used in clinical practice as a

biomarker of diabetes management[20]. Hyperglycemia appears to be a risk factor for cardiovascular disease (CVD), sudden death [21], myocardial infarction [22] and death in critically ill patients [23]. Patients with various kinds of CVD symptoms, such as chest pain and acute coronary syndrome, are typically evaluated in terms of cardiac markers [24]. Troponins, found in skeletal and cardiac muscle, are regulatory proteins that have been identified as three types; Troponin 1 (Tn1), Troponin T (TnT) and Troponin C (TnC) [25]. TN1 and TNT exist in distinct skeletal and cardiac subforms, therefore these were used for this study because immunoassays are able to differentiate between them [26] [27].

Creatine Kinase (CK-MB) used to be the biomarker of choice for the diagnosis of acute MI before cardiac troponins became available. There are two different forms of the CK-MB enzyme: CK-MB1 and CK-MB2. The Laboratory determination of the CK-MB is a simple addendum of 1 and 2. [28] A heme protein found in skeletal and cardiac muscle named myoglobin (Myo) has been used for the diagnosis of early MI, though it is not very cardio specific [29]. This enzyme is involved in energy production and is found in almost all body cells, but its highest levels are found in the cells of the heart. Although LDH has isoforms, it is not cardio-specific, but laboratory measurements have been found to be useful in diagnosing heart disorders. [30] A biomarker with these characteristics (accuracy, precision, high sensitivity and specificity) could be used objectively to measure biological processes, pathogenic processes, or even pharmacologic responses to a therapeutic intervention in type 2 diabetic subjects. Studies [31] [32] on the associated risk factors will help to reduce the risk of developing coronary heart disease among diabetics.

Material and Method

Aim

Monitoring the effect on biochemical cardiac marker activity in diabetic patient .

Objective

The objective of study is to evaluate the diagnostic performance of cardiac markers in the diabetic subjects and the goals of screening are to improve life expectancy and quality of life by preventing hypertension and heart failure through the early detection of significant CVD.

Study Area

The study was conducted on patients suffering from diabetes mellitus type -2 patients attending the Santosh Medical College, Ghaziabad ,U.P

Study population

A total of 240 Diabetes patients were recruited for this study. This comprised of 66 females and 174 males diabetic patients. Inclusion criteria were identified type 2 DM patients that presented with or without symptoms of hypertension.

Sample Collection

The study involved standard medical history questionnaires, body mass index measurements, and physical examinations in which physician investigators measured blood pressure with a mercury column sphygmomanometer and cuffs that were appropriate in size. Biomarkers were measured on baseline of blood sample collected 5 ml of venous blood.which was collected by using a disposal syringe under aspetic condition in a plain vial, EDTA vial.

Statistical Analysis

The data are expressed as mean ± standard deviation. The results obtained from this were subjected to statistical analysis carried out by using Statistical Package for Social Sciences(SPSS) version 22.

Results

The levels of FBS ,HbA1C,CK-MB, LDH and TROP-T were observed that in clinical factors systolic BP (P=0.001); FBS (P=0.004); CK-MB (P=0.001); TROP-T (P=0.001)and LDH (P=0.013) were statistically significant when compared between normotensive and hypertensive diabetic patients .The result of the study, using the tools of the cardiac markers of creatine kinase trop –t and lactate dehydrogenase in the diagnosis of type 2 DM subjects with and without hypertension is increased as the duration of diabetes increases. This is as presented in the tables.

Table 1: Descriptive statistics of demographic variable in diabetes patients with and without hypertension

S. No.	Variables		Diabetes without hypertension (n=120)	Diabetes with hypertension (n=120)
1	Gender	Female	39 (32.5%)	27 (22.5%)
		Male	81 (67.5%)	93 (77.5%)
2	Age (mean ± SD)		43.34 ± 6.357	42.16 ± 7.515
3	Duration of Diabetes (Years) (mean ± SD)		4.56 ± 1.860	6.98 ± 1.016
4	Duration of Hypertension (Years) (mean ± SD)		NA	2.48 ± 1.012

Table 2: Descriptive statistics of physiological and biochemical activity in diabetes patients with and without hypertension

S. No.	Variables	Diabetes without hypertension (mean ± SD)	Diabetes with hypertension (mean ± SD)	P-value*
1	SBP	131.09 ± 9.695	171.69 ± 24.874	0.001
2	DBP	82.53 ± 5.248	95.46 ± 6.120	0.001
3	FBS	160.297 ± 56.314	182.693 ± 61.919	0.004

4	HbA1C (%)	7.994 ± 2.272	7.808 ± 1.866	0.489
5	CK-MB (U/L)	22.783 ± 3.389	76.779 ± 87.843	0.001
6	TROP-T	0.008 ± 0.003	0.407 ± 0.799	0.001
7	LDH	210.126 ± 41.196	700.285 ± 728.014	0.001
8	MICRO ALBUMINURIA	84.194 ± 125.492	147.818 ± 71.661	0.001
9	URIC ACID	5.813 ± 1.135	7.741 ± 2.699	0.001

*Independent t test used for two group comparison

Table 3: Correlation between physiological and biochemical activity variable diabetes patients without hypertension

Variable	By Variable	Correlation Coefficient (r)	P-value*
Age	Duration of diabetes	0.822	0.001
Age	CK-MB (U/L)	0.515	0.001
Age	TROP-T	0.190	0.037
Age	LDH	0.390	0.001
Age	MICRO ALBUMINURIA	0.299	0.001
Age	URIC ACID	0.522	0.001
FBS	HbA1C (%)	0.447	0.001
CK-MB (U/L)	TROP-T	0.180	0.049
CK-MB (U/L)	LDH	0.376	0.001
CK-MB (U/L)	MICRO ALBUMINURIA	0.213	0.020
CK-MB (U/L)	URIC ACID	0.409	0.001
LDH	URIC ACID	0.234	0.010

*Pearson correlation coefficient used

Table 4: Correlation between physiological and biochemical activity variable diabetes patients with hypertension

Variable	By Variable	Correlation Coefficient (r)	P-value*
Age	SBP	0.186	0.042
SBP	DBP	0.306	0.001
DBP	FBS	-0.190	0.037
HbA1C (%)	URIC ACID	-0.218	0.017
CK-MB (U/L)	TROP-T	0.457	0.001

*Pearson correlation coefficient used

In table-2 ,the descriptive statistics of status in both diabetic with and without hypertension were studied in table . In which there is a statistical significance comparison between diabetes with and without hypertension in CK-MB (p=0.001),trop-t(p=0.001),LDH(p=0.001).

In Table 3 the Correlation between physiological and biochemical activity variable diabetes patients without hypertension were studied an statistical significance between age and duration of diabeties, CK-MB, TROP-T ,LDH , Microalbuminuria , uric acid is ($p< 0.05$). there is statistical significance between FBS and HbA1c is ($p<0.05$).there is statistical significance between CK-MB and TROP-t, LDH, uric acid. In Table 4: Correlation between physiological and biochemical activity variable diabetes patients with hypertension were studied in which there is statistical significance in CK-MB($p=0.04$),TROP-t.($p=0.001$)

Discussion

As stated in our study, men are more likely to suffer from hypertension than women, and men with diabetes have a higher risk of developing cardiovascular disease than women, but in previous studies, Huxley and his co-researchers found opposite results. Huxley R et al conclude that women with diabetes are at higher risk of suffering from hypertension and coronary diseases as well as having a higher risk of dying from these diseases than men.[33] Recently, it was found that men have a greater prevalence of diabetics and heart disease than women. For instance, one study found that only 35% of women with a heart condition or diabetes were prescribed a statin, compared to 45% of men with similar health history[34].

Compared with patients without hypertension, the LDH level was significantly higher in my study. Even though a number of studies have been conducted on LDH and diabetes mellitus, the results have generally been contradictory. Our findings are in contrast with those of Oliver et al [35], Tanaka et al [39], and Margiavichene et al [42], who did not observe any differences in LDH between diabetes and controls. Several studies have found that LDH levels are higher in patients with diabetes than those in normal subjects, including Melinkeri et al [36], Awaji et al [37], Nikolaeva et al [38], Jones et al [40], Cheshchevik [43], Zappacosta et al [44] and Goldberg et al (20). Consequently, these studies support our results.

On the other hand, Cai [38]and Ryder et al. [41] observed decreases in LDH levels in diabetic subjects. These results conflict with our own and with observations from other studies. Additionally, Fernandez et al. [45] determined that GOT levels were not altered in subjects with diabetes compared to normal controls. Tanaka et al [39], Jones et al [40], Piyachaturawat et al [46], Nanbara et al [47], Rao et al [48], Henderson et al [49], Goldberg et al [50] and Awadallah and El-Dessoukey [51] also found that GOT levels are higher in diabetes mellitus than those seen in healthy people. Our results showed that both male cases and female cases had significantly higher serum uric acid levels than their respective controls. Similarly, Emokpae and Abdu observed elevated serum uric acids in males (9.1 ±1.2) and females (8.1±1.4) . Elevated uric acid is thought to be related to hypertension and beneficial to the body, due to its antioxidant properties. Recent epidemiological studies have concluded that uric acid is a major and independent risk factor for development of cardio-vascular disorders, and also plays a significant role in the development of hypertension and renal disease[52]. The present study has shown that biochemical cardiovascular markers such as the CK-MB and LDH have a significant relationship with type 2 diabetes and

hypertension progression. Thomas r et al analyzed 57 articles involving 4,549,481 patients with T2DM. In 4,549,481 cases with type 2 diabetes, 52.0% of the individuals were male, 47.0% obese, and aged 63.6 ± 6.9 years with a T2DM duration of 10.4± 3.7 years. In terms of articles, 46.4% were produced in Europe, followed by 21.2% in the Western Pacific/China region, and 13.2% in the North America region. Overall, 32.2% of people had CVD (53 studies, N = 4,289,140); 29.1% had atherosclerosis (4 studies, N = 1153), 21.2% had coronary heart disease (42 studies, N = 3,833,200), 14.9% had heart failure (14 studies, N = 601,154), and 14.6% had angina. . In 13 studies involving 3,518,833 patients, 10.0% suffered a myocardial infarction, and in 39 studies, 7.6% suffered a stroke. CVD accounted for 50% of the deaths of these T2DM patients, Microvascular complications affect millions of people with Type II diabetes, Our study found a significant correlation between glycemic control and hypertension. There are several microvascular complications that can result in vision, renal, and neurological dysfunction, as well as increased healthcare costs for patients and society.[54]

Conclusion

The study evaluate that cardiac markers can be used as a diagnostic tool for the patients who are suffering from diabetes for a long time to stop the progression of hypertension. Cardiac markers are also used as a assessment tool for cardiovascular changes in diabetic patients , so that it cannot progress further .if these cardiac markers can be used as a routine test for diabetic patients it may help to prevent the development of hypertension in the diabetic patient.

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