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Original Article

Physiological assessment of the biomarker's atrial natriuretic peptides and cardiac troponins in patients with type 2 diabetes

Intisar Manwar[1]*, Faris Kata[1]

[1] Department of Biology, College of Education for Pure Science, University of Basrah, Basrah, Iraq

*Correspondence to: Intisar Manwar, Department of Biology, College of Education for Pure Science, University of Basrah, Basrah, 61001, Iraq. E-mail: mohammedjamal38@yahoo.com

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Abstract

Diabetes is considered a chronic metabolic disease characterized by elevated glucose levels due to either complete or relative deficiency of insulin hormone or the existence of factors antagonizing insulin action. Biomarkers are molecular, biochemical, physiological, anatomical elements, or imaging features that can be used for accurate diagnosis, disease progression assessment, prediction and monitoring of treatment effects, and determination of disease severity. This study investigated the association between two biomarkers, Atrial Natriuretic Peptides (ANP) and Cardiac Troponins (CT), and heart disease risk in diabetic women. Blood samples were collected from diabetic and healthy women, and ANP and CT levels were measured using ELISA. Diabetic women exhibited significantly higher ANP levels, potentially attributed to factors like hyperinsulinemia and elevated blood sugar. ANP is involved in cardiovascular disease development. CT levels were also significantly elevated in diabetic women and linked to vascular calcification and inflammation. ANP and CT may serve as valuable biomarkers for assessing heart disease risk in diabetic women, indicating vascular damage and inflammation. Further research is needed to validate these findings and explore their predictive value for specific cardiovascular diseases. These biomarkers show potential as early diagnostic predictors of heart diseases in diabetic women, warranting further investigation for clinical applications.

Keywords: type 2 diabetes, atrial natriuretic peptides, cardiac troponins, biomarkers, cardiovascular diseases.

Introduction

Diabetes is considered a chronic metabolic disease characterized by elevated glucose levels above the normal range due to either complete or relative deficiency of insulin hormone or the existence of factors antagonizing insulin action [1, 2].

Metabolic diseases, particularly diabetes, are always a concern for many people as it is one of the leading causes of mortality among people. It is a chronic metabolic disease that persists throughout an individual's life due to the pancreas' inability to produce sufficient insulin or the body's inability to utilize the insulin produced by the pancreas, resulting in increased glucose concentration in the blood [3, 4]. Despite the existence of various methods for preventing and treating diabetes, the disease has been recognized as a strong risk factor for cardiovascular diseases (CVD). Type 2 diabetes is strongly associated with an increased incidence of cardiovascular disease-related deaths [5].

Type 2 diabetes has been linked with an increased risk of developing cardiovascular diseases, possibly due to its correlation with common heart risk factors such as hypertension, dyslipidemia, atherosclerosis, and chronic kidney diseases, as well as non-common risk factors like ovarian calcification and osteoporosis [6, 7].

Biomarkers can be defined as molecular, biochemical, physiological, anatomical elements, or imaging features that can be used for accurate diagnosis, disease progression assessment, prediction and monitoring of treatment effects, and determination of disease severity [8, 9]. In order to understand the disease mechanism and identify new indicators, the importance of studying biomarkers involved in different inflammatory stages

of various diseases, especially cardiovascular diseases, has been increased [10]. These biomarkers include atrial natriuretic peptides (ANP) and cardiac troponins (CT).

The atrial natriuretic peptide (ANP) is a member of the family of cardiac hormones that promote sodium excretion, and it is secreted by the heart's atria in response to changes in their volume (atrial distension) and increased blood pressure. Although the ventricles also secrete it, atrial cells are the primary source of the hormone [11]. ANP is responsible for maintaining body water, sodium, potassium, and lipid balance and regulating water and electrolyte homeostasis. The atrial myocytes release it in response to high blood pressure and reduce water, sodium, and fat in the blood vessels, thus acting as a blood pressure-lowering agent. ANP plays a protective role against the development of cardiovascular diseases, microvascular inflammation, kidney disorders, accelerated atherosclerosis, and metabolic disorders such as insulin resistance and lipid metabolism disorders [12, 13]. Atrial natriuretic peptides have significant systemic effects and serve as biomarkers of mechanical and biological cardiac stress. Their secretion leads to cardiac wall stretch and plays a crucial role in regulating involuntary urination, water and electrolyte retention, vascular membrane permeability, vasodilation, heart contraction, and blood pressure changes. Therefore, they act as physiological regulators in an antagonistic manner to the renin-angiotensin-aldosterone system [14].

On the other hand, cardiac troponins are biomarkers resulting from mechanical and biological cardiac stress and ischemia. They are naturally present within cardiac cells, but when any condition of myocardial ischemia, myocardial infarction, or necrosis occurs, these enzymes are released from the damaged cells into the bloodstream. Thus, elevated enzyme levels often serve as a negative prognosis indicator for cardiovascular diseases [15]. Elevated levels of cardiac troponins in the bloodstream are common in diabetic patients due to leakage from damaged cardiac muscle cells or increased membrane permeability [16]. It has been found that elevated blood glucose levels and multiple risk factors for heart disease are associated with higher levels of cardiac troponins [17, 18]. Therefore, cardiac troponins are vital indicators of cardiovascular diseases [19].

The study aimed to evaluate two biomarkers in women with diabetes and study the physiological and immunological relationship between these biomarkers and cardiovascular diseases. Additionally, the study aimed to assess the possibility of using these biomarkers as early diagnostic predictors of heart diseases in diabetic patients.

Material and methods

A total of 60 serum samples were collected from a group of female patients with type 2 diabetes. The samples were divided based on the severity of the disease, as determined by HbA1c levels. There were 32 serum samples with HbA1c levels ranging from 7–9.9 and 28 serum samples with HbA1c levels ranging from 14–10. The samples were also divided based on the duration of the disease, with 36 serum samples from patients with a disease duration of 5–10 years and 24 serum samples from patients with a disease duration of 11–22 years. Furthermore, the samples were divided based on age, with 29 serum samples from women aged 45–54 years and 31 serum samples from women aged 55–70 years. The samples were collected from the Specialized Center for Diabetes Mellitus at Al-Faiha Hospital in Basrah/Iraq.

Control group

A total of 28 serum samples were obtained from healthy women donors after laboratory and clinical examinations conducted by a specialist to confirm that they did not have type 2 diabetes.

Serum preparation

Five ml of venous blood was drawn using a medical syringe and placed in a glass tube. The blood was left for 15 minutes and then centrifuged at 3500 rpm for 10 minutes to obtain serum. The serum was transferred to 1 ml Eppendorf tubes and stored at a temperature of -20 degrees Celsius until further testing.

Estimation of biomarker concentrations

The concentrations of the biomarkers (Atrial natriuretic peptides and cardiac troponins) were estimated using the Enzyme-Linked Immuno Sorbent Assay (ELISA) technique, specifically the Sandwich ELISA type, provided by the American company My BioSource. The measurements were taken at a wavelength of 450 nanometers, according to the instructions provided with each biomarker.

Statistical analysis

The data were analyzed using the SPSS program. Independent-sample T-tests were conducted to compare patient samples and healthy samples, as well as to

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Table 1: Concentration of natriuretic peptide in serum.

Variables		No.	Mean±SD	P-value
Participants	T2DM	60	531.824**±285.58	0.002
	Healthy women	28	355±89.858	
Age (years)	45–54	29	654.45**±286.35	0.000
	55–70	31	384.89±107.83	
Disease duration	5–10	36	533.25±203.80	0.296
	11–22	24	483.90±128.05	
Disease severity	HbA1c (7–9.9)	32	440.33±141.46	0.001
	HbA1c (10–14)	28	571.14**±145.01	

Note: ** – Significant difference at a probability level of P≤0.01.

compare patients based on disease severity, duration, and age, with a significance level of P≤0.01.

Results

Estimation of the biomarker atrial natriuretic peptide (ANP)

The results have shown a significant increase at a probability level of P≤0.01 in the concentration of natriuretic peptide in the serum of women with diabetes (531.824) compared to its concentration in healthy individuals (355). Furthermore, the results indicated a significant increase at a probability level of P≤0.01 in the concentration of natriuretic peptide in the younger age group compared to the older age group. A significant increase was observed in the high disease severity compared to moderate severity. At the same time, there were no significant differences between the first and second disease durations, as shown in Table 1.

Cardiac troponins biomarker

The current study has shown a significant increase at a probability level of p≤0.01 in the concentration of cardiac troponins among female diabetic patients (71.232) compared to healthy individuals (48.664). Additionally, the results indicated a significant elevation at a probability level of p≤0.01 in the concentration of cardiac troponins in both the second duration and high disease severity compared to the first duration and moderate disease severity. However, no significant differences were observed between the two age groups as shown in Table 2.

Discussion

The current study demonstrates a significant increase in the concentration of Atrial Natriuretic Peptides (ANP) in the plasma of women with diabetes compared to healthy individuals. Our findings were consistent with

Table 2: Concentration of cardiac troponins in serum.

Variables		No.	Mean±SD	P-value
Participants	T2DM	60	71.232**±30.983	0.000
	Healthy women	28	48.664±11.117	
Age (years)	45–54	28	69.416±15.316	0.172
	55–70	32	74.638±13.954	
Disease duration	5–10	36	65.452±12.784	0.001
	11–22	24	80.209**±19.771	
Disease severity	HbA1c (7–9.9)	33	61.076±18.581	0.007
	HbA1c (10–14)	27	74.26**±17.722	

Note: ** – Significant difference at a probability level of P≤0.01.

the results of the study [20]. These elevated levels of ANP in the current study may be attributed to the response to hyperglycemia, which is an important physiological response in diabetic patients. Insulin plays a crucial role in regulating sodium levels in the blood by signaling the renal nephron cells to increase the reabsorption of sodium ions from urine back into the bloodstream, especially in diabetic patients. This effect is known as the sodium-sparing effect of insulin, leading to an increased sodium level in the extracellular fluid and chronic stimulation of ANP [21].

Furthermore, the mechanical stretch of the atrium due to increased blood pressure in diabetic patients is considered the most important physiological mechanism that regulates the secretion of ANP. The increased atrial volume stimulates stretch-activated ion channels, resulting in ANP release. Additionally, ANP has been found to be a potent vasodilator, contributing to the body's fluid and salt balance [22]. It regulates blood pressure by dilating blood vessels, increasing glomerular filtration rate, promoting sodium excretion in urine, and increasing urine volume [23]. Moreover, it has been emphasized that ANP is released in response to atrial and vascular wall stretch, sympathetic stimulation of beta-adrenergic receptors, and elevated sodium concentration. The overall effect of ANP on the body is to counteract increased blood pressure and volume resulting from the renin-angiotensin system [24].

Additionally, the current study revealed a significant increase in the concentration of cardiac troponins in diabetic patients compared to healthy individuals, consistent with the study [25]. They have reported higher cardiac troponin levels in diabetic patients without cardiovascular diseases than in healthy individuals without cardiovascular diseases. The elevated levels of this biomarker may be attributed to increased cell membrane permeability and leakage of cardiac troponins into the bloodstream due to myocardial damage in diabetic patients with fatty toxicity and increased fat content that affects cardiac cells in addition to the cardiac steatosis and myocardial lipotoxicity which contributes to mechanical and biochemical stress, inflammation, mitochondrial dysfunction, impaired damage repair due to metabolic memory phenomenon, and compromised cellular metabolism [26].

The reasons for cardiac troponin elevation in diabetic patients can be attributed to a decrease in glomerular filtration rate, which is independently associated with the increase of troponin levels, and that is because chronic hyperglycemia reduces glomerular filtration rate and consequently decreases troponin elimination. It also affects microvascular circulation in the heart, leading to damage to the small blood vessels and myocardial ischemia, which contributes to the elevation of troponin levels [27]. All these conditions increase the risk of cardiovascular diseases and heart failure.

In the absence of cardiovascular disease, the elevation of blood troponin levels in diabetic patients can be attributed to the increased levels of ketones and free fatty acids. These substances prevent glucose metabolism in the cells and lead to energy loss in the heart muscle as ketones function differently from carbohydrates in energy production, and their utilization as fuel for cells takes much more time. Also, the accumulation of excess fatty acids in the blood can increase stress on the cardiac system due to the increased workload of the heart in dealing with these excess chemical compounds; this stress can cause damage to cardiac cells and the release of cardiac troponin into the blood stream [28].

Another possible cause of elevated cardiac troponin levels is a decrease in the pH value of the blood serum; therefore, acidosis leads to an increase in intracellular calcium, which plays a vital role in the muscle contraction process by binding to troponin [29]. Silent myocardial ischemia may also occur in diabetic patients, as silent myocardial ischemia has been detected in 21.9% of diabetic patients. Additionally, metabolic disorders accompanying diabetic ketoacidosis can lead to changes in cardiac electrophysiology and repolarization without any cardiac injury symptoms [30].

Inflammation and increased levels of cytokines due to diabetes are also among the causes that contribute to elevated troponin concentrations in the blood serum of diabetic patients [31]. Diabetic patients with inflammation and no symptoms of heart failure have higher levels of cardiac troponins compared to healthy individuals [32]. Metabolic disturbances in diabetes, such as glucose toxicity, fatty toxicity, and oxidative stress, play an important role in inflammation [33]. They cause stress on beta cells and insulin-sensitive tissues, leading to the release of cytokines and the occurrence of inflammation, which can result in the production of free radicals. These free radicals can cause damage to cardiac cells, leading to an elevation in cardiac troponin levels [34].

Elevated levels of cardiac troponin in the blood serum can lead to increased inflammation and damage to the cardiac muscle, and this leads to the heart's inability to perform its functions properly; in addition, when the heart is damaged, its function is significantly affected, and it can lead to disturbances in heart rate, difficulty in breathing, fatigue, and a feeling of tightness, and

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it also increases the risk of irregular muscle contractions in the heart, which disrupts the normal rhythm of heartbeats. Consequently, this can cause inadequate blood flow to the organs and tissues in the body and can lead to serious conditions such as blood clots, heart attacks, and other cardiovascular diseases [35].

Conclusion

In conclusion, this study investigated the levels of biomarkers, specifically Atrial Natriuretic Peptides (ANP) and Cardiac Troponins (CT), in women with type 2 diabetes and their association with heart diseases. The findings revealed a significant increase in ANP and CT concentration in the serum of diabetic women compared to healthy individuals, indicating the physiological response to hyperglycemia. Overall, the study highlights the potential of ANP and CT as biomarkers for early detection and prediction of heart diseases in diabetic women, providing insights into the pathophysiological mechanisms underlying the association between diabetes and cardiovascular complications.

Conflict of interest

The authors declare no conflict of interest.

Ethics approval

The approval for this study was obtained from the Ethics Committee of the Department of Biology, College of Education for Pure Science, University of Basrah (approval ID: 44).

Consent to participate

Written informed consent was obtained from the participants.

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