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INVESTIGATING THE INTERPLAY OF TYPE 2 DIABETES MELLITUS AND CARDIAC BIOMARKERS IN CARDIOVASCULAR RISK: A CROSS-SECTIONAL RETROSPECTIVE STUDY IN KWAZULU-NATAL.

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Abstract

Objective

This cross-sectional study investigates the relationship between glycaemic control, as indicated by HbA1c levels, and cardiovascular risk biomarkers (high-sensitivity troponin-T, troponin-I, and NT-ProBNP) in patients with Type 2 Diabetes Mellitus (T2DM). T2DM is associated with an increased risk of cardiovascular complications, including heart failure and myocardial infarction, and poor glycaemic control exacerbates these risks.

Methods

A cross-sectional study was conducted at a tertiary hospital in KwaZulu-Natal, including data from 230 patients diagnosed with T2DM. The study analyzed the correlation between HbA1c levels and cardiac biomarkers across different age groups. Demographic data, such as age and gender, were also collected to assess their influence on the relationship between glycaemic control and cardiovascular risk.

Results

The study found a significant positive correlation between elevated HbA1c levels and high-sensitivity troponin-T ($\rho = 0.250$, $p < 0.001$), indicating an increased risk of myocardial injury. Older participants exhibited higher NT-ProBNP levels ($\rho = 0.116$, $p = 0.040$), suggesting a higher risk of heart failure in this group. Additionally, higher HbA1c levels were associated with higher troponin-I levels, reinforcing the connection between poor glycaemic control and myocardial injury.

Conclusion

This study highlights the critical role of managing glycaemic control to reduce cardiovascular risk in T2DM patients, particularly in older individuals. Regular monitoring of both HbA1c and cardiac biomarkers is essential for early detection and intervention. Further research is needed to explore the combined effects of glycaemic control, comorbidities, and treatments on cardiovascular risk biomarkers.

Keywords: *Type 2 Diabetes Mellitus (T2DM), glycaemic control, HbA1c, cardiac biomarkers, high-sensitivity troponin-T, NT-ProBNP, myocardial injury.*
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Introduction

Diabetes is a chronic metabolic disorder characterized by elevated serum glucose levels in healthcare systems [1,2]. While emerging biomarkers, such as high-sensitivity cardiac troponins and natriuretic peptides, show potential for identifying cardiovascular risk in individuals with Type 2 Diabetes Mellitus (T2DM), their use remains limited in many African regions [3,4]. This research gap, particularly in South Africa, underscores the need for targeted studies investigating the role of cardiac biomarkers in the diagnosis, monitoring, and management of T2DM-related cardiovascular disease resulting from impaired insulin production or function. T2DM is characterized by insulin resistance and is a major global health issue, affecting approximately 463 million individuals worldwide as of 2022, with the prevalence expected to increase [5]. T2DM is strongly associated with an increased risk of cardiovascular diseases (CVD), including heart failure, coronary artery disease (CAD), and stroke [6].

The increasing prevalence of T2DM has been accompanied by a rise in cardiovascular complications, which are now a leading cause of morbidity and mortality in individuals with diabetes [7]. Risk factors such as hyperglycemia, dyslipidemia, and hypertension further exacerbate cardiovascular risk in individuals with T2DM

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[8]. Cardiovascular mortality due to diabetes has increased from 12 million deaths in 1990 to over 18 million in 2019 [8]. By 2045, it is projected that 783 million adults will be affected by diabetes, approximately 1 in 8 people [9].

T2DM is associated with several cardiovascular risk factors, including poor glycaemic control, as indicated by elevated glycated hemoglobin (HbA1c) levels, and dyslipidemia, which is characterized by low levels of high-density lipoprotein (HDL) cholesterol and elevated triglycerides [10]. Additionally, diabetes contributes to arterial calcification, atherosclerosis, and vascular stiffness, all of which accelerate the development of cardiovascular disease [11]. This complex relationship underscores the need for comprehensive strategies to manage both T2DM and its cardiovascular complications.

Emerging biomarkers, such as high-sensitivity cardiac troponins, natriuretic peptides, and growth differentiation factor-15, show promise in assessing cardiovascular risk in individuals with T2DM [3]. For example, cardiac troponin T (cTnT) has demonstrated sensitivity as a biomarker for myocardial infarction and provides valuable prognostic information for individuals with T2DM [4]. However, traditional biomarkers like creatine kinase MB (CK-MB) and aspartate transaminase (AST) have limited diagnostic value, particularly in the early stages of cardiovascular disease [12].

Cardiovascular Risk in Sub-Saharan Africa

In Sub-Saharan Africa (SSA), where healthcare infrastructure is limited, the burden of T2DM and its cardiovascular consequences is disproportionately high. Countries such as Nigeria and South Africa have observed significant increases in the prevalence of T2DM and associated cardiovascular complications [13,14]. In South Africa, the prevalence of T2DM is 15.25%, with KwaZulu-Natal (KZN) exhibiting even higher rates at 12.5%, along with a 14% prevalence of cardiovascular disease (CVD) [15,16]. Despite this growing burden, there is a notable lack of research on the role of cardiac biomarkers in the management of T2DM-related cardiovascular diseases, particularly in underserved regions such as KZN. KZN, although one of South Africa's more developed provinces, faces significant healthcare challenges, especially in rural and underserved areas [17]. Access to diagnostic tools, such as cardiac biomarkers, remains limited [18,19]. Studies have shown that individuals with T2DM in KZN have higher levels of cardiovascular risk factors, such as cholesterol and triglycerides, compared to non-diabetic individuals [19]. This emphasizes the need for early detection and more effective cardiovascular monitoring in this high-risk population.

The Need for Research on Cardiac Biomarkers in T2DM

Although the link between T2DM and CVD is increasingly recognized, diagnostic capabilities in many African regions remain insufficient, hindering effective disease management. The lack of access to advanced diagnostic tools, including electrocardiograms (ECGs), echocardiograms, and cardiac biomarkers, exacerbates challenges within diseases.

This study aims to address this gap by investigating the relationship between T2DM and cardiac biomarkers in a South African population, with a specific focus on KZN. By exploring the impact of T2DM on cardiovascular health and identifying potential biomarkers for early detection, this research seeks to improve healthcare outcomes and contribute to the development of effective, context-specific strategies for managing cardiovascular risk in diabetic patients.

Diabetes and Cardiovascular Risk

Individuals with T2DM face an elevated risk of cardiovascular complications, such as heart failure, stroke, and coronary artery disease [20]. T2DM is associated with common risk factors such as hypertension, dyslipidemia, and atherosclerosis, which exacerbate cardiovascular disease risk [7]. The coexistence of T2DM and cardiovascular disease worsens prognosis, increases healthcare costs, and raises the likelihood of recurrent events [21]. While some studies suggest a reduction in cardiovascular events, concerns remain regarding the potential adverse effects of certain diabetes treatments, such as hypoglycemia and weight gain [22].

Clinical Significance of Cardiac Biomarkers in T2DM

Cardiac biomarkers are essential for early identification, risk assessment, and management of cardiovascular issues in T2DM patients. Early detection can mitigate the progression of cardiovascular disease in high-risk populations, such as those with T2DM [6]. Novel biomarkers are necessary to enhance cardiovascular risk prediction in individuals with T2DM [23]. Regular monitoring of biomarkers like natriuretic peptides is recommended to detect heart failure in its early stages, enabling timely intervention [24]. The progression of T2DM can lead to diabetic cardiomyopathy (dbCM), further complicating cardiovascular health [25].

Mechanisms Linking T2DM to Cardiovascular Disease

The pathophysiological mechanisms underlying cardiovascular risks in T2DM are multifactorial. Insulin

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resistance, a hallmark of T2DM, leads to endothelial dysfunction, oxidative stress, and inflammation, all of which promote vascular damage and plaque formation [26;27]. These metabolic disruptions promote atherogenesis and increase the likelihood of thromboembolic events [28]. Lipid abnormalities, such as low HDL cholesterol and elevated triglycerides, contribute to the development of metabolic syndrome and cardiovascular disease [29].

Diagnostic and Prognostic Value of Cardiac Biomarkers

Cardiac biomarkers, such as cardiac troponin I (TnI), troponin T (TnT), and natriuretic peptides, are crucial for diagnosing myocardial injury and assessing cardiovascular risk [30]. Elevated levels of biomarkers like B-type natriuretic peptide (BNP) correlate with poor cardiovascular outcomes and can predict the risk of heart failure [30]. In individuals with diabetes, higher levels of BNP are associated with poor glycemic control and an increased risk of heart failure [31,32].

The Role of Glycated Haemoglobin (HbA1c)

HbA1c is a key marker for long-term glycaemic control and is closely associated with cardiovascular risk in individuals with T2DM [33]. Elevated HbA1c levels, indicative of poor glycaemic control, are linked to a higher risk of cardiovascular complications, cognitive decline, and dementia [34,35]. This highlights the importance of effective serum glucose management in preventing long-term cardiovascular complications. This study aims to address this gap by investigating the relationship between T2DM and cardiac biomarkers in a South African population, with a specific focus on KZN. By exploring the impact of T2DM on cardiovascular health and identifying potential biomarkers for early detection, this research seeks to improve healthcare outcomes and contribute to the development of effective, context-specific strategies for managing cardiovascular risk in diabetic patients.

Methodology

Study Design

A cross-sectional retrospective design was employed to investigate the impact of Type 2 Diabetes Mellitus (T2DM) on cardiovascular health. Data from patients' cardiac biomarkers, retrieved from the NHLS AARMS database, were analyzed for the period from January to December 2023.

Study Setting

The study utilized retrospective data from a RK Khan Hospital, KwaZulu-Natal in Durban, KwaZulu-Natal. The hospital serves a diverse population, providing a representative sample for the research.

Participants

Participants included adult patients (≥18 years) with and without T2DM. Both genders were included to account for potential differences in biomarker profiles and cardiovascular risks. The age range was chosen to focus on adult cardiac health, particularly as cardiovascular risk increases with age, especially in individuals with T2DM. A sample of 230 patients who had undergone testing for HbA1c and cardiac biomarkers during 2023 was selected. The diabetic group consisted of individuals with high HbA1c levels, while the non-diabetic group had no history of diabetes. Exclusion criteria included individuals with other cardiovascular diseases, acute illnesses, or conditions affecting cardiac biomarkers unrelated to T2DM. A non-random convenience sampling method was used based on the availability of medical records and biomarker data.

Laboratory Procedures

The methodology employed in this study involved the use of several immunoassays and diagnostic tests to assess various biomarkers associated with cardiac and metabolic conditions:

- The Elecsys® proBNP-2 immunoassay was utilized to quantitatively measure N-terminal pro-B-type natriuretic peptide (proBNP), a biomarker commonly used in diagnosing congestive heart failure and identifying minor cardiac dysfunction [36].
- The Elecsys® Troponin T immunoassay was employed to measure cardiac troponin T levels, a crucial test for diagnosing acute coronary syndrome (ACS) and myocardial infarction, as well as assessing the cardiac risk in patients with chronic renal failure [37].
- The HbA1c test was used for the quantitative detection of glycated haemoglobin, a marker for monitoring long-term glycaemic control in diabetes and diagnosing the condition [38]. These tests were selected for their established diagnostic utility in evaluating heart and metabolic conditions.

Statistical Analysis

Descriptive statistics (frequencies, percentages) summarized demographic and clinical variables. Spearman's rank correlation coefficient assessed associations between continuous variables (HbA1c and cardiac biomarkers) by age and gender, revealing patterns such as the positive correlation between HbA1c and

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Original Article

troponin T, indicating a link between poor glycaemic control and increased cardiac risk. Non-significant correlations between HbA1c and other biomarkers suggested independent factors influencing these outcomes. Data were analyzed using SPSS software.

Ethical Considerations

The study was conducted by ethical guidelines, ensuring confidentiality, voluntary participation, and the protection of patient rights. Ethical approval was obtained from the Mangosuthu University of Technology ethics committees at the university and hospital involved. All patient data was anonymized, and informed consent was obtained where necessary.

Institutional Review Board Statement

The study was conducted by the university's ethical guidelines and approved by the Research Ethics Committee of Mangosuthu University of Technology (protocol code RD5/20/2024, 19 February 2024). Ethical review and approval were waived for this study due to the use of de-identified data from the National Health Laboratory Service (NHLS) database, which did not involve direct patient contact or the need for informed consent.

Informed Consent Statement

Patient consent was waived due to the use of de-identified data from the National Health Laboratory Service (NHLS) database, which did not involve direct patient contact. Written informed consent has been obtained from the laboratory authorities to access the data utilized in this paper.

Results

Demographic Characteristics of Participants

Age Distribution

A total of 230 participant results were included in the study. *Table 1* presents the age distribution in which participants in this study were categorized into three age groups: 18-39 years, 40-64 years, and those over 65 years. Most participants fell into the 40-64 years group (57.4%), followed by the >65 years group (39.1%), while only 3.5% of the sample was between 18-39 years. This skewed age distribution suggested that the middle-aged and older populations dominated the sample.

Table 1: Age Distribution of Patients Included in the Study

Age Range	Frequency	Percent
18-39 years	8	3.5%
40-64 years	132	57.4%
>65 years	90	39.1%
Total	**230**	**100.0%**

Gender Distribution

Table 2: Gender Distribution of Patients Included in the Study

Gender	Frequency	Percent
Male	102	44.3%
Female	120	52.2%
Unknown	8	3.5%
Total	**230**	**100.0%**

Table 2 presents the gender distribution in which there was a slight female predominance in the sample, with 52.2% being female and 44.3% male. A small portion of the data (3.5%) was categorized as unknown gender. The balanced gender distribution allowed for a meaningful comparison of cardiac biomarkers and HbA1c levels between males and females.

Distribution of HbA1c Levels Across Age Groups

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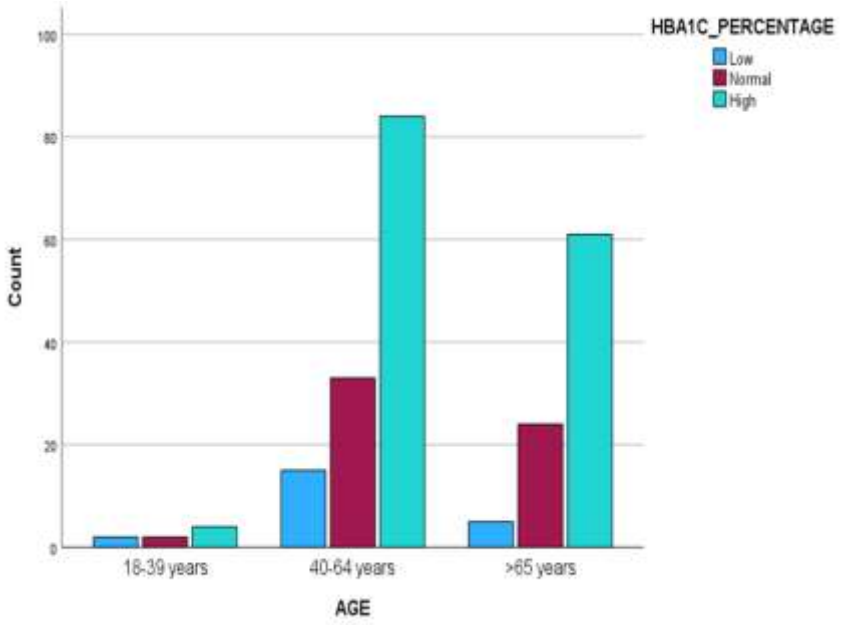

Figure 1: Distribution of HbA1c levels across age groups

The normal HbA1c range is 4% to 5.6%. Values below 5.7% are normal, 5.7% to 6.4% indicate an increased risk of developing diabetes (pre-diabetes). Pre-diabetes, and 6.5% or higher, suggests diabetes.

Figure 1 presents the distribution of HbA1c according to age. In the 18-39 years age group, few individuals (n=5) had normal and (n=7) high HbA1c levels, with (n=5) cases of low HbA1c. In the 40-64 years group, there was a noticeable increase (n=37) in normal HbA1c levels, and a substantial number (n=85) had elevated HbA1c, indicating a higher prevalence of elevated levels in this group. In those aged 65 and older, the number of individuals with low (n=8) HbA1c remained minimal, while moderate cases (n=26) of normal HbA1c were observed. A sizeable portion (n=61) of this age group had high HbA1c levels, suggesting that elevated HbA1c is more common in older adults compared to younger age groups.

Distribution of Cardiac Troponin-I Across Age Groups

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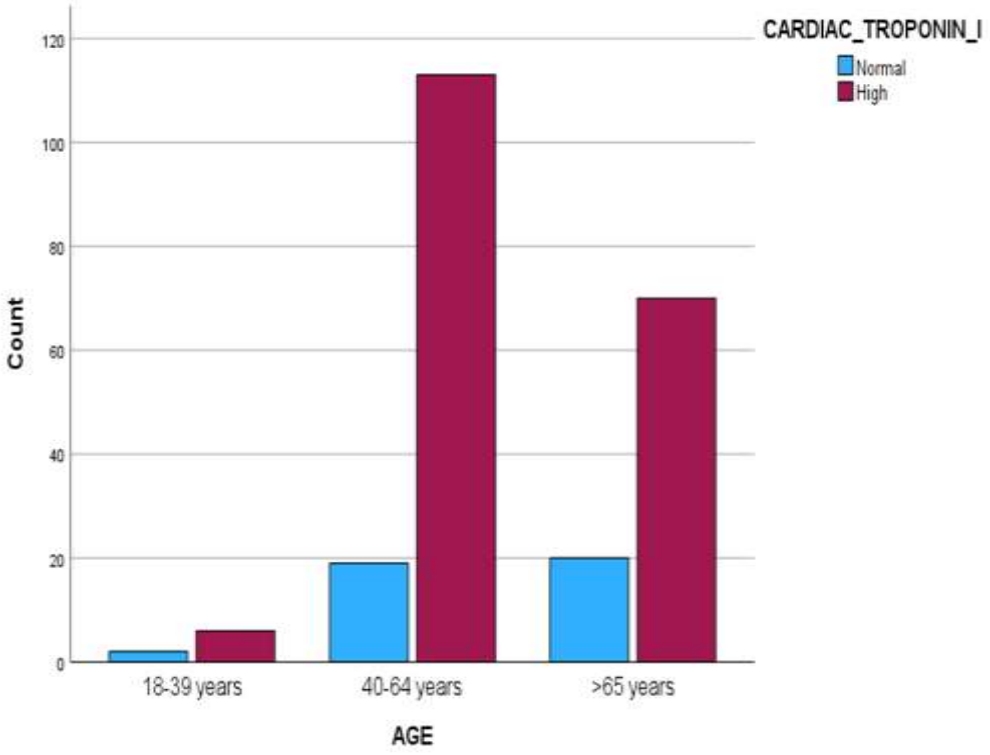

Figure 2: Distribution of Cardiac Troponin-I Across Age Groups

The normal range for Troponin I is typically less than 0.04 ng/mL, with values above this threshold indicating potential cardiac injury or acute coronary syndrome. *Figure 2* presents the distribution of Troponin-I according to age: In the 18-39 years age group, 5 individuals had normal cardiac Troponin-I levels, with a few (n=9) exhibiting elevated levels. In the 40-64 years group, a larger proportion (n=115) had high troponin-I levels, while fewer individuals (n=19) had normal levels. In the >65 years age group, a significant number (n=71) had elevated troponin-I levels, with fewer individuals (n=20) showing normal levels.

Distribution of NT-ProBNP Across Age Groups

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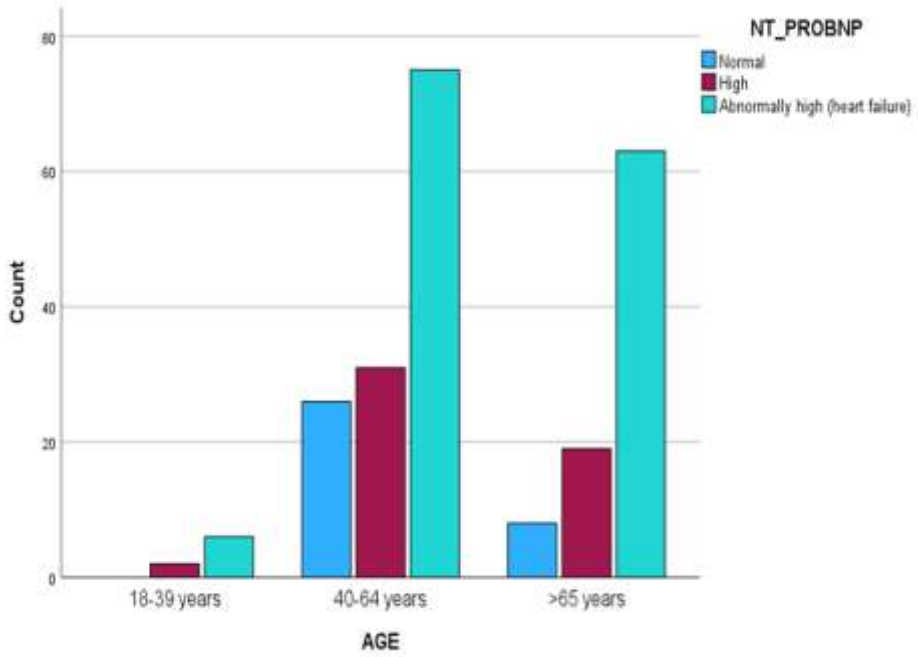

Figure 3: Distribution of NT-ProBNP Across Age Groups

Pro-BNP levels above 125 pg/mL for individuals under 75 years and 450 pg/mL for those 75 years and older are considered high and may indicate cardiac conditions such as heart failure. Abnormally high levels, significantly exceeding these thresholds (e.g., > 500 pg/mL for those under 75 years and > 1000 pg/mL for those 75 and older), suggest more severe or acute cardiac dysfunction. *Figure 3* shows the distribution of distribution across the age groups. In the 18-39 years age group, a few individuals (n=3) showed increased serum pro-BNP levels, with the majority (n=9) exhibiting abnormally elevated levels, indicative of heart failure. In the 40-64 years age group, there was a notable increase in individuals (n=75) with abnormally high NT-ProBNP levels, followed by 38 individuals with elevated NT-ProBNP results. In the >65 years age group, a high count of individuals (n=63) had abnormally high NT-ProBNP levels, indicative of heart failure, with 9 individuals showing normal results and 18 with elevated levels.

Correlation between HbA1c and Cardiac Biomarkers

Table 3: Correlation between HbA1c and Cardiac Biomarkers

		HBA1C %	TROPONIN_T	TROPONIN_I	NT_PROBNP
HBA1C %	Correlation Coefficient	1,000	,250**	-,038	-,022
	Sig. (1-tailed)	.	<,001	,283	,371
	N	230	230	230	230
TROPONIN_T	Correlation Coefficient	,250**	1,000	,325**	,310**
	Sig. (1-tailed)	<,001	.	<,001	<,001
	N	230	230	230	230

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Original Article

TROPONIN_I	Correlation Coefficient	-,038	,325**	1,000	,222**
	Sig. (1-tailed)	,283	<,001	.	<,001
	N	230	230	230	230
NT_PROBNP	Correlation Coefficient	-,022	,310**	,222**	1,000
	Sig. (1-tailed)	,371	<,001	<,001	.
	N	230	230	230	230

There was a significant positive correlation between HbA1c levels and troponin-T (Spearman's $\rho = 0.250$, $p < 0.001$), indicating that as HbA1c increases, troponin-T levels also increase, suggesting worsening cardiac function in individuals with poor glycaemic control. No significant correlation was found between HbA1c and troponin-I ($\rho = -0.038$, $p = 0.283$) or between HbA1c and NT-ProBNP ($\rho = -0.022$, $p = 0.371$), suggesting that other factors might influence these biomarkers independently of glycaemic control.

Correlation between Age and Cardiac Biomarkers

Table 4: Correlation between Age and Cardiac Biomarkers

		AGE	TROPONIN_T	TROPONIN_I	NT_PROBNP
AGE	Correlation Coefficient	1,000	,071	-,079	,116*
	Sig. (1-tailed)	.	,143	,117	,040
	N	230	230	230	230
TROPONIN_T	Correlation Coefficient	,071	1,000	,325**	,310**
	Sig. (1-tailed)	,143	.	<,001	<,001
	N	230	230	230	230
TROPONIN_I	Correlation Coefficient	-,079	,325**	1,000	,222**
	Sig. (1-tailed)	,117	<,001	.	<,001
	N	230	230	230	230
NT_PROBNP	Correlation Coefficient	,116*	,310**	,222**	1,000
	Sig. (1-tailed)	,040	<,001	<,001	.
	N	230	230	230	230

Age was positively correlated with NT-ProBNP ($\rho = 0.116$, $p = 0.040$), indicating that older individuals are more likely to have elevated NT-ProBNP, which could point to an increased risk of heart failure with age. No significant correlation was found between age and troponin-T ($\rho = 0.071$, $p = 0.143$) or troponin-I ($\rho = -0.079$, $p = 0.117$), suggesting that age may not have had a direct relationship with these biomarkers in the sample.

Correlation between Gender and Cardiac Biomarkers

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Original Article

Table 5: Correlation between Gender and Cardiac Biomarkers

			GENDER	TROPONIN_T	TROPONIN_I	NT_PROBNP
Spearman's rho	GENDER	Correlation Coefficient	1,000	,051	-,011	,109
		Sig. (1-tailed)	.	,223	,433	,050
		N	230	230	230	230
	TROPONIN_T	Correlation Coefficient	,051	1,000	,325**	,310**
		Sig. (1-tailed)	,223	.	<,001	<,001
		N	230	230	230	230
	TROPONIN_I	Correlation Coefficient	-,011	,325**	1,000	,222**
		Sig. (1-tailed)	,433	<,001	.	<,001
		N	230	230	230	230
	NT_PROBNP	Correlation Coefficient	,109	,310**	,222**	1,000
		Sig. (1-tailed)	,050	<,001	<,001	.
		N	230	230	230	230

Gender did not significantly correlate with troponin-T ($\rho = 0.051$, $p = 0.223$), troponin-I ($\rho = -0.011$, $p = 0.433$), or NT-ProBNP ($\rho = 0.109$, $p = 0.050$). This suggested that gender did not play a significant role in the distribution of these biomarkers in this sample.

Discussion

This study investigated the relationship between T2DM and cardiac biomarkers—specifically high-sensitivity troponin-T, cardiac troponin-I, and NT-ProBNP in a sample population from KwaZulu-Natal. The primary objective was to explore the association between glycaemic control, as indicated by HbA1c, and these biomarkers, while considering the impact of demographic factors such as age and gender. The results demonstrate a significant link between poor glycaemic control and increased cardiac risk, with notable trends in the distribution of biomarkers across different age groups.

A key finding was the significant correlation between elevated HbA1c levels and high-sensitivity troponin-T, a marker of myocardial injury. Elevated HbA1c levels reflect poor glucose control, which increases the risk of complications such as myocardial injury, as indicated by high high-sensitivity troponin-T levels [37]. The observed relationship ($\rho = 0.250$, $p < 0.001$) suggests that poor glycaemic control contributes to increased myocardial stress, which is consistent with studies by Simic et al. (2019), who reported elevated troponin levels in individuals with poor glycaemic control [38]. This finding aligns with Longo et al. (2022), who confirmed a correlation between poor glycaemic control and an increased risk of heart failure in patients with diabetes [39].

The distribution of cardiac biomarkers also varied by age group, with older participants (especially those over 65) showing significantly higher levels of all three biomarkers. This finding is consistent with previous research, such as Forman et al. (2020), which noted an increase in cardiac biomarkers with aging, likely due to the higher prevalence of comorbidities like hypertension and heart failure [40]. The positive correlation between age and NT-ProBNP ($\rho = 0.116$, $p = 0.040$) further supports the established link between aging and an increased risk of heart failure, as NT-ProBNP serves as a reliable marker for ventricular strain and heart failure [41]. Additionally, it has been reported that HbA1c levels naturally increase with age due to changes in glucose tolerance, even in individuals without diabetes. This increase is independent of glucose levels, insulin resistance, or body mass index [42].

Gender differences in cardiac biomarkers have been highlighted in earlier studies, with women generally presenting lower levels of troponins, creatine kinase, and other cardiac markers compared to men [43,44]. However, women tend to have higher levels of inflammatory markers and adipokines, such as C-reactive protein and leptin [45,46], a pattern that persists even in pre-diabetic states [46]. In contrast, this study found no significant influence of gender on cardiac biomarker

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levels. Despite a slight female predominance in the sample, no significant differences in biomarker levels between males and females were observed ($p > 0.05$). This contrasts with previous research suggesting that women with T2DM may be more susceptible to cardiovascular disease [47]. The lack of significant gender differences in this study may reflect the balanced gender distribution or specific characteristics of the sample. Further studies with larger, more diverse populations are needed to explore these gender-related differences more thoroughly.

Despite these gender differences in biomarker profiles, women are less frequently diagnosed with cardiac disorders and referred for coronary angiography [44]. The underlying reasons for these disparities remain unclear, but they may involve gender-related pathophysiological differences in the presentation of cardiac disorders. These findings suggest that a multi-marker approach, considering gender-specific biomarker patterns, could improve the risk assessment and diagnosis of cardiac disorders, particularly in women [43,45].

The association between poor glycaemic control and elevated troponin further emphasizes the importance of maintaining optimal HbA1c levels to mitigate cardiovascular risk in T2DM patients. These findings support the idea that regular monitoring of both HbA1c and cardiac biomarkers is essential for the early detection of myocardial injury and other cardiovascular risks. Elevated NT-ProBNP levels in individuals with high HbA1c further suggest an increased risk of heart failure, a finding consistent with the work of previous scholars who identified NT-ProBNP as a potential predictor of heart failure in patients with poor glycaemic control [48]. Future studies should further investigate how glycaemic control interacts with cardiac biomarkers to predict long-term cardiovascular outcomes and explore the effects of different diabetes treatments on these biomarkers. Prospective studies are needed to establish causality and provide more effective diagnostic and management strategies for diabetic patients at risk of heart failure.

Conclusions

In conclusion, this study underscores the significant association between poor glycaemic control, as reflected by elevated HbA1c levels, and increased cardiovascular risk in individuals with Type 2 Diabetes Mellitus (T2DM). A notable finding was the positive correlation between elevated HbA1c and high-sensitivity troponin-T, suggesting that poor glycaemic control contributes to myocardial injury risk. Furthermore, the distribution of cardiac biomarkers across age groups revealed that older participants, particularly those over 65, exhibited higher levels of troponin-T, troponin-I, and NT-ProBNP, indicating an increased cardiovascular risk associated with aging. However, no significant gender-related differences in biomarker levels were observed, challenging some previous findings on gender disparities in cardiac health. These results highlight the importance of monitoring both HbA1c and cardiac biomarkers to assess and manage cardiovascular risks in T2DM patients. Despite the study's limitations, including a sample from a single region and a cross-sectional design, the findings provide valuable insights into the relationship between glycaemic control and cardiovascular risk markers.

Study Limitations

While this study provides valuable insights, it is not without limitations. The sample was exclusively from KwaZulu-Natal, which may limit the generalizability of the findings to broader populations. Additionally, the small sample size may have limited the power to detect subtle associations, particularly in subgroup analyses. The cross-sectional design of the study restricts the ability to draw causal conclusions about the relationship between glycaemic control and cardiac biomarkers. Furthermore, the study did not account for the potential impact of common comorbidities in older adults, which may have confounded the results. Finally, the absence of longitudinal data restricts the ability to assess how changes in glycaemic control over time affect cardiac biomarker levels and long-term cardiovascular risk.

Generalizability of the Study

The generalizability of this study is limited by several factors. First, the sample was exclusively from KwaZulu-Natal, which may not represent the broader South African or international population, potentially limiting the applicability of the findings to different geographic or demographic groups. Second, the cross-sectional design restricts the ability to infer causal relationships, as it only provides a snapshot of the associations between glycaemic control and cardiovascular biomarkers at a single point in time. Additionally, the study's sample size may not be large enough to detect subtle differences in subgroups, such as those based on gender, race, or comorbidities. Lastly, the absence of longitudinal data prevents an examination of how changes in glycemic control over time might influence cardiovascular outcomes. These factors must be considered when interpreting the study's findings and their potential application to other populations or settings.

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Author Contributions

Siyabonga Mncedisi Mkhabela (Research Student) was responsible for the conceptualization of the study, data

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collection, data analysis, and interpretation. He also drafted the manuscript and ensured the accuracy of the data presented. Zinging Nobuhle Jaya (Main Supervisor) provided overall supervision of the study, contributed to the research design, offered critical insights during data analysis, and reviewed and revised the manuscript. Nokukhanya Thembane (Co-supervisor) contributed to the research design, assisted in data analysis, and provided feedback and revisions to the manuscript.

Data Availability Statement

The data supporting the reported results of this study can be found in the National Health Laboratory Service (NHLS) database. Due to privacy and ethical restrictions, the data is not publicly available. However, the data used in this study was de-identified to maintain confidentiality. Further information regarding data access can be requested from the corresponding author.

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Conflicts of Interest

The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:
T2DM: Type 2 Diabetes Mellitus
CVD: Cardiovascular Disease
CAD: Coronary Artery Disease
SSA: Sub-Saharan Africa
KZN: KwaZulu-Natal
HbA1c: Glycated Haemoglobin
HDL: High-Density Lipoprotein
CK-MB: Creatine Kinase MB
AST: Aspartate Transaminase
ECGs: Electrocardiograms
BNP: B-type Natriuretic Peptide
Dba: Diabetic Cardiomyopathy
TnI: Troponin I
TnT: Troponin T
proBNP: N-terminal pro B-type Natriuretic Peptide
ACS: Acute Coronary Syndrome
NHLS: National Health Laboratory Service
AARMS: Academic Affairs and Research Management System

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