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Original Article

Effect of HbA1c on The Severity of Diastolic Dysfunction in Type Two Diabetic Patients Presenting to the Cardiology Department, Mardan Medical Complex: A Cross-Sectional Study

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Abstract

Objectives: This study aimed to delineate the graded impact of HbA1c levels on the severity of diastolic dysfunction among patients presenting to the cardiology department at Mardan Medical Complex.

Methodology: A total of 151 consenting T2DM patients, aged 20 to 65, were enrolled in the study. Participants were categorized into three groups based on their HbA1c levels: <8, 8-10, and >10. Transthoracic echocardiography was utilized to assess left ventricular diastolic dysfunction.

Results: Of the participants, 61 were male and 90 were female. Notably, 85 patients (56.30%) exhibited HbA1c levels >10, among whom 18 (21%) were diagnosed with LVDD grade III, 51 (60%) with LVDD grade II, and 16 (19%) with LVDD grade I ($p<0.001$). Females were predominantly affected, constituting 59.6% of the study cohort. A significantly positive correlation was observed between LVDD and HbA1c levels ($r=0.841$; $p<0.001$).

Conclusion: This study underscores a significant relationship between the severity of diastolic dysfunction and HbA1c levels in T2DM patients. Poor glycemic control, as evidenced by elevated HbA1c levels, correlates with heightened diastolic dysfunction. The findings highlight the critical importance of optimizing glycemic control in individuals with T2DM to mitigate the risk of cardiovascular complications, particularly diastolic dysfunction.

Keywords: Type 2 diabetes mellitus, Diastolic dysfunction, HbA1c, 2D echocardiography

INTRODUCTION

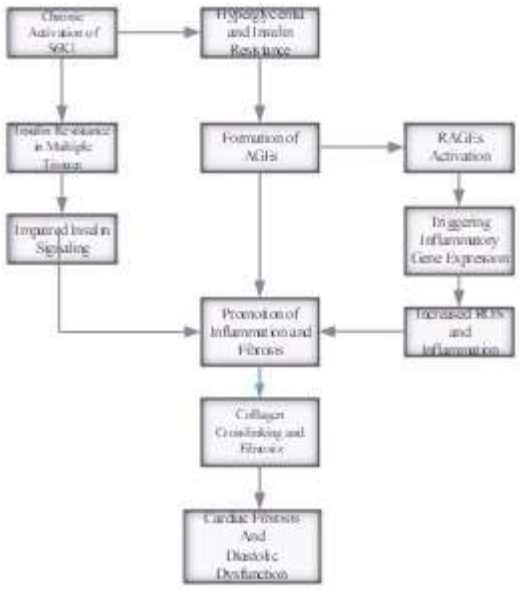
Diabetes mellitus (DM) stands as one of the most rapidly escalating public health challenges globally [1]. Its detrimental effects extend to the cardiovascular system, contributing to elevated blood pressure and coronary artery disease [2]. The International Diabetes Federation estimates that by 2021, approximately 537 million individuals worldwide will grapple with diabetes, with Pakistan expected to witness its impact on 30.8% of the adult population [3]. With an estimated four million deaths directly attributed to the condition in 2017, diabetes ranks among the top 10 causes of adult mortality, underscoring its profound impact on individuals, families, and communities worldwide [4].

DM is stratified into two principal subtypes: type 1, which typically emerges in infancy and is often immune-mediated, and type 2, which typically manifests in adulthood and is frequently associated with pancreatic pathology [1]. Studies have consistently highlighted the strong correlation between type 2 diabetes mellitus (T2DM) and heart failure with preserved ejection fraction (HFpEF) [5]. A chronic illness with an alarmingly escalating prevalence, diabetes mellitus (DM) is primarily driven by sedentary lifestyles and escalating obesity rates, poised to afflict approximately 9.9% of the global population by 2045, with over 90% of cases being type 2 diabetes [1,6].

DM precipitates a myriad of comorbidities and mortalities, including microvascular cardiac damage, believed to underlie diabetic cardiomyopathy (DCM). In instances where alternative etiologies for heart failure are absent, DCM may emerge as the underlying pathology, with left ventricular (LV) diastolic dysfunction representing its initial subclinical manifestation, which may eventually progress to symptomatic heart failure [7]. Numerous studies, including those by Paul Poirier et al., have demonstrated impaired diastolic function in diabetic patients devoid of overt clinical signs of heart disease, even in the presence of preserved systolic function [8]. Echocardiographic assessments by Boonman et al. further corroborate these findings, revealing diastolic dysfunction in nearly half of elderly individuals with diabetes [9]. Hyperglycemia, independently of enzymatic involvement, exerts deleterious effects on the myocardium, with every 1% reduction in mean HbA1c levels potentially corresponding to a 37% reduction in microvascular complications [10]. Accordingly, glycated hemoglobin emerges as a pivotal determinant in gauging the likelihood and severity of diabetic cardiovascular complications [8]. Additionally, studies by Giorda et al. underscore the association between advanced age, elevated HbA1c levels, and LV diastolic dysfunction [11].

This study aims to deepen our understanding of the impact of glycemic control on cardiac function, potentially paving the way for targeted therapeutic interventions aimed at optimizing patient outcomes. Specifically, the study seeks to determine the graded effect of HbA1c levels in T2DM on diastolic dysfunction and to evaluate the degree of diastolic dysfunction across different age cohorts.

Figure 1: pathophysiology of diastolic dysfunction in T2DM



METHODOLOGY

Study Design: This study employed a cross-sectional design to investigate the association between the severity of diastolic dysfunction in type 2 diabetic patients and their HbA1c levels. Cross-sectional studies are well-suited for examining relationships between variables at a single point in time, allowing for the assessment of prevalence and associations within a defined population.

Setting: The study was conducted in the Cardiology Department at Mardan Medical Complex, a tertiary care hospital in Mardan, Pakistan. The department's diverse patient population, drawn from both the local community and surrounding areas, provided a representative sample of individuals with type 2 diabetes seeking cardiac care.

Participants: Inclusion criteria encompassed patients with type 2 diabetes mellitus (T2DM) undergoing echocardiography, regardless of gender, within the age range of 20 to 65 years. Exclusion criteria included patients with type 1 diabetes mellitus, hypertension, congenital heart diseases, valvular heart disease, cardiomyopathy, coronary artery disease, atrial fibrillation, cardiac tumors, and amyloidosis.

Variables: The independent variable of interest was the HbA1c level, a measure of long-term blood glucose control in diabetic patients. The dependent variable was the severity of diastolic dysfunction, assessed through echocardiographic parameters such as transmitral peak early diastolic velocity (E wave), peak early diastolic velocity at the mitral annulus (e' wave), peak late diastolic velocity (A wave), E/A ratio, and isovolumic relaxation time (IVRT).

Data Sources/Measurement: Data collection involved obtaining ethical approval from the Institutional Ethics Committee (IEC) and informed consent from eligible patients. Clinical evaluation included ruling out coronary artery disease, hypertension, and prior myocardial infarction or arrhythmias. Diabetes status was determined based on recent HbA1c levels, and echocardiography was performed by trained personnel following standardized guidelines.

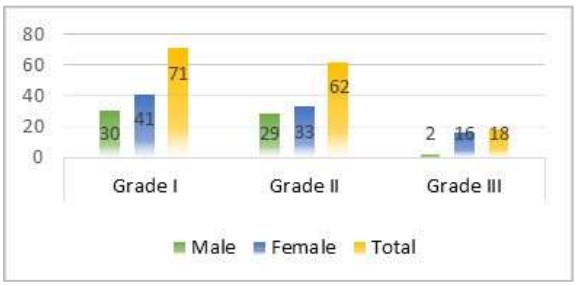
Bias: Efforts were made to minimize bias by employing standardized procedures for data collection and analysis. Additionally, the use of purposive sampling aimed to include a diverse range of participants representative of the population seeking cardiac care at the study site.

Study Size: The sample size of 151 participants was determined using OpenEpi, with a margin of error of 5% and a confidence level of 95%, accounting for an anticipated frequency of 11% [12].

Quantitative Variables: Quantitative variables included age, HbA1c levels, and various echocardiographic parameters such as E wave, e' wave, A wave, E/A ratio, and IVRT.

Ethical Considerations: Ethical approval was obtained from the Ethical Committee of BKMC, Mardan, prior to data collection, ensuring compliance with ethical standards. Informed consent was obtained from all study participants, prioritizing their confidentiality, privacy, and voluntary participation in the study. These ethical considerations are paramount in maintaining the integrity and trustworthiness of our research findings.

Figure 2: Gender and DD Grade



Statistical Methods: Data analysis was performed using SPSS software. Descriptive statistics, including means and standard deviations, were calculated for age, HbA1c levels, and echocardiographic parameters. Linear regression analysis was employed to predict the relationship between continuous variables (duration of diabetes, random blood sugar, E/e') and HbA1c levels. The Chi-square test was utilized to assess the statistical significance of the relationship between diastolic dysfunction grades and HbA1c levels.

RESULTS

Participants: The study involved 151 participants with type 2 diabetes mellitus (T2DM) undergoing echocardiography, with an average age of 48.34 years. Participants were divided into three age groups: 21-35 years (5.3%), 36-50 years (53.0%), and 51-65 years (41.7%). The average duration of T2DM was 7.68 years, with the majority having a diabetic duration of less than 10 years.

Descriptive Data: The mean random blood sugar (RBS) was 323.35 mg/dL, and the mean HbA1c level was 11.34%. Echocardiographic parameters, including E wave, A wave, e', E/A ratio, E/e', left atrial (LA) size, isovolumic relaxation time (IVRT), and left atrial volume index (LAVI), were also recorded.

Table 1: Quantitative Variables

Variables		Mean	Std. Deviation
Age (years)		48.34	8.74
T2DM duration (years)		7.68	4.85
RBS (mg/dL)		323.35	92.7
	Male	10.75	3.22
HbA1c level %	**female**	11.72	3.27
	Total	11.34	3.28
E wave (cm/s)		56.63	11.25
A wave (cm/s)		62.16	18.29
e' (cm/s)		6.07	1.13
E/A		1.02	0.48
E/e'		9.68	2.78
LA Size (cm)		3.66	0.46
IVRT (ms)		92.73	18.12
LAVI (mL/m²)		34.28	7.39

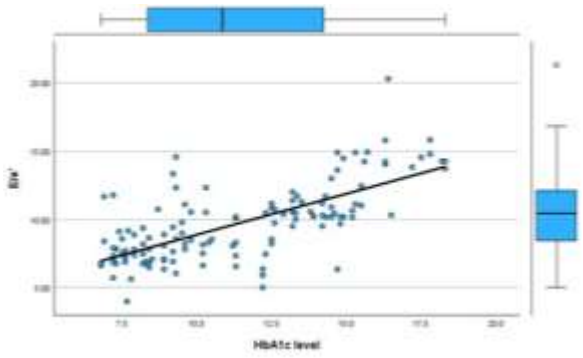
Outcome Data: The study found a statistically significant association between HbA1c levels and various parameters of left ventricular diastolic dysfunction (LVDD), including E/e' ratio ($p<0.001$), RBS levels ($p<0.001$), and age (chi-square, $p<0.001$). The correlation between HbA1c and LVDD was particularly strong, with higher HbA1c levels correlating with more severe LVDD.

Table 2: Age, HbA1c, and LVDD Cross tabulation

LVDD Grade	HbA1c (%)			P-value
	<8	8 to 10	>10	
21-35 years				
Grade I	2	0	1	0.101
Grade II	0	1	4	
36-50 years				
Grade I	21	17	7	
Grade II	1	5	24	<0.001
Grade III	0	0	5	
51-65 years				
Grade I	5	10	8	
Grade II	0	4	23	<0.001
Grade III	0	0	13	
Total				
Grade I	28	27	16	
Grade II	1	10	51	<0.001
Grade III	0	0	18	

Main Results: In the age group of 21-35 years, there was no statistically significant association between HbA1c levels and LVDD. However, in the age groups of 36-50 years and 51-65 years, higher HbA1c levels were significantly associated with more severe LVDD, indicating the impact of glycemic control on cardiac function, particularly in older individuals. Regression analysis further supported these findings, showing a robust positive correlation between HbA1c levels and LVDD. Additionally, HbA1c levels were found to be associated with other echocardiographic parameters, such as E/e' ratio and LAVI, highlighting the broader impact of glycemic control on cardiac structure and function. See Table 2 for a detailed breakdown of the association between age, HbA1c levels, and LVDD grades. Figure 3 illustrates the correlation between HbA1c levels and E/e' ratio.

Figure 3: Correlation of HbA1c and E/e'



DISCUSSION

Diabetes mellitus (DM) has become a global epidemic, posing significant health challenges worldwide. Cardiovascular disease, which often accompanies diabetes, manifests earlier and more severely in individuals with type 2 diabetes mellitus (T2DM) compared to those without diabetes [13]. In this study, we investigated left ventricular diastolic dysfunction (LVDD) in 151 participants with T2DM, revealing notable associations and insights into the interplay between glycemic control, duration of diabetes, and cardiac function.

The prevalence of LVDD in our study population was substantial, with 47.0% classified as grade I, 41.1% as grade II, and 11.9% as grade III. This distribution aligns with findings from previous research, underscoring the high burden of LVDD in individuals with T2DM [14]. Consistent with existing literature, we observed a significant correlation between age and LVDD, reinforcing the notion that advancing age is a risk factor for cardiac dysfunction in diabetic patients [14,15].

Our study revealed a moderate positive correlation between the duration of T2DM and LVDD, echoing findings from Arshad et al. [16] and Hassan Ayman et al. [17] Prolonged exposure to hyperglycemia may contribute to the development and progression of LVDD, highlighting the importance of early

intervention and tight glycemic control in mitigating diabetic complications.

Elevated HbA1c levels emerged as a significant predictor of LVDD severity in our study. Participants with higher HbA1c levels demonstrated a greater likelihood of advanced LVDD grades, consistent with prior research by Kumar et al. [18], Guria et al. [19], and others. These findings underscore the critical role of glycemic control in preserving cardiac function and reducing the risk of diabetic cardiomyopathy [20,21].

Echocardiographic parameters such as E/A ratio and E/e' ratio serve as valuable indicators of diastolic function. Our study revealed associations between HbA1c levels and these parameters, corroborating previous research by Reddy et al. and others [22,23]. These findings emphasize the multifactorial nature of LVDD pathogenesis, wherein glycemic control influences cardiac structure and function through various mechanisms [24].

Of note, our study identified a lack of association between HbA1c levels and LVDD in the youngest age group (21-35 years). This divergence from older age groups suggests potential differences in disease pathophysiology and risk factors across age cohorts [25]. Further investigation into the unique characteristics of diabetic cardiomyopathy in young adults is warranted to inform targeted prevention and management strategies.

Our study contributes to the growing body of evidence linking glycemic control, duration of diabetes, and LVDD in individuals with T2DM. By elucidating these relationships, our findings underscore the importance of comprehensive diabetes management strategies aimed at optimizing cardiovascular health and reducing the burden of diabetic complications. Further longitudinal studies are needed to validate these findings and explore additional factors influencing diabetic cardiomyopathy across different age groups and populations.

RECOMMENDATIONS

Based on the insights gleaned from this cross-sectional study, further research is warranted to explore and evaluate intervention strategies aimed at optimizing glycemic control in T2DM patients. While our study provides valuable insights, longitudinal investigations with larger sample sizes are recommended to establish causality and elucidate the long-term effects of HbA1c on LVDD. Longitudinal data can also facilitate the identification of trends and the impact of changes in HbA1c levels on diastolic function over time. Multidisciplinary collaboration among cardiologists, endocrinologists, and primary care providers is imperative for comprehensive management of T2DM patients, with a focus on glycemic control to mitigate the risk of LVDD. Health promotion and patient education programs may prove beneficial in empowering individuals to manage their diabetes effectively. Additionally, the development of risk stratification tools incorporating HbA1c levels and other clinical parameters could aid in identifying T2DM patients at higher risk of diastolic dysfunction, enabling targeted interventions and closer monitoring of at-risk individuals.

LIMITATION

It is important to acknowledge several limitations of our study. The sample size of 151 T2DM patients may not fully represent the diversity within the T2DM population. Additionally, as a cross-sectional study, our findings may not be generalizable to other populations, and causality cannot be inferred. The single-center nature of the study may limit the external validity of our results. Furthermore, potential errors and incompleteness in medical records and patient-reported data may have introduced biases. While coronary artery disease was ruled out through electrocardiography and echocardiography, the lack of recorded cholesterol levels is a notable limitation that should be addressed in future studies.

CONCLUSION

A significant proportion of individuals with type 2 diabetes mellitus (T2DM) exhibit left ventricular diastolic dysfunction (LVDD), underscoring the importance of glycemic management in mitigating this risk, particularly among older patients. Our study indicates a slightly higher level of HbA1c in females compared to males, suggesting potential gender-specific considerations in diabetes management. Additionally, we observed a worsening severity of LVDD with advanced age and higher HbA1c levels. Furthermore, our findings demonstrate a robust and highly significant positive correlation between HbA1c levels and various echocardiographic parameters

associated with LVDD, highlighting the impact of glycemic control on diastolic function.

AUTHORS' CONTRIBUTION

AA, AAK, SB, and SK: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. AA, AAK, SB, and SK: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

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