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Research Article

Histomorphological and Physiological Assessment of Diabetic Cardiomyopathy in Rats

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ABSTRACT
Background: Diabetic cardiomyopathy is a major cardiovascular complication of diabetes mellitus characterized by structural and functional abnormalities of the myocardium independent of hypertension or coronary artery disease. Persistent hyperglycemia contributes to oxidative stress, inflammation, and impaired cardiac physiology, leading to progressive myocardial damage. This study aimed to perform a histological and physiological assessment of diabetic cardiomyopathy in streptozotocin-induced diabetic rats.
Methods: An experimental study was conducted in July-December 2025, on 20 adult male albino rats divided into two groups: control (n=10) and diabetic (n=10). Diabetes mellitus was induced by intraperitoneal injection of streptozotocin (55 mg/kg). Rats with fasting blood glucose levels ≥250 mg/dL after 72 hours were considered diabetic. After 8 weeks, physiological parameters including fasting blood glucose levels and myocardial thickness were evaluated. Heart tissues were collected and processed using standard histological techniques. Hematoxylin and eosin-stained sections were examined microscopically for myocardial fiber disorganization, cellular degeneration, edema, inflammatory infiltration, vascular congestion, hypertrophy, and fibrosis.
Results: Diabetic rats demonstrated significantly elevated fasting blood glucose levels (312.4 ± 28.6 mg/dL) compared to controls (96.8 ± 11.2 mg/dL) ($p<0.001$). Histological examination revealed marked myocardial abnormalities in diabetic rats, including myocardial fiber disorganization in 80% of specimens, cytoplasmic vacuolar degeneration in 70%, vascular congestion in 70%, interstitial edema in 60%, inflammatory infiltration in 50%, cardiomyocyte hypertrophy in 50%, and focal fibrosis in 40% of cases. Mean myocardial thickness was significantly increased in diabetic rats (18.6 ± 2.4 µm) compared to controls (12.9 ± 1.8 µm) ($p=0.002$). Fibrotic tissue area was also significantly higher in diabetic myocardium (16.3% ± 3.1%) than in controls (<3%) ($p<0.001$).
Conclusion: Diabetes mellitus induces significant histological and physiological alterations in myocardial tissue, resulting in structural degeneration, fibrosis, inflammation, and cardiac hypertrophy. These findings support the role of chronic hyperglycemia in the pathogenesis of diabetic cardiomyopathy and highlight the importance of early cardiovascular assessment in diabetes-related cardiac dysfunction.

Keywords: Diabetic Cardiomyopathy, Cardiovascular Complication, Diabetes Mellitus, Histological and Physiological Alterations.

INTRODUCTION

Diabetes mellitus (DM) is one of the most prevalent metabolic disorders worldwide and is associated with substantial cardiovascular morbidity and mortality. Among the various cardiovascular complications, diabetic cardiomyopathy (DCM) has emerged as a distinct clinical entity characterized by structural and functional abnormalities of the myocardium independent of hypertension, coronary artery disease, or valvular heart disease [1,2]. The increasing prevalence of diabetes has contributed significantly to the growing burden of heart failure, making DCM

an important area of cardiovascular research [3].

The pathogenesis of diabetic cardiomyopathy is multifactorial and involves hyperglycemia-induced oxidative stress, chronic inflammation, mitochondrial dysfunction, altered myocardial energy metabolism, and impaired insulin signaling [4,5]. Persistent hyperglycemia promotes the production of reactive oxygen species and advanced glycation end products, leading to cellular injury and myocardial remodeling [6]. These molecular alterations result in cardiomyocyte hypertrophy, apoptosis, interstitial fibrosis, and ventricular dysfunction, ultimately compromising cardiac performance [5,7].

Histological studies have demonstrated characteristic myocardial changes in diabetes, including myofibrillar disorganization, cytoplasmic degeneration, inflammatory cell infiltration, vascular congestion, edema, and excessive collagen deposition [6,8]. These structural abnormalities correlate closely with physiological impairments and contribute to the progression of diabetic cardiomyopathy. Experimental animal models, particularly streptozotocin-induced diabetic rats, are extensively used to investigate the underlying mechanisms of diabetes-associated cardiac injury because they reproduce many pathological features observed in human disease [9].

Therefore, the present study aimed to evaluate the histological and physiological alterations associated with diabetic cardiomyopathy in streptozotocin-induced diabetic rats and to determine the relationship between myocardial structural changes and cardiac dysfunction.

METHODOLOGY

This experimental laboratory-based study was conducted in July-December 2025, to evaluate the histological and physiological alterations associated with diabetic cardiomyopathy in streptozotocin-induced diabetic rats. A total of 20 healthy adult male albino rats weighing 180–250 g were obtained from the animal house and acclimatized under standard laboratory conditions with a 12-hour light-dark

Cycle, controlled temperature (22–25°C), and free access to food and water. The animals were randomly divided into two equal groups: a control group (n=10) and a diabetic group (n=10).

Diabetes mellitus was induced in the experimental group through a single intraperitoneal injection of streptozotocin (STZ) at a dose of 55 mg/kg body weight dissolved in freshly prepared citrate buffer (pH 4.5). Control animals received an equivalent volume of citrate buffer. After 72 hours, fasting blood glucose levels were measured using a glucometer from tail vein blood samples. Rats with fasting blood glucose levels ≥250 mg/dL were considered diabetic and included in the study. The experimental period continued for eight weeks, during which animals were monitored regularly for body weight, general health status, and blood glucose levels.

At the end of the experimental period, all animals were anesthetized using ketamine-xylazine and sacrificed humanely according to institutional ethical guidelines. The hearts were carefully excised, washed with normal saline to remove blood clots, and fixed in 10% neutral buffered formalin for 24–48 hours. Tissue samples from the left ventricular myocardium were processed using standard histological techniques, including dehydration through ascending grades of alcohol, clearing in xylene, and embedding in paraffin wax. Sections of 4–5 µm thickness were prepared using a rotary microtome and stained with hematoxylin and eosin (H&E).

Histological examination was performed under a light microscope to assess myocardial fiber organization, cytoplasmic degeneration, interstitial edema, inflammatory cell infiltration, vascular congestion, cardiomyocyte hypertrophy, and fibrosis. Physiological assessment included measurement of fasting blood glucose levels and myocardial thickness. Data were analyzed using SPSS version 25. Quantitative variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Statistical comparisons between groups were performed using the independent t-test and Chi-square test, with a p-value <0.05 considered statistically significant.

RESULTS

Tables 1–3 demonstrate significant physiological and histopathological alterations in the myocardium of streptozotocin-induced diabetic rats. As shown in Table 1, fasting blood glucose levels were markedly elevated in the diabetic group compared with the control group (312.4 ± 28.6 mg/dL vs. 96.8 ± 11.2 mg/dL, $p<0.001$), confirming successful induction of diabetes. In addition, diabetic rats exhibited significantly greater myocardial thickness (18.6 ± 2.4 µm vs. 12.9 ± 1.8 µm, $p=0.002$) and a substantially larger fibrotic tissue area (16.3 ±

3.1% vs. 2.7 ± 0.8%, p<0.001), indicating myocardial hypertrophy and fibrosis. These findings suggest that chronic hyperglycemia leads to structural remodeling of cardiac tissue and contributes to the development of diabetic cardiomyopathy.

The histopathological findings presented in Tables 2 and 3 further support these observations. Myocardial fiber disorganization was the most common abnormality, affecting 80% of diabetic rats, followed by cytoplasmic vacuolar degeneration and vascular congestion, each observed in 70% of specimens. Interstitial edema was present in 60% of diabetic rats, whereas inflammatory cell infiltration and cardiomyocyte hypertrophy were detected in 50% of cases. Focal fibrosis was observed in 40% of myocardial sections. Comparison with the control group revealed statistically significant increases in all evaluated histopathological parameters, including myocardial fiber disorganization (p<0.001), cytoplasmic degeneration (p<0.001), vascular congestion (p=0.008), interstitial edema (p=0.003), inflammatory infiltration (p=0.011), cardiomyocyte hypertrophy (p=0.011), and fibrosis (p=0.029). These results indicate that diabetes induces marked cellular injury, inflammation, edema, vascular disturbances, and fibrotic remodeling within the myocardium.

The overall severity of myocardial damage is summarized in Table 4. The mean histopathological severity score was significantly higher in the diabetic group (7.8 ± 1.4) compared with the control group (1.9 ± 0.7) (p<0.001). This composite score, based on myocardial fiber disorganization, degeneration, edema, inflammation, congestion, hypertrophy, and fibrosis, reflects the cumulative impact of diabetes on myocardial architecture. The significantly elevated score in diabetic rats confirms the presence of extensive myocardial injury and highlights the progressive nature of diabetic cardiomyopathy in this experimental model.

Table 1. Comparison of Physiological Parameters between Control and Diabetic Rats

Parameter	Control Group (N=10) Mean ± SD	Diabetic Group (N=10) Mean ± SD	P-Value
Fasting Blood Glucose (Mg/Dl)	96.8 ± 11.2	312.4 ± 28.6	<0.001
Myocardial Thickness (µm)	12.9 ± 1.8	18.6 ± 2.4	0.002
Fibrotic Tissue Area (%)	2.7 ± 0.8	16.3 ± 3.1	<0.001

Table 2. Frequency of Histopathological Changes in Diabetic Rats (n=10)

Histopathological Finding	Frequency (N)	Percentage (%)
Myocardial Fiber Disorganization	8	80
Cytoplasmic Vacuolar Degeneration	7	70
Vascular Congestion	7	70
Interstitial Edema	6	60
Inflammatory Cell Infiltration	5	50
Cardiomyocyte Hypertrophy	5	50
Focal Fibrosis	4	40

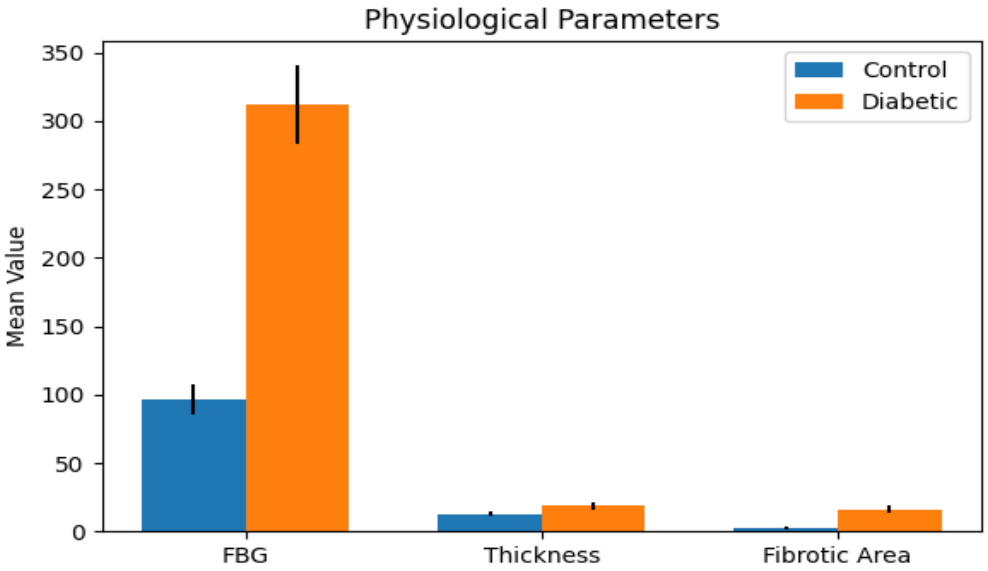
Table 3. Comparison of Histopathological Findings between Control and Diabetic Groups

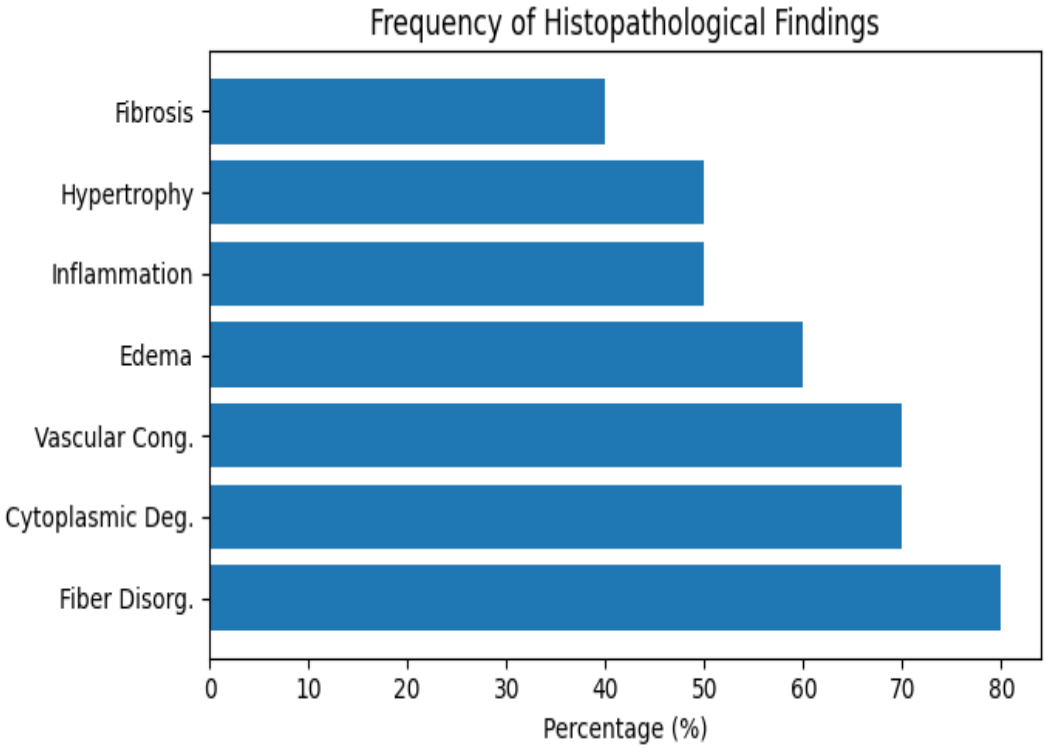
Histopathological Parameter	Control Group n (%)	Diabetic Group n (%)	p-value
Myocardial Fiber Disorganization	0 (0%)	8 (80%)	<0.001
Cytoplasmic Degeneration	0 (0%)	7 (70%)	<0.001
Vascular Congestion	1 (10%)	7 (70%)	0.008
Interstitial Edema	0 (0%)	6 (60%)	0.003
Inflammatory Cell Infiltration	0 (0%)	5 (50%)	0.011
Cardiomyocyte Hypertrophy	0 (0%)	5 (50%)	0.011
Fibrosis	0 (0%)	4 (40%)	0.029

Table 4. Overall Histopathological Severity Score

Parameter	Control Group Mean ± SD	Diabetic Group Mean ± SD	P-Value
Histopathological Severity Score	1.9 ± 0.7	7.8 ± 1.4	<0.001

Scoring Criteria: Composite score based on myocardial fiber disorganization, degeneration, edema, inflammation, congestion, hypertrophy, and fibrosis. Higher scores indicate greatermyocardial injury.





Histological Figures for Diabetic Cardiomyopathy

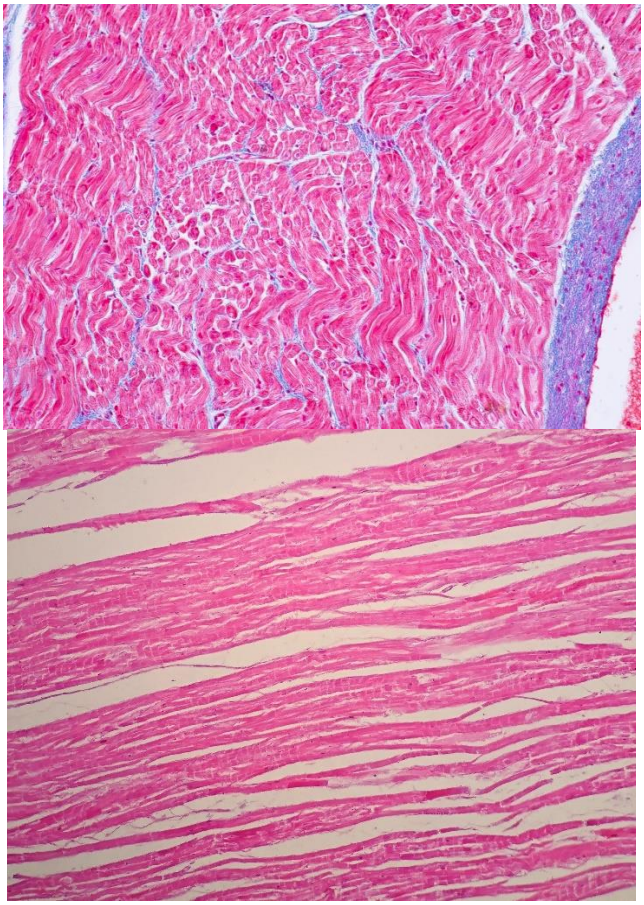


Figure 1. Normal Myocardium (Control).

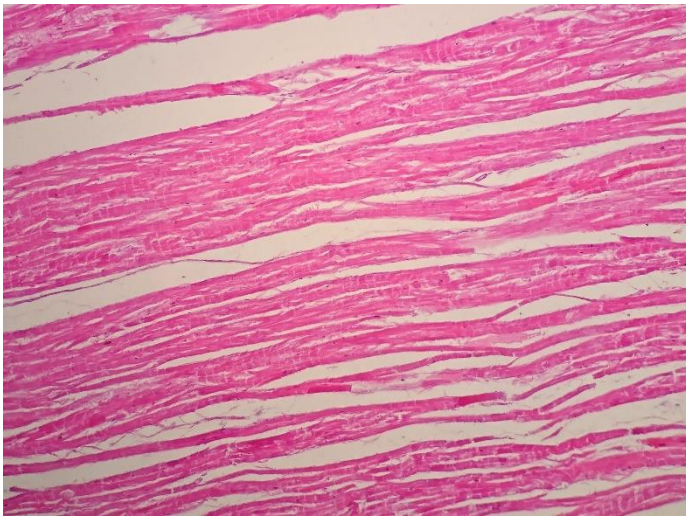


Figure 2. Myocardial Fiber Disorganization.

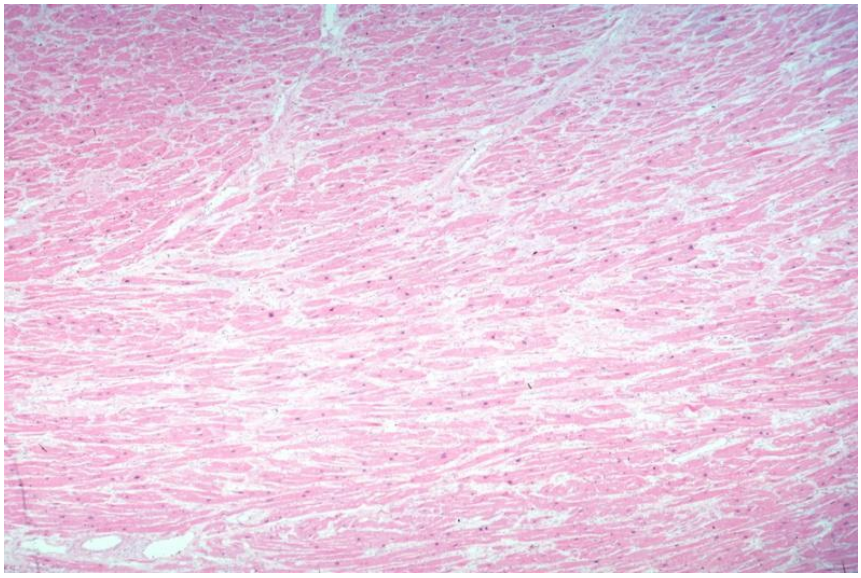


Figure 3. Cardiomyocyte Hypertrophy and Vacuolar Degeneration.

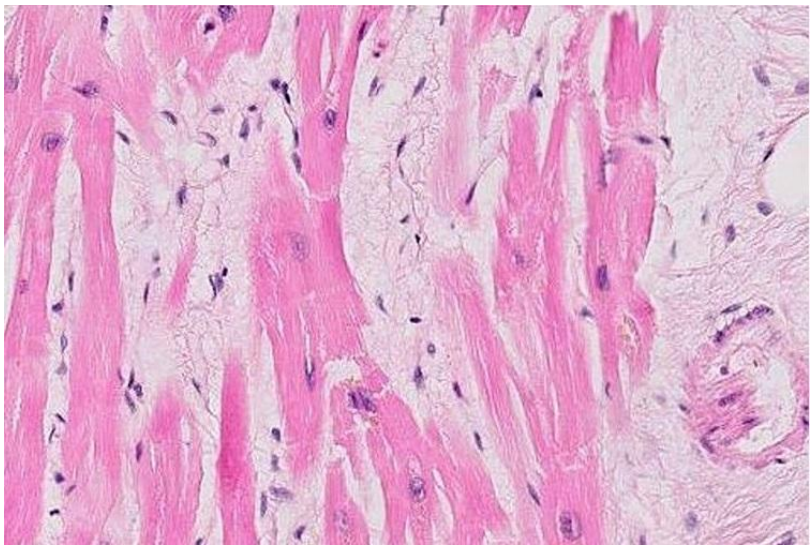


Figure 4. Interstitial Edema and Inflammatory Infiltration.

DISCUSSION

The present study demonstrated significant histological and physiological alterations in the myocardium of streptozotocin-induced diabetic rats, supporting the development of diabetic cardiomyopathy as a consequence of chronic hyperglycemia. Diabetic rats exhibited markedly elevated fasting blood glucose levels, accompanied by myocardial fiber disorganization, cytoplasmic degeneration, vascular congestion, interstitial edema, inflammatory cell infiltration, cardiomyocyte hypertrophy, and fibrosis. These findings are consistent with previous studies that identified structural remodeling and myocardial dysfunction as characteristic features of diabetic cardiomyopathy [10,11].

The observed myocardial fiber disorganization and cytoplasmic vacuolation may be attributed to hyperglycemia-induced oxidative stress and mitochondrial dysfunction. Excessive production of reactive oxygen species damages cellular proteins, lipids, and nucleic acids, resulting in cardiomyocyte degeneration and impaired contractile function [12]. Furthermore, persistent hyperglycemia promotes the formation of advanced glycation end products, which accelerate myocardial remodeling and stiffness through collagen cross-linking and extracellular matrix deposition [13].

Inflammatory cell infiltration observed in 50% of diabetic specimens supports the role of chronic low-grade inflammation in the pathogenesis of diabetic cardiomyopathy. Pro-inflammatory cytokines such as tumor necrosis factor-α and interleukin-6 contribute to myocardial injury, apoptosis, and fibrosis [14].

Similar findings have been reported in experimental diabetic models where inflammation was strongly associated with ventricular dysfunction and adverse cardiac remodeling [15].

A notable finding of this study was the significant increase in myocardial thickness and fibrotic tissue area in diabetic rats. Cardiac hypertrophy and fibrosis are recognized hallmarks of diabetic cardiomyopathy and contribute to reduced ventricular compliance and impaired cardiac performance [16]. Increased collagen deposition within the myocardial interstitium disrupts normal tissue architecture and adversely affects both systolic and diastolic function [17].

The present findings are in agreement with recent experimental and clinical studies demonstrating that chronic hyperglycemia induces progressive structural and functional deterioration of the myocardium [18]. Therefore, early glycemic control and interventions targeting oxidative stress, inflammation, and fibrosis may play an important role in preventing the progression of diabetic cardiomyopathy [19].

CONCLUSION

The present study demonstrated that streptozotocin-induced diabetes mellitus produces significant physiological and histopathological alterations in the myocardium of rats, indicative of diabetic cardiomyopathy. Diabetic rats exhibited markedly elevated fasting blood glucose levels, increased myocardial thickness, and greater fibrotic tissue deposition compared to the control group. Histological examination revealed myocardial fiber disorganization, cytoplasmic degeneration, vascular congestion, interstitial edema, inflammatory cell infiltration, cardiomyocyte hypertrophy, and fibrosis, all of which occurred with significantly greater frequency in diabetic animals.

These findings suggest that chronic hyperglycemia induces progressive myocardial remodeling through mechanisms involving cellular injury, inflammation, and extracellular matrix deposition. The significantly higher histopathological severity score observed in diabetic rats further confirms the extensive myocardial damage associated with diabetes mellitus. Collectively, the results highlight the detrimental effects of diabetes on both the structure and function of cardiac tissue and emphasize the importance of early diagnosis and effective glycemic control in preventing the development and progression of diabetic cardiomyopathy. Further studies are warranted to explore potential therapeutic strategies aimed at reducing myocardial injury and improving cardiovascular outcomes in diabetic patients.

Authors' Contribution

Concept & Design of Study: Avais Ahmad, Aliya Shabbir, Aleena Younis,

Drafting: Safiya Javed, Sana Shahzad, Ayesha Imtiaz

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Critical Review: Avais Ahmad, Aliya Shabbir, Aleena Younis,

Final Approval of Version: All authors approved the final version.

Conflict of Interest: None

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