International Journal of Bio-resource and Stress Management https://ojs.pphouse.org/index.php/IJBSM

Crossref

IJBSM June 2026, 17(6): 01-09 **Article** AR6989

Research Article *Natural Resource Management*

DOI: HTTPS://DOI.ORG/10.23910/1.2026.6989

Effect of High Fat Diet (HFD) on Progression of Cardiomyopathy and Nephropathy

Aruna B.[1], Sujith S.[1], Sanis Juliet[1], Ranjith D.[1], Pradeep M.[2], Divya P. D.[3], Adheena Xavier[1], Bindu Shree R.[1], Ananthu Vijayakrishnan[1] and Deepanjaly S.[1]

[1]Dept. of Veterinary Pharmacology and Toxicology, [2]Dept. of Veterinary Pathology, [3]Dept. of Veterinary Biochemistry, College of Veterinary and Animal Sciences, Pookode, Kerala Veterinary and Animal Sciences University, Wayanad, Kerala (673 576), India

Open Access

Corresponding sujith@kvasu.ac.in

0000-0001-5205-2986

ABSTRACT

The experiment was conducted during April, 2025 at the College of Veterinary and Animal Sciences, Pookode, to investigate the effect of a high-fat diet (HFD) on the progression of cardiomyopathy and nephropathy. Diabetes mellitus was identified as a chronic metabolic disorder characterized by persistent hyperglycemia, which contributed to severe complications such as cardiomyopathy and nephropathy. High-fat diet intake further aggravated metabolic imbalances, thereby accelerating the progression of these systemic complications. The present study evaluated cardiac and renal functions in Wistar rats fed an HFD following streptozotocin (STZ)-induced diabetes. Diabetes was induced using STZ (40 mg kg^{-1}, i.p.) in HFD-fed rats, and animals with blood glucose levels exceeding 300 mg dl^{-1} four days post-induction were considered diabetic. Diabetic animals were compared with normal rats to assess metabolic, renal, and cardiac alterations. Body weight, blood glucose, total cholesterol, triglycerides, blood urea nitrogen (BUN), creatinine, and creatine kinase-myoglobin binding (CK-MB) were assessed at baseline, pre-induction, and on days 1, 14, and 28. Diabetic rats on HFD showed persistent hyperglycemia, progressive weight loss, and severe dyslipidemia. Elevated renal markers, specifically BUN and creatinine, and increased CK-MB levels indicated the progression of nephropathy and cardiomyopathy. These results demonstrated that HFD accelerated metabolic disturbances and promoted significant target organ damage in diabetes. The findings highlighted that sustained lipid abnormalities and hyperglycemia synergistically worsened myocardial and renal injury over the experimental period

KEYWORDS: Diabetes mellitus, high-fat diet (HFD), cardiomyopathy, nephropathy, streptozotocin

***Citation* (VANCOUVER):** Aruna et al., Effect of High Fat Diet (HFD) on Progression of Cardiomyopathy and Nephropathy. *International Journal of Bio-resource and Stress Management,* 2026; 17(6), 01-09. HTTPS://DOI.ORG/10.23910/1.2026.6989.

Data Availability Statement: Legal restrictions are imposed on the public sharing of raw data. However, author have full right to transfer or share the data in raw form upon request subject to either meeting the conditions of the original consents and the original research study. Further, access of data needs to meet whether the user complies with the ethical and legal obligations as data controllers to allow for secondary use of the data outside of the original study.

Conflict of interests: The author has declared that no conflict of interest exists.

RECEIVED on 18th February 2026 RECEIVED in revised form on 05th June 2026 ACCEPTED in final form on 22nd June 2026 PUBLISHED on 29th June 2026

1. INTRODUCTION

Diabetes mellitus is a collection of metabolic diseases characterised by high blood glucose levels, or hyperglycaemia (Olefsky, 2001). This hyperglycaemia arises from a relative or total lack of insulin secretion, a resistance to the action of insulin, or both of these factors (Babu et al., 2013). According to the International Diabetes Federation, approximately 537 million adults worldwide were living with diabetes in 2021, and this number is projected to rise to 783 million by 2045, highlighting the escalating global health burden. Based on etiopathogenesis, DM is classified into Type 1 and Type 2 diabetes mellitus (Nicolle et al., 2011), type 1, which results from the immune system's destruction of the body's own insulin-producing pancreatic cells, and type 2, the more prevalent form, which is characterized by the body's resistance to insulin in conjunction with an insufficient secretory response (Skyler, 2004). Persistent hyperglycaemia results in progressive macrovascular and microvascular complications, among which diabetic cardiomyopathy and nephropathy are major contributors to diabetes-associated morbidity and mortality (Forbes and Cooper, 2013). The development of diabetic complications is mediated by several interconnected biochemical mechanisms. Chronic hyperglycaemia activates protein kinase C (PKC), enhances flux through the polyol and hexosamine biosynthetic pathways, promotes the accumulation of advanced glycation end-products (AGEs), and increases oxidative stress. These alterations converge to induce endothelial dysfunction, inflammatory signaling, and progressive organ damage (Zhang et al., 2016). Diabetes mellitus is associated with distinct microvascular alterations, including excessive extracellular matrix deposition and thickening of the capillary basement membrane, resulting in diabetic microangiopathy. Persistent hyperglycaemia, along with oxidative stress and inflammation, further contributes to the development of macrovascular complications. Additionally, microvascular injury may aggravate atherosclerotic progression through hypoxia and vasa vasorum dysfunction (Chawla et al., 2016). Advanced glycation end-products (AGEs) have been implicated in the progression of chronic kidney disease in diabetes. Their reactive precursor, methylglyoxal, has been shown to accelerate renal injury, particularly under conditions of reduced glyoxalase-1 activity. Furthermore, AGEs may aggravate diabetic nephropathy by upregulating angiotensinogen expression, thereby contributing to renal dysfunction (Parveen et al., 2021). Chronic hyperglycaemia in diabetes induces microvascular alterations, oxidative stress, inflammation, impairment of the IRS–PI3K/Akt signaling pathway leading to insulin resistance, and accumulation of advanced glycation end-products and methylglyoxal under reduced glyoxalase-1 activity, collectively accelerating renal injury, angiotensinogen expression, and the progression of diabetic nephropathy and cardiovascular complications (Guo, 2014). Consumption of a high-fat diet (HFD) plays a pivotal role in the development of Type 2 diabetes by promoting insulin resistance, dyslipidaemia, and metabolic stress (Lozano et al., 2016). The combination of a high-fat diet (HFD) and low-dose streptozotocin (STZ) induces diabetic complications in rats, characterized by micro- and macrovascular lesions, renal injury, and pathological features that resemble human diabetic nephropathy and vascular abnormalities (Rather et al., 2023). Sustained hyperglycaemia and lipid abnormalities exacerbate myocardial and renal injury, which can be evaluated through alterations in glycaemic status, lipid profile, cardiac injury markers, renal function indices, and body weight parameters. Therefore, the present study was undertaken to evaluate the effect of a high-fat diet on the progression of cardiomyopathy and nephropathy in streptozotocin-induced diabetic rats.

2. MATERIALS AND METHODS

The experiment was conducted during April, 2025 at the College of Veterinary and animal sceinces pookode to study the effect of high fat diet on the progression of cardiomyopathy and nephropathy.

2.1. Experimental animals

Twenty-four healthy adult male Wistar albino rats (≈150 g) were used in the present study. The animals were procured from an approved animal facility and housed under standard laboratory conditions with controlled temperature, relative humidity, and a 12 h light/dark cycle, with free access to standard pellet diet and water unless otherwise specified. All experimental procedures were conducted in accordance with the guidelines of the Institutional Animal Ethics Committee (IAEC), College of Veterinary and Animal Sciences, Pookode, and the study was approved under the protocol number IAEC/COVAS/PKD/25/10/2025.

2.2. Induction of type 2 diabetes mellitus

Type 2 diabetes mellitus was induced using a high-fat diet (HFD) and streptozotocin (STZ) model (Zhang et al. 2016). Rats were fed a high-fat diet for six weeks, followed by a single intraperitoneal injection of streptozotocin (STZ). Fasting blood glucose levels were measured on the fourth day after STZ injection, and rats showing blood glucose levels >300 mg dl^{-1} were considered diabetic and included in the study.

A high-fat diet (HFD) was prepared for the induction of Type 2 diabetes in rats. The diet was formulated using 55% normal pelleted feed, 29% lard, 10% casein, 5% vitamin and mineral mixture, and 1% cholesterol, yielding a total composition of 100%. The formulated HFD was designed to provide a higher fat and energy content compared with

the normal pellet diet.

Proximate analysis of both normal and high-fat diets was conducted in accordance with the guidelines of the Association of Official Analytical Chemists (AOAC). The normal pellet diet was found to contain 12.5% moisture, 17.4% crude protein, 7.5% total ash, and 4.5% ether extract. In contrast, the high-fat diet contained 7.4% moisture, 23.2% crude protein, 8.94% total ash, and 27.54% ether extract, confirming the elevated lipid content of the experimental diet.

2.3. Experimental design

Adult Wistar albino rats were randomly allocated into two experimental groups, with twelve animals in each group. The normal control group received a standard pellet diet and served as non-diabetic controls. The diabetic control group was fed a high-fat diet, and diabetes was induced by administration of streptozotocin (STZ).

To evaluate the temporal progression of diabetic cardiomyopathy and nephropathy, six rats from each group were sacrificed on day 14, and the remaining six rats on day 28 post-diabetes induction.

2.4. Sample collection

Blood samples were collected from all animals before initiation of the high-fat diet, before diabetes induction, and on days 1, 14, and 28 post-induction under aseptic conditions. Blood samples were centrifuged to obtain serum, which was stored appropriately and used for biochemical estimations.

2.5. Biochemical analysis

The following biochemical parameters were assessed using spectrophotometry with commercial kits from Aagappe Diagnostics, Kerala:

• Fasting blood glucose (mg dl^{-1})

• Serum lipid profile, including total cholesterol (mg dl^{-1}) and triglycerides (mmol l^{-1})

• Renal function markers, including blood urea nitrogen (BUN) (mg dl^{-1}) and serum creatinine (mg dl^{-1})

• Cardiac injury marker, creatine kinase-MB (CK-MB) (U/L)

2.6. Statistical analysis

Data were expressed as mean±standard error. Statistical analysis was performed using SPSS software version 24.0. Differences between groups were analyzed using appropriate statistical tests, and a value of $p<0.01$ was considered statistically significant.

3. RESULTS AND DISCUSSION

3.1. Effect of high-fat diet and STZ on blood glucose

Rats fed with high fat diet followed by streptozotocin (HFD–STZ) administration exhibited a significant ($p<0.01$) elevation in fasting blood glucose levels compared to normal control rats (Table 1 and Figure 1). In diabetic groups, blood glucose levels increased markedly by day 4 post-STZ and remained persistently elevated on day 14. In animals extended up to day 28, hyperglycaemia further progressed, indicating sustained diabetic status. Normal control rats maintained stable glucose levels throughout the experimental period. Persistent hyperglycaemia observed in HFD–STZ rats plays a central role in initiating metabolic disturbances that contribute to the development of diabetic cardiomyopathy and nephropathy, as reported by Prabhakar (2016).

Hyperglycaemia in the HFD–STZ model is attributed to the combined effects of diet-induced insulin resistance

Table 1: Effect of high-fat diet and streptozotocin in the blood glucose level of rats

Group	Before the administration of HFD	On the day of administration of STZ (Day zero)	Day 4	Day 14	Day 28
Normal animals (Group I)	88.45 ± 6.42^{aA}	90.45 ± 8.23^{aA}	94.45 ± 7.12^{aA}	89.65 ± 8.35^{aA}	92.35 ± 5.31^{aA}
Animals fed with HFD and STZ (Group II)	93.2625 ± 12.34^{aB}	139.6625 ± 14.29^{bB}	340.155 ± 39.81^{cB}	310.355 ± 21.26^{dB}	NA
Animals fed with HFD and STZ (Group II) were extended till 28th day	74.5 ± 7.67^{aC}	131.5475 ± 9.31^{bB}	362.0225 ± 29.31^{cB}	375.54 ± 57.15^{cC}	$388.02+88.12^{cB}$

Means having different superscripts differ significantly at 1% level; Alphabets a-e signifies row wise and A-C signifies column wise comparison

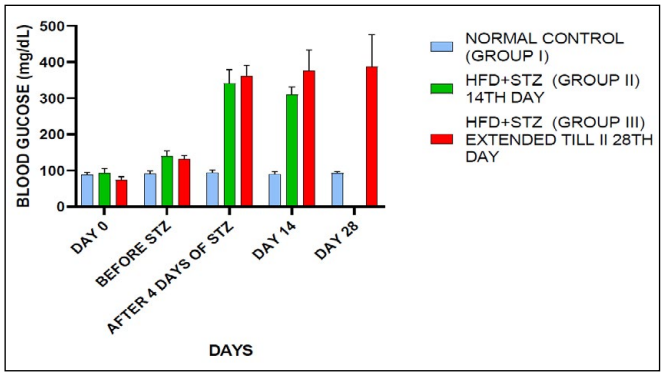

Figure 1: Effect of high-fat diet and streptozotocin on the blood glucose level of rats

and streptozotocin-mediated pancreatic β-cell injury. High-fat feeding reduces peripheral insulin sensitivity, while streptozotocin selectively impairs β-cell function, resulting in decreased insulin secretion and disturbed glucose homeostasis. This dual insult leads to sustained dysregulation of glycaemic control through impaired insulin action and altered glucose metabolism, a mechanism consistently reported in experimental models of Type 2 diabetes (Wickramasinghe et al., 2022).

Prolonged HFD causes intracellular accumulation of diacylglycerols and ceramides in the liver and muscles. These lipid metabolites trigger proinflammatory JNK and IKKβ pathways, inducing serine phosphorylation of IRS-1. This disrupts insulin signalling and blocks the translocation of GLUT-4 transporters to the cell surface, effectively preventing glucose uptake (Samuel and Shulman, 2012).

3.2. *Effect of high-fat diet and STZ on total cholesterol*

Serum total cholesterol levels were significantly (p<0.01) elevated in HFD–STZ–treated rats compared to normal controls (Table 2). A progressive increase in cholesterol concentration was observed from day zero to day 28, with the highest levels recorded in extended diabetic rats. The rise in cholesterol may be attributed to insulin resistance–induced impairment of lipid metabolism, decreased lipoprotein lipase activity, and increased hepatic cholesterol synthesis. Hypercholesterolaemia contributes to lipotoxicity and accelerates both myocardial and renal damage under diabetic conditions, supporting earlier observations reported by Tam et al. (2024).

The observed lipid metabolic dysregulation in experimental diabetes has been attributed primarily to high-fat diet–induced insulin resistance and impaired hepatic insulin signaling. Under these conditions, insulin fails to effectively suppress hepatic synthesis and secretion of very-low-density lipoproteins (VLDL), leading to elevated circulating cholesterol and triglycerides (Brito et al., 2025). Furthermore, the combined influence of high-fat feeding and streptozotocin-induced insulin deficiency disrupts lipid homeostasis, resulting in increased low-density lipoprotein (LDL) and VLDL levels along with a reduction in high-density lipoprotein (HDL) cholesterol. Such alterations contribute to the development of an atherogenic lipid profile commonly reported in untreated diabetic animal models (Wickramasinghe et al., 2022).

In the HFD+STZ model, hypercholesterolaemia occurs because the lack of effective insulin inhibits Lipoprotein Lipase (LPL) activity, preventing the clearance of cholesterol-rich lipoproteins from the blood. Simultaneously, the insulin-resistant liver fails to suppress HMG-CoA reductase, leading to continuous endogenous cholesterol synthesis despite high dietary intake. Furthermore, the conversion of cholesterol into bile acids is blocked, resulting in significant systemic accumulation of total cholesterol (Goldberg et al., 1996).

3.3. *Effect of high-fat diet and STZ on serum triglyceride concentration*

Serum triglyceride concentrations showed a significant

Table 2: Effect of high-fat diet and streptozotocin in the total cholesterol level of rats

Group	Before the administration of HFD	On the day of administration of STZ (Day zero)	Day 4	Day 14	Day 28
Normal animals (Group I)	52.1425 ± 4.28^{aA}	$56.23+4.25^{aA}$	57.18 ± 4.69^{aA}	57.23 ± 4.43^{aA}	59.85 ± 4.23^{aA}
Animals fed with HFD and STZ (Group II)	52.1425 ± 4.87^{aA}	72.83 ± 3.14^{bB}	95.38 ± 4.23^{cB}	125.57 ± 5.9^{dB}	
Animals fed with HFD and STZ (Group II) were extended till 28th day	54.65 ± 8.06^{aA}	95.19 ± 17.52^{bC}	97.88 ± 5.42^{cB}	166.63 ± 37.42^{dC}	170.015 ± 22.04^{dB}

(p<0.01) (Figure 2) and time-dependent increase in HFD–STZ–treated rats compared to normal animals. Triglyceride levels rose sharply following STZ administration and continued to increase up to day 28 in extended diabetic rats. This elevation reflects enhanced lipolysis, increased hepatic triglyceride synthesis, and reduced peripheral lipid utilization due to insulin deficiency and resistance. Elevated triglycerides are known to exacerbate oxidative stress and inflammatory responses, thereby contributing to the progression of diabetic cardiomyopathy and nephropathy. Tam et al. (2024).

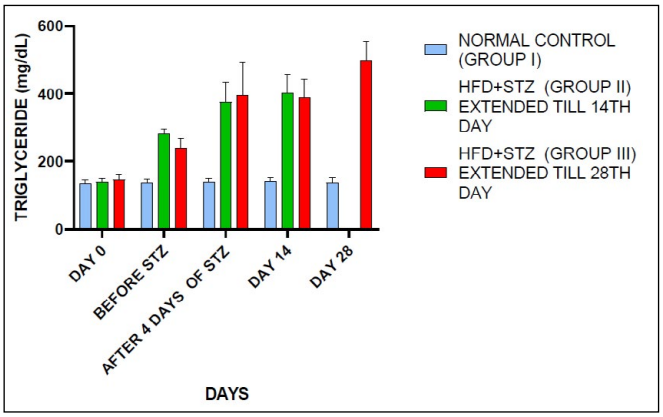

Figure 2: Effect of high-fat diet and streptozotocin in the serum triglyceride level of rats

Hypertriglyceridemia in HFD–STZ–induced diabetes is primarily attributed to insulin resistance–related disturbances in lipid metabolism. Defective insulin action impairs triglyceride clearance, enhances lipolysis in adipose tissue with increased free fatty acid flux, and stimulates hepatic triglyceride synthesis, collectively leading to elevated circulating triglyceride levels (Lewis et al., 2002). Moreover, the synergistic effect of high dietary lipid intake and streptozotocin-induced β-cell dysfunction markedly disrupts lipid homeostasis, producing a dyslipidemic profile that closely resembles the metabolic abnormalities characteristic of human Type 2 diabetes.

In the HFD+STZ-induced diabetic state, hepatic insulin resistance triggers an upregulation of Microsomal Triglyceride Transfer Protein (MTP), stimulating the over-assembly and secretion of large, triglyceride-dense VLDL particles. This process is further exacerbated by a continuous influx of free fatty acids derived from both dietary intake and accelerated adipose tissue lipolysis, providing an abundant substrate for hepatic triglyceride synthesis (Adiels et al., 2008).

3.4. *Effect of high-fat diet and STZ on blood urea nitrogen (BUN)*

Blood urea nitrogen levels were significantly (p<0.01) increased in HFD–STZ–treated rats compared to normal controls. BUN levels showed a progressive rise from day 4 onwards, with maximum values observed on day 28 in extended diabetic animals. The elevation in BUN indicates impaired renal excretory function and increased protein catabolism associated with chronic hyperglycaemia. These findings confirm the onset and progression of diabetic nephropathy, in agreement with previous reports by Hao et al. (2012).

Elevated blood urea nitrogen (BUN) levels in HFD–STZ–induced diabetes are indicative of compromised renal function and progressive nephropathic changes. Chronic hyperglycaemia promotes glomerular injury through oxidative stress and inflammatory mechanisms, leading to impaired renal filtration and reduced urea excretion. Consequently, the accumulation of nitrogenous waste products in the circulation reflects declining renal clearance, a feature commonly reported in experimental diabetic nephropathy models (Al-Qabbaa et al., 2023).

3.5. *Effect of high-fat diet and STZ on serum creatinine concentration*

Serum creatinine levels were significantly (p<0.01) elevated in diabetic rats fed with HFD and STZ (Table 3) when compared to normal animals. A gradual increase in creatinine concentration was observed from day 4 to day 28, suggesting a reduction in glomerular filtration rate due to glomerular and tubular damage. Normal control rats showed no significant changes in creatinine levels throughout the study. The observed rise in serum creatinine further substantiates the development of renal dysfunction in diabetic rats, as reported by King (2012).

Elevated serum creatinine levels in HFD–STZ–induced diabetes are indicative of impaired renal filtration and progressive nephropathic alterations. Chronic hyperglycaemia induces oxidative stress–mediated damage and structural changes in both glomerular and tubular compartments, resulting in reduced creatinine clearance and its subsequent accumulation in the circulation. Similar increases in serum creatinine have been consistently reported in experimental diabetic models, supporting its utility as a reliable biochemical marker for the progression of diabetic nephropathy and declining renal function (Tesch and Allen, 2007).

In the HFD+STZ model, persistent hyperglycemia triggers the intrarenal renin-angiotensin-aldosterone system (RAAS), causing efferent arteriolar constriction and subsequent glomerular hyperfiltration. This increased mechanical pressure eventually induces podocyte damage and basement membrane thickening, leading to glomerulosclerosis. Consequently, the reduction in functional glomerular surface area impairs the kidney's filtration capacity, resulting in the systemic accumulation of serum creatinine (Ziyadeh, 1993).

Table 3: Effect of high-fat diet and streptozotocin in the blood urea nitrogen level of rats

Group	Before the administration of HFD	On the day of administration of STZ (Day zero)	Day 4	Day 14	Day 28
Normal animals (Group I)	83.15±4.18^{aA}	85.15±3.25^{aA}	82.24±4.59^{aA}	83.43±4.49^{aA}	85.03 +3.23^{aA}
Animals fed with HFD and STZ (Group II)	84.15±4.87^{aA}	122.69±20.92^{bB}	185.48±22.23^{cB}	264.37±24.05^{dB}	
Animals fed with HFD and STZ (Group II) were extended till 28th day	88.57±7.45^{aA}	141.22±11.52^{cC}	171.505±5.57^{cB}	205.63 +10.42^{eC}	295.99 +29.51^{eB}

3.6. Effect of high-fat diet and STZ on creatine kinase–myoglobin binding (CK-MB)

Serum creatine kinase–myoglobin binding (CK-MB) levels were significantly (p<0.01) elevated in HFD–STZ–treated rats compared to normal controls (Table 4 and figure 3). CK-MB levels increased progressively with the duration of diabetes, with the highest values recorded in extended diabetic rats. Elevated CK-MB reflects myocardial cell membrane damage and leakage of cardiac enzymes into circulation, indicating the presence of diabetic cardiomyopathy. These findings are consistent with earlier studies demonstrating myocardial injury in experimental diabetic models (Youssef et al., 2022).

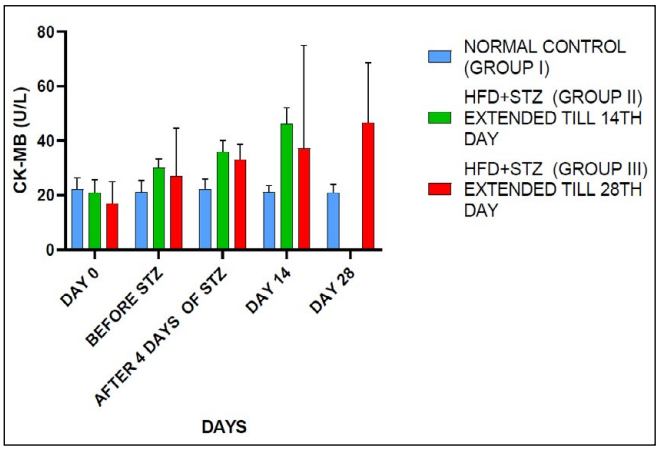

Figure 3: Effect of high-fat diet and streptozotocin on the serum creatine kinase-myoglobin binding concentration of rats

Elevated creatine kinase–MB (CK-MB) activity in HFD–STZ–induced diabetes reflects hyperglycaemia-mediated myocardial injury. Sustained hyperglycaemia enhances glucose flux into cardiomyocytes, leading to excessive generation of reactive oxygen species through mitochondrial dysfunction, increased polyol pathway activity, and accelerated formation of advanced glycation end products. The resulting oxidative stress promotes lipid peroxidation of cardiomyocyte membranes, increasing membrane permeability and facilitating the release of CK-MB into the circulation (Ansley and Wang, 2013). In parallel, activation of IKK-dependent NF-κB signaling amplifies inflammatory and profibrotic responses, contributing to cardiomyocyte apoptosis, hypertrophy, and progressive cardiac dysfunction. Such mechanisms collectively underpin the elevation of

Table 4: Effect of high-fat diet and streptozotocin in the serum creatinine concentration of rats

Group	Before the administration of HFD	On the day of administration of STZ (Day zero)	Day 4	Day 14	Day 28
Normal animals (Group I)	0.27±0.01^{aA}	0.27±0.03^{aA}	0.26±0.02^{aA}	0.27±0.01^{aA}	0.27±0.01^{aA}
Animals fed with HFD and STZ (Group II)	0.27±0.03^{aA}	0.393±0.044^{bB}	0.51±0.033^{cB}	0.64 +0.11^{cB}	
Animals fed with HFD and STZ (Group II) were extended till 28th day	0.21±0.02^{aA}	0.28±002^{aA}	0.35±0.34^{cC}	0.46 +0.06^{cC}	0.4 +0.03^{cB}

CK-MB as a sensitive biochemical indicator of diabetes-associated myocardial damage.

In the HFD+STZ model, persistent hyperglycemia promotes the formation of advanced glycation end-products (AGEs) and reactive oxygen species, leading to oxidative damage of the cardiac sarcolemma. This loss of membrane integrity allows the leakage of the intracellular CK-MB isoenzyme into the systemic circulation, serving as a definitive marker of myocardial injury and diabetic cardiomyopathy (Cai and Kang, 2003) of rats.

3.7. Effect of high-fat diet and STZ on body weight

Normal control rats exhibited a gradual increase in body weight throughout the experimental period. In contrast, HFD–STZ–treated rats (Table 5) showed an initial increase in body weight following HFD feeding, followed by a significant (p<0.01) reduction after STZ administration. Progressive weight loss was evident by day 14 and day 28, despite persistent hyperglycaemia. This reduction in body weight may be attributed to enhanced proteolysis, lipolysis, and impaired glucose utilization, reflecting systemic metabolic dysfunction associated with diabetes (Tam et al., 2024).

Body weight alterations in HFD–STZ–induced diabetes are primarily attributed to insulin deficiency–and insulin resistance–associated metabolic disturbances. Impaired insulin action promotes enhanced proteolysis and lipolysis, leading to negative energy balance and progressive weight loss despite adequate nutritional intake. Similar reductions in body weight have been consistently reported in streptozotocin-induced and HFD–STZ

diabetic models, reflecting disrupted metabolic regulation and increased catabolic activity characteristic of experimental Type 2 diabetes (Huang et al., 2024).

Consistent with the findings of Akbarzadeh et al. (2007), rats rendered diabetic with streptozotocin showed a marked decline in body weight when compared to non-diabetic controls. This reduction may be attributed to insulin deficiency–induced metabolic disturbances, leading to enhanced breakdown of proteins and lipids and subsequent loss of body mass.

In the HFD+STZ model, an initial increase in body weight during the HFD phase is followed by a significant decline post-STZ administration. This weight loss is driven by the depletion of fat and muscle stores through accelerated catabolism and the massive loss of calories and fluids through glucose-induced osmotic diuresis (Srinivasan et al., 2005).

Table 5: Effect of high-fat diet and STZ on the body weight of rats

Group	Before the administration of HFD	On the day of administration of STZ (Day zero)	Day 4	Day 14	Day 28
Normal animals (Group I)	152.5±4.28^{a}	161.5±4.25^{b}	148.23±3.69^{a}	162.48±2.43^{b}	168.32±3.21^{b}
Animals fed with HFD and STZ (Group II)	156.5±4.66^{a}	310.25±16.23^{b}	305.25±16.23^{b}	277.25±13.76^{c}	
Animals fed with HFD and STZ (Group II) were extended till 28th day	176.5±10.15^{a}	318±30^{b}	306.25±30.11^{b}	272±13.27^{c}	238.5±4.03^{d}

4. CONCLUSION

The present investigation demonstrated that high-fat diet feeding significantly aggravated metabolic derangements and accelerated the progression of cardiac and renal dysfunction in streptozotocin-induced diabetic rats. Persistent hyperglycaemia, progressive dyslipidaemia, and marked body weight reduction reflected severe metabolic imbalance. Significant elevations in blood urea nitrogen, serum creatinine, and CK-MB substantiated the development of diabetic nephropathy and cardiomyopathy. The progressive deterioration observed from day 14 to day 28 indicated time-dependent exacerbation of target organ damage under sustained hyperglycaemic conditions.

5. REFERENCE

Abdel-Rahim, E.A., Rashed, M.M., El-Hawary, Z.M., Abdelkader, M.M., Kassem, S.S., Mohamed, R.S., 2016. Anti-diabetic effect of Cichorium intybus leaves and Plantago ovata seeds in high-fat diet-streptozotocin induced diabetic rats. Journal of Food and Nutrition Research 4(5), 276–281. DOI: 10.12691/jfnr-4-5-2.

Adiels, M., Olofsson, S.O., Taskinen, M.R., Boren, J., 2008. Overproduction of very low–density lipoproteins is the hallmark of dyslipidemia in the metabolic syndrome. Arteriosclerosis, Thrombosis, and Vascular Biology 28(7), 1225–1236. DOI: https://doi.org/10.1161/atvbaha.107.160192.

Akbarzadeh, A., Norouzian, D., Mehrabi, M.R., Jamshidi, S.H., Farhangi, A., Verdi, A.A., Rad, B.L., 2007. Induction of diabetes by streptozotocin in rats. Indian Journal of Clinical Biochemistry 22(2), 60–64. DOI: https://doi.org/10.1007/bf02913315.

Al-Qabbaa, S.M., Qaboli, S.I., Alshammari, T.K., Alamin, M.A., Alrajeh, H.M., Almuthnabi, L.A., Alrasheed, N.M., 2023. Sitagliptin mitigates diabetic nephropathy in a rat model of streptozotocin-induced type 2 diabetes: possible role of PTP1B/JAK-STAT pathway. International Journal of Molecular Sciences 24(7), 6532. DOI: 10.3390/ijms24076532.

Ansley, D.M., Wang, B., 2013. Oxidative stress and myocardial injury in the diabetic heart. The Journal of Pathology 229(2), 232–241. DOI: 10.1002/path. 4113.

Babu, P.V.A., Liu, D., Gilbert, E.R., 2013. Recent advances in understanding the anti-diabetic actions of dietary flavonoids. The Journal of Nutritional Biochemistry 24, 1777–1789. DOI: 10.1016/j. jnutbio.2013.06.003.

Brito, A.K.D.S., Mendes, A.V.D.S., Timah Acha, B., Santos Oliveira, A.S.D.S., Lopes Macedo, J., Suzuki Cruzio, A., Arcanjo, D.D.R., 2025. Experimental models of type 2 diabetes mellitus induced by combining hyperlipidemic diet (HFD) and streptozotocin administration in rats: an integrative review. Biomedicines 13(5), 1158. DOI: 10.3390/ biomedicines13051158.

Cai, L., Kang, Y.J., 2003. Cell death and diabetic cardiomyopathy. Cardiovascular Toxicology 3(3), 219–228. DOI: https://doi.org/10.1385/ct:3:3:219.

Chawla, A., Chawla, R., Jaggi, S., 2016. Microvascular and macrovascular complications in diabetes mellitus: distinct or continuum? Indian Journal of Endocrinology and Metabolism 20(4), 546–551. DOI: 10.4103/2230-8210.183480.

Forbes, J.M., Cooper, M.E., 2013. Mechanisms of diabetic complications. Physiological Reviews 93, 137–188. DOI: https://doi.org/10.1152/physrev.00045.2011.

Goldberg, I.J., 1996. Lipoprotein lipase and lipolysis: central roles in lipoprotein metabolism and atherogenesis. Journal of Lipid Research, 37(4), 693–707. PMID: 8732771. DOI: https://doi.org/10.1016/S0022-2275(20)37569-6.

Guo, S., 2014. Insulin signaling, resistance, and the metabolic syndrome: insights from mouse models to disease mechanisms. The Journal of Endocrinology 220(2), T1–T23. DOI: 10.1530/JOE-13-0327.

Hao, H.H., Shao, Z.M., Tang, D.Q., Lu, Q., Chen, X., Yin, X.X., Wu, J., Chen, H., 2012. Preventive effects of rutin on the development of experimental diabetic nephropathy in rats. Life Sciences 91(19-20), 959–967. DOI: 10.1016/j.lfs.2012.09.003.

Huang, K.C., Chuang, P.Y., Yang, T.Y., Tsai, Y.H., Li, Y.Y., Chang, S.F., 2024. Diabetic rats induced using a high-fat diet and low-dose streptozotocin treatment exhibit gut microbiota dysbiosis and osteoporotic bone pathologies. Nutrients 16(8), 1220. DOI: 10.3390/ nu16081220.

International Diabetes Federation, 2021. https://www.ncbi.nlm.nih.gov/books/NBK581934/. DOI: http://dx.doi.org/10.5772.

King, A.J., 2012. The use of animal models in diabetes research. British Journal of Pharmacology 166(3), 877–894.DOI: https://doi.org/10.1111/j.1476-5381.2012.01911.x.

Lewis, G.F., Carpentier, A., Adeli, K., Giacca, A., 2002. Disordered fat storage and mobilization in the pathogenesis of insulin resistance and type 2 diabetes. Endocrine Reviews 23(2), 201–229. DOI: doi.org/10.1210/edrv.23.2.0461.

Lozano, I., Van der Werf, R., Bietiger, W., Seyfritz, E., Peronet, C., Pinget, M., Dal, S., 2016. High-fructose and high-fat diet-induced disorders in rats: impact on diabetes risk, hepatic and vascular complications. Nutrition and Metabolism 13(1), 15. DOI: 10.1186/s 12986-016-0074-1.

Nicolle, E., Souard, F., Faure, P., Boumendjel, A., 2011. Flavonoids as promising lead compounds in type 2 diabetes mellitus: molecules of interest and structure-activity relationship. Current Medicinal Chemistry 18, 2661–2672. DOI: 10.2174/092986711795933777.

Olefsky, J.M., 2001. Prospects for research in diabetes mellitus. JAMA 285(5), 628–632. DOI: 10.1001/ jama.285.5.628.

Parveen, A., Sultana, R., Lee, S.M., Kim, T.H., Kim, S.Y., 2021. Phytochemicals against anti-diabetic complications: Targeting the advanced glycation end product signaling pathway. Archives of Pharmacal Research 44(4), 378–401. https://doi.org/10.1007/ s12272-021-01323-9.

Prabhakar, P.K., 2016. Pathophysiology of secondary complications of diabetes mellitus. Pathophysiology 9(1), 32–36. Available from: https://www.researchgate.net/ publication/290455800_Pathophysiology_of_ secondary_complications_of_diabetes_mellitus.

Rather, I.A., Khan, N., Kushwah, A.S., Surampalli,

G., Kumar, M., 2023. Nephroprotective effects of honokiol in a high-fat diet-streptozotocin rat model of diabetic nephropathy. Life Sciences 320, 121543. DOI: 10.1016/j.lfs.2023.121543.

Samuel, V.T., Shulman, G.I., 2012. Mechanisms for insulin resistance: common threads and missing links. Cell 148(5), 852–871. DOI: https://doi.org/10.1016/j.cell.2012.02.017.

Skyler, J.S., 2004. Diabetes mellitus: Pathogenesis and treatment strategies. Journal of Medicinal Chemistry 47(17), 4113–4117. DOI: https://doi.org/10.1021/jm0306273.

Srinivasan, K., Viswanad, B., Asrat, L., Kaul, C.L. Ramarao, P.J.P.R., 2005. Combination of high-fat diet-fed and low-dose streptozotocin-treated rat: a model for type 2 diabetes and pharmacological screening. Pharmacological Research 52(4), 313–320. https://doi.org/10.1016/j.phrs.2005.05.004.

Tam, A.A., Altay, F.P., Demir, P., Ozdemir, D., Topaloglu, O., Ersoy, R., Cakır, B., 2024. The association between diabetic nephropathy and triglyceride/glucose index and Triglyceride/high-density lipoprotein cholesterol ratio in patients with type 2 diabetes mellitus. Journal of Clinical Medicine 13(22), 6954. DOI: https://doi.org/10.3390/jcm13226954.

Tesch, G.H., Allen, T.J., 2007. Rodent models of streptozotocin-induced diabetic nephropathy (Methods in Renal Research). Nephrology 12(3), 261–266. DOI: https://doi.org/10.1111/j.1440-1797.2007.00796.

Wickramasinghe, A.S.D., Attanayake, A.P., Kalansuriya, P., 2022. Biochemical characterization of high-fat diet-fed and low-dose streptozotocin-induced diabetic Wistar rat model. Journal of Pharmacological and Toxicological Methods 113, 107144. DOI: https://doi.org/10.1016/j.vascn.2021.107144.

Wu, T., Ding, L., Andoh, V., Zhang, J., Chen, L., 2023. The mechanism of hyperglycemia-induced renal cell injury in diabetic nephropathy disease: an update. Life 13(2), 539. DOI: doi.org/10.3390/life13020539.

Youssef, M.E., El-Azab, M.F., Abdel-Dayem, M.A., Yahya, G., Alanazi, I.S., Saber, S., 2022. Electrocardiographic and histopathological characterizations of diabetic cardiomyopathy in rats. Environmental Science and Pollution Research 29(17), 25723–25732. Available from: https://ncmrjournal.com.tr/wp-content/uploads/2025/08/ncmr-vol-2.2.2.pdf.

Zhang, Y., Wang, P., Xu, Y., Meng, X., Zhang, Y., 2016. Metabolomic analysis of biochemical changes in the plasma of high-fat diet- and streptozotocin-induced diabetic rats after treatment with isoflavone extract of *Radix Puerariae*. Evidence-Based Complementary and Alternative Medicine, 2016, 4701890. DOI: https://doi.org/10.1155/2016/4701890.

Ziyadeh, F.N., 1993. The extracellular matrix in diabetic nephropathy. American Journal of Kidney Diseases 22(5), 736–744. DOI: https://doi.org/10.1016/s0272-6386(12)80440-9.