Original Article

Experimentally-induced Diabetes and Dyslipidaemia in Rats: Biochemical Monitoring

Harikar Salih Mahmood, Nashaat Ghalib Mustafa

Department of Physiology, Biochemistry, and Pharmacology, College of Veterinary Medicine, University of Mosul, Mosul, Iraq

Abstract

Background: Diabetes mellitus as a group of metabolic disorder still be one of the most common diseases of pet animals and humans. **Aims and Objectives:** To uncover the impact interaction of both disorder on the biochemical central pathways, this project was conducted. **Materials and Methods:** Sixty-four adult male rats were utilised, and experimentally diabetes (by injection of streptozotocine) and dyslipidaemia (by high fat diet) were done. **Results:** demonstrated that diabetes and dyslipidaemia cause significant changes in lipid profile, insulin resistance and body weight parameters. The body mass index in the dyslipidaemia group (0.66 ± 0.015) has a greater value compared to other groups, followed by the control group gained (0.60 ± 0.016) then the diabetic and dyslipidaemia group (0.58 ± 0.015) and finally diabetic group (0.54 ± 0.06). Lipid profiles reveal a greater elevation of cholesterol in the diabetic and dyslipidaemia group (110 ± 13.09). Also, all treated groups have a significantly ($P \leq 0.05$) higher cholesterol level when compared with the other groups. **Conclusion:** It could be concluded that the comorbidity of diabetes and dyslipidaemia worsens most biochemical parameters and seems to be more synergistic harmful than a single disorder alone.

Keywords: Diabetes mellitus, dyslipidaemia, insulin resistance, lipid profile, rats

Introduction

Diabetes mellitus (DM) is the main metabolic disease in humans and animals (especially in pet animals)(1) unfortunately, diabetes always coexists with many other metabolic disorders of carbohydrates, proteins and lipids. DM is a chronic and progressive metabolic disorder marked by persistent high blood sugar levels, resulting from defect with insulin secretion, its action or both (2). DM is mainly classified into three types (3,4): Type 1 DM (IDDM), Type 2 diabetes and gestational diabetes. Type 1 diabetes, also referred to as insulin-dependent DM, occurs when the body fail to produce insulin. Type 2 DM (T2DM), also known as non-insulin-dependent DM, is caused by insulin resistance, which occurs when cells do not effectively utilise insulin, with or without a deficiency of insulin (5,6). The third main type of diabetes is gestational diabetes, which happens when a female without a prior history of diabetes experiences high blood glucose levels during her pregnancy. This condition may increase the risk of developing T2DM later on (4). While insulin resistance is typically associated with type 2 diabetes, studies have also indicated the presence of insulin resistance in type 1 diabetes in certain circumstances (7). Additionally, diabetes is often associated with a condition known as diabetic dyslipidaemia, which is characterised by increased serum levels of total serum cholesterol (TC), triacylglycerol and low-density lipoproteins (LDLs), coupled with a decrease in high-density lipoprotein (HDL) cholesterol (8). A typical diabetic dyslipidaemia is characterised by low levels of HDL cholesterol (HDL-c) and high triacylglycerol (TGs). This condition is often accompanied by mildly elevated or even normal levels of LDL cholesterol (LDL-c). The moderate increase in LDL is attributed to the presence of atherogenic small dense LDL particles. Common risk factors for dyslipidaemia include genetic predisposition, obesity, physical inactivity, alcohol abuse and poorly controlled

Access this article online

Quick Response Code:

Website: https://journals.lww.com/ajvs

DOI: 10.4103/AJVS.AJVS_16_25

Address for correspondence: Prof. Nashaat Ghalib Mustafa, Department of Physiology, Biochemistry, and Pharmacology, College of Veterinary Medicine, University of Mosul, Mosul, Iraq.
E-mail: nashaat74@uomsul.edu.iq

How to cite this article: Mahmood HS, Mustafa NG. Experimentally-induced diabetes and dyslipidaemia in rats: Biochemical monitoring. Al-Anbar J Vet Sci 2026;19:33-7.

Received: 01-08-2025, **Revised:** 04-03-2026,
Accepted: 09-03-2026, **Published:** 31-07-2026

blood glucose levels (9). Configurations of dyslipidaemia in DM and the principal risk factors have been defined in many reports (10). Atherosclerosis, cardiovascular disease, stroke and hypertension are the leading causes of increasing mortality rates among patients with DM (11). Dyslipidaemia, which refers to the imbalance of normal pattern of plasma lipids, is characterised by elevated TC and TG levels. It is a key component of metabolic syndrome and serves as a significant risk factor for the development of atheroma, heart disease and strokes (12). Dyslipidaemia abnormalities can be quantitative, qualitative or both. Quantitatively, it is characterised by elevated levels of TC, LDL-c and TGs, along with decreased levels of HDL-c. These changes may occur individually or in various combinations. Qualitatively, dyslipidaemia involves changes in the composition of LDL-c, which may include the presence of small, dense LDL-c particles, an increase in TG content or heightened electronegativity of LDL-c (13). Dyslipidaemia can be caused by various factors, including genetic, secondary and environmental causes (14). Secondary dyslipidaemia can be caused by diabetes, endocrine disorders, nephrotic syndrome, renal failure, medication, hypothyroidism, alcohol, unhealthy diet and metabolic disorders (12). Inherited factors, diseases of the thyroid and kidneys, and lack of activity can also contribute to dyslipidaemia (15).

Materials and Methods

Laboratory animals

This study involved sixty-four adult male rats aged between 2 and 3 months and weighing 200–240 g. All experimental procedures were conducted in accordance with the guidelines for the care and use of laboratory animals set by the National Institute of Health (16) and the laboratory animal care committee of the College of Veterinary Medicine, University of Mosul, approved these procedures. The rats were maintained under appropriate environmental conditions, including a temperature of 22°C ± 2°C, suitable humidity levels and a 12-h light/dark cycle (14,17,18).

Study approval

This study obtained approval from the Ethics Committee of the Institutional Animal Care Committee at the College of Veterinary Medicine, University of Mosul, Iraq, under certification number UM.VET.2024.009.

Animal groups

Animals are divided into the following groups:

Control group (group A)

The control group was composed of fifteen adult male rats that were given a standard diet for 45 days without the use of any additional chemicals.

Dyslipidaemia group (group B)

The dyslipidaemia group consisted of fifteen adult male rats that were fed a high-fat diet (HFD)(14,19) for 45 days, without the introduction of other chemicals.

Diabetic and dyslipidaemia group or mixed group (group C)

The Diabetic and Dyslipidaemia group was composed of 17 adult male rats that received an HFD (14,19) for 45 days in conjunction with a streptozotocin (STZ) injection at a single dose of 50 mg/kg via intraperitoneal (IP) administration (20,21). Only 8 rats out of 34 rats injected with STZ from groups C and D required a second dose of STZ.

Diabetic group (group D)

The diabetic group was comprised of seventeen adult male rats that were given a standard diet for 45 days and received an STZ at a dose of 50 mg/kg (20,21) single dose of STZ was injected via IP administration.

Streptozotocin

STZ is the most well-known diabetogenic chemical (22) that is commonly employed in experimental animals for making animal models of diabetes (23).

High-fat diet

The HFD was used to induce dyslipidaemia in groups B and C. HFD was prepared with 1.5% cholesterol, 3% olive oil and 17% butter added to the standard diet (14,19), and it was given to rats in groups B and C for a duration of 45 days.

Body measurement

Regarding body weight, an electronic weighing scale with an accuracy of 0.01 g was used, while body length and abdominal circumference were measured by a scale tape at the beginning and end (45 days later) of the experiment. Body length measurement was taken from the nose to the origin of the tail (24). Abdominal circumference was determined about the anterior region of the abdomen. Body weight gain was calculated from values of initial and final weight.

Body mass index

Body mass index (BMI) was found as BMI = body weight (g)/ body length^2 (cm^2)(25,26).

Biochemical tests

Blood was collected from the retro-ocular vein of each animal using a heparinised capillary tube. The collected blood was then centrifuged at 3000 × g for 15 min to separate the serum. The serum was subsequently stored at −20°C for biochemical analysis. Serum insulin levels were measured using a sandwich ELISA kit (Ideal, China) specifically designed for rats, with readings taken at 450 nm using a microtiter reader (Biotek, USA). Serum glucose levels were determined using an enzymatic method (oxidase-peroxidase) with a kit (Giesse, Italy), and the concentration was measured at 505 nm using a chemistry analyser (Smart 120, USA).

Serum lipid profile

Total serum cholesterol (TC), triacylglycerol (TG), HDL, LDL-C and very LDL-C were measured using an enzymatic colorimetric method with a kit from Giesse, (Italy). The

concentrations were determined at a wavelength of 500 nm using a Smart 120 chemistry analyser from the USA.

Homeostatic model assessment for insulin resistance

Insulin resistance was evaluated by Homeostatic Model Assessment for Insulin Resistance (HOMA-IR)(17,27) as follows:

- HOMA-IR = Fasting insulin (µU/ml) × Fasting glucose (mmol/L)/22.5.

The quantitative insulin-sensitivity check index

Insulin resistance was evaluated by the quantitative insulin-sensitivity check index (QUICKI)(28) as follows:

- QUICKI = 1/(log fasting insulin [µU/ml] +log fasting glucose [mmol/L]).

Statistical analysis

The results are presented as means ± standard deviation (SD). The values were analysed using a one-way analysis of variance (ANOVA). Differences were considered significant when the *P* value was < 0.05. The analysis was conducted using SigmaPlot, Systat Software Inc., San Jose, CA, USA (29).

Results and Discussion

DM was successfully induced in albino rats using STZ. The induction process directly impacts the beta cells of the islets of Langerhans (10). Experimentally induced dyslipidaemia in laboratory animals, especially rats, is commonly achieved both through the use of transgenic animals or by feeding them an HFD. In this way, we can achieve a comprehensive understanding of dyslipidaemia's pathophysiology. Dyslipidaemia is characterised by an imbalance in cholesterol levels (30). An elevated TC level is one of the critical factors contributing to dyslipidaemia. Cholesterol homeostasis relies on the balance between the absorption, synthesis and excretion pathways (31).

As shown in Table 1, all experimental groups gained weight during the study period; however, the dyslipidaemia group exhibited a significantly greater increase in body weight (95 ± 4.7 g) than the other groups the control group gained (71.58 ± 5.3), followed by the diabetic and dyslipidaemia group (44.54 ± 2.9). In contrast, the diabetic group lost weight (−16.2 ± 1.6). In the same manner, the BMI in the dyslipidaemia group (0.66 ± 0.015) has a greater value compared to other groups, followed by the control group gained (0.60 ± 0.016) then the diabetic and dyslipidaemia group (0.58 ± 0.015) and finally diabetic group (0.54 ± 0.06). These changes mainly due to excessive energy consumed (as a high fat diet) which converted into adipose tissue positioned around internal organs and in between the tissues (14) and these results agree with many similar works (17,18,20). HFDs are known to disrupt lipid metabolism, leading to dyslipidaemia. Studies have shown that rats fed with HFDs exhibit significant increases in TC, TGs and LDL-C, along with a decrease in HDL-C(32,33). The administration of STZ significantly reduces body weight in rats because it destroys pancreatic beta cells, resulting in insulin deficiency and hyperglycaemia. This metabolic disruption forces the body to break down fat and muscle for energy, ultimately leading to weight loss (34).

Table 1: Body physiological parameters

Groups	Body weight (g)	Weight change (g)	Length (cm)	BMI	Abdominal circumference (cm)
Control	290.40±11.77^{b}	71.58±5.3^{b}	21.93±0.84^{b}	0.60±0.016^{b}	17.42±0.997^{b}
Dyslipidemia	321.38±8.84^{a}	95±4.7^{a}	22.03±0.48^{a}	0.66±0.015^{a}	17.933±0.799^{a}
Diabetic and Dyslipidemia	279.77±8.53^{c}	44.54±2.9^{c}	21.96±1.03^{c}	0.58±0.015^{c}	17.23±1.129^{c}
Diabetic	213.13±11.19^{d}	-16.2±1.6^{d}	19.85±1.16^{d}	0.54±0.06^{d}	15.600±1.41^{d}

Each value represents mean±S.D, *n*=15. Different letters within each column mean a significant difference between groups ($P \leq 0.05$)

Table 2: Biochemical Parameters of control and treated groups

Groups	Serum glucose mg/dl	Insulin pmol/dl	HOMA-IR
Control	112.12±15.60^{d}	45.19±4.58^{a}	1.8±0.04^{d}
Dyslipidemia	131.64±6.22^{c}	41.49±3.34^{b}	1.94±0.04^{c}
Diabetic and Dyslipidemia	290±14.77^{b}	30.74±3.97^{d}	3.14±0.12^{b}
Diabetic	460±12.21^{a}	31.80±3.29^{c}	4.97±0.23^{a}

Each value represents mean±S.D, *n*=15. Different letters within each column mean a significant difference between groups ($P \leq 0.05$)

Table 3: Lipid profile of control and treated groups

Groups	TC (mg/dl)	TG (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)
Control	55.64±12.45^{d}	61.08±11.85^{d}	51±5.861^{a}	17.08±2.53^{c}	12.22±1.5^{d}
Dyslipidemia	80.55±8.62^{b}	120.1±11.88^{b}	41.667±4.419^{c}	23.67±3.56^{b}	24.02±2.954^{b}
Diabetic and Dyslipidemia	110±13.09^{a}	146±18.74^{a}	48.1±10.318^{b}	36±10.21^{a}	29.4±5.712^{a}
Diabetic	64.3±11.59^{c}	74.6±8.13^{c}	36.4±5.147^{d}	14.5±1.72^{d}	14.92±1.512^{c}

Each value represents mean±S.D, *n*=15. Different letters within each column mean a significant difference between groups ($P \leq 0.05$)

As shown in Table 2, the diabetic group exhibited the highest serum glucose level (460 ± 12.21 mg/dL), which was markedly higher than those of the diabetic and dyslipidaemia group (290 ± 14.77 mg/dL), dyslipidaemia group (131.64 ± 6.22 mg/dL), and control group (112.12 ± 15.60 mg/dL). While insulin in the control group (45.19 ± 4.58) has the highest value compared to other groups, followed by the dyslipidaemia group (41.49 ± 3.34), then the diabetic group (31.80 ± 3.29) and finally, the diabetic and dyslipidaemia group (30.74 ± 3.97). Hence, it is clear that experimentally induced diabetes (like other types) causes hyperglycaemia due to beta cell damage (here by streptozotocin) that results in partial or complete insulin loss (35), in addition it seems that dyslipidaemia deteriorates the condition (17).

Lipid profiles [Table 3] reveal a greater elevation of cholesterol in the diabetic and dyslipidaemia group (110 ± 13.09). Furthermore, all treated groups have a significantly ($P \leq 0.05$) higher cholesterol level when compared with the other groups. In the same manner, serum triacylglycerol, LDL and VLDL are greater in a diabetic and dyslipidaemia group. While HDL (36.4 ± 5.147) is the lowest in the diabetic group compared to the other groups. These outcomes agree with (17,18); in addition, dyslipidaemia induction was successful by high fat diet in rats through 45 days of experiments. Elevated levels of lipid profile with HDL reduction confirm that, and these state were more obvious in the diabetic and dyslipidaemia group, which may be due to the synergistic deteriorated impact of diabetes and dyslipidaemia (36). HFD leads to increased body weight and lipid accumulation, which elevates serum TGs, TC, LDL and VLDL levels while reducing HDL levels (37). While STZ-induced diabetes increases TC, TGs, LDL and VLDL cholesterol levels. This occurs due to insulin deficiency, which disrupts lipid metabolism, leading to heightened lipolysis and increased hepatic lipid synthesis (38).

Conclusion

Successful DM has been developed experimentally in adult male rats by the administration of 50 mg/kg of STZ intraperitoneally. While experimental induction of dyslipidaemia in male adult rats was acceptable, through a HFD for 45 days, also the comorbidity of diabetes and dyslipidaemia worsens most biochemical parameters and seems to be more synergistic harmful than a single disorder alone.

Acknowledgement

The authors are grateful to the College of Veterinary Medicine, University of Mosul, for providing non-financial support for this project.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Kee OT, Harun H, Mustafa N, Abdul Murad NA, Chin SF, Jaafar R, *et al*. Cardiovascular complications in a diabetes prediction model using machine learning: A systematic review. Cardiovasc Diabetol 2023;22:13.
2. Yameny AA. Diabetes mellitus overview 2024. J Biosci Appl Res 2024;10:641-5.
3. Dilworth L, Facey A, Omoruyi F. Diabetes mellitus and its metabolic complications: The role of adipose tissues. Int J Mol Sci 2021;22:7644.
4. Chaudhari YS, Bhujbal SS, Walunj VA, Bhor NS, Vyavhare RD. 7. Diabetes mellitus: A review. Int J Adv Res Sci Commun Technol 2023;3:1.
5. Holt RI, DeVries JH, Hess-Fischl A, Hirsch IB, Kirkman MS, Klupa T, *et al*. The management of type 1 diabetes in adults. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care 2021;44:2589-625.
6. Pashayeva SR, Gasimova FN, Mirzazade V. Insulin secretion and insulin resistance in type 2 diabetes mellitus. The Med & Sci 2024;1:14-21.
7. Vladu M, Clenciu D, Efrem IC, Forțofoiu MC, Amzolini A, Micu ST, *et al*. Insulin resistance and chronic kidney disease in patients with type 1 diabetes mellitus. J Nutr Metab 2017:2017:6425359. [doi: 10.1155/2017/6425359]
8. Laios K, Karamanou M, Saridaki Z, Androutsos G. Aretaeus of Cappadocia and the first description of diabetes. Hormones (Athens) 2012;11:109-13.
9. Kalra S, Raizada N. Dyslipidemia in diabetes. Indian Heart J 2024;76 Suppl 1:S80-2.
10. O'Rahilly S, Farooqi IS. Obesity, diabetes mellitus, and metabolic syndrome. In: Loscalzo J, editor. Harrison's Principles of Internal Medicine. 21st ed. New York, NY: McGraw-Hill Co. Inc.; 2022. p. 3080-156.
11. Mansurah A. Effect of Peristrophe bicalyculata on lipid profile of P-407-induced hyperlipidemic Wistar rats. J Med Plants Res 2011;5:490-4.
12. Bethell HJ, Brodie D. Dyslipidemia. In: CABI; 2023. p. 61-3. Exercise: A Scientific and Clinical Overview. [doi: 10.1079/9781800621855.0012].
13. Oguejiofor OC, Onwukwe CH, Odenigbo CU. Dyslipidemia in Nigeria: Prevalence and pattern. Ann Afr Med 2012;11:197-202.
14. Hussein AA, Mustafa NG. Impact of a high-fat diet on dyslipidemia and gene expression of low density lipoprotein receptors in male rats. Iraqi J Vet Sci 2024;38:133-8.
15. Merlo G, Berra K. (Eds). Lifestyle Nursing (1st ed.) CRC Press. 2022. [doi: 10.1201/9781003178330].
16. Institute of Laboratory Animal Resources (US), Committee on Care and Use of Laboratory Animals. Guide for the Care and Use of Laboratory Animals. No. 86. Bethesda (MD): US Department of Health and Human Services, Public Health Service, National Institutes of Health; 1986.
17. Mustafa NG, Hasan MK. Biochemical investigation of an experimentally induced metabolic syndrome in rats. Indian J Anim Res 2020;54:168-72.
18. Salih SS, Al-Khashab EM. Role of rosuvastatin in bone metabolism of ovariectomized adult rats. Iraqi J Vet Sci 2023;37:267-73.
19. Udomkasemsab A, Prangthip P. High fat diet for induced dyslipidemia and cardiac pathological alterations in Wistar rats compared to Sprague Dawley rats. Clin Investig Arterioscler 2019;31:56-62.
20. Ali MA, Mustafa NG. A comparative histopathological study of pancreas, intestine, and liver of experimentally induced diabetes in rats. Iraqi J Vet Sci 2023;37:971-8.
21. Sharma M, Chan HK, Lavilla CA Jr., Uy MM, Froemming GR, Okechukwu PN. Induction of a single dose of streptozotocin (50 mg) in rat model causes insulin resistance with type 2 diabetes mellitus. Fundam Clin Pharmacol 2023;37:769-78.
22. Ghasemi A, Khalifi S, Jedi S. Streptozotocin-nicotinamide-induced rat model of type 2 diabetes (review). Acta Physiol Hung 2014;101:408-20.
23. Samuel RO, Gomes-Filho JE, Dezan-Júnior E, Cintra LT. Streptozotocin-induced rodent models of diabetes: Protocol comparisons. In: Elizabeth GL, editor. Streptozotocin: Uses, Mechanism of Action and Side Effects. New York: Nova Science Publishers; 2014. p. 61-80.
24. Poudyal H, Campbell F, Brown L. Olive leaf extract attenuates cardiac,

hepatic, and metabolic changes in high carbohydrate-, high fat-fed rats. J Nutr 2010;140:946-53.
25. Novelli EL, Diniz YS, Galhardi CM, Ebaid GM, Rodrigues HG, Mani F, *et al.* Anthropometrical parameters and markers of obesity in rats. Lab Anim 2007;41:111-9.
26. Kochar GK. Impact of diet regime at naturopathy centers on the nutritional status of non insulin dependent diabetes mellitus (NIDDM) patients. Asian Journal of Dairy and Food Research. 2014;33:62-6.
27. Haffner SM. Coronary heart disease in patients with diabetes. N Engl J Med 2000;342:1040-2.
28. Perseghin G, Caumo A, Caloni M, Testolin G, Luzi L. Incorporation of the fasting plasma FFA concentration into QUICKI improves its association with insulin sensitivity in nonobese individuals. J Clin Endocrinol Metab 2001;86:4776-81.
29. Sweet SA, Grace-Martin KA. Data Analysis with SPSS. A First Course in Applied Statistics. 4th ed. USA: Pearson Pub Ltd; 2011.
30. Al-Safo AA, AlDulaimi LH. Effect of orlistat and aquatic extract of *Rosmarinus officinalis* leaves in histopathological changes in kidney of albino rat. Iraqi J Vet Sci 2022;36:393-400.
31. Jasim RF, Allwsh TA. Effect of plasma isolated orexin-A on the regulation of metabolites in male rats. Iraqi J Vet Sci 2021;35:451-7.
32. Nasution LS, Mustika AA, Andriyanto A. The effects of high fat diets on body weight and lipid profile changes of Sprague-Dawley rats. Bul Farmatera 2022;7:51.
33. Ramalho L, da Jornada MN, Antunes LC, Hidalgo MP. Metabolic disturbances due to a high-fat diet in a non-insulin-resistant animal model. Nutr Diabetes 2017;7:e245.
34. Scridon A, Perian M, Mărginean A, Fisca C, Vantu A, Ghertescu D, *et al*. Wistar rats with long-term streptozotocin-induced type 1 diabetes mellitus replicate the most relevant clinical, biochemical, and hematologic features of human diabetes. Rev Rom Med Lab Sciendo 2015;23:263-74.
35. Syed RU, Moni SS, Hussein W, Alhaidan TM, Abumilha SM, Alnahdi LK, *et al.* Effect of cubebin against streptozotocin-induced diabetic nephropathy rats via inhibition TNF-α/NF-κB/TGF-β: *In vivo* and *in silico* study. Sci Rep 2025;15:4369.
36. But VM, Rus V, Ilyés T, Gherman ML, Stănescu IC, Bolboacă SD, *et al*. Therapeutic effects of lavender oil on streptozotocin-induced diabetes mellitus and experimental thrombosis. Antioxidants (Basel) 2025;14:166.
37. Xia ZH, Chen WB, Shi L, Jiang X, Li K, Wang YX, *et al.* The underlying mechanisms of curcumin inhibition of hyperglycemia and hyperlipidemia in rats fed a high-fat diet combined with STZ treatment. Molecules 2020;25:271.
38. Komolafe OA, Adeyemi DO, Adewole SO, Obuotor EM. Streptozotocin-induced diabetes alters the serum lipid profiles of adult Wistar rats. Internet Journal of Thoracic and Cardiovascular Surgery 2008;7.