

Diabetogenic Effect of Diet-Induced Obesity among Male Wistar Rats

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How to cite this paper: Kwarteng, J.K., Laing, E.F., Obirikorang, C. and Akollor, M.E. (2025) Diabetogenic Effect of Diet-Induced Obesity among Male Wistar Rats. *Open Journal of Endocrine and Metabolic Diseases*, 15, 265-278.
<https://doi.org/10.4236/ojemd.2025.1511023>

Received: September 10, 2025

Accepted: November 23, 2025

Published: November 26, 2025

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Abstract

Background: Globally, obesity has become an epidemic. It has been implicated in chronic non-communicable diseases such as diabetes. The risk of diabetes among the obese population has been conjectured based on limited data. The aim of this study was therefore to evaluate the outcome of various diabetogenic indices among diet-induced obese male Wistar rats. **Method:** Male Wistar rats were randomly put into two groups and fed a high-fat diet (HFD) and normal rat chow (NFD) for ten (10) weeks ad libitum. Zoometric, morphometric, and serum biochemical measurements were made during and after the dietary treatment. Student t-test, one-way ANOVA, the Pearson correlation, and logistic regression analysis were used to evaluate the association between biochemical indices, BMI, and diabetes among the experimental animal population after the dietary treatment. **Results:** The study revealed significant weight gain (83 ± 18.4 , $p < 0.0001$) and marked morphometric changes characterized by increased weight of kidney (1.17 ± 0.08 , $p < 0.01$), liver (8.57 ± 3.04 , $p < 0.01$) pancreas (1.15 ± 0.045 , $p = 0.027$) and abdominal fat (5.2 ± 1.40 , $p < 0.0001$) among most (>80%) of the animal population rationed on the HFD. There was hyperglycemia (5.5 ± 0.69 , $p = 0.028$), hyperinsulinemia (11.29 ± 3.27 , $p = 0.043$), and dyslipidemia characterized by elevated triglyceride (1.50 ± 0.83 , $p < 0.001$) and total cholesterol (4.68 ± 1.70 , $p < 0.035$). On Pearson correlation and logistic regression analysis, elevated BMI correlated positively with HOMA-IR (OR: 25.0; 95% CI: 1.8 - 346.7; $p < 0.0001$) and negatively with HOMA-S (OR: 0.89; 95% CI: 0.047 - 16.66; $p < 0.001$) and HOMA-B (OR: 1.0; 95% CI: 0.156 - 6.42; $p < 0.05$). **Conclusion:** Obesity is a strong risk factor for type 2 diabetes mellitus.

Keywords

Obesity, Hyperglycemia, Diabetes, Insulin Resistance, High Fat Diet

1. Introduction

Data from global population studies present obesity as a major epidemic of the 21st century spreading across developed, emerging, and underdeveloped countries [1] [2]. Reports from the Global Burden of Disease study rank obesity as the 5th leading cause of death—accounting for the death of ~4.7 million (8% of global deaths) in 2017 [3]. This is a marked increase from 4.5% in 1990. The risk of obesity is predicted to rise globally owing to increased global wealth and the availability of processed and high-calorie foods, which are affordable [4] [5]. This proposition is corroborated by observations of increased prevalence of obesity and overweight in lower-middle-income countries in West Africa, including Ghana [6]-[10]. Several risk factors, such as gentrification exposure, age, gender, genetic predisposition, ethnicity, smoking, alcohol consumption, sedentariness, educational level, income, etc., have all been implicated in the cross-links between diabetes and obesity [11]-[15]. In one simulated population-wide study, by adjusting for gender and lifestyle, Nianogo and Arah (2022) reported an increased risk of obesity and T2DM (81%) among adults (18 - 65 years) compared with a relatively lower risk of 31% among children (2 - 17 years) [16] [17]. Even among children, Ganle *et al.* reported an increased prevalence of obesity with aging. In a cross-sectional study among randomly sampled school children in Ghana, they observed that children aged 11-16 years had six times more risk of becoming obese compared with those in the 5-10 years cohort [10]. In addition, they reported a higher incidence of overweight and obesity among female adolescents than their male counterparts [10].

Pathophysiologically, obesity is a disorder resulting from excessive fat storage in body tissues [18] [19]. It is characterized by elevated body-mass-index (BMI) (>30 kg/m²) in adults, poor quality of life [6], shortened lifespan [6], increased hospitalizations and costs of hospitalizations [7], increased risk to communicable [18] [19] and non-communicable diseases including COVID-19 [8], cancers, coronary artery disease, kidney disease, asthma, stroke, diabetes, decreased reproductive fecundity, among others [8] [18] [20]-[22]. This has been reported to be due to dysregulation of the plasma levels of pro-inflammatory adipokines such as interleukin (IL)-6, tumor necrosis factor (TNF)- α , C-reactive protein (CRP), IL-18, resistin, and visfatin [23] [24] due to increased adipogenesis in obesity. These factors induce oxidative stress, endothelial dysfunction, chronic inflammation, and increased risk of vascular degenerative diseases such as atherosclerosis, myocardial infarction, and hypertension [24]-[28]. Obesity can be categorized as class 1 (low risk) obesity (BMI of 30 to <35), class 2 (moderate risk) obesity (BMI of 35 to <40), and class 3 (high risk) or morbid obesity (BMI of >40) [29]. Prolonged oxidative stress and chronic inflammation due to pancreatic lipotoxicity observed in high-risk and morbid obesity induce mitochondrial damage, endoplasmic reticulum (ER) stress, and beta-cell degeneration, resulting in insulin insufficiency, dysregulated glucose homeostasis, and increased risk of type-2 diabetes [26] [27].

To deal with this emerging pandemic of obesity, there is an urgent need for the development of novel, potent, and effective treatments. This can be achieved by the use of appropriate animal models—human and non-human primates. Diet-induced obesity (DIO) in animal models has the advantages of being cost-effective, polygenic, as in most human obese conditions, and requiring a relatively short time to achieve [30]-[32]. In this study, we induced obesity in male Wistar rats using a high-fat diet (HFD) and measured how this influenced the diabetogenic indices in the rats. This would help us predict the probable pathophysiological cross-link between obesity and diabetes.

2. Materials and Methods

High-Fat Diet Preparation

The high-fat diet (HFD) was formulated by mixing soya-bean oil and melted pork tallow with commercial rat chow at room temperature to provide 31.25% of the total energy from fat. The mixture was stirred to produce dispersed semi-solid pellets and used for feeding animals of the HFD group.

Animal Care and Ethical Considerations

In all, forty (40) eight-week-old male Wistar rats (180 g ± 15 g) obtained from the Department of Animal Science, Faculty of Agriculture and Natural Resources, Kwame Nkrumah University of Science & Technology (KNUST), were randomly distributed into two equal-sized groups (n = 20). The test group was fed a HFD ad libitum, while the control group was fed a normal rat chow (NFD). The rats were housed in metal cages (five animals per cage) and were maintained at 28°C ± 2°C under a cycle of 12 hours of light and 12 hours of darkness, being allowed free access to food and water. The animals were housed and kept under conditions in accordance with the National Institute of Health Guidelines for the care of Laboratory Animals (NIH) (Department of Health Service Publication No. 83-23, revised 1985). All attempts were made to reduce suffering and death among animals used for the study. The dietary treatment lasted for 10 weeks, after which anesthesia was induced in animals following intraperitoneal injection of 0.5 ml of 45 mg/kg BW of pentobarbitone (TCI Ltd, Chou-ku, Tokyo, Japan). Blood and tissue samples were taken for further analysis.

Zoometric Measurements

During the period of dietary treatment, body weight, nose-anal length, body mass index (BMI), changes in weight, and adiposity index were measured weekly. Body weight of rats was measured to the nearest 0.01 g using a digital scale (Shanghai Huachao Industrial Co. Ltd., Shanghai, China), and naso-anal length (to the nearest 0.1cm) using a plastic centimeter ruler (Suzhou Chaosheng Stationery Co. Ltd., Anhui, China). The BMI and adiposity index were determined by calculation from the formula [32]:

$$\text{BMI} = \frac{\text{mass of rat (kg)}}{(\text{naso - anal length})^2} \quad \text{kg/m}^2$$

$$\text{Adiposity Index} = \frac{\sqrt[3]{\text{Body mass}}}{\text{naso - anal length}} \text{ cm/g}^3$$

Sacrifice

Before the anesthesia, the final body weight of animals in each group was recorded. Anesthesia was achieved by intraperitoneal injection of 1 ml (40 mg/kg body weight) of pentobarbital (Taj Pharmaceutical Ltd., Mumbai, India). About 5 ml of blood was collected by cardiopuncture using disposable syringes (Changzhou Standard Medical Devices Co., Xinbei, Changzhou, China) into sterile serum separator tubes (Becton, Dickinson and Company, New Jersey, US). The samples were made to stand for 1 hr to clot, after which they were centrifuged (Life Technologies Ltd., Paisley PA4 9RF, UK) at 3000 g for 5 minutes, and the serum was aliquoted into clean Eppendorf tubes and stored at -80°C to be used for the various biochemical assays.

3. Biochemical Assays

Fasting Blood Glucose, Random Blood Glucose, and Oral Glucose Tolerance

Having fasted for 10 - 12 hrs overnight, the fasting blood glucose (FBG) was determined using a commercially available OneTouch® Glucometer device and its test strips (Lifescan, PA 19355, USA). Using the prick, a puncture was made in the tail capillary, and the blood drop was stained onto a strip inserted into the OneTouch Select glucometer device. The reading on the glucometer was noted. This was repeated for each animal, and the average values were noted for the analysis.

The random blood glucose (RBG) was determined on ordinary days when the animals were not fasting. Just as with FBG described above, the tails of the animals were punctured, and the capillary blood drop was stained onto a strip inserted into the OneTouch® Select glucometer device.

Serum Lipid Profile

The serum total cholesterol (TC), high density lipoprotein (HDL), and triglyceride (TG) levels were measured by semi-automated technique using commercially available reagents (Fortress Diagnostics®, Antrim, N. Ireland) and KENZA Max BioChemisTry (Biolabo Diagnostics, Lyon, France). The serum LDL-C, VLDL-C, and HDL-C/LDL-C ratio were determined by calculation, respectively, as follows:

$$\text{LDL} = \text{TC} - \text{HDL}(0.2 \times \text{TG}) \quad (1)$$

$$\text{VLDL} = \text{TG}/5 \quad (2)$$

NB: Equations (1) and (2) are used when triglyceride is measured in mg/dl.

Fasting Insulin Levels

The serum fasting insulin levels were assayed by enzyme-linked immunosorbent assay (ELISA) technique using a commercially available kit according to the manufacturer's instructions (Shanghai Chemical Ltd., Shanghai, China) and 10 μl of serum sample [33].

Diabetogenic Indices

The principal diabetogenic indices—homeostatic model assessment of insulin resistance (HOMA-IR), homeostatic model assessment of beta cell function (HOMA-B), homeostatic model assessment of insulin sensitivity (HOMA-S), quantitative insulin sensitivity check index (QUICKI), and disposition index were calculated using the formulae below [19] [33] [34]:

$$\text{HOMA-IR} = \left(\frac{\text{fasting insulin (mU/L)} \times \text{fasting glucose (mmol/l)}}{22.5} \right)$$

$$\text{HOMA-B} = \left(\frac{(20 \times \text{fasting insulin (mU/L)})}{(\text{fasting glucose (mmol/L)} - 3.5)} \right)$$

$$\text{HOMA-S} = \frac{1}{\text{HOMA-IR}} \times 100\%$$

$$\text{Disposition index (DI)} = \left(\left(\frac{\text{HOMA-S}}{100} \right) \times \left(\frac{\text{HOMA-B}}{100} \right) \right)$$

$$\text{QUICKI} = \left(\frac{1}{(\log \text{fasting glucose [mg/dl]} + \log \text{fasting insulin [\mu U/ml]})} \right)$$

4. Statistical Analysis

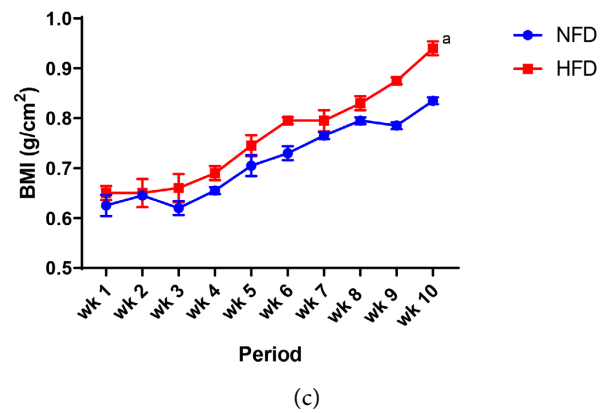
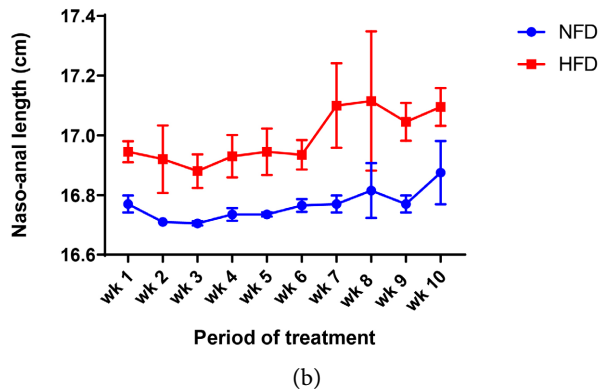
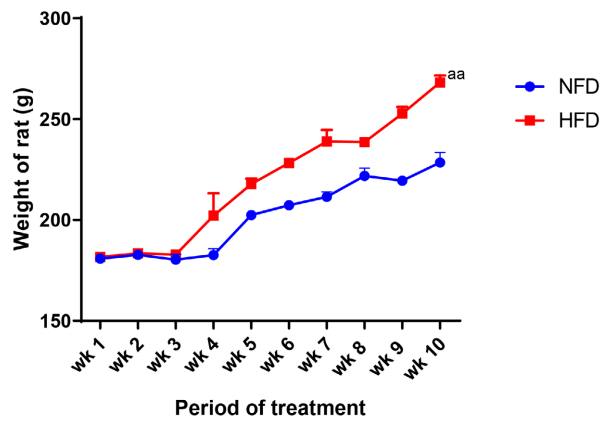
The data from the study were analyzed using GraphPad Prism® software version 8.0 (San Diego, California). All data were expressed as mean ± standard deviation. For continuous variables, group differences were determined using the Student t-test or the one-way ANOVA, depending on which was appropriate. The Pearson correlation and logistic regression analysis were used to evaluate the association between biochemical indices, BMI, and diabetes among the experimental animal population after the dietary treatment. From the analysis, all p-values < 0.05 were considered significant.

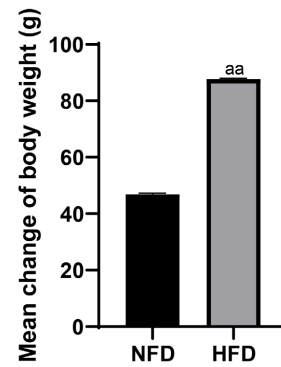
5. Results and Discussion

Common environmental factors such as prolonged consumption of a diet rich in fat (≥25% w/w) have been implicated as a common cause of increased adiposity, whole body insulin resistance (**Table 1**), β-cell dysfunction, gross obesity, and diabetes mellitus [19] [34]-[39]. The result from our study corroborates this evidence. From our study, most of the rats fed with the HFD over the 10-week period had a significant weight gain (**Figures 1(a)-(d)**), owing most probably to increased abdominal fat accumulation as observed from **Table 2**. Common clinical and biochemical presentations of obesity include elevated alanine transaminase levels (AST) [40] due to hepatic steatosis, dyslipidemia [40]-[42], elevated BMI [43], depression [36], decreased adaptive immunity [44] [45]. Obesity, among other things, is also characterized by derangement of nutrient metabolism [46].

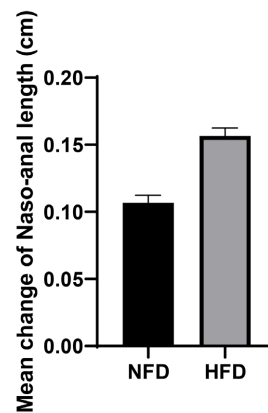
Table 1. Composition of diets for experimental rats.

Composition (p/p)	Normal Rat Chow	High-Fat Diet (HFD)
	% Weight	% Weight
Carbohydrate	41.475	30.500
Protein	18.850	17.475
Fat/Lipids	1.975	31.250
Fibre	7.700	8.350
Mineral/Vitamins	5.625	5.325
Energy (kCal/kg)	2590.75	4731.50

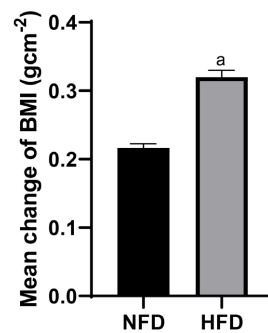




(d)



(e)



(f)

Figure 1. Zoometric measurements of experimental animals. (a) Body weight evaluation; (b) Nose-Anal length changes; (c) Body mass index (BMI) evaluation; (d) Mean change in body weight; (e) Mean change of nose-anal length; (f) Mean change of BMI of Wistar rats after the 10 weeks of dietary treatment. Results are presented as mean \pm S.E.M. and n represents the number of animals used in each group. (^a) $p < 0.05$ vs NFD group. (^{aa}) $p < 0.01$ vs NFD group.

One of the dangers associated with morbid obesity is its negative effect on the functional integrity of the vital organs—liver, lung, heart, kidney, pancreas, and sympathetic nerves [37]. Our findings in **Table 2** reveals significantly increased weights of liver, kidney, pancreas, and abdominal fat among the subjects rationed on the HFD compared with those subsisted on the NFD. There have been reports

from literature implicating obesity in chronic kidney disease and end-stage renal disease owing to the hyperfiltration resulting in sustained increase in intraglomerular pressure to compensate for the additional metabolic homeostatic demand imposed by the additional body weight [45]. Abdominal fat mass produces pro-inflammatory free fatty acids and adipokines, which infiltrate most visceral organs, causing inflammation of the liver and pancreas [41] [47].

Available evidences reveal that there is a significant decrease in the expression of glucose transporter-4 (GLUT4) in muscles and adipose tissues of obese animals [48] [49]. Another study reported that the translocation, docking, and fusion of GLUT4-containing vesicles with the plasma membrane in adipocytes of obese rats [50]-[52]. Ultimately, these result in impaired insulin sensitivity by various body tissues, hyperinsulinemia, and hyperglycemia among the obese. Even though our results from **Table 3** concur with the above findings, it also produces further biomarkers that strengthen the relationship between obesity and diabetes. It shows a marked increase in some common diabetogenic indices, such as HOMA-IR and HOMA-S, with an increase in body weight gain from prolonged dependence on HFD. While hitherto, HOMA-IR as an index is known to be elevated in pathological type 2 diabetes, our findings indicate that it is also elevated in the obese. However, further investigation is required to review the extent of increase in the above index between obesity and type 2 diabetes and to set diametrical cut-off ranges for distinguishing between them. Our study showed a positive correlation between weight gain and HOMA-IR, as has been reported in other studies [38] [39] [53] [54]. On the other hand, there was a negative correlation between weight gain and the other diabetogenic indices, *i.e.*, HOMA-S ($r^2 = -0.8787$, $p < 0.0001$), HOMA-B ($r^2 = -0.8805$, $p < 0.0001$), and disposition index ($r^2 = -0.7827$, $p < 0.0001$) (**Table 4** and **Figure 2**).

Table 2. Morphometric measurements of Wistar rats after 10 weeks of treatment with normal chow and HFD.

Morphometric Indices	NFD (n = 20)	HFD (n = 18)	p-value
Weight gain (g)	41.0 ± 5.88	83.5 ± 18.4 ^{aa}	<0.001
Liver weight (g)	5.68 ± 1.41	8.57 ± 3.03 ^a	<0.01
Abdominal fat (g)	0.43 ± 0.27	5.2 ± 1.40 ^a	<0.0001
Adiposity index	0.28 ± 0.08	0.35 ± 0.13 ^a	0.042
Kidney weight (g)	0.62 ± 0.25	1.17 ± 0.08 ^a	<0.01
Pancreas weight (g)	0.69 ± 0.11	1.15 ± 0.45 ^a	0.027
Weight gain/pancreas weight	36.2 ± 10.49	63.3 ± 21.57 ^a	<0.001

Results are presented as mean ± S.E.M. and n represents the number of animals used in each group; the p-values were determined using the unpaired t-test, NFD versus HFD; (^a) $p < 0.05$ was considered significant when compared against the NFD group, (^{aa}) $p < 0.01$ when compared against the NFD group; NFD: Normal Fed Diet; HFD: High Fat Diet.

Table 3. Biochemical characteristics of study animals.

Biochemical Indices	BMI (<0.65 g·cm ⁻²) (n = 9)	BMI (0.65 ≤ BMI ≤ 0.70 g·cm ⁻²) (n = 16)	BMI (≥0.71 g·cm ⁻²) (n = 15)	p-value
FBG (mmol/l)	4.3 ± 0.52	4.60 ± 0.28	5.5 ± 0.69 ^a	0.028
RBG (mmol/l)	6.20 ± 0.08	6.13 ± 0.45	6.7 ± 0.28	0.076
VLDL-C (mmol/l)	0.16 ± 0.11	0.13 ± 0.08	0.30 ± 0.06 ^a	<0.01
Triglyceride (mmol/l)	0.80 ± 0.17	0.65 ± 0.12	1.50 ± 0.83 ^a	<0.01
Total Chol. (mmol/l)	2.46 ± 0.13	3.01 ± 0.18	4.68 ± 1.70 ^a	0.035
HDL-C (mmol/l)	1.20 ± 0.60	1.50 ± 0.72	1.90 ± 0.59	0.082
LDL-C (mmol/l)	0.44 ± 0.17	1.21 ± 0.05	2.10 ± 0.23 ^a	0.017
LDL-C/HDL-C	0.37 ± 0.04	0.81 ± 0.29	1.11 ± 0.02 ^a	0.041
TC/HDL-C	2.05 ± 0.18	2.01 ± 0.58	2.46 ± 0.73	0.069
TG/HDL-C	0.67 ± 0.33	0.43 ± 0.11	0.79 ± 0.29 ^a	0.025
Fasting Insulin (μU/l)	10.45 ± 2.71	10.68 ± 2.93	11.29 ± 3.27	0.043
HOMA-IR	2.00 ± 0.69	2.18 ± 0.52	7.16 ± 1.88 ^a	<0.001
HOMA-B	268.7 ± 10.84	194.18 ± 12.68	112.9 ± 5.83 ^a	<0.001
HOMA-S	50.0 ± 7.31	45.90 ± 3.59	14.0 ± 1.75 ^a	<0.001
QUICKI	0.34 ± 0.02	0.34 ± 0.17	0.33 ± 0.07	0.180
Disposition Index	1.34 ± 0.92	0.87 ± 0.05	0.16 ± 0.10 ^a	0.037

Results are presented as mean ± S.E.M. and n represents the number of animals used in each group; the p-value was determined by the one-way analysis of variance; $p < 0.05$ was considered significant. (^a) p-value < 0.05. Abbreviations: BMI: Body Mass Index; FBG: Fasting Blood Glucose; RBG: Random Blood Glucose; VLDL-c: Very Low Density Lipoprotein Cholesterol; HDL-c: High Density Lipoprotein; LDL-c: Low Density Lipoprotein; TC: Total Cholesterol; TG: Triglyceride; HOMA-IR: Homeostasis Model Assessment of Insulin Resistance; HOMA-B: Homeostatic Model Assessment of β -cell Function Index; HOMA-S: Homeostasis Model Assessment of Insulin Sensitivity; QUICKI: Quantitative Insulin Sensitivity Check Index.

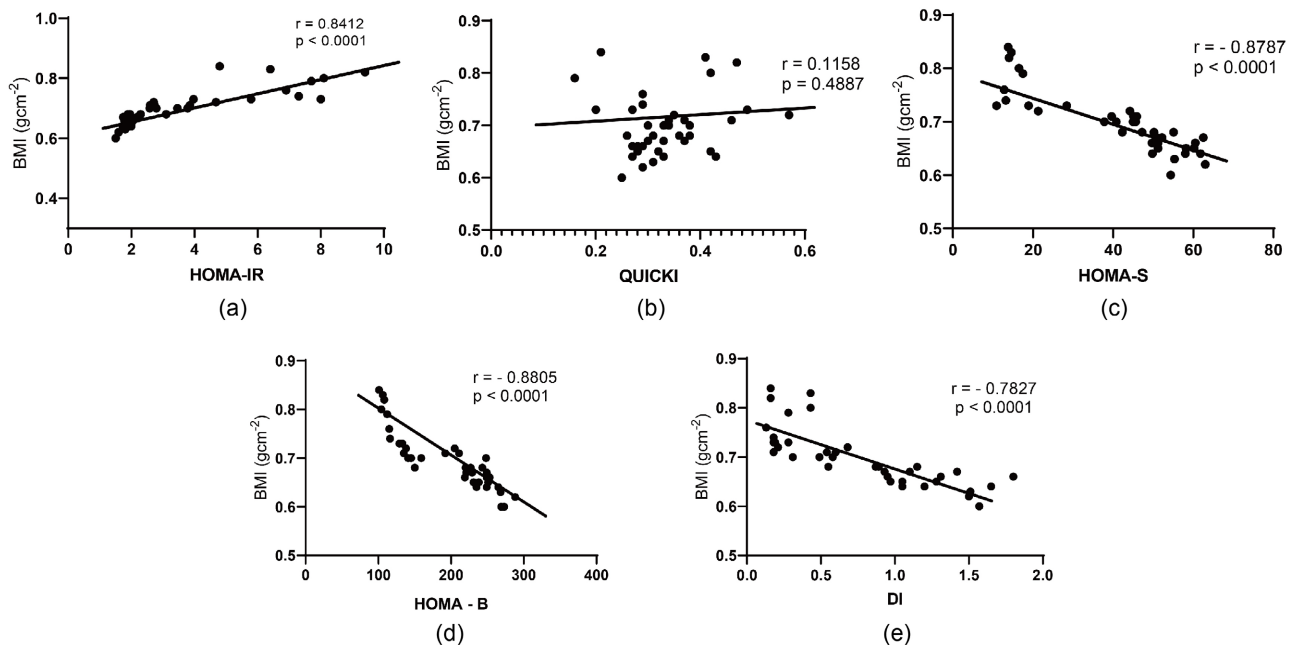


Figure 2. Scatter plot showing significant correlations between some diabetogenic indices and BMI among experimental animals used in the study.

Table 4. Logistic linear regression analysis of diabetogenic indices and BMI.

Variable	p-value	Odds Ratio	95% CI
HOMA-IR	p < 0.001	25.0	1.80 - 346.7
HOMA-B	p < 0.01	0.1	0.0085 - 1.17
HOMA-S	p < 0.01	0.89	0.047 - 16.66
QUCIKI	p < 0.05	1.0	0.156 - 6.42
Disposition Index	p < 0.001	0.089	0.0077 - 1.03

6. Limitations of Our Study

The use of laboratory animals as research subjects limits the extrapolation of our findings to humans. Again, the number of animals used poses a statistical constraint on the application of our findings for the management and monitoring of obesity in humans. Nonetheless, our findings were consistent with findings from studies using human subjects. It additionally reveals novel biomarkers that could help further account for the clinical and pathophysiological implications of obesity.

7. Conclusion

Our study reveals that subjects with high BMI have increased insulin resistance and decreased insulin sensitivity and secretion compared with those of lower BMI. Total cholesterol, fasting plasma glucose, fasting plasma insulin, and triglycerides were significantly elevated among subjects with higher BMI. Obesity, therefore, presents itself as a strong risk factor for type 2 diabetes. There is therefore an urgent need for an effective public health policy for the prevention of the epidemic of obesity.

Acknowledgements

The authors hereby acknowledge Mr. Gyan at the Animal House, Department of Pharmacology, Faculty of Pharmacy, KNUST, Ghana, for his technical support in keeping and maintaining the animals used in the study. We also appreciate Mr. Joseph Frempong at the Central Laboratory for his assistance in analyzing the biochemical assays.

Disclaimer

The data and opinions expressed in this paper are new and solely the responsibility of the authors and do not necessarily represent the official views of any auxiliary agencies.

Ethical Consideration

The above study was approved by the Animal Research and Ethics Committee—Kwame Nkrumah University of Science and Technology, Kumasi, Ghana. All conditions and protocols pertaining to animal care and treatments were done in accordance with the National Institute of Health Guidelines for the care of Labora-

tory Animals (NIH) (Department of Health Service Publication No. 83-23, revised 1985).

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

- [1] Ng, M., Fleming, T., Robinson, M., Thomson, B., Graetz, N., Margono, C., *et al.* (2014) Global, Regional, and National Prevalence of Overweight and Obesity in Children and Adults during 1980-2013: A Systematic Analysis for the Global Burden of Disease Study 2013. *The Lancet*, **384**, 766-781. [https://doi.org/10.1016/s0140-6736\(14\)60460-8](https://doi.org/10.1016/s0140-6736(14)60460-8)
- [2] World Health Organization (2020) Obesity. https://www.who.int/health-topics/obesity#tab=tab_1
- [3] Stanaway, J., Murray, C.J.L. and Ashkan, A. (2018) Global, Regional, and National Comparative Risk Assessment of 84 Behavioural, Environmental and Occupational, and Metabolic Risks or Clusters of Risks for 195 Countries and Territories, 1990-2017: A Systematic Analysis for the Global Burden of Disease Study 2017. *The Lancet*, **392**, 1923-1994.
- [4] Emanuel-Frith, M.N. (2020) Obese and Hungry: Two Faces of a Nation. *BMJ*, **370**, m3084.
- [5] Clemmensen, C., Petersen, M.B. and Sørensen, T.I.A. (2020) Will the COVID-19 Pandemic Worsen the Obesity Epidemic? *Nature Reviews Endocrinology*, **16**, 469-470. <https://doi.org/10.1038/s41574-020-0387-z>
- [6] Asosega, K.A., Adebajji, A.O. and Abdul, I.W. (2021) Spatial Analysis of the Prevalence of Obesity and Overweight among Women in Ghana. *BMJ Open*, **11**, e041659. <https://doi.org/10.1136/bmjopen-2020-041659>
- [7] Amoah, A.G. (2003) Obesity in Adult Residents of Accra, Ghana. *Ethnicity & Disease*, **13**, S29-S101.
- [8] Chu, Y., Yang, J., Shi, J., Zhang, P. and Wang, X. (2020) Obesity Is Associated with Increased Severity of Disease in COVID-19 Pneumonia: A Systematic Review and Meta-Analysis. *European Journal of Medical Research*, **25**, Article No. 64. <https://doi.org/10.1186/s40001-020-00464-9>
- [9] Biritwum, R., Gyapong, J. and Mensah, G. (2005) The Epidemiology of Obesity in Ghana. *Ghana Medical Journal*, **39**, 82-85.
- [10] Ganle, J.K., Boakyee, P.P. and Baatiema, L. (2019) Childhood Obesity in Urban Ghana: Evidence from a Cross-Sectional Survey of In-School Children Aged 5-16 Years. *BMC Public Health*, **19**, Article No. 1561. <https://doi.org/10.1186/s12889-019-7898-3>
- [11] Ofori-Asenso, R., Agyeman, A.A., Laar, A. and Boateng, D. (2016) Overweight and Obesity Epidemic in Ghana—A Systematic Review and Meta-Analysis. *BMC Public Health*, **16**, Article No. 1239. <https://doi.org/10.1186/s12889-016-3901-4>
- [12] Dixon, J.B., Dixon, A.F. and O'Brien, P.E. (2003) Improvements in Insulin Sensitivity and β -Cell Function (HOMA) with Weight Loss in the Severely Obese. *Diabetic Medicine*, **20**, 127-134. <https://doi.org/10.1046/j.1464-5491.2003.00889.x>
- [13] Antoni, R., Johnston, K.L., Collins, A.L. and Robertson, M.D. (2017) Effects of Intermittent Fasting on Glucose and Lipid Metabolism. *Proceedings of the Nutrition Society*, **76**, 361-368. <https://doi.org/10.1017/S0029665116002986>
- [14] Kovesdy, C.P., Furth, S.L. and Zoccali, C. (2017) Obesity and Kidney Disease: Hidden

- Consequences of the Epidemic. *Canadian Journal of Kidney Health and Disease*, **4**, 1-10. <https://doi.org/10.1177/2054358117698669>
- [15] Wree, A., Kahraman, A., Gerken, G. and Canbay, A. (2010) Obesity Affects the Liver—The Link between Adipocytes and Hepatocytes. *Digestion*, **83**, 124-133. <https://doi.org/10.1159/000318741>
- [16] Kim, H.G. and Han, J. (2012) Obesity and Pancreatic Diseases. *The Korean Journal of Gastroenterology*, **59**, 35-39. <https://doi.org/10.4166/kjg.2012.59.1.35>
- [17] Nianogo, R.A. and Arah, O.A. (2022) Forecasting Obesity and Type 2 Diabetes Incidence and Burden: The Vila-Obesity Simulation Model. *Frontiers in Public Health*, **10**, Article ID: 818816. <https://doi.org/10.3389/fpubh.2022.818816>
- [18] Nowosad, K. and Sujka, M. (2021) Effect of Various Types of Intermittent Fasting (IF) on Weight Loss and Improvement of Diabetic Parameters in Human. *Current Nutrition Reports*, **10**, 146-154. <https://doi.org/10.1007/s13668-021-00353-5>
- [19] Taylor, V.H., Forhan, M., Vigod, S.N., McIntyre, R.S. and Morrison, K.M. (2013) The Impact of Obesity on Quality of Life. *Best Practice & Research Clinical Endocrinology & Metabolism*, **27**, 139-146. <https://doi.org/10.1016/j.beem.2013.04.004>
- [20] Raebel, M.A., Malone, D.C., Conner, D.A., Xu, S., Porter, J.A. and Lantý, F.A. (2004) Health Services Use and Health Care Costs of Obese and Nonobese Individuals. *Archives of Internal Medicine*, **164**, 2135-2140. <https://doi.org/10.1001/archinte.164.19.2135>
- [21] Silvestris, E., de Pergola, G., Rosania, R. and Loverro, G. (2018) Obesity as Disruptor of the Female Fertility. *Reproductive Biology and Endocrinology*, **16**, e490-e497. <https://doi.org/10.1186/s12958-018-0336-z>
- [22] Grover, S.A., Kaouache, M., Rempel, P., Joseph, L., Dawes, M., Lau, D.C.W., *et al.* (2015) Years of Life Lost and Healthy Life-Years Lost from Diabetes and Cardiovascular Disease in Overweight and Obese People: A Modelling Study. *The Lancet Diabetes & Endocrinology*, **3**, 114-122. [https://doi.org/10.1016/s2213-8587\(14\)70229-3](https://doi.org/10.1016/s2213-8587(14)70229-3)
- [23] Nyberg, S.T., Batty, G.D., Pentti, J., Virtanen, M., Alfredsson, L., Fransson, E.I., *et al.* (2018) Obesity and Loss of Disease-Free Years Owing to Major Non-Communicable Diseases: A Multicohort Study. *The Lancet Public Health*, **3**, e490-e497. [https://doi.org/10.1016/s2468-2667\(18\)30139-7](https://doi.org/10.1016/s2468-2667(18)30139-7)
- [24] Bulló, M., García-Lorda, P., Megias, I. and Salas-Salvadó, J. (2003) Systemic Inflammation, Adipose Tissue Tumor Necrosis Factor, and Leptin Expression. *Obesity Research*, **11**, 525-531. <https://doi.org/10.1038/oby.2003.74>
- [25] Festa, A., D'Agostino Jr, R., Williams, K., Karter, A., Mayer-Davis, E., Tracy, R., *et al.* (2001) The Relation of Body Fat Mass and Distribution to Markers of Chronic Inflammation. *International Journal of Obesity*, **25**, 1407-1415. <https://doi.org/10.1038/sj.ijo.0801792>
- [26] Kuneš, J., Hojná, S., Mráziková, L., Montezano, A., Touyz, R. and Maletínská, L. (2023) Obesity, Cardiovascular and Neurodegenerative Diseases: Potential Common Mechanisms. *Physiological Research*, **72**, S73-S90. <https://doi.org/10.33549/physiolres.935109>
- [27] Vilas-Boas, E.A., Almeida, D.C., Roma, L.P., Ortis, F. and Carpinelli, A.R. (2021) Lipotoxicity and β -Cell Failure in Type 2 Diabetes: Oxidative Stress Linked to NADPH Oxidase and ER Stress. *Cells*, **10**, Article 3328. <https://doi.org/10.3390/cells10123328>
- [28] Zakaria, Z., Othman, Z.A., Suleiman, J.B., Ghazali, W.S.W. and Mohamed, M. (2025) Obesity-Induced Pancreas Lipotoxicity, Oxidative Stress and Inflammation: Protective and Therapeutic Effects of Bee Bread. *Journal of the American Nutrition Associ-*

- ation, 1-12. <https://doi.org/10.1080/27697061.2025.2536769>
- [29] Nakamura, M. (2024) Lipotoxicity as a Therapeutic Target in Obesity and Diabetic Cardiomyopathy. *Journal of Pharmacy & Pharmaceutical Sciences*, **27**, Article No. 12568. <https://doi.org/10.3389/jpps.2024.12568>
- [30] Pandey, S. and Dvorakova, M.C. (2020) Future Perspective of Diabetic Animal Models. *Endocrine, Metabolic & Immune Disorders-Drug Targets*, **20**, 25-38. <https://doi.org/10.2174/1871530319666190626143832>
- [31] Suleiman, J., Mohamed, M. and Bakar, A. (2020) A Systematic Review on Different Models of Inducing Obesity in Animals: Advantages and Limitations. *Journal of Advanced Veterinary and Animal Research*, **7**, 103-114. <https://doi.org/10.5455/javar.2020.g399>
- [32] Lutz, T.A. and Woods, S.C. (2012) Overview of Animal Models of Obesity. In: Enna, S.J., *et al.*, Eds., *Current Protocols in Pharmacology*, Wiley, 5.61.1-5.61.18. <https://doi.org/10.1002/0471141755.ph0561s58>
- [33] Niemczyk, S., Szamotulska, K., Giers, K., *et al.* (2013) Homeostatic Model Assessment Indices in Evaluation of Insulin Resistance and Secretion in Hemodialysis Patients. *Medical Science Monitor*, **19**, 592-598. <https://doi.org/10.12659/msm.883978>
- [34] Lavie, C.J., De Schutter, A. and Milani, R.V. (2015) Healthy Obese versus Unhealthy Lean: The Obesity Paradox. *Nature Reviews Endocrinology*, **11**, 55-62. <https://doi.org/10.1038/nrendo.2014.165>
- [35] Guh, D.P., Zhang, W., Bansback, N., Amarsi, Z., Birmingham, C.L. and Anis, A.H. (2009) The Incidence of Co-Morbidities Related to Obesity and Overweight: A Systematic Review and Meta-Analysis. *BMC Public Health*, **9**, Article No. 88. <https://doi.org/10.1186/1471-2458-9-88>
- [36] Lauby-Secretan, B., Scoccianti, C., Loomis, D., Grosse, Y., Bianchini, F. and Straif, K. (2016) Body Fatness and Cancer—Viewpoint of the IARC Working Group. *New England Journal of Medicine*, **375**, 794-798. <https://doi.org/10.1056/nejmsr1606602>
- [37] Black, M.H., Watanabe, R.M., Trigo, E., Takayanagi, M., Lawrence, J.M., Buchanan, T.A., *et al.* (2013) High-Fat Diet Is Associated with Obesity-Mediated Insulin Resistance and β -Cell Dysfunction in Mexican Americans. *The Journal of Nutrition*, **143**, 479-485. <https://doi.org/10.3945/jn.112.170449>
- [38] Okura, T., Nakamura, R., Fujioka, Y., Kawamoto-Kitao, S., Ito, Y., Matsumoto, K., *et al.* (2018) Body Mass Index ≥ 23 Is a Risk Factor for Insulin Resistance and Diabetes in Japanese People: A Brief Report. *PLOS ONE*, **13**, e0201052. <https://doi.org/10.1371/journal.pone.0201052>
- [39] Johansen, M.J., Gade, J., Stender, S., Frithioff-Bøjsøe, C., Lund, M.A.V., Chabanova, E., *et al.* (2020) The Effect of Overweight and Obesity on Liver Biochemical Markers in Children and Adolescents. *The Journal of Clinical Endocrinology & Metabolism*, **105**, 430-442. <https://doi.org/10.1210/clinem/dgz010>
- [40] Klop, B., Elte, J. and Cabezas, M. (2013) Dyslipidemia in Obesity: Mechanisms and Potential Targets. *Nutrients*, **5**, 1218-1240. <https://doi.org/10.3390/nu5041218>
- [41] Geloneze, B., Vasques, A.C.J., Stabe, C.F.C., Pareja, J.C., Rosado, L.E.F., *et al.* (2009) HOMA1-IR and HOMA2-IR Indexes in Identifying Insulin Resistance and Metabolic Syndrome: Brazilian Metabolic Syndrome Study (Brams). *Arquivos Brasileiros de Endocrinologia & Metabologia*, **53**, 281-287. <https://doi.org/10.1590/s0004-27302009000200020>
- [42] Vekic, J., Zeljkovic, A., Stefanovic, A., Jelic-Ivanovic, Z. and Spasojevic-Kalimanovska, V. (2019) Obesity and Dyslipidemia. *Metabolism*, **92**, 71-81.

- <https://doi.org/10.1016/j.metabol.2018.11.005>
- [43] Liew, P.-L., Lee, W.-J., Lee, Y.-C., Wang, H.-H., Wang, W. and Lin, Y.-C. (2006) Hepatic Histopathology of Morbid Obesity: Concurrence of Other Forms of Chronic liver Disease. *Obesity Surgery*, **16**, 1584-1593. <https://doi.org/10.1381/096089206779319392>
- [44] Lee, H. and Koh, D.H. (2020) Obesity and Pancreatobiliary Disease. *Korean Journal of Gastroenterology*, **75**, 240-245. <https://doi.org/10.4166/kjg.2020.75.5.240>
- [45] Green, W.D. and Beck, M.A. (2017) Obesity Impairs the Adaptive Immune Response to Influenza Virus. *Annals of the American Thoracic Society*, **14**, S406-S409. <https://doi.org/10.1513/annalsats.201706-447aw>
- [46] Ma, H., Wu, X., Guo, X., Yang, J., Ma, X., Lv, M., *et al.* (2018) Optimal Body Mass Index Cut-off Points for Prediction of Incident Diabetes in a Chinese Population. *Journal of Diabetes*, **10**, 926-933. <https://doi.org/10.1111/1753-0407.12785>
- [47] Andersen, C.J., Murphy, K.E. and Fernandez, M.L. (2016) Impact of Obesity and Metabolic Syndrome on Immunity. *Advances in Nutrition*, **7**, 66-75. <https://doi.org/10.3945/an.115.010207>
- [48] Yamauchi, K., Oka, R., Yagi, K., Hayashi, K., Kawashiri, M., Yamagishi, M., *et al.* (2014) Population Impact of Increased Body Mass Index and Attenuated Beta-Cell Function on Worsening of Glucose Metabolism in Subjects with Normal Glucose Tolerance: A Pilot Study. *Acta Diabetologica*, **51**, 441-445. <https://doi.org/10.1007/s00592-013-0535-1>
- [49] Shepherd, P.R., Gnudi, L., Tozzo, E., Yang, H., Leach, F. and Kahn, B.B. (1993) Adipose Cell Hyperplasia and Enhanced Glucose Disposal in Transgenic Mice Overexpressing GLUT4 Selectively in Adipose Tissue. *Journal of Biological Chemistry*, **268**, 22243-22246. [https://doi.org/10.1016/s0021-9258\(18\)41516-5](https://doi.org/10.1016/s0021-9258(18)41516-5)
- [50] Tozzo, E., Gnudi, L. and Kahn, B.B. (1997) Amelioration of Insulin Resistance in Streptozotocin Diabetic Mice by Transgenic Overexpression of GLUT4 Driven by an Adipose-Specific Promoter. *Endocrinology*, **138**, 1604-1611. <https://doi.org/10.1210/en.138.4.1604>
- [51] Brennan, C.L., Hoenig, M. and Ferguson, D.C. (2004) GLUT4 but Not GLUT1 Expression Decreases Early in the Development of Feline Obesity. *Domestic Animal Endocrinology*, **26**, 291-301. <https://doi.org/10.1016/j.domaniend.2003.11.003>
- [52] Schwartz, M.W., Seeley, R.J., Zeltser, L.M., Drewnowski, A., Ravussin, E., Redman, L.M., *et al.* (2017) Obesity Pathogenesis: An Endocrine Society Scientific Statement. *Endocrine Reviews*, **38**, 267-296. <https://doi.org/10.1210/er.2017-00111>
- [53] Luppino, F.S., de Wit, L.M., Bouvy, P.F., Stijnen, T., Cuijpers, P., Penninx, B.W.J.H., *et al.* (2010) Overweight, Obesity, and Depression: A Systematic Review and Meta-Analysis of Longitudinal Studies. *Archives of General Psychiatry*, **67**, 220-229. <https://doi.org/10.1001/archgenpsychiatry.2010.2>
- [54] Singla, P., Bardoloi, A. and Parkash, A.A. (2010) Metabolic Effects of Obesity: A Review. *World Journal of Diabetes*, **1**, 76-88. <https://doi.org/10.4239/wjd.v1.i3.76>