

Serum Resistin and Glucose Among Obese and Non-Obese Diabetic RatsBanya, R.J. ^{1*}, Dallatu, M.K. ², Nnamah, N.K. ⁴ and Tambuwal, F.M. ³

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Author for Correspondence*: banyajarich@gmail.com <https://dx.doi.org/10.4314/sokjmls.v9i4.22>**Abstract**

The role of resistin in response to obesity in T2DM patients is still obscure. The aim of this was to evaluate serum resistin and lipid profiles in obese and non-obese diabetic rats. Obesity was induced by the administration of high-fat diet (HFD) for 35 days, while DM was induced by injecting 150 mg/kg body weight of alloxan monohydrate into the rats. Serum resistin was assayed using the ELISA technique, serum glucose, TC, HDL-C, and TG using spectrophotometric techniques. The results of body weight and BMI were significantly higher ($P < 0.05$) in HFD-fed groups compared with those of control. Serum resistin results show no significant difference ($P > 0.05$) in all the study groups but show a positive correlation ($P > 0.05$) with BMI in all the experimental groups. The results of TC, TG, LDL-C, and VLDL-C were significantly higher ($P < 0.05$), while HDL-C was significantly lower ($P < 0.05$) in the obese and diabetic groups compared with the control. In conclusion, the findings of this study show that a relationship exists between serum resistin and BMI. Dyslipidemia is associated with obesity.

Keywords: Resistin, Lipid profile, Obese, Non-obese

Introduction

Obesity is defined as a condition characterized by excess accumulation and storage of fat in the body (CDC, 2016; WHO, 2021). It is more specifically defined as having 25% or more total body fat in men and 35% or more in women. The condition occurs when caloric intake exceeds energy expenditure, resulting in a negative

caloric balance. Technically, obesity is diagnosed by simple anthropometric measurements, such as a body mass index (BMI)

30 kg/m² or a waist-to-hip ratio > 0.95 in men and > 0.80 in women (Rashid, 2013). Waist circumference: 77 cm in men and 62 cm in women (Sonuyi *et al.*, 2013). This condition can be classified into three classes: class I (BMI of $30 < 35$ kg/m²), class II (BMI of $35 < 40$ kg/m²), and class III (> 40 kg/m²). These classes are also known as moderate, severe, and very severe obesity, respectively (CDC, 2016). Obesity is associated with an increased risk of developing insulin resistance and type 2 diabetes mellitus. In obese individuals, adipose tissue releases increased amounts of non-esterified fatty acids, glycerol, hormones, proinflammatory cytokines, and other factors that are involved in the development of insulin resistance. Abnormalities in β -cell function are therefore critical in defining the risk of developing type 2 diabetes (Kahn *et al.*, 2006; Li *et al.*, 2022). Obesity and noninsulin-dependent diabetes mellitus are global epidemics. Insulin resistance is a major contributor to the pathogenesis of type II diabetes and plays a role in numerous other metabolic disorders, including hypertension, dyslipidemia, and atherosclerosis. Obesity, in particular visceral adiposity, is positively correlated with insulin resistance. Although this correlation between adiposity and insulin resistance is well established in human beings as well as in rodent models, the mechanisms involved in obesity-related insulin resistance are not fully defined (Steppan and Lazar, 2011; Dilworth *et al.*, 2021).

Lipid profile, or lipid panel, is the collective term given to the estimation of, typically, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and triglycerides. An extended lipid profile may include very low-density lipoproteins. This is used to identify hyperlipidaemia (various disturbances of cholesterol and triglyceride levels), many of which are recognized risk factors for cardiovascular disease and sometimes pancreatitis. It has been demonstrated that high levels of serum total cholesterol (TC), triglycerides (TG), LDL cholesterol, very-low-density lipoprotein (VLDL), low concentrations of HDL cholesterol, and increased body mass index (BMI) are significantly associated with CHD. Dyslipidemia is one of the top five major risk factors leading to cardiovascular disorders. It is characterized by elevated LDL cholesterol and TG and decreased HDL (Rizvi and Nagra, 2012; Hedayatnia *et al.*, 2020).

Over the years, there have been great strides in understanding the pathophysiological mechanisms by which obesity induces or amplifies its major adverse consequences. In particular, the role of adipose tissue was highlighted, no longer regarded as a tissue with simply trophic and mechanical properties but as an organ with endocrine functions and the ability to secrete bioactive molecules. It is now considered a key player in the development of lifestyle-related diseases (Di Raimo *et al.*, 2015; Clemente-Suárez *et al.*, 2023).

Adipose tissue acts as a fat storage site as well as an endocrine organ that produces certain proteins, known as adipocytokines. An association between some of these proteins and the development of insulin resistance (IR) has been well documented. Among the proteins released from the adipose tissue is resistin (Demir, 2015; Lin *et al.*, 2022). Resistin belongs to a family of cysteine-rich secretory proteins called resistin-like molecules, or FIZ proteins. Resistin is derived almost exclusively from fat tissue, and adipose expression and serum levels are elevated in models of obesity and insulin resistance. Hyperresistinaemia impairs glucose tolerance and induces hepatic insulin resistance in rodents, whereas mice deficient in resistin are protected

from obesity-associated insulin resistance (Reilly *et al.*, 2005; Mohammed and Yacir, 2021).

The role of resistin in response to obesity and insulin resistance in diabetics is still obscure. Several studies have reported increased resistin levels in association with obesity and insulin resistance in type 2 diabetes, whereas other studies have failed to detect any change in resistin levels under such conditions. Yet other studies found that circulating resistin levels are involved in promoting adiposity but have no effect on the degree of insulin resistance. These observations suggest that the role of resistin in the pathogenesis of diabetes remains controversial (Gharibeh *et al.*, 2010; Davoud *et al.*, 2015; Mohammed and Yacir, 2021). Two independent studies in which recombinant resistin was administered to rodents both argued that resistin can cause insulin resistance. When resistin protein (32 µg/mouse) was administered intraperitoneally to C57BL/6J mice, glucose homeostasis and insulin action were impaired. Infusion of resistin protein (5 µg h⁻¹) into Sprague-Dawley rats worsened glucose homeostasis because of increased hepatic glucose production without apparent changes in glucose utilization by skeletal muscle and adipose tissue (Rajala *et al.*, 2003). Interestingly, circulating levels of counterregulatory hormones such as glucagon and corticosterone were not altered by resistin infusion (Rajala *et al.*, 2003; Raje *et al.*, 2020).

Recombinant bacterially produced resistin has been demonstrated to inhibit glucose uptake in L6 skeletal muscle cells following acute exposure (Moon *et al.*, 2003; Raje *et al.*, 2020). Previously, it was demonstrated that recombinant resistin inhibits insulin-stimulated glucose uptake in 3T3-L1 adipocytes (Steppan *et al.*, 2001). These studies suggest that resistin may contribute to insulin resistance and diabetes mellitus (Steppan and Lazar, 2011; Deeksha *et al.*, 2020).

Circulating resistin levels are decreased by the anti-diabetic drug rosiglitazone and increased in diet-induced and genetic forms of obesity. Administration of an anti-resistin antibody improves blood glucose and insulin action in mice with diet-induced obesity. Moreover, treatment of normal mice with recombinant resistin impairs glucose tolerance and insulin action. Insulin-stimulated glucose uptake by

adipocytes is enhanced by the neutralization of resistin and reduced by resistin treatment. Resistin is thus a hormone that potentially links obesity to diabetes (Steppan and Lazar, 2011).

Materials and Methods

Experimental Animals

Forty (40) Albino Westar male rats (180-180g) were purchased from the Animal House, Faculty of Pharmaceutical Sciences, Usmanu Danfodiyo University, Sokoto. These rats were used for the study. All animals were kept at constant room temperature (25–30 °C) and a 12-hour light-dark cycle with free access to food and water ad libitum. The rats were acclimatized to the normal diet for one week before introducing the experimental diets for five weeks (35 days). Before the induction of DM, only rats that satisfied the definition of obesity were included in the study (Novelli *et al.*, 2007).

Induction of Obesity

The normal diet was sourced from Grand Cereals and Oil Mills Ltd., Jos, and the high-fat diet (HFD) was prepared by mixing 40% of the normal diet (Grow Maxx) from Grand Cereals and Oil Mills Ltd., Jos, and 60% of groundnut cake (Michael and Omotayo, 2015). Obesity was induced by feeding the rats with HFD for five (5) weeks (35 days).

Method of Calculating Body Mass Index in Rats

The obesity in the rats was determined by taking body weight (g) and measuring the length (cm) of the rats using a tape from the nose to the anus. The weight of the rats was divided by the length per square (Novelli *et al.*, 2007).

Induction of Diabetes Mellitus in the Rats

Before the induction of diabetes mellitus, the rats were allowed to fast for 24 hours. Fasting blood glucose was measured as a basal level. Freshly prepared alloxan monohydrate, dissolved in sterile normal saline at a single dose of 150 mg/kg body weight, was administered intraperitoneally to rats in diabetic and obese diabetic groups. The rats were placed on 5% glucose water for 24 hours as their drinking water to avoid hypoglycemia. Blood glucose was measured from the 3rd to the 5th day, and only rats with fasting blood glucose of 10 mmol/l

were included in the study. Five (5) days after the confirmation of diabetes, a blood sample was collected for biochemical analysis.

RESEARCH DESIGN

Forty (40) male rats were divided into four (4) groups as follows

- Group 1: Ten (10) non -diabetic non obese rats as control
- Group 2: Ten (10) non- obese diabetic rats as diabetic group
- Group 3 Ten (10) obese non-diabetic rats as obese group
- Group 4: Ten (10) obese diabetic rats as diabetic obese group

Sample Collection

At the end of the five (5) days, experimental animals were anesthetized by dropping them in a transparent plastic jar saturated with chloroform. Insertion in the abdomen was made, about 7mL of blood sample was collected through cardiac puncture (Dallatu *et al.*, 2009), in which three millilitres (3mls) was transfer into fluoride oxalate and 4mL into plain containers.

Laboratory Analyses

3.7.1 Serum Resistin

Serum resistin was estimated by Enzyme Linked Immunosorbent Assay Technique using supplied kits by (WKEA MEDICAL SUPPLIES In Indian) according to Steppan and Lazar, (2011).

Principle

Immunoenzymometric assay: the essential reagents for immunoenzymometric assay include high affinity and specificity antibodies (enzyme conjugated and immobilized), with different and distinct epitope recognition in excess, and native antigens. The immobilization takes place during the assay at the surface of a microplate well through the interaction of streptavidin coated on the well with an exogenously added biotinylated monoclonal anti-resistin antibody. Upon mixing monoclonal biotinylated antibody, the enzymes labeled antibody, and a serum containing the native antigen, reaction results between the native antigen and the antibodies, without competition or steric hindrance, to form a soluble sandwich complex.

Test Procedure

Hundred microliters (100 μ l) of standard were added into the first and second wells of the microtitre plate, followed by the addition of fifty microliters (50 μ l) of standard dilution into the first and second wells, and the mixture was properly mixed. After mixing the wells, 100 microliters (100 μ l) were taken from the first and second wells into the third and fourth wells, respectively. Fifty microliters (50 μ l) of standard dilute were added to the third and fourth wells and mixed properly. After mixing, fifty microliters (50 μ l) were removed from the third and fourth wells separately and discarded. Fifty microliters (50 μ l) were taken from the third and fourth wells separately and dispensed into the fifth and sixth wells, respectively. Follow by adding fifty microliters (50 μ l) of standard dilute and mixing properly. Fifty microliters (50 μ l) were taken from the fifth and sixth wells separately and dispensed into the seventh and eighth wells, respectively. Follow by adding fifty microliters (50 μ l) of standard dilute and mixing properly. Fifty microliters (50 μ l) were taken from the seventh and eighth wells separately and dispensed into the ninth and tenth wells, respectively. Follow by adding fifty microliters (50 μ l) of standard dilute and mixing properly. After the mixing, fifty microliters (50 μ l) of the mixture in the ninth and tenth wells were taken and discarded.

Note: After this process, we expect that fifty microliters (50 μ l) of dilution are in each well with a concentration of 18 μ l g/l, 12 μ g/l, 6 μ g/l, 3 μ g/l, and 1.5 μ g/l, respectively.

A well is set as blank, and the sample and enzyme conjugate were not added to the well. Wells were labeled based on the number of samples. Forty microliters (40 μ l) of sample dilute were added into all the sample wells, followed by adding ten microliters (10 μ l) of the samples into their respective wells without touching the bottom of the wells and mixing gently. After making a dilution of the standard and samples well, the microtitre plate was covered with a plate membrane and incubated for 30 minutes at 37 $^{\circ}$ C. A wash solution was prepared (30-fold with distilled water and reserve before use). After the incubation, the late was washed manually by adding the wash solution to each well and filling it. The wash solution was aspirated into a sink. This procedure was repeated five times for proper washing. After washing, the plate was inverted and blotted dry by

hitting the plate onto absorbent paper until no moisture appeared. Fifty microliters (50 μ l) of enzyme conjugate reagent were added to all the wells except the blank well.

The plate was covered and incubated as in 8 above. After the incubation, it was washed as in 10 above. Fifty microliters (50 μ l) of substrates A and B were added to all the wells, respectively, covered with membrane, and incubated for 15 minutes at 37 $^{\circ}$ C. The reaction was stopped by adding fifty microliters (50 μ l) of stop solution to each well and mixing properly. The plate was read within 15 minutes using a microplate reader.

Plasma Glucose—Oxidase-Peroxidase Method (Burtis *et al.*, 1999).

Principle

Glucose oxidase (GOD) catalyzes the oxidation of glucose to give hydrogen peroxide (H₂O₂) and gluconic acid. In the presence of the enzyme Peroxidase (POD), the hydrogen peroxide is broken down, and the oxygen released reacts with 4-aminophenazone (4-aminoantipyrine) and phenol to give it a pink color. The absorbance of the pink color is directly proportional to the concentration of glucose in the sample.

Procedure

Ten microliters (10 μ l) of samples were added into the respective label test tube for the samples. Ten microliters of the glucose standard were added to the test tube label standard. Five milliliters (5 ml) of glucose reagent were added to all the tubes, including the blank test tube. The mixtures were incubated for 15 minutes at 37 $^{\circ}$ C. After the incubation, the absorbance was read at 490nm.

Calculation

$$\frac{\text{absorbance of test}}{\text{absorbance of standard}} \times \text{conc. of standard (5.5mmol/L)}$$

Total cholesterol (TC) Enzymatic Colorimetric Method (Trinder, 1969).

Principle

Cholesterol ester + H₂O cholesterol esterase
cholesterol + fatty acid

Cholesterol + O₂ cholesterol oxidase 4-cholesten-3-one + H₂O₂
 2H₂O₂ + phenol + aminoantipyrin Peroxidase
 Red quinone + 4H₂O

The absorbance of red colour is proportional to the concentration of cholesterol in the sample.

Procedure

One milliliter (1 ml) of cholesterol reagents was added to the test, standard, and blank tubes. Ten micrometers (10 µl) of serum sample were added to the test tube, and ten microliters (10 µl) of standard were added to the standard tube. The tubes were mixed and incubated at 37°C for 5 minutes. Absorbance was read within 60 minutes at 505nm.

Calculation

$$\frac{\text{absorbance of test}}{\text{absorbance of standard}} \times \text{conc. of standard (200mg/dl)}$$

High Density Lipoprotein-Cholesterol (HDL-C) (Trinder, 1969).

Principle

The chylomicrons, very low-density lipoprotein (VLDL) and low-density lipoprotein (LDL), are precipitated by phosphotungstic acid and magnesium ions. After centrifugation, HDL remained in the supernatant and was measured by the enzymatic method as in cholesterol above.

Procedure

Precipitation

Three hundred microliters (300 µl) of sample were pipetted into a test tube. Three hundred microliters (300 µl) of HDL reagent were added and mixed well. It was incubated at room temperature for 10 minutes, mixed, and centrifuged at 4000 rpm for 10 minutes. The mixture was separated to collect the clear supernatant for determination of the HDL-C concentration using a cholesterol reagent.

HDL-C Determination

One thousand microliters (1000µl) of cholesterol reagent was pipetted into labeled test, standard, and blank test tubes. Fifty microliters (50µl) of HDL-C supernatant were added to the test tube,

and fifty microliters (50µl) of standard were added to the standard tube; they were mixed and incubated at 37°C for 5 minutes. The absorbance was read at 505nm.

Calculation

N²

N= Standard concentration (50mg/dl)

2= Dilution factor

Low Density Lipoprotein-Cholesterol (LDL-C) (Friedewald *et al.*, 1972).

Very Low-Density Lipoprotein Cholesterol (VLDL-C) (Friedewald, *et al.*, 1972).

VLDL-C = TG/5

Triglycerides (TG) (Tinder, 1969).

Principle

Triglycerides and H₂O lipoprotein lipase Glycerol and fatty acids Glycerol + ATP glycerol kinase Glycerol-3-phosphate and ADP Glycerol-3-phosphate + O₂ glycerol-3-phosphate Dihydroxyacetone phosphate + H₂O₂ + 4-aminoantipyrine + P-chlorophenol Peroxidase Red quinoimine. The absorbance is proportional to the concentration of TG in the sample.

Procedure

One milliliter (1 ml) each of TG reagents was pipetted into the test, standard, and blank tubes. Ten microliters (10µl) of serum, standard, and distilled water were pipetted into the test, standard, and blank, respectively. It was mixed and incubated at 37 °C for 5 minutes. The absorbance was read against the blank within 60 minutes at 505nm.

Calculation

$$\frac{\text{absorbance of test}}{\text{absorbance of standard}} \times \text{conc. of standard (200mmol/l)}$$

Body Weight

Body weight of the animals was taken by gravimetric method.

Data Analysis

The results were analyzed using analysis of variance (ANOVA). Post-hoc tests and multiple

comparisons using LSD were utilized to identify differences in means. The Pearson correlation coefficient was used to correlate the studied variables. The difference was considered statistically significant at 5% ($p < 0.05$) only. Statistical Package for Social Science (SPSS) Windows Version 20 was employed for the analysis.

Ethics

Ethical clearance was obtained from the ethical committee of Usmanu Danfodiyo University,

Sokoto Nigeria.

Results The results obtained in the current study are presented in tables 1 to 4. Table 1 shows the mean body weight was significantly higher ($p < 0.05$) in obese and obese diabetic groups when compared with those of control. The Mean body mass index was significantly higher ($p < 0.05$) in obese and obese- diabetic groups when compared with those of control.

Table 1: Anthropometric measurements, Height, body weight and body mass index in experimental rats and control.

Groups	Body weight(g)	BMI g/cm ²)
Group 1 (n=10)	204.50±12.68	0.59±0.01
Group 2 (n=10)	182.11±11.69*	0.53±0.02*
Group 3 (n=10)	285.57±7.37*	0.69±0.02*
Group 4(n=10)	290.57±14.35	0.71±0.02*
f-values	21.791	29.541
p-values	0.000	0.000
Post hoc using LSD		
Grp 1 vs Grp 2	0.177	0.004
Grp 1 vs Grp 3	0.000	0.000
Grp 1 vs Grp 4	0.000	0.000
Grp 2 vs Grp 3	0.000	0.000
Grp 2 vs Grp 4	0.000	0.000
Grp 3 vs Grp 4	0.780	0.256

Values are mean ± SEM, n = number of subjects, group 1 = control, group 2 =diabetic, group 3 = obese, group 4 =obese-diabetic controls. * = value differs significantly when compared with controls.

Table 2: The mean serum total cholesterol concentration was significantly higher ($p < 0.05$) in obese and obese diabetic groups when compared with those of the control. The mean total serum Triglyceride concentration was significantly higher ($p < 0.05$) in obese and obese diabetic groups when compared with those of the control. The mean total serum High density lipoprotein – cholesterol (HDL-C concentration was significantly lower ($p < 0.05$) in obese and obese diabetic groups when compared with those of the control.

Table 2: Serum lipid profile in experimental rats and controls

Groups	TC (mmol/L)	TG (mmol/L)	HDL-C (mmol/L)
Group 1 (n=10)	84.88±2.51	86.38±7.13	58.50±2.46
Group 2 (n=10)	83.00 ±5.10	79.67±7.05	56.22±4.12
Group 3 (n=10)	106.43±5.32*	146.71±8.75*	45.43±5.32*
Group 4(n=10)	100.57±15.14*	147.57±18.20*	39.43±5.29*
f-values	5.461	23.695	3.453
p-values	0.005	0.000	0.030
Post hoc using LSD			
Grp 1 vs Grp 2	0.781	0.626	0.689
Grp 1 vs Grp 3	0.005	0.000	0.038
Grp 1 vs Grp 4	0.036	0.000	0.014
Grp 2 vs Grp 3	0.002	0.000	0.075
Grp 2 vs Grp 4	0.017	0.000	0.029
Grp 3 vs Grp 4	0.432	0.024	0.665

Values are mean ± SEM, n = number of subjects, group 1 = control, group 2 =diabetic, group 3 = obese, group 4 =obese-diabetic controls. * = value differs significantly when compared with controls.

Table 3 shows the mean Serum Fasting Blood Glucose level was significantly higher (p<0.05) in diabetic and diabetic obese groups when compared with those of the control The Mean Serum Resistin concentration shows no statistically significant difference (p>0.05) in all the experimental groups when compared with those the control

Table 3: Serum Fasting blood glucose and resistin levels in experimental rats and control.

Groups	Glucose (mmol/l)	Resistin (µg/l)
Group 1 (n=10)	5.41±0.73	1.62±0.09
Group 2 (n=10)	13.91±3.74*	1.68±0.14
Group 3 (n=10)	5.91±0.31	1.68±0.11
Group 4(n=10)	13.14±2.73*	1.67±0.10
f-values	3.302	0.059
p-values	0.035	0.981
Post hoc using LSD		
Grp 1 vs Grp 2	0.019	0.717
Grp 1 vs Grp 3	0.891	0.727
Grp 1 vs Grp 4	0.043	0.772
Grp 2 vs Grp 3	0,032	0.993
Grp 2 vs Grp 4	0.830	0.958
Grp 3 vs Grp 4	0.065	0.954

Values are mean ± SEM, n = number of subjects, group 1 = control, group 2 =diabetic, group 3 = obese, group 4 =obese-diabetic controls. * = value differs significantly when compared with controls.

Table 4. The correlation coefficients for BMI of diabetic, obese and obese-diabetic rats and serum resistin concentration show no significant difference ($P>0.05$), but serum resistin correlates positively with Body Mass Index (BMI) in all the experimental groups.

Table 4: Correlation between BMI and serum resistin in obese and non-obese Diabetic Obese rats

Groups	Correlation (r)	p-values
Diabetic	0.345	0,363
Obese	0384	0.395
Obese diabetic	0.701	0.079

All results show statistically not significant. There was a negative correlation between BMI and serum resistin in the diabetic, obese group. While positive correlations exist between BMI and serum resistin in obese diabetic group.

Discussion

In the current study, we are able to show a significant variation in the BMI of the controls and the experimental rats. A high BMI is associated with the risk of developing diabetes mellitus and cardiovascular disorders. Previous reports (Gholizalleh *et al.*, 2015; Marie *et al.*, 2015; Shoaib *et al.*, 2015 and Bhowmik *et al.*, 2018) shows that obesity and diabetes mellitus are associated with a significant increase in serum triglycerides (TG), very low-density lipoprotein (LDL), total cholesterol, low-density lipoprotein (LDL), and a decrease in high-density lipoprotein (HDL-C). At the commencement of this study, the body weight of the experimental rats was between 150 and 180 g, which rose significantly before the end of the study. With a significantly higher level of BMI, this brought to light a clear relationship between obesity and possible cardiovascular disorders. Our findings is consistent with earlier reports (Mahmoud *et al.*, 2013; Michael and Omatayo, 2015) which found a significant increase in the body mass index of experimental rats post-fed with a high-fat diet (HFD) and that total dietary fat intake is linked to an increased risk of obesity and diabetes (Ma *et al.*, 2006; Astrup, 2008; Bhandari *et al.*, 2010).

At the commencement of the current study, the mean serum fasting blood glucose concentration of all the rats was 4.4 ± 0.11 mmol/l. After diabetes induction, FBG significantly rose in diabetic groups. Our finding is consistent with previous report (Choi *et al.*, 2008; Adeyi *et*

al., 2012) which indicated that alloxan monohydrate, when administered intraperitoneally, has an effect on the metabolism of glucose due to its toxic and destructive effect on the beta cells of the pancreas. Obesity seems to have no significant effect on serum fasting blood glucose levels. Our result is contrary to the report by Akter *et al.* (2017), which found that fasting serum glucose is significantly increased in obese people. In obese subjects, the values of FBS indicate they are prone to developing cardiovascular and metabolic diseases. This could be due to the fact that the degree of obesity in the present study was not enough to elicit effects on glucose metabolism. The destruction of the beta cells is responsible for the inability of the pancreas to synthesize and secrete an adequate amount of insulin needed for the metabolism of the circulating glucose concentration. Over the years, studies in humans and rats have examined the relationship between lipid profiles in experimentally obese and indicated that an increase in serum total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL), and a decrease in high-density lipoprotein (HDL-C) is seen in diabetic rats fed a high-fat diet (HFD) rats (Brai *et al.*, 2007; Otunola *et al.*, 2010; Gupta *et al.*, 2011; Gholizalleh *et al.*, 2015; Marie *et al.*, 2015; Shoaib *et al.*, 2015). These may be due to an abnormality in lipid metabolism. Fat intake in any of its forms has long been investigated in relation to human health, and a number of observational studies (Ma *et al.*, 2006; Astrup,

2008; Erkkiila *et al.*, 2008) have reported a link between dietary fat consumption and metabolic and cardiovascular disorders. It is also shown that hyperlipidaemia leads to pancreatic endocrine and exocrine alterations, with the possible risk of pancreatic cancer (Chowdhury *et al.*, 2000; Popov *et al.*, 2003; Karpińska and Czauderna, 2022). It has been established in previous reports that individuals with diabetes and obesity have complications in their lipid metabolism and stand a risk of developing cardiovascular disorders (Di Raimo *et al.*, 2015; Bhupathiraju and Hu, 2016). Obesity is linked to an increased prevalence of dyslipidaemia, and dyslipidaemia is primarily characterized by increased levels of plasma free fatty acids and triglycerides, decreased levels of high-density lipoprotein (HDL), and abnormal low-density lipoprotein (LDL) composition (Jung and Choi, 2014). The most significant contributing factor for obesity-related dyslipidemia is likely uncontrolled fatty acid release from adipose tissue, especially visceral adipose tissue, through lipolysis, which causes increased delivery of fatty acids to the liver and the synthesis of very low-density lipoprotein (VLDL) (Jung and Choi, 2014). Diabetes mellitus has the potential to cause abnormalities in lipid metabolism, with an increased tendency to develop dyslipidaemia, thereby increasing the risk factors for cardiovascular disease (Mensink *et al.*, 2003; Hu *et al.*, 2012; Mahmoud *et al.*, 2013; Micheal and Omatayo, 2015) Abnormalities in lipid metabolism observed in this study may be associated with an increased intake of high-fat diets (HFD) and diabetes (Mensink *et al.*, 2003; Hu *et al.*, 2012; Mahmoud *et al.*, 2013; Micheal and Omatayo, 2015).

In the current study, the mean serum resistin concentration shows no significant difference ($P > 0.05$) in all the study groups when compared with the control. An increase in body weight invariably increases the BMI, which directly influences the adipose tissue to secrete adipocytokines (Christine *et al.*, 2005). Previous research has reported that resistin is derived almost exclusively from fat tissue, and adipose expression and serum levels are elevated in models of obesity and insulin resistance. Earlier studies in humans and rats showed that obesity is

associated with elevated serum resistin levels in proportion to the degree of adiposity (Gharibeh *et al.*, 2010; Davoud *et al.*, 2015). However, there are conflicting results regarding the increase in serum resistin concentration among obese and non-obese individuals. Documented evidence (Silha *et al.*, 2003; Gerber *et al.*, 2006; and Rajkovic *et al.*, 2014; Musialik *et al.*, 2022) indicates that there is no significant difference ($P > 0.05$) in serum resistin level among obese and non-obese individuals, as opposed to the reports of Amirhakimi *et al.* (2011) and Bulduk and Günbatar (2023), who reported a significantly higher ($p < 0.05$) serum resistin concentration in obese groups when compared with non-obese individuals. Also, findings of the current study disagreed with previous reports (Keleshadi *et al.*, 2013; Urbanovych *et al.*, 2015; Tofangchiha *et al.*, 2020) that serum resistin was significantly higher ($p < 0.05$) in type 2 diabetes mellitus (T2DM) patients when compared with those of normal healthy individuals, but agreed with that of Mohammadzadeh *et al.* (2008), which state that serum resistin concentration shows no significant difference ($p > 0.05$) in type 2 diabetes mellitus (T2DM) obese patients when compared with those of type 2 diabetes mellitus patients.

In the current study, the relationship between serum resistin level and body mass index was observed in all the experimental groups, which showed a positive correlation between serum resistin level and BMI. This signifies that an increase in body weight and body mass index may cause a significant increase in serum resistin level. Individuals with an increase in the intake of a high-fat diet may have a tendency to increase their serum resistin level as obesity increases. Many studies have shown that serum resistin levels rise in parallel with an increase in BMI in obese T2DM patients, which shows that there is a relationship between an increase in serum resistin concentration and an increase in BMI (Hui-ling *et al.*, 2006; Mohammadzadeh *et al.*, 2008; Rajkovic *et al.*, 2014). Recently, Khalil *et al.* (2014) and Al-Sowayan (2015) also reported a positive correlation between serum resistin concentration and BMI in T2DM patients. This report corroborates the findings of the current study.

Limitations

Our study was faced with several limitations. The sample size was too small, and the duration was too long. An increase in the number of laboratory animals, the duration of exposure to diabetes, and an increase in BMI may have more effects. Further studies should be carried out to have a clear understanding of the effects of long-term exposure to diabetes and obesity on the study parameters.

Conclusions

At the end of this study the following conclusions were made:

1. The serum resistin concentration was not affected by diabetes and obesity, however, it correlated positively with body mass index in all the experimental groups.
2. Fasting blood glucose was significantly higher in diabetic and obese diabetic groups when compared with those of control group.
3. Dyslipidemia is associated with obesity.

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References

- Adeyi A.O., Idowu B.A., Mafiana C.F., Oluwalana O.A., Akiloye O.A., (2012): Rats model of food-induced non-obese type 2 diabetes mellitus: Comparative pathophysiology and Histopathology. *International Journal of Physiology Pharmacology*; **4(1)**: 51-58.
- Akter R, Nessa A, Husain MF, Wahed F, Khatun N, Yesmin M, Nasreen S, Tajkia T. (2017) Effect of Obesity on Fasting Blood Sugar. *Mymensingh Medical Journal*; **26(1)**:7-11.
- Al-Sowayan, N.S. (2015): Exploration of the relationship between adipocytokines, Tradition risk markers, nontraditional risk markers and anthropometric measurements in T2DM Patients. *Journal of Biomedical Science and Engineering*; **8**:184-200.
- Amirhakimi, A., Karamifar, H., Moravej, H., Amirhakimi, G. (2011): Serum resistin Level in obese male children. *Journal of Obesity*, **3**: 4-5.
- Astrup, A. (2008): Dietary management of obesity. *Journal of Parenteral Enteral Nutrition*; **32**: 575-577.
- Bhandari, U., Kumar, K.V. Khanna, N. and Panda, B.P. (2010) The effect of high-fat diet-induced obesity on cardiovascular toxicity in wistar albino rats. *Human and Experimental Toxicology*; **30(9)**:1313–1321
- Bhowmik B, Siddiquee T, Mujumder A, Afsana F, Ahmed T, Mdala IA, do V Moreira NC, Khan AKA, Hussain A, Holmboe-Ottesen G, Omsland TK. (2018).Serum Lipid Profile and Its Association with Diabetes and Prediabetes in a Rural Bangladeshi Population. *International Journal of Environmental Research Public Health*; **15(9)**:1944.
- Bhupathiraju, S.N. and Hu, F.B. (2016). Epidemiology of Obesity and Diabetes and Their Cardiovascular Complications. *Circulation Research*; **118(11)**:1723-35.
- Brai B. I. C., Odetola A. A., Agomo P. U. (2007): Effect of Porsea American leaf extracts on body weight and liver lipids in rats fed hyperlipidemia diet. *African Journal of Biotechnology*; **6(8)**: 1007 -1011.
- Bulduk, B. and Günbatar, N. (2023). The Effect of Exercise on Serum Resistin and Leptin Values in Rats Fed with a High Fat Diet. *Journal of Contemporary Medicine*; **13(1)**:82-85
- Burtis, A. (1999): Tietz Textbook of Clinical Chemistry, 3rd edn. Saunders an imprint Elsevier Inc: 675-682
- Center for Disease Control and Prevention (2016). Defining adult overweight and obesity.
- Choi Y.H., Lee M.G., Lee. I., (2008): Effect of diabetes mellitus induced by Alloxan on the pharmacokinetic of melformin in rats : restoration of pharmacokinetic parameters to the control state by insulin treatment. *Journal of Pharmacology, Pharmaceutical Science*; **11(1)**: 80-103.
- Chowdhury, P., Nishikawa, M., Blevins, G.W., Rayford, P.L. (2000): Response of rat's exocrine pancreas to high-fat and high-carbohydrate diets. *Proceedings of the Society for Experimental Biology and Medicine*; **223**: 310-315.
- Christine, M., Kusminski, Philip, G.M., and

- Sudhesh, K. (2005): Role of resistin in obesity, insulin resistance and Type II diabetes. *Clinical Science*; **109**: 243–256.
- Clemente-Suárez, V.J.; Redondo-Flórez, L.; Beltrán-Velasco, A.I.; Martín-Rodríguez, A.; Martínez-Guardado, I.; Navarro-Jiménez, E.; Laborde-Cárdenas, C.C.; Tornero-Aguilera, J.F. (2023) The Role of Adipokines in Health and Disease. *Biomedicines*; **11**: 1290.
- Dallatu, M.K., Anaja, P.O., Bilbis, L.S., Mujiminiyi, F.B.O. (2009): Lipid profile and Antioxidant status of Alloxan –induced diabetic rats supplemented with micronutrients. *Nigeria Journal of Basic and Apply Science*; **17(1)**: 112-117.
- Deeksha Tripathi¹, Sashi Kant², Saurabh Pandey³ and Nasreen Z. Ehtesham (2020). Resistin in metabolism, inflammation, and disease. *The Federation of European Biochemical Societies Journal*; **287**: 3141–3149
- Demir, N., Ahishel, E., Daloplioglu, C., Ercan, S., Kaptanagos, A.O., Dabak, R., Yucel, N., Sargan, M., Bayamicil, O.U. (2015): The relationship between serum adiponectin and resistin level, insulin resistance and colorectal adenomas. *Turkish Journal of Gastroenterology*; **26**: 20-24.
- Di Raimo, T., Gabriella, A., Mariangela, C., Daria, C., Vincenza, Vasco, R. L., and Businaro, I.R. (2015): Adipokines and their Involvement as a Target of New Drugs. *Journal of Pharmacovigilance*; **3(3)**: 166
- Dilworth, L.; Facey, A.; Omoruyi, F. (2021). Diabetes Mellitus and Its Metabolic Complications: The Role of Adipose Tissues. *International Journal of Molecular Sciences*; **22**: 7644.
- Erkkilä, A., de Mello, V.D., Risérus, U., Laaksonen, D. E. (2008): Dietary fatty acids and cardiovascular disease: an epidemiological approach. *Progress in Lipid Research*; **47**: 172-187.
- Friedewald, W.T., Levy, R.I., Fredrickson, D.S. (1972): Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clinical Chemistry*; **18**: 499–502.
- Gerber, M., Boettner, A., Seide, B., Lammert, A., Ba, r. J., Schuster, .E., Thiery. J., Kiess, W., Kratzsch, J. (2006): Serum resistin Levels of obese and lean children and adolescents: biochemical analysis and clinical relevance. *The Journal of Clinical Endocrinology & Metabolism*; **90(8)**: 4503–4509.
- Gharibeh M.Y., Al-Tawalbeh G.M., Abboud M.M., Radaideh A., Alhader A.A., Khabour O.F., (2010): Correlation of plasma resistin with obesity and insulin resistance in type 2 diabetic patients. *Journal of Diabetes*; **36(1)**: 443-449.
- Gholizadeh, D., Rahmati-Yamchi, .M., Zonouzi, A.P., Maleksabet, A., Moghaddam, M.P., Zarghami, S .N. (2015): Variations of serum leptin and resistin levels in healthy non-diabetic women with different degrees of obesity. *Environmental Pharmacology Life Science*; **4(2)**: 2015: 49-54.
- Gupta P., Tyagi S., Mukhiya M., Saini A.S., Goyal R., Sharma P.L., (2011): Obesity: An introduction and evaluation: *Journal of Advanced Pharmacy Education and Research*; **2**: 125-137.
- Hedayatnia M, Asadi Z, Zare-Feyzabadi R, Yaghooti-Khorasani M, Ghazizadeh H, Ghaffarian-Zirak R, Nosrati-Tirkani A, Mohammadi-Bajgiran M, Rohban M, Sadabadi F, Rahimi HR, Ghalandari M, Ghaffari MS, Yousefi A, Pouresmaeili E, Besharatlou MR, Moohebaty M, Ferns GA, Esmaily H, Ghayour-Mobarhan. M. (2020) Dyslipidemia and cardiovascular disease risk among the MASHAD study population. *Lipids Health Disuse*; **19(1)**: 42
- Hu, T., Mills, K.T., Yao, L., Demanelis, K., Eloustaz, M., Yancy, W.S. (2012). Effects of low-carbohydrate diets versus low-fat diets on metabolic risk factors: a metaanalysis of randomized controlled clinical trials. *American Journal of Epidemiology*; **176(7)**: 44-54.
- Hui-Ling, L., Hong-Wei, W., Yu, W., Mu-Xun, Z., Han-Hua, L. (2006). Roles of adipocyte derived hormone adiponectin and resistin in insulin resistance of type diabetes. *World Journal of Gastroenterology*; **12(11)**: 1747-1751.
- Jung, U. J., and Choi, M.S., (2014). Obesity and Its Metabolic Complications: The Role of

- Adipokines and the Relationship between Obesity, Inflammation, Insulin Resistance, Dyslipidemia and Nonalcoholic Fatty Liver Disease. *International Journal of Molecular Sciences*; **15**: 6184-6223.
- Kahn, S.E., Hull, R., Mutzsehneider, K. (2006). Mechanism of linking obesity to insulin resistance and type 2 diabetes. *Nature*:444-447
- Karpińska M, and Czauderna M. (2022) Pancreas-Its Functions, Disorders, and Physiological Impact on the Mammals' Organism. *Frontiers Physiology*; **13**:807632.
- Kelishadi, R., Hajizadeh, M., Ardalan, G., Poursafa, P., Fakhri, M. (2013). Association of resistin and hs-CRP with liver enzymes and components of the metabolic syndrome in Iranian adolescents with excess weight: the CASPIAN-III Study. *Pakistan Journal of Medical Science*; **29(1)**:290-295.
- Khalil, O. A., Alsayed, G. M., Fawzy, S., Ibrahim, M., Raafat, N., and Samy, W. (2014). Does Resistin gene polymorphisms +299 (G>A) Participate in Insulin Resistance in Egyptian Non- obese Type 2 Diabetes. *International Journal of Genomic Medicine*; **2**:1
- Li, M, Chi, X, Wang, Y. Setrerrahmane, S. Xie, W, and Xu H. (2022). Trends in insulin resistance: insights into mechanisms and therapeutic strategy. *Signal Transduction and Targeted Therapy*; **7**: 216
- Lin Y, Fan R, Hao Z, Li J, Yang X, Zhang Y and Xia Y (2022) The Association Between Physical Activity and Insulin Level Under Different Levels of Lipid Indices and Serum Uric Acid. *Frontiers in Physiology*; **13**:809669.
- Ma, Y., Olendzki, B.C., Hafner, A.R., Chiriboga, D.E., Culver, A.L., Andersen, V.A.(2006). Low-carbohydrate and high-fat intake among adult patients with poorly controlled type 2 diabetes mellitus. *Nutrition*; **22**: 1129- 1136.
- Mahmoud R.H., Elnour W.A., (2013). Comparative evaluation of the efficacy of ginger and orlistat on obesity management, pancreatic lipase and liver peroxisomal catalase enzyme in male albino rats. *European Review for Medical and Pharmacological Sciences*; **17**: 75-83.
- Marie, M.S., Arafa, N. M. S., Alazimi, S.A.M. (2015). Effect of canagliflozin metformin on metabolic disorders in obese diabetic rats. *African Journal Pharmacy and Pharmacology*, **9(46)**:1071-1079.
- Mensink, R.P., Zock, P.L., Kester, A.D., Katan, M.B. (2003) Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. *American Journal Clinical Nutrition*; **77**: 1146-1155.
- Michael, C. A. M., and Omotayo, P, (2015). Effects of High Dietary Fat Intake on Biochemical Variables and Pancreas Histoarchitecture in Diabetic Rats. *Journal Human Nutrition Food Science*; **3(1)**: 1053.
- Mohammadzadeh, G., Zarghami, N., Mobaseri, M. (2008). Serum Resistin Concentration in Obese Diabetic patients: Any Possible Relation to Insulin Resistance Indices. *International Journal of Endocrinology Metabolism*; **4**: 183-193.
- Mohammed, T. and Yacir, B. (2021). Is resistin the master link between inflammation and inflammation-related chronic diseases?. *Molecular and Cellular Endocrinology*; **533**:111341.
- Moon, B., Kwan, J.J., Duddy, N., Sweeney, G., Begum, N. 2003 Resistin inhibits glucose uptake in L6 skeletal muscle cells independent of changes in insulin signalin components and glut-4 translocation. *American Journal of Physiology and Endocrinology Metabolism*; **285**: 106–115.
- Musialik, K.; Miller-Kasprzak, E.; Walczak, M.; Markuszewski, L.; Bogda ński, P.(2022) The Association between Serum Resistin Level, Resistin (- 420C/G) Single Nucleotide Variant, and Markers of Endothelial Dysfunction, including Salt Taste Preference in Hypertensive Patients. *Nutrients*; **14**: 1789.
- .Novelli, E. L .B., Diniz, Y. S., Galhardi, C. M., Ebaid, G. M. X., Rodrigues, H. G., Mani, F., Fernandes, A. A. H., Cicogna, A. C., and Filho, N. (2007). Anthropometrical parameters and markers of Obesity in rats. *Laboratory Animals*; **41**: 111–119.
- Otunola, G. A., Oloyede, O. B., Oladiji, A. T., Afolayan, A.A. (2010) Effects of diet induced hypercholesterolemia on the lipid profile and some enzyme activities in female

- Wistar rats. *African Journal of Biochemistry Research*; **4 (6)**:149-154.
- Popov, D., Simionescu, M., Shepherd, P. (2003) Saturated-fat diet induces moderate diabetes and severe glomerulosclerosis in hamsters. *Diabetologia*; **46**: 1408-1418.
- Rajala, M.W., Obici, S., Scherer, P.E., Rossetti, L. (2003). Adipose-derived resistin and gut derived resistin-like molecule-beta selectively impair insulin action on glucose production. *Journal of Clinical Investigations*; **111**: 225–230.
- Raje V, Ahern KW, Martinez BA, Howell NL, Oenarto V, Granade ME, Kim JW, Tundup S, Bottermann, K, Gödecke, A., Keller, S.R., Kadl, A., Bland, M.L., Harris, T.E. (2020) Adipocyte lipolysis drives acute stress-induced insulin resistance. *Scientific Reports*; **10(1)**:18166.
- Rajkovic, N.A., Zamaklar, .M., Lalic, K., Jotic, A., Lukic, L., Milicic, .T., Singh, .S. Stosic. .L., Lalic, N. M. (2014). Relationship between Obesity, Adipocytokines and Inflammatory Markers in Type 2 Diabetes: Relevance for Cardiovascular Risk Prevention International. *Journal Environmental Research Public Health*; **11**: 4049-4065.
- Rashid, S. (2013). Mechanism by which elevated resistin levels accelerate atherosclerotic cardiovascular disease. *Rheumatology Current Research*; **3 (1)**:56-60.
- Reilly, M.P., Lehrke, M., Megan, L., Wolfe, .B.S., Anand, R., Lazar, A.M., Rader, D.J (2005). Resistin is an inflammatory marker of atherosclerosis in humans. *Journal American Heart Association*; **111(932-939)**.
- Rizvi, N. B., and Nagra, S. A. 2012. Minerals and Lipids Profiles in Cardiovascular Disorders in South Asia: 9-11
- Shoaib, O.M., Nourein, I. H., Abusharib, A. B., Elbadri, M.A. (2015). Changes in Lipids Profile and Insulin Level in Obese Sudanese Women. *Global Advanced Research Journal of Medicine and Medical Science*; **4(10)**: 449-454.
- Silha J.V, Krsek M, Skrha J.V, Sucharda P, Nyomba BLG, Murphy LJ. (2003). Plasma resistin, adiponectin and leptin levels in lean and obese subjects: correlations with insulin resistance. *Europe Journal of Endocrinology*; **149**: 331-335.
- Sonuyi, A.O., Akinpelu, A.O., Odole, A.C., AND Akinbo, S.R.A. (2013). Normative values of selected Anthropometric variables in Lagos Nigeria population. *Orthopedic and Molecular System Current Research*, **2**:133
- Steppan, C.M., Bailey, S.T., Bhat, S., Brown, E.J., Banerjee, R.R. (2001) The hormone resistin links obesity to diabetes. *Nature*; **409**: 307-312.
- Steppan, C.M., Lazar M.A. (2011). The current biology of resistin. *Journal of Internal Medicine*; **255**: 439-447.
- Steppan, C.M., Wang, J., Whiteman, E.L., Birnbaum, M.J., Lazar, M.A. (2005). Activation of SOCS-3 by resistin. *Molecular Cell Biology*; **25**: 1569-1575.
- Tofangchiha, S., Rahimi Dizgah, I.M., Isazadeh, M., Mansournia, N., Taghavi, Y., and Larijani, A.M. (2020). The Relationship between Serum Resistin Levels and Diabetic Nephropathy in Type 2 Diabetic Patients. *Ann Mil Health Science Research*; **18(4)**: e107878
- Trinder, P. (1969). Determination of total cholesterol. *Annals of Clinical Biochemistry*; **6**:24–27.
- Urbanovych, A. (2015). The blood resistin level in patients with DM2, depending on the duration of the disease. *Current Issues in Pharmacy and Medical Sciences*; **28(2)**:111-114.
- World Health Organization (2021) Obesity and overweight.

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