Kirkuk Journal of Science Vol. 20, Iss. 1, p. 43-53, 2025 doi:10.32894/kujss.2025.157067.1193

Assessing the Role of GSK3 β and Arrestin Beta1 in Regulating Oxidative Stress that Causes Metabolic Disorders

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Article Information

Article Type:
Research Article

Keywords:
oxidative stress, metabolic disorders, GSK3 β, Arrestin Beta 1, obesity.

History:
Received: 30 January 2025
Revised: 11 March 2025
Accepted: 21 March 2025
Available Online: 27 March 2025

Citation: Ali Mahmood Monef, Assessing the Role of GSK3 β and Arrestin Beta1 in Regulating Oxidative Stress that Causes Metabolic Disorders, Kirkuk Journal of Science, 20(1), p. 43-53, 2025, https://doi.org/10.32894/kujss.2025.157067.1193

Abstract

Metabolic syndrome is intricately associated with diabetes and obesity. Elevated obesity fosters inflammation and oxidative stress, which are precursors to several problems, including elements of metabolic disorders such as insulin resistance and hyper lipidaemia. This study aims to show that the GSK3 β and Arrestin beta 1 serve as effective biomarkers for predicting metabolic disorders Such as diabetes and obesity, which leads to increased oxidative stress that enhances inflammatory reactions, and this contributes to obesity and type 2 diabetes. The research was performed at Al-Yarmouk Teaching Hospital. Out of 180 collected samples, only 135 were measured. The patients were categorized into three groups. The biomarkers Arrestien Beta 1 and GSK3 β were measured by ELISA technology, the lipid profile, FBS, and total protein were assessed using a spectrophotometer. Arrestin Beta 1 and GSK3 β in the serum showed a significant increase in type 2 diabetic patients with obesity compared to the group of metabolic disorders. The atherosclerosis index (AIP) was measured using a logarithm TG/HDL-cholesterol. conclude from this study the GSK3 β and Arrestin beta1 serve as effective biomarkers for predicting metabolic disorders based on the results obtained Which leads to increased production of free radicals in the body, causing diabetes, which may lead to the accumulation of glucose in the blood, which increases levels of oxidative stress. This condition leads to increased production of free radicals and reactive molecules that contribute to the activation of NF-$_K$B inflammatory pathways, which in turn affects the metabolic balance in the body.

1. Introduction:

Metabolic syndrome is intricately associated with diabetes and obesity. Elevated obesity fosters inflammation and oxidative stress, which are precursors to several problems, including elements of metabolic syndrome such as insulin resistance and hyper lipidaemia. Numerous variables influence the pathophysiology of metabolic disorders; nonetheless, extensive research indicates that oxidative stress is fundamental to the onset of these illnesses [1]. Oxidative stress is characterized as an imbalance between oxidants and antioxidants inside the cell, resulting in a diminished capacity of the cell to counteract oxidation. Excessive generation of reactive oxygen species (ROS) is detrimental to cellular components, particularly proteins and lipids, resulting in cellular damage. Oxidative stress has been associated with several medical disorders, including diabetes and atherosclerosis [2].

Oxidative stress is closely associated with GSK3 β. Glycogen synthase kinase-3β (GSK-3β) (EC 2.7.11.26) is a serine-threonine kinase ubiquitously expressed and involved in cellular organization. It comprises two homologous kinds, alpha and beta, exhibiting 98% sequence identity in the particular kinase domains, differing in their N and C terminals [3]. Oxidative stress activates GSK3 β via impairing the PI3K/AKT pathway due to oxidative damage [4]. It also contributes

to redox equilibrium by modulating the levels of reactive oxygen species in mitochondria. The generation of reactive oxygen species (ROS) significantly impacts metabolic control by affecting energy metabolism, hence contributing to the development of diabetes and obesity, a factor associated with impaired metabolism [5].

Obesity is a multifaceted condition that significantly affects global public health. The outcome is the consequence of a complex interplay of variables, including genetic predisposition, food, metabolism, and physical activity. It is associated with several ailments, including metabolic disorders, type 2 diabetes, and cardiovascular dysfunction [6]. The Arrestin beta 1 family has two types, Arrestin 1 and Arrestin 2, which exhibit significant structural similarities. Arrestin beta 1 functions as a molecular scaffold for several signaling proteins. Specific investigations have suggested it is a crucial cellular organizer with multifunctional capabilities [7]. It is crucial in controlling oxidative stress and synthesizing superoxide for mitochondria [8].

This study aims to show that the GSK3 β and Arrestin beta 1 serve as effective biomarkers for predicting metabolic disorders such as diabetes and obesity, which leads to increased oxidative stress that enhances inflammatory reactions, and this contributes to obesity and type 2 diabetes.

2. Subjects and Methods:

One hundred eighty samples were obtained, excluding all patients with type 1 diabetes, those receiving insulin injections, individuals with heart, renal, or liver illness, and pregnant women. A total of 135 samples were measured and specifically selected for the research investigation. The study encompassed individuals aged 30 to 55 years, categorized into three groups: control group G1 (46 participants), metabolic disorders group G2 (45 participants) have excessive obesity. By calculating the body mass index, the value is greater than 30 kg/m^2, they recently developed diabetes without taking any diabetes treatment and they suffer from dyslipidemia through high levels of cholesterol and triglycerides and low levels of high-density lipoprotein cholesterol (TG/HDL-C), and obesity and type 2 diabetes group G3 (44 participants).

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The specimens were obtained from AL-Yarmouk Teaching Hospital. The body mass index was determined using the accompanying formula: weight in kg/m^2 [9]. for all participants, including both sick and healthy individuals. A 10 ml syringe was employed to collect 6 ml of venous blood, which was subsequently put in a gel tube. The tube was allowed to separate before being centrifuged at 3000 rpm for 10 minutes to get serum, which was then frozen at -8 degrees Celsius. An assessment of each of our biomarkers was conducted, Arrestin beta 1, GSK3 β, and insulin, with ELISA technology from Huma Reader HS in U.S.A. Tests of quantifying total protein, lipid profile, and fasting blood glucose were performed utilizing a UV-visible spectrophotometer from Huma Reader HS in U.S.A.

The atherosclerosis index (API) was calculated using a logarithmic function of TG/HDL-C [10]. Homeostasis Model Assessment (HOMA) IR estimation of insulin resistance using HOMA IR = (FBG $\times$ Insulin / 405) [11].

3. Statistical Analysis:

The study employed version 26 of the Statistical Package for the Social Sciences (SPSS Inc., Chicago, U.S.A.). The data was provided as (mean $\pm$ standard error). This study encompassed many assessments, including the ANOVA test to evaluate the correlation coefficient (r) among parameters, the Tukey test, the ROC curve, and the examination of differences among three independent variables the statistical test utilized linear regression analysis for estimates. The anticipated value, deemed significant at $p \leq 0.05$ and non-significant at $p > 0.05$, was employed to ascertain statistical significance.

4. Results:

The results indicate no significant difference in the ages of the three groups, However, a significant difference in W/H ratio and BMI (kg/m^2) was observed among the groups: G1 (22.85 $\pm$ 0.17), G2 (36.51 $\pm$ 0.74), and G3 (34.01 $\pm$ 0.65) and W/H G1(0.87$\pm$0.01), G2(1.12 $\pm$ 0.02), andG3(1.04 $\pm$ 0.02), ($p<0.001$) as indicated in Table 1. Additionally, the lipid profile showed significant differences, with mean values $\pm$ SE for cholesterol (mg/dL), Triglycerides TG (mg/dL), Low-Density Lipoprotein LDL-C (mg/dL) and Very Low-Density Lipoprotein VLDL (mg/dL) as indicated in Table 1 also, High Density Lipoprotein HDL (mg/dL) demonstrated significant differences among the groups: [G1 (38.67$\pm$0.69), G2 (18.05$\pm$0.48), and G3 (21.46$\pm$1.71)].

The atherosclerosis index (API) was mathematically calculated using the logarithm TG/HDL-C, The atherosclerosis index (AIP)[G1(0.609 $\pm$0.008), G2(1.059 $\pm$ 0.013), G3(1.051 $\pm$ 0.028)]. Additionally, a significant difference was observed among the three groups concerning insulin, insulin resistance, and fasting blood sugar. The mean values $\pm$ SE of insulin

(SI/ml) are as follows: G1 (3.36 $\pm$ 0.11), G2 (6.05 $\pm$ 0.12), G3 (7.66 $\pm$ 0.17).Insulin resistance (SI \ mL) was done using HOMA-IR equation [G1 (0.79 $\pm$ 0.02), G2 (1.91 $\pm$ 0.06), G3 (4.05 $\pm$ 0.19)] There is significant difference between G1 ,G2 and G3, Total Protein (g \ dL) [G1 (5.48 $\pm$ 0.12), G2 (6.02 $\pm$ 0.07), G3 (6.93 $\pm$ 0.14)],There is no significant difference between G1 and G2, but there is a significant difference between G2 and G3 GSK3 β (ng \ ML)[G1 3.53 $\pm$ 0.06, G2 3.20 $\pm$ 0.0.5 and G3 16.16 $\pm$ 0.62)] and Arrestin Beta1 (pg \ ML) [G1(273.98 $\pm$ 21.30) G2 (311.16 $\pm$ 20.23) G3 (520.75 $\pm$ 27.25)] as indicated in Table 1. Data were presented as Mean $\pm$ SE **Significant difference between means using ANOVA -test at 0.01 level. a, b, and c are significant variants that are denoted by different small letters, and non-significant variations are denoted by identical small letters.

Table 2: indicates a positive correlation in G3 between GSK3 β and triglycerides (0.485) as well as VLDL (0.482), with statistical significance ($p < 0.01$). In G3 and G2, a positive correlation between GSK3 β and insulin was observed, with values of 0.423 ($p<0.01$) and 0.347 ($p<0.05$), respectively. In G3, a positive correlation is observed with insulin resistance (0.312, $p<0.05$) and arrestin beta 1 (0.385, $p<0.01$). Conversely, G2 negatively correlates with Arrestin Beta1 (-0.408, $p<0.01$). In Table 3, in G3, there is a positive correlation between Arrestin beta 1 and FBS (0.659), triglycerides(0.619), VLDL(0.618), insulin(0.774), insulin resistance(0.714), and GSK3 β(0.385), a negative correlation with total protein(-0.385) ($p < 0.01$). While in G2, there is a negative correlation between Arrestin beta 1, insulin(-0.514), and GSK3 β(-0.408), G1, a positive correlation between Arrestin beta 1 and age(0.321), and a negative correlation. With FBS(-0.345), HDL(-0.307) ($p<0.05$) Table 4 indicates that the area under the curve for the enzyme glycogen synthase kinase 3 beta is 0.999, which signifies an excellent result. This suggests that the indicator is highly effective for both groups, G1 and G2. Figure 1 Table 5 indicates that the area under the curve of Arrestin Beta1 gave a very good result = 0.817. This suggests that the indicator is highly effective for both groups, G1 and G2. Figure 2

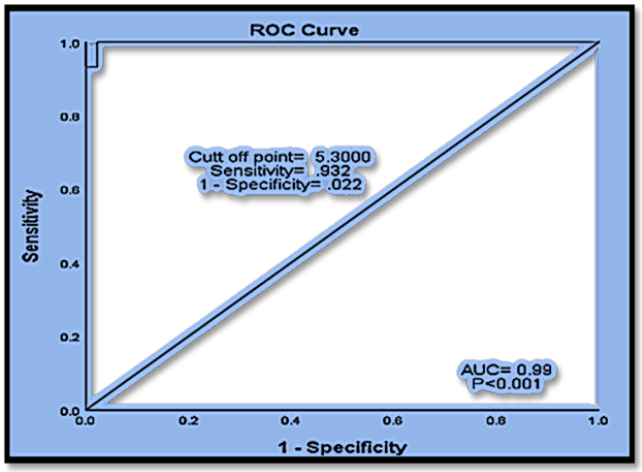

Figure 1. ROC curve analysis of GSK3 β between control and Metabolic disorders.

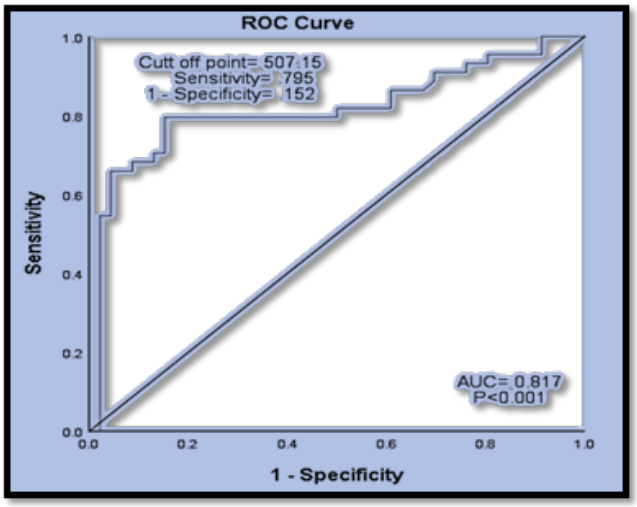

Figure 2. ROC curve analysis of Arrestin Beta1 between control and metabolic disorders.

5. Discussion:

Table 1 indicates no significant difference among the ages, as the samples were selected from the range of 30 to 55 years. Both groups, G2 and G3, exhibit a considerable difference from G1 regarding insulin resistance and fasting blood sugar. This suggests that both factors are predictive of metabolic disease development, particularly type 2 diabetes, alongside an increase in AIP, a notable risk indicator for type 2 diabetes. The atherosclerosis index AIP was found to be associated with an elevated risk. The prevalence of insulin resistance and diabetes aligns with the findings of Yin B et al [12]. Both groups exhibit a body mass index exceeding 30 kg/m^2. This suggests

Table 1. mean $\pm$ SE of biochemical parameters and GSK3 β between studied group.

Parameters	Groups			
	Control Group G1 No. (46)	Metabolic disorders Group G2 No. (45)	Type 2 diabetes with Obesity Group G3 No. (44)	P-value
Age (year)	40.82 ± 1.28^{a}	40.84 ± 1.10^{a}	44.45 ± 1.04^{a}	0.071
BMI (kg/m^2)	22.85 ± 0.17^{a}	36.51 ± 0.74^{c}	34.01 ± 0.65^{b}	0.001**
W/H ratio	0.87 ± 0.01^{a}	1.12 ± 0.02^{c}	1.04 ± 0.02^{b}	0.001**
FBS (mg/dL)	97.79 ± 1.96^{a}	131.58 ± 2.34^{b}	212.67 ± 6.71^{c}	0.001**
Insulin (SI \ Ml)	3.36 ± 0.11^{a}	6.05 ± 0.12^{b}	7.66 ± 0.17^{c}	0.001**
Insulin resistance (SI \ ML)	0.79 ± 0.02^{a}	1.91 ± 0.06^{c}	4.05 ± 0.19^{b}	0.001**
Cholesterol (mg/dL)	173.91 ± 1.11^{a}	209.17 ± 2.30^{b}	213.56 ± 2.45^{b}	0.001**
Triglyceride (mg/dL)	156.49 ± 1.16^{a}	204.38 ± 2.97^{b}	217.87 ± 1.91^{c}	0.001**
HDL-C (mg/dL)	38.67 ± 0.69^{b}	18.05 ± 0.48^{a}	21.46 ± 1.71^{a}	0.001**
LDL-C (mg/dL)	103.39 ± 1.58^{a}	150.06 ± 2.58^{b}	148.59 ± 1.80^{b}	0.001**
VLDL-C (mg/dL)	31.00 ± 0.22^{b}	40.80 ± 0.59^{b}	43.46 ± 0.38^{c}	0.001**
AIP (mg/dL)	0.609 ± 0.008^{a}	1.059 ± 0.013^{a}	1.051 ± 0.028^{b}	0.001**
GSK3β (ng \ ML)	3.53 ± 0.06^{a}	3.20 ± 0.05^{a}	16.16 ± 0.62^{b}	0.001**
Arrestin Beta1 (pg \ ML)	273.98 ± 21.30^{a}	311.16 ± 20.23^{a}	520.75 ± 27.25^{b}	0.001**

that obesity arises from low-quality food intake, leading to increased oxidative stress, a critical factor in the development of obesity and diabetes and its associated metabolic complications. This suggests that oxidative stress in mitochondria may contribute to obesity, leading to metabolic disorders [13].

An increase in the waist-to-hip index is observed in groups G2 and G3, indicating the presence of abdominal fat. The increased likelihood of developing additional conditions, including high cholesterol, diabetes, or atherosclerosis. This aligns with numerous studies that have validated body mass index and waist-to-hip ratio use. Identifying metabolic disorders in clinical and epidemiological investigations is essential due to its direct and non-invasive nature [14]. Both groups, G2 and G3, exhibit a significant difference from G1 in the lipid profile, characterized by elevated triglyceride levels, reduced HDL, and increased LDL and VLDL levels. This results from several factors, notably elevated oxidative stress in the mitochondria, leading to the oxidation of LDL, as supported by Hazart J et al [15].

Oxidation of fats generates reactive oxygen species that damage cellular structures, including membranes and proteins. Excessive fat accumulation results in oxidative stress. Conversely, one cause of metabolic disorders is fat accumulation, which is associated with metabolic syndrome resulting from a weakened defense system. Systemic antioxidants [16]. Research indicates that elevated protein levels correlate with high consumption of substantial quantities of meat, dairy products, and fish. This high protein intake is associated with an increase in insulin resistance and a heightened risk of developing type 2 diabetes. This aligns with our findings, as total protein levels were elevated in groups G2 and G3 [17]. The findings align with the work of Liu X et al., who established a correlation between an increased fat profile and elevated total protein levels in the body [18].

The quality of protein intake is essential, as it enhances the overall protein quality relative to its quantity. Essential amino acids in food enhance glycaemic and metabolic indicators overall. This study confirms that a protein-rich diet enhances blood sugar indicators. Blood parameters and anthropometric indicators are improved by reducing fatty factors, enhancing insulin sensitivity, and promoting glycogen formation, which aligns with previous studies [19], [20].

There exists a significant relationship between oxidative stress and protein, as research indicates that oxidative stress contributes to protein aggregation and its elevation. Research suggests that oxidative stress imbalance leads to protein oxidation, particularly in individuals with type 2 diabetes [21]. Our findings align with this observation, as we noted increased protein levels in patients with type 2 diabetes. An increase in atherosclerosis index (AIP) is observed in both groups of metabolic disorders and type 2 diabetes with obesity compared to the control group. This finding aligns with studies indicating that the atherosclerosis index and the total cholesterol to HDL ratio are significantly elevated in patients with

Table 2. The correlation coefficient between difference parameters with GSK3 β.

Parameters		Groups		
		Control Group G1 No. (46)	Metabolic disorders Group G2 No. (45)	Type 2 diabetes with Obesity Group G3 No. (44)
Age (years)	r	-0.049	-0.279	-0.154
	P	0.745	0.064	0.318
BMI (kg/m^2)	r	0.086	-0.096	-0.249
	P	0.571	0.530	0.103
W/H ratio	r	-0.079	0.223	-0.327*
	P	0.603	0.140	0.030
FBS (mg/dL)	r	0.292*	0.046	0.234
	P	0.049	0.765	0.127
Cholesterol (mg/dL)	r	0.180	-0.048	-0.017
	P	0.230	0.756	0.912
Triglyceride (mg/dL)	r	0.144	0.286	0.485**
	P	0.339	0.056	0.001
HDL-C (mg/dL)	r	0.092	-0.058	0.092
	P	0.545	0.707	0.551
LDL-C (mg/dL)	r	0.038	-0.083	-0.217
	P	0.802	0.588	0.157
VLDL-C (mg/dL)	r	0.182	0.276	0.482**
	P	0.226	0.067	0.001
Insulin (SI \ ml)	r	-0.192	0.347*	0.423**
	P	0.202	0.020	0.004
Insulin resistance (SI \ mL)	r	0.008	0.262	0.312*
	P	0.960	0.082	0.039
Arrestin Beta1 (pg \ mL)	r	-0.268	-0.408**	0.385**
	P	0.072	0.005	0.010
Total Protein (g \ dL)	r	-0.158	-0.014	-0.281
	P	0.295	0.927	0.065

*Correlation is significant at the 0.05 level.
**Correlation is significant at the 0.01 level.

diabetes and obesity, which are primary contributors to these disorders. Metabolism refers to the biochemical processes that occur within a living organism to maintain life, encompassing both catabolic and anabolic pathways. The role of atherosclerosis index (AIP)underscores the connection between metabolic factors and cardiovascular health [22]. The GSK3 β enzyme exhibited a significant difference between G2 patients with metabolic disorders and G3 patients with type 2 diabetes with obesity.

This is attributable to its significant function and its presence within cells. It is located in the cytoplasm, nucleus, and mitochondria. It is produced in all body tissues and plays a role in regulating metabolic processes, cell proliferation, and apoptosis. Research indicates When oxidative stress occurs, it leads to an increase in the levels of free radicals in the cells, which leads to the activation of GSK3 β. This affects many cellular pathways, including those that control the activity of GSK3 β. Oxidative stress also leads to a change in phosphorylation levels, which leads to the activation of GSK3 β. This in turn leads to insulin resistance, which means that the cells do not respond effectively to insulin, which in turn leads to diabetes, which is one of the metabolic diseases. [23]. Mitochondria play a crucial role in energy generation within the cell, contributing to fundamental cellular functions, the production and elimination of reactive oxygen species, and the relationship between mitochondrial dysfunction and oxidative stress in developing and progressing various diseases, including metabolic disorders [24].

Also, in Arrestin beta 1, no significant difference is observed between G2 and G1 however, The results showed a significant difference between G2 patients with metabolic disorders and patients with type 2 diabetes with obesityG3.This highlights the crucial role of Arrestin beta 1 in coordinating various essential signaling proteins. The function of Arrestin

Table 3. The correlation coefficient between difference parameters with Arrestin Beta1.

		Groups		
		Control Group G1 No. (46)	Metabolic disorders G2 No. (45)	Type 2 diabetes with Obesity Group G3 No. (44)
Age (years)	r	0.321 *	-0.245	0.202
	P	0.030	0.105	0.188
BMI (kg/m^2)	r	0.011	-0.172	0.124
	P	0.943	0.258	0.421
W/H ratio	r	0.166	-0.012	-0.108
	P	0.271	0.940	0.485
FBS (mg/dL)	r	-0.345*	0.088	0.659**
	P	0.019	0.563	0.000
Cholesterol (mg/dL)	r	-0.111	0.167	0.191
	P	0.462	0.273	0.214
Triglyceride (mg/dL)	r	-0.104	0.092	0.619**
	P	0.492	0.548	0.000
HDL-C (mg/dL)	r	-0.307*	-0.096	0.151
	P	0.038	0.530	0.326
LDL-C (mg/dL)	r	0.261	0.137	-0.017
	P	0.080	0.370	0.911
VLDL-C (mg/dL)	r	-0.061	0.087	0.618**
	P	0.686	0.571	0.000
Insulin (SI)	r	0.136	-0.514**	0.774**
	P	0.367	0.000	0.000
Insulin resistance (SI \ mL)	r	-0.078	-0.243	0.714**
	P	0.606	0.108	0.000
GSK3 β (ng \ mL)	r	-0.268	-0.408**	0.385**
	P	0.072	0.005	0.010
Total Protein (g \ dL)	r	-0.033	-0.146	-0.385**
	P	0.825	0.337	0.010

*Correlation is significant at the 0.05 level.
**Correlation is significant at the 0.01 level.

beta 1 proteins is attributed to the phosphorylation of G protein receptors, a significant factor in cellular responses [25]. It is a crucial element in the functioning of adipocytes and the regulation of glucose and energy homeostasis. Any disruption in this balance contributes to the prevalence of diabetes and obesity, resulting in metabolic disorders .It also plays an important role in regulating cellular signals that are affected by oxidative stress through its effect on cellular receptors and signaling pathways.

In the normal state, Arrestien beta 1 interacts with GPCRS receptors to stop or modify the receptor response, but when oxidative stress occurs, this interaction changes as free radicals lead to structural changes in the receptor proteins or in Arrestien beta1 it self. These changes contribute to disrupting insulin related signals, increasing insulin resistance, and causing metabolic problems. As shown in Table 2 presents results indicating an association between the GSK3 β enzyme, triglycerides, and VLDL. Our results indicate that It causes an increase in body fat, and visceral fat leads to oxidative stress, which leads to an abnormal increase in the activity of GSK3 β. This causes negative effects on cells, such as disturbances in cellular processes and an increased risk of metabolic diseases, the most important of which is diabetes. obesity disrupts the regulation of the metabolic pathways associated with GSK3 β. This subsequently results in dyslipidaemia and various cardiovascular diseases [26].

A positive correlation between insulin resistance and GSK3 β is observed, underscoring the enzyme's considerable role in insulin regulation. An imbalance in oxidative stress and defects in mitochondrial functions contribute to metabolic disorders, resulting in a deficiency of the GSK3 β enzyme. An imbalance in oxidative stress or a defect in mitochondrial function has been associated. Both factors contribute to insulin resistance and induce cellular stresses related to this condition, including stress on the endoplasmic reticulum. It also results in unstable insulin resistance [27]. Consequently,

Table 4. ROC Curve Analysis of GSK3 β between control and metabolic disorders.

Area Under the Curve				
Test Result Variable(s): GSK3 β				
Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.999	0.002	0.000	0.995	1.000
a. Under the nonparametric assumption				
b. Null hypothesis: true area = 0.5				

Table 5. ROC Curve Analysis of Arrestin Beta1 between control and metabolic disorders.

Test Result Variable(s): Arrestin Beta1				
Area	Std. Errora	Asymptotic Sig.b	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.817	0.049	0.000	0.722	0.912
a. Under the nonparametric assumption				
b. Null hypothesis: true area = 0.5				

We note that there is a relationship between Arrestien beta1 and GSK3 β. Studies have indicated that Arrestien beta1 has an influential role in signaling pathways and in the same biological pathways that GSK3 β joins, which plays a role in many signaling pathways that include cell growth and oxidative stress, indicating that both may interact in the same way [28].

This explanation is associated in Table 3 illustrates the correlation between age and Arrestin beta 1. Age significantly influences the pathophysiology. An increase in the expression and functional effect of Arrestin beta 1 has been observed. To regulate Arrestin beta1, addressing the elevated levels of reactive oxygen species (ROS) present in nearly all cells is essential to reduce the associated oxidative damage. When the body fails to regulate reactive oxygen species (ROS), oxidative stress and damage ensue, leading to detrimental modifications. Regarding proteins and fats, arrestin beta 1 is significant in regulating oxidative stress [29]. An important connection exists between Arrestin beta 1 and total protein.

The function of G-protein receptors in the plasma membrane serves as information channels, facilitating communication between the external environment and the interior of the cells. Signal transmission relies on the physical interaction between receptors and stimuli within cells, following activation through ligand interaction outside the cells. G protein receptors interact with diverse proteins in the human body [30]. Arrestin beta1 plays a significant role in insulin secretion via the glycogen-like peptide receptor-1, which is relevant to novel anti diabetic therapies. Arrestin beta 1 mediates the capacity of GLP-1 to stimulate cAMP and insulin secretion in pancreatic beta cells, thereby regulating their function, highlighting its importance. In the regulation of metabolic pathways due to impaired glucose regulation [31].

Arrestin beta1 is a multifunctional protein that plays a significant role in signal transmission. G protein receptors are crucial for regulating metabolic pathways, including those involved in diabetes management. Arrestin beta 1 contributes to the development of dyslipidaemia, a factor associated with heart disease and heart failure, by attenuating signaling pathways. 4 β-adrenergic and angiotensin II receptors mitigate the detrimental effects of excessive sympathetic stimulation by concurrently activating cardiac protective signaling pathways that preserve the structure and function of the heart in response to injury [32].

Table 4 indicates that the area under the curve for the enzyme GSK3 β kinase is 0.999, which is an excellent result. Recent discussions have highlighted the significant role of GSK3 β in regulating metabolic pathways and its involvement in oxidative stress, a contributing factor to obesity associated with metabolic disorders. The indicator demonstrates strong performance for both groups G1 and G2. We prove through it that the GSK3 β enzyme is an important biomarker that predicts metabolic disorders resulting from one of the diseases, which is diabetes, as it is characterized by high levels of glucose in the blood [33].

This condition leads to increased production of free radicals and reactive molecules that contribute to activating the inflammatory pathways (Nuclear Factor kappa-light-chain-enhancer of activated B cells))NF-KB(, which affects insulin regulation. GSK3 β plays an important role in regulating the (Nuclear Factor kappa-light-chain-enhancer of activated B cells)) NF-KB(pathway, Ser9 phosphorylation at the amino terminal of GSK-3β may considerably reduce its activity, whilst Tyr216 phosphorylation may increase it [34]. (Nuclear Factor kappa-light-chain-enhancer of activated B cells) (NF-KB) which is a signaling pathway that plays an important role in the cells, response to free radicals and damage resulting from oxidative stress and the occurrence of any defect in this pathway will lead to increased activation of GSK3 β, which leads to a defect in the body's response to insulin, which contributes to insulin resistance and is one of the causes of diabetes aligns with the findings of Xianyi W et al [35].

In Table 5, the ROC analysis of Arrestin beta 1 gave a very good result (0.817), as it proved that Arrestin beta 1 is a clear indicator for both Groups G1 and G2. Arrestin beta 1 is a plasma membrane that has a role in regulating the cell cycle and also has a role in functions related to the G protein. Arrestin beta1 and NF-KB play a role in regulating the response to oxidative stress by affecting GPCR signals or the cells' response to radicals. This is due to the role of Arrestin beta 1 in regulating NF-KB signals through its interaction with GPCR. Arrestin beta 1 can enhance or inhibit the activation of NK-KB and thus plays a crucial role in maintaining cellular balance and modifying responses to oxidative stress. This confirms that it is a very good biomarker in predicting metabolic diseases, including diabetes, as when blood sugar levels rise in the body, we notice a significant activity in the biomarker, Arrestien beta 1 aligns with the findings of Juan Li et al [36].

6. Conclusion:

This study concluded that GSK3 β and Arrestin beta 1 act as effective biomarkers for pre-existing metabolic disorders according to the results obtained through the area under the curve of the Roc, where the GSK3 enzyme gave an excellent result and Arrestien beta 1 gave and from the results we conclude that both are biomarkers for metabolic disorders that lead to increased production of free radicals in the body, for example in the case of obesity, diabetes or dyslipidemia, This may lead to the accumulation of glucose in the blood, which increases the levels of oxidative stress. This condition leads to increased production of free radicals and reactive molecules that contribute to the activation of NF-$_k$B inflammatory pathways, which in turn affects the metabolic balance in the body.

Acknowledgments: The authors acknowledge with sincere gratitude all staff of "AL-Yarmouk Teaching Hospital" for their help in obtaining samples for the current study.

Funding: There is no financial support or sponsorship from any institute.

Data Availability Statement: All of the data supporting the findings of the presented study are available from corresponding author on request.

Declarations:

Conflict of interest: The authors declare that they have no conflict of interest.

Ethical approval: The Declaration of Helsinki's ethical guidelines guided the research. We conducted the procedure after obtaining the patients' verbal and analytical consent prior to sample collection. The research protocol, subject information, and permission form underwent assessment and approval by the local Ethical Committee at the University of Baghdad.

Author contributions: Asmaa Mohammed AbdalJalil was responsible for collecting samples, conducting analysis, interpreting data, writing the manuscript, and proofreading it. Fayhaa Muqdad Khaleel conceived the idea, supervised the research, and read the manuscript.

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تقييم دور $GSK3\beta$ و $Arrestin\ Beta1$ في تنظيم الإجهاد التأكسدي الذي يسبب الاضطرابات الأيضية

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الخلاصة

ترتبط متلازمة التمثيل الغذائي بشكل معقد بمرض السكري والسمنة. تؤدي السمنة المرتفعة إلى تعزيز الالتهابات والإجهاد التأكسدي، وهي مقدمة للعديد من المشاكل، بما في ذلك عناصر الاضطرابات الأيضية مثل مقاومة الأنسولين وفرط الدهون في الدم.

تهدف هذه الدراسة إلى أن يكون $GSK3\beta$ و $Arrestin\ Beta1$ بمثابة مؤشرات حيوية فعالة للتنبؤ بالاضطرابات الأيضية مثل مرض السكري والسمنة، مما يؤدي إلى زيادة الإجهاد التأكسدي الذي يعزز التفاعلات الالتهابية، وهذا يساهم في الإصابة بالسمنة ومرض السكري من النوع الثانيتم إجراء البحث في مستشفى اليرموك التعليمي. ومن بين 180 عينة تم جمعها، تم قياس 135 عينة فقط. تم تصنيف المرضى إلى ثلاث مجموعات. تم قياس المؤشرات الحيوية $GSK3\beta$ و $Arrestin\ Beta1$ بواسطة تقنية $ELISA$ ، وتم تقييم ملف الدهون و FBS والبروتين الكلي باستخدام مقياس الطيف الضوئي. أظهر النتائج $GSK3\beta$ و $Arrestin\ Beta1$ في المصل زيادة ملحوظة في مرضى السكري من النوع 2 الذين يعانون من السمنة مقارنة بمجموعة الاضطرابات الأيضية. تم قياس مؤشر تصلب الشرايين (AIP) باستخدام لوغاريتم $TG/HDL-C$ وخلصت هذه الدراسة إلى أن $GSK3\beta$ و $Arrestin\ Beta1$ يعملان كمؤشرات حيوية فعالة للتنبؤ بالاضطرابات الأيضية بناءً على النتائج التي تم الحصول عليها مما يؤدي إلى زيادة إنتاج الجذور الحرة في الجسم ، على سبيل المثال في حالة مرض السكري، مما قد يؤدي إلى تراكم الجلوكوز في الدم، مما يزيد من مستويات الإجهاد التأكسدي، وتؤدي هذه الحالة إلى زيادة إنتاج الجذور الحرة والجزيئات التفاعلية التي تساهم في تنشيط مسارات الالتهاب $NF-_kB$ ، مما يؤثر بدوره على التوازن الأيضي في الجسم.

الكلمات الدالة : الإجهاد التأكسدي، الاضطرابات الأيضية، السمنه ، $Arrestin\ beta1$ ، $GSK3\ \beta$.

التمويل: لايوجد.

بيان توفر البيانات: جميع البيانات الداعمة لنتائج الدراسة المقدمة يمكن طلبها من المؤلف المسؤول.

اقرارات:

تضارب المصالح: يقر المؤلفون أنه ليس لديهم تضارب في المصالح.

الموافقة الأخلاقية: استرشد البحث بالمبادئ الأخلاقية لإعلان هلسنكي. أجرينا الإجراء بعد الحصول على موافقة المرضى الشفهية والتحليلية قبل جمع العينات. خضع بروتوكول البحث، ومعلومات المريض، ونموذج الإذن للتقييم والموافقة من قبل اللجنة الأخلاقية المحلية في جامعة بغداد.