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Metabolic Mechanisms of Fat Accumulation and Effects of a Healthy Lifestyle Intervention on Obesity Indicators in Adults A Case-Control Study

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ABSTRACT

Obesity is a complex condition resulting from a long-term positive energy balance, in which energy intake exceeds energy expenditure, leading to excessive accumulation of adipose tissue. This study evaluated the impact of a six-month healthy lifestyle intervention on anthropometric, metabolic, and lipid parameters among obese adults. Participants were divided into three groups: obese individuals pre-intervention, the same group post-intervention, and normal-weight controls. Body composition was measured, and lipid profile and metabolic parameters were assessed before and after the intervention. The study was designed as a quasi-experimental longitudinal controlled study, done from 2024 to 2025. The intervention included a healthy lifestyle program was designed for obese group. The results showed significantly higher body composition and metabolic indices in obese group compared to normal-weight individuals. Lipid profile were significantly higher ($P<0.05$), with the exception of high-density lipoprotein, which was low in the obese group before the intervention. Post-intervention, a significant decrease was observed in body compositions indicators, lipid profile, and metabolic indicators compared to the values recorded before the intervention. These values, however, remaining higher than the levels of healthy individuals. High-density lipoprotein increased slightly post-intervention, but did not reach the level of normal weight individuals. The results reflect the positive effect of fat loss on reducing chronic inflammation associated with obesity and improving metabolic and lipid profiles, confirming the effectiveness of a healthy lifestyle in obesity management.

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1. INTRODUCTION

The human body is evolutionarily programmed to be responsive to fat stores because it is the ultimate energy source for survival, especially during periods of food deprivation, such as during fasting or starvation. Obesity is a chronic condition characterized by excessive accumulation of body fat that poses a health risk. In obesity, the body does not have strong mechanisms to prevent the accumulation of excess fat. Obesity has not been such a significant health threat throughout human evolutionary history as it is in the modern era, where excessive fat accumulation has become associated with an increased susceptibility to metabolic disorders and associated diseases [1]. In the pathophysiology of obesity, chronic overconsumption of calorie-dense foods plays a crucial role in generating a positive energy balance, where caloric consumption exceeds expenditure, finally stimulating fat storage [2]. In overeating, the brain's reward system, which generally drives eating conducts associated with delight, is over-catalyzed and becomes the main driver for food consume. Highly palatable food (high in fat and sugar), can spur dopaminergic neurons and prompt a release of dopamine in regions, which includes the striatum, nucleus accumbens, and prefrontal cortex, essentially overriding the brain's hunger and satiety signals [3]. This leads to compulsive eating behaviors. When this pattern persists, it causes chronic energy excess, a key feature of obesity.

Overfeeding not only regulates appetite but also activates specific metabolic pathways that contribute to fat storage and metabolic imbalance [4]. In response to an excess of calories, whether from carbohydrates, lipids, or proteins, insulin secretion is promoted from beta cells in the pancreas as a regulatory mechanism to keep metabolic balance. Insulin stimulates several actions, including: timulates nutrient absorption and storage in various tissues, make facilitates glucose uptake into liver and muscle [5], which is used to produce energy or stored as glycogen, but the excess stored in adipose tissue, as well as prevents lipolysis. These coordinated actions help regulate blood glucose levels and control the body's energy homeostasis [6] .

When extreme quantities of carbohydrates, particularly glucose and fructose (such as high-fructose corn syrup), are intake, and the glycogen storages in the liver and muscles are saturated, the body starts to exchange this excess into fat [7]. Glucose is firstly metabolized through the glycolysis path to pyruvate, a vital intermediate that is subsequently converted to acetyl-CoA via the enzyme pyruvate dehydrogenase complex. Acetyl-CoA is the structure block for the production of fatty acids, which are later stored as triglycerides in fat tissues. While, fructose is mainly metabolized in the liver, which leads to increased acetyl-CoA creation, particularly when glycogen stores are full [8]. After acetyl-CoA is created in the cell, it is transported to the cytoplasm to start the process of lipid production (de novo lipogenesis). In this metabolic path, acetyl-CoA is transformed to malonyl-CoA by the enzyme acetyl-CoA carboxylase (ACC). This malonyl-CoA then acts as a substrate for the enzyme fatty acid synthase (FAS), which utilizes it to synthesis saturated fatty acid chains [9]. This pathway is catalyzed through plentiful carbohydrates and increased in insulin levels, leading to the production of fatty acids and the collection of triglycerides in the liver and fat tissue, which is associated with the development of obesity and metabolic disorders [10].

Dietary fats are in fact stored further directly than surplus carbohydrates. Whereas converting carbohydrates into fat (lipogenesis) is a many step process, dietary fats, after being absorbed as triglycerides, are packaged into chylomicrons, which are transported through the lymphatic system and then into the bloodstream [11]. Once, they reach the target tissues, particularly adipose and muscle tissue, where the enzyme Capillary lipoprotein lipase (LPL) breaks down these triglycerides into free fatty acids. These free fatty acids are taken up by adipocytes, re-esterified into triglycerides, and stored as fat without the need for complex metabolic conversions [12]. So, dietary fats are among the most rapidly stored nutrients, and their efficiency in accumulating as fat is very high. This is because fats are a highly concentrated energy source, providing more calories per gram than carbohydrates or proteins, making their excess a direct contributor to the development of obesity [13].

Proteins are broken down into amino acids through digestion process. These amino acids are thereafter used by the body as the building blocks for new proteins, repairing tissues, as well for numerous other essential functions as hormone and enzyme product. Nevertheless, when the body's protein needs surpass, the amino acids go through deamination process, and the over nitrogen is disposed of throughout the urea cycle and finally excreted in the urine [14]. While, the resulting carbon skeletons are directed into diverse metabolic pathways be contingent on the body's needs; they either converted into intermediates of the Krebs cycle, which ultimately lead to the production of ATP [15], or be converted into precursors for glucose production (gluconeogenesis) especially when blood sugar levels are decreased, or it is converted to acetyl-CoA and used to form fatty acids in the event of a surplus of energy. Though protein is not the main source of fat creation, extra protein can indirectly contribute to fat storing, particularly when intake in surplus as part of a high-calorie diet [16].

Therefore, the metabolic pathways of macronutrients are primarily aimed at supporting vital functions and providing energy. However, consuming them in quantities exceeding the body's needs leads to the excess being converted, especially after glycogen stores are saturated, into fats that are stored in adipose tissue [17]. This persistent fat accumulation is one of the most prominent physiological mechanisms contributing to the development of obesity, a chronic disease associated with a group of metabolic disorders, such as insulin resistance, low-grade inflammation, and neuroendocrine axis disruption. The figure 1 below illustrates the metabolic pathways of macronutrients and their role in the development of obesity [18].

Because of the increasing prevalence of obesity at the current time, which is mostly attributed to unbalanced lifestyles, particularly undue calorie consuming, therefore, the present study aims to investigate the physiological mechanisms that contribute to the accumulation of fat, while evaluating the effect of adopting a healthy lifestyle (including healthy diet and regular physical activity) on metabolic indicators and body composition.

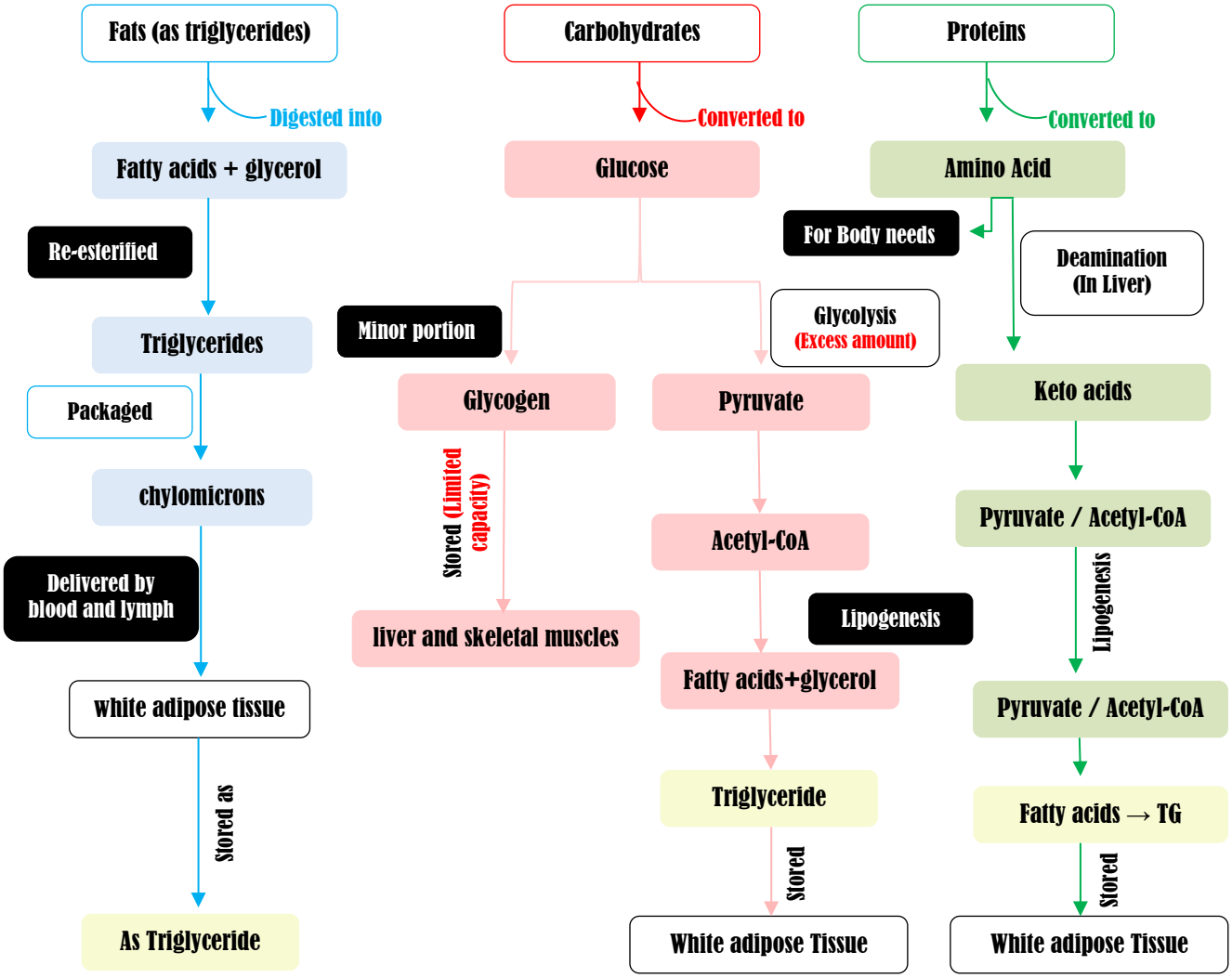

Figure 1. Metabolic pathway of fat, carbohydrate and protein and conversion excess of them to stored fat. The figure illustrates the metabolic pathway of macronutrients after they are consumed, and how the body uses them for energy or stores excess. Excess carbohydrates are stored as glycogen in the liver and muscles (in limited quantities), and then the excess is converted to fat. Dietary fats are stored directly in adipose tissue, while proteins are used according to the body's needs, and excess protein is converted into fat. The accumulation of these fats leads to the development of obesity when the energy surplus persists (Designed by researcher).

2. METHOD

2.1. Study Design

The current quasi-experimental longitudinal controlled study was conducted from December 2024 to July 2025, in Al-Anbar and Baghdad Governorates to estimate the effect of undergoing a healthy lifestyle (including a tailored diet and regular physical activity) on body composition in adult obese groupresulting compared to a control group of healthy, normal-weight participants who did not receive any intervention.

Licensed clinical nutrition specialists designed the individualized dietary plans based on InBody body composition assessments. The researcher monitored adherence and supervised the 6-month lifestyle program, including diet and physical activity.

- **Participants**

The study included a total of 100 (participants were recruited from therapeutic nutrition clinics, and their obesity status was confirmed using InBody body composition analysis) adult participants (male and female), aged 20-40 years, and they were classified into two groups:

- **A- Obesity Group**

The study involved 50 obese group(30 males/ 20 females). Obesity was identified based on body composition analysis by the InBody device, which offers accurate data on all body compositions includes: weight, length, visceral fat(VF),body fat percentage (BFP%), skeletal muscle mass(SMM), body fat(BF), waist-to-hipp ratio(HER), basal betaolism rate (BMR), rather than just traditional BMI.

Participants' weights ranged from 100 to 130 kg, and analysis showed that their body fat percentage fell within the ranges clinically classified as Class II or III obesity (In this study, obesity status of participants were determined using comprehensive body composition analysis with the InBody device, rather than solely relying on BMI classification. This method provides a more precise assessment of body fat and obesity).

All results in this group had a clear history of consuming a high-calorie food, without any chronic diseases or metabolic disorders. The dietary plans were not determined by the research team. Each participant received an individualized diet designed by a clinical nutrition specialist according to their body composition.

- **B-Control Group**

It consisted of 50 healthy participants with normal weight (37 male/13 female), who did not undergo any dietary or exercise intervention during the study period.

- **Inclusion Criteria:**
  - Adults (20– 40 years) (The age group was chose because it represents young and middle-aged adults, a phase characterized by active metabolic functions and lower age-related disorders. Thus, minimizes confounding agents, allowing a clearer estimate of obesity-related hormonal and metabolic changes)
  - Body Fat Percentage indicates obesity, as determined by the InBody analysis.
  - Being free of chronic diseases, such as diabetes and heart disease.
  - A desire to follow a healthy lifestyle.
- **Exclusion Criteria:**
  - Use of medications affecting appetite.
  - Weight loss surgery.
  - Pregnancy or breastfeeding.
  - Individuals, who were hard dieting, taking hormonal supplements

2.2.Ethical Considerations

The study was approved by the Ethical approval committee from University of Anbar. All participants signed an informed consent form after receiving a full explanation of the nature and objectives of the study, and the confidentiality of participants' data and their identity were confirmed.

2.3.Study Hypothesis

Scientific researches indicates that more consumption of high-calorie foods, particularly those rich in sugars and saturated fats, contributes to a disturbance in the signs of hunger and satiety controlled by the central nervous system, leading to overeating, weight gain, and body fat accumulation [19].

Therefore, the study hypotheses that following a healthy diet accompanied by a regular exercise program leads to regulate appetite and energy and improving weight management in obese group, thus improving their overall health.

2.4.Body Composition Analysis

Body composition including: Body weight, skeletal muscle, body fat, body fat percentage, waist-hip fat ration, basal metabolism and visceral fat was accurately assessed using the InBody bioelectrical impedance analyzer (InBody Co., Ltd., Seoul, South Korea), which is an advanced device in the field and widely used in clinical and physiological research.

The principle work of the InBody device based on the Bioelectrical Impedance Analysis (BIA) through the various body's tissue, when an electrical current is transmitted through lean tissue, the resistance is small, while the resistance is larger in tissue that contains fat. Dependent on these readings, the InBody device can determine anthropometric measurements.

2.5.Measurement of Metabolic indicators and Lipids profile

Blood samples were collected from all participants after fasting for 8-12-hour to estimate metabolic markers and lipid profiles. Blood samples were drawn from obese group twice, once before the intervention and once after 6 months of undergoing a healthy lifestyle (By adopting a balanced diet and engaging in regular physical activity) while samples were drawn from normal weight participants (control group)only once.

Metabolic markers, including fasting glucose and insulin, were measured using a Cobas e411 device (Roche Diagnostics, Germany). Insulin resistance was measured using the homeostatic model assessment for insulin resistance (HOMA-IR), a widely used method dependent on fasting blood glucose and fasting insulin concentrations. According to [20], HOMA-IR is calculated using the following formula bellow:

$$HOMA - IR = \frac{Fasting\ Glucose\left(\frac{mg}{dL}\right) \times Fasting Insulin\left(\frac{\mu U}{mL}\right)}{405} \quad (1)$$

Lipid profile indicators, including total cholesterol (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides (TG), were measured using the enzymatic colorimetric method (endpoint) with the CHOLESTEROL MR kit (Linear Chemicals S.L., Barcelona, Spain) on a spectrophotometer.

2.6.Healthy Lifestyle Intervention

All obese group underwent a healthy lifestyle intervention lasting 6 months, which included two main components:

A- Dietary Intervention

An individual nutrition plan was designed for each participant based on body composition analysis using the InBody device. The diet focused on: Increasing protein intake to stimulate satiety and maintain muscle mass, reducing sugars and saturated fats, and increasing fiber intake through fruits, vegetables, and whole grains. Participants were monitored through monthly diaries, with the dietitian re-evaluating and adjusting the diet based on periodic body changes.

B- Physical Activity Intervention

A regular physical activity program was prescribed for obese group, aimed at improving body composition in a safe and sustainable manner.The program included exercise five days a week and included:

- Moderate-intensity walking exercises
- Guided yoga sessions to improve flexibility and reduce stress
- Simple home bodyweight exercises

This type of exercise was chosen to minimize costs, avoid excessive physical stress, and ensure participants' continued adherence.

2.7.Statistical Analysis

All data were analyzed using statistical software program. Statistics were presented as mean ± standard deviation. To compare differences among the three groups: healthy controls, obese group pre-intervention, and obese group 6 months post-intervention, a one-way analysis of variance (ANOVA) was used. Pearson correlation analysis was conducted to explore associations between studied variables before and after the intervention of obese group. Additionally, stratified analyses were performed to examine all variables based on age among obese individuals. A p-value less than 0.05 was considered statistically significant.

3. RESULTS AND DISCUSSION

3.1. Demographic Characteristics of Study Participants

The results of the statistical analysis showed no statistically significant differences between the three participants groups with regard to mean age and age group distribution, Table 1. Also, no significant differences (P <0.05) were observed in the gender distribution ratios or the geographical distribution of participants between urban and rural areas. This demographic balance between groups decreases the likelihood of confounders impacting study results, enhancing the credibility of inferences about the effects of health interventions on studied variables in the current study. Scientific studies [21] have emphasized the importance of achieving demographic balance between study groups to reduce the influence of confounding factors and ensure the reliability of the results.

Table 1. The general demographic characteristics of in Healthy Controls, Obese group Pre-intervention, and Obese Group 6 months Post-intervention, Presented as Mean ± Standard Deviation.

Variables		Healthy Controls	Obese Group		X^2 F	p-value
			Pre-intervention	Post-intervention		
Age (Years)	Mean±SD	29.9±5.9	30.06±5.9	30.06±5.9	0.007	0.993 N.S
Age periods (Years) (%)	20 – 25	16	13	13	3.92	0.685 N.S
	26 – 30	9	15	15		
	31 – 35	15	10	10		
	36 – 40	10	12	12		
Sex (%)	Male	37	30	30	2.85	0.239 N.S
	Female	13	20	20		
Region (%)	Urban	31	33	32	0.174	0.917 N.S
	Rural	19	17	18		

*Significant differences (p-value less than 0.05), Abbreviation: SD: Standard deviation. Min.: Minimum, Max.: Maximum, N.S: No significant difference between groups.

3.2. Body Composition

The results in Table 2 show the means of body compositions variables of the participants in the three groups. The obese group recorded higher mean pre-intervention of weight, body fat, PBF%, WHR, visceral fat, BMR, and muscle mass compared to the normal weigh participants group. After 6 months of undergoing to a healthy lifestyle, these indicators decreased significantly ($P < 0.05$) compared to pre-intervention values, but remained higher significantly ($P < 0.05$) than the values recorded in the normal weight participants group. While no significant differences ($P < 0.05$) were recorded in the average height between the three groups, indicating the homogeneity of the participants in this variable.

Table 2. Body Composition Variables in Healthy Controls, Obese group Pre-intervention, and Obese Group 6 months Post-intervention, Presented as Mean ± Standard Deviation.

Variables		Healthy Control (n=50)	Obese Group (n=50)		F	p-value
			Pre-intervention	Pre-intervention		
Weight (Kg)	Mean±SD	79.3±9.24 a	116.3±12.05 b	92.1±11.04 c	150.08	0.0001
	Min.–Max.	56.2-99.1	100.1-140.1	74.2-114.0		
Length (Cm)	Mean±SD	173.6±9.03	171.7±11.1	171.3±10.9	0.674	0.511 N.S
	Min.–Max.	154-190	148-190	148-190		
Body fat (Kg)	Mean±SD	14.4±1.90 a	41.2±5.31 b	31.4±4.42 c	535.9	0.0001
	Min.– Max.	7.71–18.03	32.3–51.2	25.1–41.2		
BFP (%)	Mean±SD	14.3±2.9 a	38.3±5.7 b	29.06±5.3 c	313.7	0.0001
	Min.–Max.	9.9–20.9	29.01–49.7	21.01–45.1		
WHR	Mean±SD	0.68±0.11 a	1.23±0.77 b	0.82±0.15 c	6.59	0.002
	Min.–Max.	0.43–0.92	0.87–10.50	0.54–1.4		
BMR(Kcal)	Mean±SD	1303.7±200.1 a	2086.2±267.3 b	1932.9±328.8 c	117.3	0.0001
	Min.–Max.	1023-1803	1350-2516	1219-2354		
Visceral fat (Kg)	Mean±SD	3.62±0.971 a	17.71±3.10 b	9.84±2.40 c	455.5	0.0001
	Min.–Max.	1.97–6.0	13.0–28.9	2.60–17.9		
Skeletal muscle mass (Kg)	Mean±SD	25.1±3.66 a	32.62±4.6 b	30.1±4.9c	37.20	0.0001
	Min.–Max.	18.02–32.11	22.1–41.2	18.9–38.0		

*Significant differences (p-value less than 0.05), Abbreviation: a: control group, b: Obese group before, c: Obese group after, Different superscript letters (a, b, c) indicate statistically significant differences between groups, N.S: No significant difference between groups, SD: Standard deviation, Min.: Minimum, Max.: Maximum, BFP%: Body fat percentage, WHR: Waist to Hip ratio, BMR: Basal metabolism rate.

The impact of age groups on body anthropometric variables was evaluated before undergoing a healthy lifestyle intervention in the case group. Statistical analysis results showed no significant differences between the different age groups in the following variables: weight, length, body fat mass, BFP%, WHR, BMR, skeletal muscle mass ($p < 0.05$) (Figure 2). This indicates that age did not significantly influence the body composition status of this sample before weight loss.The results of the current study are consistent with previous studies that confirm that increased in consumption of highly palatable foods (High-calories foods) is related with body fat accumulation, highlighting the essential role of dietary quality in the development of obesity. This attribute to the capability of these type of foods, although their low nutritional value, to bypass satiety cues due to their small size and high calorie content, which leads to an energy excess that is stored as fat in adipose tissue, especially in areas of visceral fat [22,23].

The results of the current study show that an unhealthy life style is associated with increased in body fat accumulation, especially visceral fat, which is reflected in a noticeable increase in metabolic parameters. A significant direct correlation was observed between body weight with the HOMA-IR index and fasting glucose ($r = 0.238$, $p = 0.048$; $r = 0.25$, $p = 0.039$) respectively. As well as between body fat and fasting insulin concentrations ($r = 0.25$, $p = 0.039$). A strong positive relationship was also recorded between visceral fat with fasting insulin and HOMA-IR ($r = 0.33$, $p = 0.009$; $r = 0.296$, $p = 0.018$) respectively.

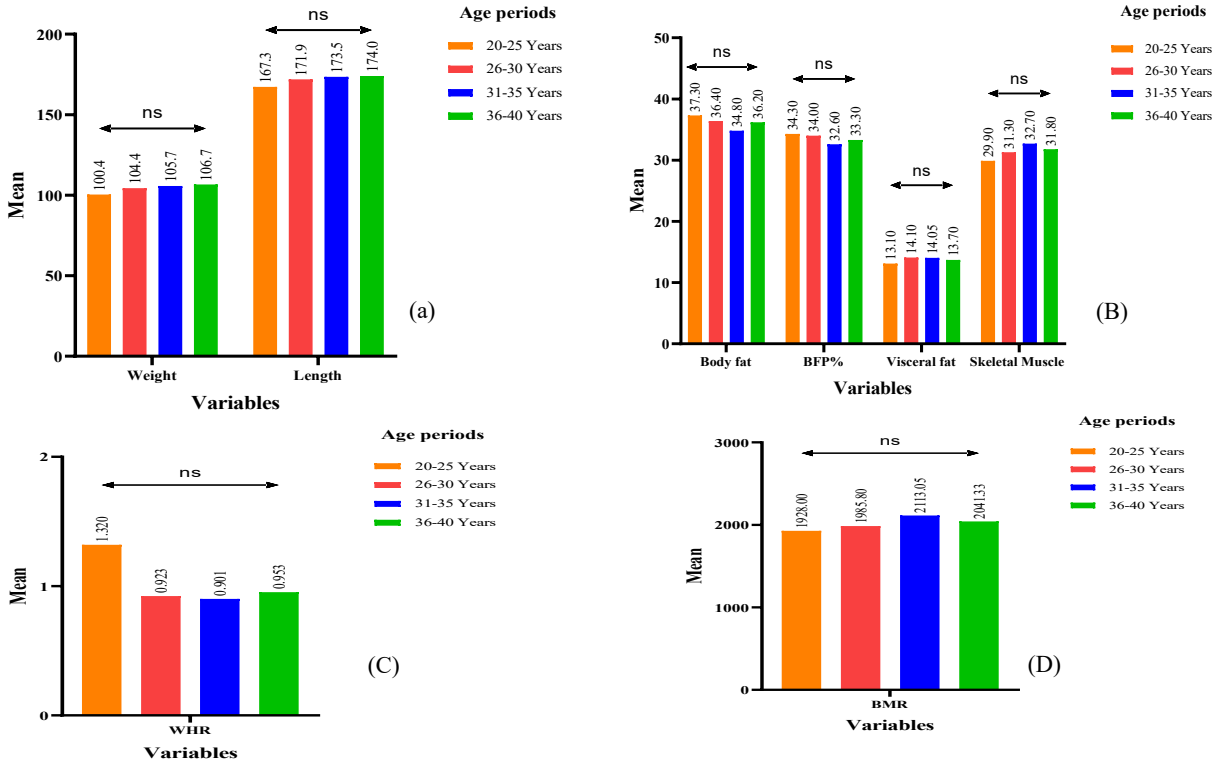

Figure 2. Relation between age and (a-weight, length), (b-body fat, BFP%, visceral fat, skeletal muscle), (c-WHR), (d-BMR) in obese group pre-intervention.

These correlations indicate that fat accumulation, mainly in the visceral area, plays a key role in disrupting metabolic homeostasis and stimulating insulin resistance, which supports the studies on the negative metabolic influence of lifestyle-related obesity [24]. The cumulative pattern of obesity in the current study participants reflects an obvious impact of neural and hormonal mechanisms on fat distribution, particularly in leptin resistance and leptin-POMC axis disorder, which impairs the effectiveness of appetite-inhibiting neural cues and enhances accumulation the visceral fat [25]. The significantly increase in body fat, BFP%, visceral fat, skeletal muscle mass, and BMR in obese individuals references a metabolic imbalance [26]. Valenzuela and his colleagues [27] pointed that the high levels of muscle mass may be as a compensatory response to increase in body weight . Nevertheless, this an increase does not necessarily reflect higher functional muscle quality. Rather, it is usually joined by excessive fat accumulation and an imbalance between lean muscle and body fat mass, contributing to a status of functional metabolic insufficiency.

In spite of high levels of skeletal muscle mass has been observed in obese group, this increase is not necessarily a positive indicator. This may be due to the mechanical stress resulting from more weight, which enhances skeletal muscle growth as a compensatory mechanism to accommodate the increased body weight [28]. However, this excess skeletal muscle mass is frequently related with a decrease in muscle quality, rather than effectiveness, as a result of the influence of obesity on the muscle's metabolic environment, involving low-grade chronic inflammation, oxidative stress, resistance to anabolism, the changes in muscle fibers, and interfibrillar lipid accumulation, which restricts functional muscle performance in despite of the increase in mass [29]. Many studies as study by Karagun & Baklaci [30], have documented an increase in metabolic rate in obese people, and stated that the basal metabolic rate increases with weight gain, especially the increase in skeletal muscle mass. However, this increase is viewed as a metabolic burden, reflecting tissue hypertrophy and increased energy demands, and not necessarily an indicator of metabolic efficiency, as noted by Guan et al., [31].

Post-intervention results (Table 2) show a clear improvement in body composition, reflecting the effectiveness of the healthy lifestyle. Despite this improvement, values remain higher than normal levels compared to the control group, indicating the need to continue adopting a healthy lifestyle for a longer period to achieve optimal results.This improvement in body composition was mostly attributed to the obese group adherence to a balanced low-calories, diet in terms of protein, fat, carbohydrate and fiber content, which produced a measured energy deficit.

This energy deficit contributes to stimulating the process of lipolysis by activating the sympathetic nervous system and increasing the secretion of norepinephrine, which in turn activates the hormone-sensitive lipase enzyme, which accelerates the breakdown of stored fats and their use as an alternative energy source [32]. The results of the current study are in agreement with the results of a previous study conducted by Rezaieg [33] the researcher on a sample of male overweight and obese individuals, a healthy dietary program were applied, which characterized food with high fiber content, low amounts of simple and complex carbohydrates, high protein content, and low fat content, in addition to regular physical activity. The results of the study showed a significant improvement in BMI, Waist Circumference, Fat%. These findings and results of current study support the hypothesis that actual lifestyle modifications can bring about positive changes without resorting to strict dietary restrictions.

3.3. Metabolic Indicator

Table 3 show the means of metabolic indicators of the participants in the three groups. The obese group recorded higher mean pre-intervention of Fasting insulin and glucose concentrations and HOMA-IR compared to the normal weigh participants group. After 6 months of undergoing to a healthy lifestyle, these indicators decreased significantly ($P < 0.05$) compared to pre-intervention values, but remained higher significantly ($P < 0.05$) than the values recorded in the normal weight participants group.

Table 3. Metabolic Indicators in Healthy Controls, Obese Group Pre-intervention, and Obese Group 6 months Post-intervention, Presented as Mean ± Standard Deviation.

Variables		Healthy Control (n=50)	Obese group (n=50)		F	p-value
			Pre-intervention	Post-intervention		
Glucose (mg/dl)	Mean±SD	77.01±5.2 a	101.3±7.8 b	90.6±3.8 c	216.7	0.0001
	Min.–Max.	70.0–90.0	89.1–119	82–101.7		
HOMA- IR	Mean±SD	1.01±0.20 a	3.74±0.61 b	2.22±0.32 c	536.5	0.0001
	Min.–Max.	0.69–1.82	2.85–5.01	1.55–3.27		
Insulin (µU/mL)	Mean±SD	6.31±0.80 a	13.9±1.39 b	10.0±1.18 c	862.6	0.0001
	Min.–Max.	4.01–8.22	12.9–17.8	8.24–14.0		

*Significant differences (p-value less than 0.05), Abbreviation: a: control group, b: Obese group before, c: Obese group after, Different superscript letters (a, b, c) indicate statistically significant differences between groups, N.S: No significant difference between groups, SD: Standard deviation, Min.: Minimum, Max.: Maximum.

A statistical analysis was done to investigate the impact of age on metabolic indicators (fasting insulin, glucose, and HOMA-IR) in obese group. That results recorded that the age period did not show any significant effect of these parameters ($p<0.05$), revealing that these variables are relatively stable across the age obese group pre-intervention (Figure3). This interpretation is supported by a recent study that indicated that the relationship between insulin resistance index (HOMA-IR) and obesity remains strong regardless of age, indicating that obesity is the primary influencing variable, not age itself [34].

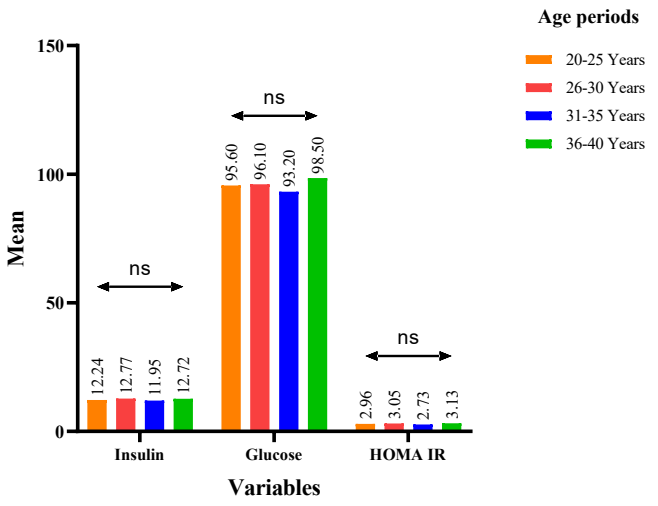

Figure 3. Relation between age and metabolic indicators (fasting insulin and glucose and HOMA-IR).

The observed elevations of fasting insulin and glucose concentrations in obese group in the current study is consistent with recent literatures referencing that these increases are a main characteristics of the metabolic status associated with obesity [35,36]. At the peripheral level, insulin resistance is a crucial factor; peripheral tissues, especially skeletal muscle and liver, reveal a decreased response to insulin, leading to weak glucose transfer into cells, increased hepatic glucose production through the gluconeogenesis mechanism, and thus elevated concentrations of fasting blood glucose. These changes are related by a compensatory rise in insulin secretion from the pancreas, which demonstrates the observed hyperinsulinemia [37].

In contrast, the latest study done by Rezaieg and Awad, [38] have reported the role of the CNS, particularly the hypothalamus, in exacerbating energy and glucose imbalances in individuals with obesity. The ARC of the hypothalamus plays an important role in receiving and processing insulin cues that control appetite and glucose balance. The chronic neuro-inflammation associated with obesity have been a negatively affects the efficiency of these cues, reducing the HT capability to prevent hepatic gluconeogenesis and control food intake, contributing to persistently elevated fasting insulin and glucose concentrations [39]. HOMA-IR is a common characteristics of obese individuals and its a represents a physiological status in target tissues as the liver and skeletal muscle are minus responsive to insulin influences, and thus be in need of higher concentrations of insulin to achieve the same typical metabolic impact [40]. This metabolic imbalance is reflected in impaired glucose regulation and increased insulin load, which predisposes to broader metabolic abnormalities as type 2 diabetes.

Fasting insulin and glucose concentrations, and HOMA-IR decreased significantly, after 6 months of adopting a healthy lifestyle. This may be due to improve sensitivity of target tissues, like skeletal muscle and liver, as a result of increased effectiveness of glucose transporters (GLUT-4) and improved signaling related with insulin receptors [41]. Yet, a degree of insulin resistance might persevere because of pre-existing structural changes in receptors and transporters, which may explain the failure to achieve levels comparable to those of healthy controls during the follow-up time [42].

Masoodian et al., [43] mentioned that the doesn't reach normal levels of metabolic markers after weight loss is attributed to several physiological factors that may persist even after improvement in body weight, including: the dysfunction of pancreatic beta cells, resulting from chronic fatigue because of overstimulation during obesity. On the another hand, the chronic low-grade inflammation, which is connected with obesity, may continue to disrupt metabolic signaling. and limit full improvement in insulin response [44].

After 6 months of lifestyle modification, WHR preserve a significant independent correlation with fasting glucose concentrations($r= 0.47$, $p= 0.0001$) and insulin resistance ($r= 0.33$, $p =0.008$). Similarly, visceral fat mass remained independently correlated with fasting insulin concentrations ($r= 0.329$, $p = 0.010$). These findings underscore the robustness of central adiposity indicators as independent predictors of metabolic impairment, beyond the confounding effect of age. The data of current study demonstrate that central fat distribution (as measured by WHR and visceral fat) is a crucial mediator of the relation between weight loss and improvement the metabolic indicators. Even post weight loss, the correlations between WHR/visceral fat and glucose and insulin concentrations remain strong, pointing that targeting visceral fat decreasing might have a major influence on restoring insulin sensitivity compared depending on just overall weight loss [45].

Returning the metabolic homeostasis after weight loss remains a complex physiological problem, particularly in obese individuals. This problem appears to include not only superficial factors such as insulin resistance or low-grade inflammation, but also deeper impacts known as metabolic memory, a phenomenon that refers that molecular and epigenetic changes that occur as a result of obesity may persist even after clinical indicators improve, therefore impacting metabolic balance in the long term [46].

The study by Le Thuc and García-Cáceres, [47], reinforced the results of the current study, which confirm that exercise contributes effectively of improving insulin receptor sensitivity and promotes muscle mitochondrial effectiveness, which permits for major dependence on fatty acids as an energy source, especially after exercise when glucose reliance is decreased, Jurczewska and his colleagues [48] mentioned that this amended metabolic flexibility is a crucial benefit of exercise, especially for persons managing conditions as insulin resistance or type 2 diabetes.

3.4. Lipid Profile Parameters

Table 4 show the means of lipid profile for participants in the three groups. The obese group group recorded higher significantly ($P <0.05$) mean pre-intervention of total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL) compared to the normal weigh participants group, while high-density lipoprotein (LDL) was lower significantly ($P <0.05$) in the obese group. After 6 months of undergoing a healthy lifestyle, these indicators decreased significantly ($P <0.05$) compared to pre-intervention values, but remained higher significantly ($P <0.05$) than the values recorded in the normal weight participants group. In contrast, HDL-C concentrations increased after the intervention, but remained below normal concentrations.

Table 4. Lipid profile parameters in Healthy Controls, Obese Group Pre-intervention, and Obese Group 6 months Post-intervention, Presented as Mean ± Standard Deviation.

Variables		Healthy Control (n=50)	Obese group (n=50)		F	p-value
			Pre-intervention	Post-intervention		
TC (mmol/L)	Mean±SD	3.82±0.733 a	6.33±0.74 b	4.59±0.87 c	134.3	0.0001
	Min.–Max.	1.99 – 6.0	5.0 – 8.0	2.0 – 7.0		
TG (mmol/L)	Mean±SD	1.60±0.52 a	4.82±0.95 b	3.34±0.65 c	239.2	0.0001
	Min.–Max.	0.84 – 2.78	2.65 – 7.03	1.87 – 5.03		
HDL (mmol/L)	Mean±SD	1.83±0.39 a	0.82±0.34 b	1.44±0.47 c	77.69	0.0001
	Min.–Max.	1.0 – 3.02	0.16 – 2.0	0.61 – 3.0		
LDL (mmol/L)	Mean±SD	2.66±0.70 a	4.76±1.08 b	3.32±0.60 c	85.13	0.0001
	Min.–Max.	1.24 – 6.0	3.28 – 9.0	2.0 – 5.21		

*Significant differences (p-value less than 0.05), Abbreviation: a: control group, b: Obese group before, c: Obese group after, Different superscript letters (a, b, c) indicate statistically significant differences between groups, N.S: No significant difference between groups, SD: Standard deviation, Min.: Minimum, Max.: Maximum. TC: total cholesterol, TG: triglyceride, HDL: high-density lipoprotein, LDL-: low-density lipoprotein.

Obese Group were divided into four groups according to age periods for assessing the impact age on lipid profile indices. Statistical analysis results recorded no significant ($p < 0.05$) differences between the age groups in TC, TG, , LDL, and HDL concentrations, obviously indicating that age does not significantly impact lipid profile variables in the case groups (Figure 4). The results of the current study differ from recent study by Huang et al., [49], which showed clear impact of age on specific types of fat in obese patients. This difference may be attributed to various factors such as sample size, demographic characteristics, and different measurement methods, which explain the variability in results between studies.

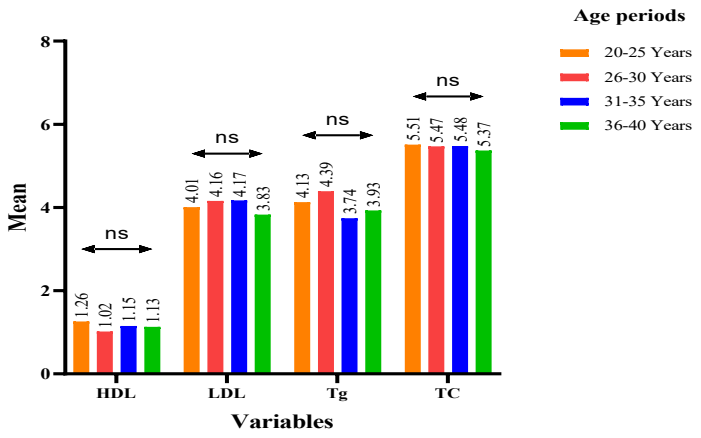

Figure 4. Relation between age and lipid profile variables (TC, TG, LDL and HDL).

There are several physiological explanations for the lipid disorders associated with obesity, the most prominent of which is the increased lipolysis in adipose tissue, whereby fat cells (adipocytes) become more sensitivity to catecholamines as adrenaline, While its response to the effects of insulin on fat storage is reduced [50]. This leads to an increased release of free fatty acids (FFAs) into the circulation, which contributes to stimulating the liver to produce more very-low-density lipoproteins (VLDL), which are rich in triglycerides. This mechanism explains the marked increase in TG concentrations in obese individuals [51]. In addition, Wang and his colleagues [52] reported that obesity, especially in the presence of insulin resistance, leads to the accumulation of fat within liver cells, this buildup can lead to the development of non-alcoholic fatty liver disease (NAFLD). This buildup activates the biological pathways responsible for de novo lipogenesis thus leading to raised triglyceride concentrations in the blood. Insulin resistance, a notable characteristic of obesity, plays a pivotal role in lipid metabolism disorders, throughout the failure of insulin to do its basic function, which is to prohibit the breakdown of fats in fat cells via inhibiting the enzyme Hormone-sensitive lipase (HSL) and stimulating the storage of triglycerides. In insulin resistance, adipocytes lose this response, leading to an uncontrolled rise in the release of free fatty acids (FFA) into the bloodstream [53].

Statistical analysis showed that at baseline, there was a significant positive correlation between body and TG concentrations ($r = 0.25$, $p = 0.037$), alongside a strong inverse association between skeletal muscle mass and HDL concentrations ($r = -0.34$, $p < 0.007$). Post-intervention, an inverse correlation emerged between WHR and HDL concentrations ($r = -0.25$, $p = 0.035$), indicating that visceral fat distribution continued to exert an unfavorable impact on lipid profile parameters in despite of the overall improvement in body composition measurements. In obesity, decreased HDL concentrations is linked with increased activity of cholesterol ester transfer protein (CETP), which stimulates the transfer of cholesterol esters from HDL to VLDL in exchange for triglycerides.

This exchange leads to HDL being overloaded with triglycerides, which increases in its degradation by hepatic lipase (HL) and reduces its functional half-life, thus impairing its efficiency in reverse clearance of the TC, increasing the risk of atherosclerosis that associated with obesity [54]. It's worth noting that the accumulation of visceral fat in obese individuals contributes to an increased in rate of partial degradation of HDL molecules, leading to their destabilization, accelerated degradation, and reduced duration of their survival in the blood. These mechanisms explain the physiological reason why visceral obesity is associated with an increased in risk of cardiovascular disease [55]. It is serious to understand that obesity is not necessarily the result of over consuming of fat but it may result from surplus calorie ingestion from many source as carbohydrates or proteins. This confirms that the type of nutrients is not the only factor that influences, but rather the total amount of energy consumed [56].

Any lifestyle intervention program that includes healthy dieting and regular exercise could effectively improve the nutritional pattern, contribute to body weight control, and improve serum lipid profiles. This type of intervention was applied in the current study to obese group. The results of the current study indicated that after a 6 months of undergoing to healthy lifestyle enhancement program, obese group managed to reduce their body compositions variables (Table 2) and serum TC, TG, LDL concentrations (Table 4). These results are in agreement with previous studies done by Thomse et al., [57] pointed that female finishing the weight loss period (12 weeks) of a private program succeed to reduce their body weight, BMI, PBF% and WHR, increased in their HDL and decreased their risks for CVD. On the other hand, the increase in serum HDL concentration in the current study is consistent with previous finding (Gannamani *et al*., 2024), just the results contradicts another study that did not show improvement in cholesterol concentrations in cases of energy restriction [58], reflecting a difference that may be results to many factors as the type of diet, period of intervention, density of exercises, or person differences among participants.

Although the known interest of weight loss, the contribution of weight decreasing compared to energy consume modification stays debated. Results from study done by Dou et al., [59] showed that changes in energy consume may have a more impacts on cholesterol concentrations than changes in weight alone . In contrast, the findings of Eichelmann and his colleagues [60] complemented that the weight loss significantly enhances the lipid-lowering impact of a low-fat diet. These mixed results show the difficulty of lipid response to lifestyle interventions, as numerous studies have reported inconsistent results in lipid profiles before and after weight loss. A systematic review of overweight or obese adults concluded that dietary interventions even within 6 months led to a significant reduction in TG by an average of approximately (~21.7 mg/dL) [61]. On the other hand, although the results of the current study showed that reducing calories and increasing physical activity were indeed associated with an improvement in the lipid profile, TC, TG, LDL and HDL concentrations remained outside the ideal ranges after 6 months of following a healthy lifestyle.

These results are consistent with a recent study published in Obesity (Silver Spring) in December 2024, in 21 participants underwent a comprehensive lifestyle program (diet and regular physical activity) for 3 months. The results resulted in a ~10% reduction in body mass index, a 57% improvement in insulin sensitivity, and significant reductions in triglycerides and lipid types associated with insulin resistance, including dihydroceramides and sphingolipids [62].

4. CONCLUSION

The study highlighted the role of metabolic pathways in the accumulation of adipose tissue associated with obesity in adults. The study results showed that adopting a healthy lifestyle led to a significant improvement in anthropometric measurements after the intervention compared to pre-intervention values. Metabolic indices and lipid profiles also improved, but remained lower than the normal reference range. This improvement is partially attributed to what is known as obesity memory, whereby prior obesity leads to long-term metabolic changes despite adherence to a healthy lifestyle. These findings highlight the importance of continuous follow-up health interventions to understand the dynamics of metabolic improvement and effectively of manage obesity.

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