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Exploring omentin-1 gene expression and insulin-resistance modulation in diabetic and obese male albino rats

Noorah Saleh Al-Sowayan, Aiesha Mohammed Almutawa
Department of Biology, College of Science, Qassim University, Buraydah, Saudi Arabia

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ABSTRACT

Omentin-1, a cytokine secreted by adipose tissue, plays a role in metabolic regulation and insulin sensitivity. However, there is a lack of understanding about the specific effects of high-intensity training (HIT) in diabetic and obese individuals. The present study investigates the effect of a 5-week HIT program on the omentin-1 gene expression and insulin resistance in diabetic and obese male albino rats. Thirty-two rats weighing between 100-120 grams, were procured and divided into groups: the control group (receiving a normal diet), the high-fat diet group (non-diabetic obese rats), the HIT diabetic group (induced diabetes through streptozotocin administration and subjected to HIT), and the diabetic control group (induced diabetes but not subjected to HIT). The HIT diabetic and HIT obese groups underwent a 5-week HIT protocol, involving treadmill running for 60 minutes at 34 m/min speed, five sessions per week. At the end of the experiment, various parameters including glucose, insulin, insulin resistance, LDL, HDL, TC, TG levels, and omentin-1 gene expression assessed using samples obtained from visceral tissue. SPSS version 25 was used to perform statistical analysis, results as mean±SE. One-way ANOVA identified group differences, with significance level (p-value) of less than 0.05. The findings revealed that omentin-1 gene expression significantly increased in the HIT diabetic group following five weeks of training. Both training groups exhibited reductions in insulin, glucose, and insulin resistance levels. It is concluded that a 5-week HIT program can lead to enhanced omentin-1 gene expression and improved insulin resistance in diabetic and obese male albino rats.

Corresponding Author:

Noorah Saleh Al-Sowayan
Department of Biology, College of Science, Qassim University
Buraydah, Saudi Arabia
Email: nsaoiean@qu.edu.sa

1. INTRODUCTION

The rise in sedentary lifestyles, easy availability of unhealthy food, and lack of physical activity have led to an increasing prevalence of various metabolic disorders such as cardiovascular diseases, type 2 diabetes (T2D), dyslipidemia, and different cancers [1], [2]. These lifestyle changes have contributed to a global increase in obesity rates. Hyperinsulinemia, insulin resistance, and hypertriglyceridemia observed in obese individuals serve as precursors to the development of T2D [3]. Projections estimate that by 2040, the incidence of diabetes may reach 640 million, highlighting the significant impact of this disease and its associated complications on global health [4]. T2D comprises around 90-95% of all diabetes cases [5]. In T2D, there is a defect in the insulin secretion process from beta cells, and the insulin's action in insulin-sensitive tissues, like liver, muscles, and adipose tissue, is compromised, leading to a condition known as

insulin resistance (IR) [4]. Obesity is closely associated with T2D and promotes the onset of insulin resistance in patients affected by the disease [6]. Zheng *et al.* [4] noted that 61% of T2D cases are attributable to being overweight, defined as a body mass index (BMI) of <25 m^2/kg, with a particular emphasis on the accumulation of visceral fat around the waist and hips. Visceral fat itself serves as a significant risk indicator for T2D [7].

Omentin, an amino peptide encoded by gene 313 located on chromosome q22, q23 associated with type 2 diabetes, is primarily expressed in visceral tissues [8]. Omentin-1 plays modulate insulin resistance and lipolysis in individuals with obesity [9]. The research conducted by Hou *et al.* [10] has demonstrated a significant correlation between the level of omentin-1 and T2D development. Omentin-1 levels are reduced in patients with metabolic syndrome, diabetes, and obesity; whereas individuals with a lean body composition exhibit higher omentin-1 levels. Moreover, serum levels of omentin-1 serum increase following weight loss achieved through dietary interventions and regular physical activity [11].

Obesity is closely linked to insulin resistance and individuals with decreased levels of omentin-1 tend to exhibit this condition [11]. It is important to maintain insulin resistance in diabetes management, which can be achieved through various approaches such as dietary interventions, physical activity, pharmacotherapy, and stimulation of insulin secretion [12]. Notably, advanced age, body weight, and exercise are considered significant factors influencing omentin-1 levels in the body [11]. In particular, exercise-induced elevation of omentin-1 levels has been shown to positively impact glucose homeostasis and enhance lipolysis [13].

Physical activity is considered a highly effective non-pharmacological approach for addressing insulin resistance, exerting notable effects on various metabolic and physiological processes [14]. High-intensity training (HIT) represents an exercise modality characterized by intensities surpassing 65% of maximum speed. This form of exercise has emerged as a valuable alternative to conventional exercise regimens, which typically involve low to moderate intensities sustained over longer durations. HIT has demonstrated effectiveness and has been proposed as an intervention for weight reduction [15].

According to American diabetes association (ADA) [16], absence of regular exercise is considered the fourth risk factor for developing coronary artery/heart disease. Resistance exercise is likely to improve glucose control, insulin resistance, lipid mass, and blood pressure [17]. Notably, a study reported an increase in omentin-1 concentrations in the blood of obese children following a 16-week program combining resistance and aerobic exercises, leading to weight reduction and enhanced insulin sensitivity [18]. Golestani *et al.* [19] highlighted that physical exercise is the optimal strategy for reducing total cholesterol (TC), body fat percentage (BFP), low-density lipoprotein (LDL), and triglyceride (TG). Increasing high-density lipoprotein (HDL) serves as a protective factor against cardiovascular diseases. Previous research has demonstrated a negative association between omentin-1 gene expression and obesity, body mass, insulin resistance, and leptin levels, along with a positive relationship between adiponectin and HDL [12].

The study aims to focus on investigating the efficacy of HIT in modulating omentin-1 gene expression, insulin resistance, and lipid profile in individuals with diabetes and obesity. Furthermore, it also investigates the relationships between omentin-1 levels and insulin, glucose, insulin resistance, TC, TG, HDL, and LDL. This study contributes to the field by examining the HIT's impact on omentin-1 gene expression in the context of diabetes and obesity, providing valuable insights into its potential therapeutic effects. The present study hypothesizes that HIT will significantly impact metabolic and molecular markers in rat models with diabetes and obesity. Specifically, it is expected that HIT intervention is likely to reduce body weight, improve lipid profiles, elevate omentin-1 gene expression, lower fasting insulin and glucose levels, and enhance insulin sensitivity compared to control and diabetic control groups.

2. METHOD

2.1. Experimental setup

Thirty-two male Wistar rats weighing between 110-120 g were sourced from the Animal House at King Saud University in Riyadh. Upon arrival, a two-week adaptation period was implemented to acclimate the rats to their environment. The animals were housed in plastic cages with metal doors, measuring 20×20×40 cm, accommodating four rats per cage. The room conditions were maintained at a temperature of 20-24 °C, humidity ranging from 50-65%, and a light-dark cycle of 12 hours each. Sterilization procedures were rigorously followed throughout the experiment to ensure consistent hygiene and cleanliness standards.

Before commencing the experiment, all animals underwent an adaptation period to acclimate to the experimental conditions. During this period, they were provided with a normal diet (commercial fodder) obtained from the College of Agriculture and Veterinary Medicine at King Saud University. A total of eight rats were assigned to the control group, which received a normal diet throughout the study. The rest of the rats were fed a high-fat diet, utilizing Diet D12451, comprising 20% kcal protein, 35% kcal carbohydrates,

and 45% kcal fat for eight weeks, as described by Morrison *et al*. [20]. All rats were allowed unrestricted access to water and food.

Diabetes condition was triggered in 16 rats through the injection of streptozotocin at a dosage of 60 mg/kg body weight dissolved in 0.09 mg citrate buffer with a pH of 4.5, administered intraperitoneally, following the protocol outlined by Altun *et al*. [21]. After 72 hours of diabetic induction, blood samples were collected from the tails of the rats to check blood glucose levels using a glucometer. Rats with blood glucose values exceeding 300 mg/dl were categorized as diabetic, following the criteria established by Alizadeh *et al*. [12].

Subsequently, the diabetic rats were categorized into two groups: the diabetic control group, comprising eight rats with a mean weight of (264.8±4.47) grams, and the HIT diabetic group, consisting of eight rats with an average weight of (273.4±3.13) grams. The remaining eight rats, which were not induced to develop diabetes, were assigned to the HIT Obese group.

2.2. HIT protocol

The HIT diabetic and HIT Obese groups underwent a training protocol using a 5-lane treadmill designed for rats. Initially, for one week, they underwent five sessions of adaptation to the device, running at speeds ranging from 0 to 15 m/min for 15 minutes, aimed at familiarizing them with the treadmill setup. Subsequently, a heating phase of 5 minutes followed by a cooling phase at a speed of 0 to 10 m/min for 5 minutes was implemented to prepare the animals for the subsequent training regimen, as described by Kartinah *et al*. [22]. After the adaptation period, the rats underwent a continuous training program for five consecutive weeks, with each week consisting of five sessions. During these sessions, the animals were subjected to a training duration at a speed of 34 m/min for 60 minutes, as reported by Kim *et al*. [23].

2.3. Obtaining blood samples and autopsies

Obtaining blood samples and performing autopsies were carried out following established procedures. After final training and following a 72-hour recovery period, the rats were subjected to anesthesia using chloroform inhalation, as described by Aguwa *et al*. [24]. Blood samples were taken from posterior vein of the rats' eyes using capillary tubes and immediately transferred into gel and clot activator tubes to facilitate appropriate preservation and analysis of the samples. Before blood collection, the animals underwent a 12-hour fasting period to ensure consistent conditions. The blood samples were centrifuged at a speed of 4,000 rpm for 15 minutes to obtain plasma.

After blood collection, the animals were carefully dissected, and samples of visceral fat were excised. These fat samples were then thoroughly washed with isotonic saline solution to remove any extraneous contaminants. The cleaned samples were subsequently placed in cryotubes and stored in liquid nitrogen to maintain their molecular integrity, following the protocols outlined by Alizadeh *et al*. [12].

All animals were humanely sacrificed following approved ethical guidelines. The remains of the animals were appropriately disposed of by incineration in the incinerator of the College of Agriculture and Veterinary Medicine of Qassim University, adhering to proper waste management practices. Finally, in compliance with local laws and regulations, the animal remains were buried deeply [25].

2.4. Measurement of insulin, glucose, insulin resistance, and lipid profile

Insulin levels were quantified using the liaison-insulin assay (DiaSorin Saluggia, Italy) with the LIAISON®XL model number 10050 and the cobas integra system (manufactured in Germany, distributed in the USA by Roche Diagnostics, Indianapolis) for the measurement of glucose, TC, TG, HDL, and LDL levels. The Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) formula was used to assess insulin resistance [12] (p.31). The formula below was used for calculating HOMA-IR index:

$$\text{HOMA-IR} = (\text{fasting plasma insulin [microunit/mL]}) \times (\text{fasting plasma glucose [mg/dL]}) / 405$$

Omentin-1 gene expression mensuration. The real-time quantitative polymerase chain reaction (RT-PCR) was used to assess the Omentin-1 gene expression.

2.5. RNA extraction

Tissue homogenization was performed to ensure ice removal. A column-based technique (BIO BASIC, Canada) was used to extract total RNA from visceral tissues. cDNA synthesis and RT-PCR preparation. The ultraviolet spectrophotometer (PCRmaxLambada, Japan) was used to determine DNA's concentration. Complementary DNA (cDNA) synthesis was carried out using 500 ng of RNA from each sample. For qRT-PCR, SYBR Premix Ex Taq was employed. Omentin-1 was selected as the target gene, while beta 2 microglobulin (B2M) was considered as reference gene for normalization (TaKaRa Inc., Japan) using the Rotor-Gene 6000 qPCR machine (Qiagen, Germany). The primers used for B2M and omentin include; F-5′-GCTGAAGAGAACCTGGAC-3′ and R-5′-AATAGAGACCATCTTGTGC-3′, and F-5′-

CTTCAGCAAGGACTGGTC-3′ and R-5′-TCTCGATCCCAGTAGACG-3′, respectively. The relative gene expressions were determined using the 2^−ΔΔCT method [26].

$$\Delta Ct = Ct\,(target\ gene) - Ct\,(housekeeping\ gene)$$
$$\Delta\Delta Ct = \Delta Ct\,(test\ sample) - \Delta Ct\,(control\ sample)$$
$$Relative\ fold\ change\ in\ gene\ expression = 2\text{^} - \Delta\Delta Ct\ [12]\ (p.31).$$

2.6. Data analysis

Statistical package of social sciences (SPSS) version 25 was used to conduct the statistical analysis and the findings were presented as mean ± standard error. The group differences were determined using one-way analysis of variance (ANOVA) test at < 0.05 significance value. Figure 1 outlines the overview of stages of methods followed in the study.

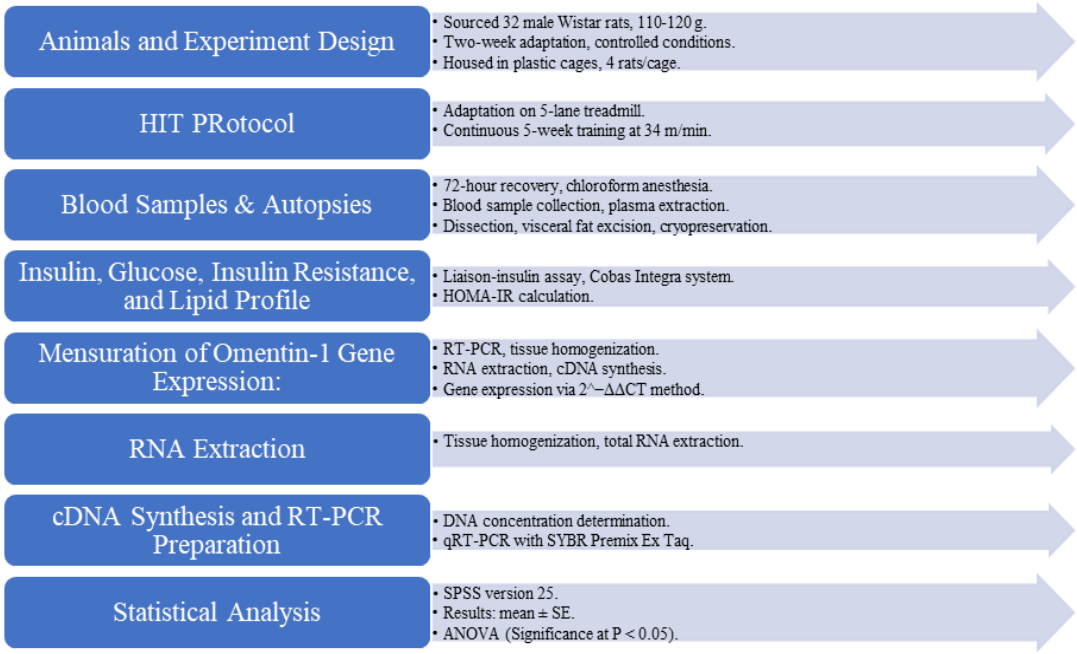


Figure 1. Schematic diagram of methods' stages

2.7. Ethical consideration

The study was carried on by the policy statement by the Declaration of Helsinki. This study was conducted with the approval of Qassim University and adhered to the regulations for the Administration of Affairs Concerning Experimental Animals. All necessary measures were taken to minimize animal suffering. The protocols involving animal experimentation were approved by the Committee of Research Ethics, Deanship of Scientific Research, Qassim University, under permit number 22-18-05, on 29 December 2022.

3. RESULTS

The results presented in Table 1 show the mean body weights along with their standard errors (SE) for different groups throughout the study. At the beginning of the experiment, no significant differences were observed in body weight among all groups (p=0.65). Similarly, after the adaptation period, no significant differences were found (p=0.43). However, significant differences were observed in body weight at the end of the experiment among the four categories (p<0.01). The final mean body weight of the control group was 293.7±7.79, while the Diabetic Control, HIT Diabetic, and HIT Obese groups exhibited weights of 266.3±2.35*, 249.6±3.88*#, and 297.4±3.56#+, respectively. The asterisk (*) denotes a significant difference in comparison to the control group, indicating that the diabetic control group had decreased body weight (P<0.05). The hash symbol (#) depicts a significant difference compared to the diabetic control group, highlighting that the HIT Diabetic group had a further reduced body weight (p<0.05). Finally, the plus

symbol (+) signifies a significant difference compared to the HIT diabetic group, demonstrating that the HIT obese group had a higher body weight ($p<0.05$). These findings suggest that the intervention protocols, particularly HIT, influenced the body weight outcomes, leading to significant differences among the groups at the end of the experiment.

Table 1. The effect of HIT on body weight (gm) in the normal control group and different-treated groups (n=8)

Groups body weight	Control group (Mean±SE)	Diabetic control (Mean±SE)	HIT diabetic (Mean±SE)	HIT obese (Mean±SE)
Primary	107.3±4.26	107.2±3.51	110.5±3.56	113.0±3.23
After adaptation	127.1±1.50	125.7±2.27	127.3±2.77	131.3±2.52
After 8 weeks of diet	-------	294.2±3.31	300.0±2.44	309.3±3.75
After indicating diabetes	-------	264.8±4.47	273.4±3.13	-------
Final	293.7±7.79	266.3±2.35*	249.6±3.88*#	297.4±3.56#+

* Significant difference in comparison to the control
\# Significant difference in comparison to the diabetic control group
\+ Significant difference in comparison to the HIT diabetic group

Table 2 illustrates the levels of TC, HDL, TG, and LDL in different groups after the intervention. In the HIT diabetic group, following HIT, the TC levels significantly decreased to 77.4±2.55 mg/dl. This reduction was notable compared to the diabetic control group (106.1±4.21 mg/dl) and the HIT obese group (101.1±4.33 mg/dl). Regarding HDL levels, after five weeks of training, the HIT diabetic group exhibited a significant elevation to 39.8±1.28 mg/dl. In contrast, the HIT obese group (31±1.25 mg/dl), the control diabetic group (30.3±1.26 mg/dl), and the control group (32±1.54 mg/dl) demonstrated relatively lower HDL levels. TG levels showed a decrease after five weeks of HIT in the HIT diabetic group (85±2.20 mg/dl) compared to the control diabetic group (115±6.11 mg/dl) and the HIT obese group (107.2±7.58 mg/dl). Furthermore, LDL levels exhibited a significant decrease in both the HIT diabetic group (50.4±1.73 mg/dl) and the HIT obese group (53.2±3.82 mg/dl) compared to the control group (67.1±1.75 mg/dl) and the diabetic control group (60.9±1.99 mg/dl). The HIT diabetic group showed reduced TC levels, increased HDL levels, decreased TG levels, and lower LDL levels compared to other groups, highlighting the benefits of HIT on lipid metabolism in individuals with diabetes.

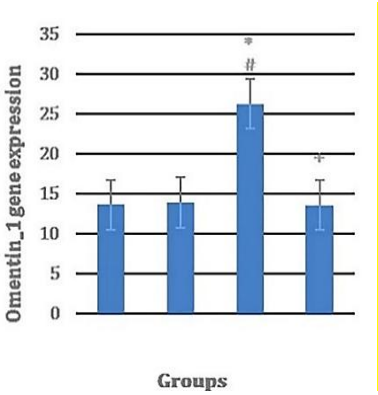
Table 2. The effect of HIT on lipid profile in normal group and different-treated groups (n=8)

Groups lipid levels	Control group (Mean±SE)	Diabetic control (Mean±SE)	HIT diabetic (Mean±SE)	HIT obese (Mean±SE)
TC	78.3±4.20	106.1±4.21*	77.4±2.55#	101.1±4.33*+
TG	83.1±4.02	115±6.11*	85±2.20#	107.2±7.58*+
LDL	67.1±1.75	60.9±1.99	50.4±1.73*#	53.2±3.82*#
HDL	32±1.54	30.3±1.26	39.8±1.28*#	31±1.25+

*Significant difference in comparison to the control
#Significant difference in comparison to the diabetic control group
+Significant difference in comparison to the HIT diabetic group

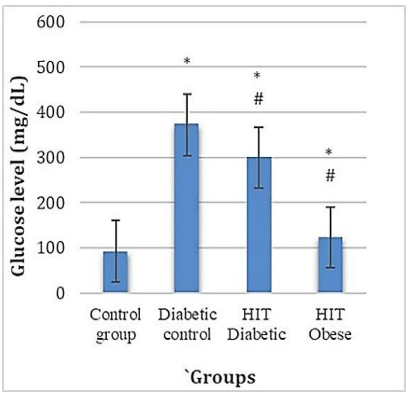
The level of the omentin-1 gene expression was significantly increased in the HIT diabetic group after five weeks of HIT (26.2±1.09) as compared to the other groups as shown in Figure 2. This suggests that HIT has a positive impact on omentin-1 gene expression, particularly in individuals with diabetes. Fasting glucose levels also exhibited notable changes after five weeks of training. The HIT diabetic group (299.5±2.01 mg/dl) and the HIT obese group (122.9±1.14 mg/dl) demonstrated lower fasting glucose levels compared to the diabetic control group (372.5±1.06 mg/dl) as presented in Figure 3. These findings indicate that HIT can contribute to improved glucose regulation in individuals with diabetes and obesity.

Furthermore, fasting insulin levels showed a decrease following five weeks of HIT. Both the HIT diabetic group (4.6±0.142 mU/ml) and the HIT obese group (4.5±0.024 mU/ml) exhibited lower insulin levels compared to the diabetic control group (8±0.157 mU/ml) and the control group (5.6±0.024 mU/ml) as shown in Figure 4. These results suggest that HIT may enhance insulin sensitivity and reduce insulin levels in diabetic and obese individuals.



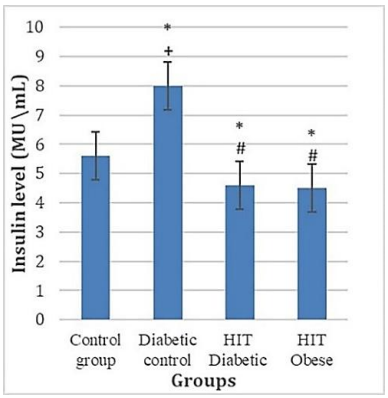
Note: *Shows a considerable difference with the control group, #shows a considerable difference with the diabetic control group, + shows a considerable difference with HIT diabetic

Figure 2. Effect of HIT on omentin-1 gene expression in normal group and different-treated groups



Note: *Shows a considerable difference with the control group, #shows a considerable difference with the diabetic control group, + shows a considerable difference with HIT diabetic

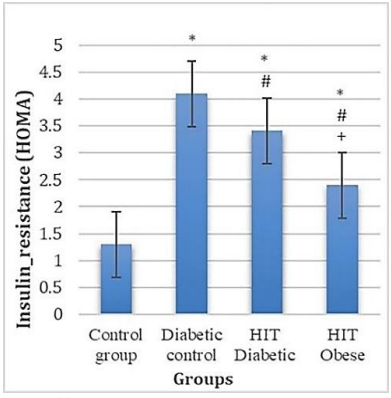
Figure 3. Effect of HIT on glucose levels in the normal group and different-treated groups



Note: *Shows a considerable difference with the control group, #shows a considerable difference with the diabetic control group, + shows a considerable difference with HIT diabetic

Figure 4. Effect of HIT on insulin levels in normal group and different-treated groups

Insulin resistance, as measured by the HOMA index, also demonstrated favorable outcomes after five weeks of HIT. The HIT diabetic group (3.4±0.098) and the HIT obese group (2.4±0.060) had lower levels of insulin resistance compared to the diabetic control group (4.1±0.16) as shown in Figure 5. These findings suggest that HIT can improve insulin sensitivity in individuals with diabetes and obesity.



Note: *shows a considerable difference with the control group, #shows a considerable difference with the diabetic control group, + shows a considerable difference with HIT diabetic

Figure 5. Effect of HIT on insulin resistance levels in normal group and different-treated groups

4. DISCUSSION

The present study investigated the impact of a five-week HIT program on omentin-1 gene expression in diabetic and obese rats and revealed a significant increase in its expression specifically in the HIT diabetic group. However, there were no significant changes observed in the HIT-obese group. These findings align with the results presented by Amanat *et al*. [27], demonstrating increased omentin-1 levels following aerobic exercise in diabetic women. The increase in omentin-1 gene expression further provides evidence for the potential beneficial effects of exercise on regulating omentin-1 diabetic individuals. Moreover, omentin-1 gene expression can be influenced by different exercise modalities. Castro *et al*. [28] investigated the effects of various exercises on omentin-1 gene expression in the visceral tissues of diabetic mice. Their study demonstrated different types of exercise-induced changes in omentin-1 gene expression, highlighting the exercise-specific effects on omentin-1 regulation. These collective findings underscore the potential role of exercise, particularly HIT, in modulating omentin-1 gene expression in the context of diabetes. While our study focused on rats, the results are consistent with previous research in humans, suggesting the translational relevance of our findings. A similar study investigated the impact of HIT training for 8 weeks on insulin resistance and omentin-1 gene expression and showed an increase in its gene expression in obese and diabetic rats [12].

Surprisingly, the study found that the concentration of omentin-1 expression did not show any significant changes following the five-week HIT intervention. These results are in agreement with Urbanová *et al*. [29], where the study observed no alteration in omentin-1 levels after training program of three months duration, despite the positive impact on hormonal and biochemical parameters in humans. Another study investigated the impact of HIT on insulin resistance, omentin-1 level, and lipid profile among diabetic and obese human males. The findings were in agreement with the present study as 12 weeks of HIT training improved levels of omentin-1, insulin sensitivity, and lipid profile [30]. On the other hand, our result contradicts the findings of Alizadeh *et al*. [12], demonstrating high levels of omentin-1 gene expression in obese rats after 8 weeks of high-intensity interval training (HIIT). It is important to note that omentin-1 is a complex adipokine that affects different physiological processes, like insulin resistance and inflammation. The regulation of omentin-1 expression is still not fully understood, and it appears to be influenced by multiple factors, including exercise modality, duration, and individual characteristics.

The lack of omentin-1 gene expression in the HIT obese group in our study may be attributed to the ongoing state of obesity among the rats. A longer duration of training may be required to elicit changes in omentin-1 expression. This notion is supported by Amanat *et al*. [27], who demonstrated that resistance or aerobic exercise over 12 weeks resulted in weight loss, leading to increased levels of omentin-1. Furthermore, a study conducted by Li *et al*. [11] provided evidence that consistent adherence to daily exercise regimens can regulate body composition, thereby influencing the level of omentin-1 in serum. Specifically, increased levels of omentin-1 in serum were observed after twelve weeks of exercise, consisting of five sessions per week of medium continuous training (MCT) and HIIT. This indicates that longer and more regular exercise programs may be necessary to induce changes in omentin-1 expression. Moreover, Ross *et al*. [31] conducted a study involving both MCT and HIIT and found that these exercise modalities resulted in a decrease in the total percentage of body and leg fat, as well as a reduction in subcutaneous fat accumulation, after twelve weeks of training. These findings suggest that sustained exercise regimens that combine MCT and HIIT have the potential to positively impact body composition, which may, in turn, influence omentin-1 levels.

Adipose tissue serves as the primary source of Omentin-1 production, and its levels are influenced by the expansion or reduction of adipose tissue. There is proliferation of fat cells due to increase in adipose tissue, resulting in increased secretion of pro-inflammatory adipokines and decrease in anti-inflammatory adipokines. Consequently, the size of fat cells plays a crucial role in regulating Omentin-1 levels. HIIT has been shown to effectively reduce visceral fat in individuals with obesity. This reduction in visceral fat is linked with improved indicators of metabolic syndrome, along with increased levels of Omentin-1 [19]. By engaging in HIIT, obese individuals can experience a reduction in fat deposition around their internal organs, leading to beneficial changes in metabolic health. This decrease in visceral fat is accompanied by an upregulation of Omentin-1, having anti-inflammatory effects that result in amelioration of metabolic dysregulation. These findings highlight the importance of fat cell size and its influence on Omentin-1 levels. HIIT serves as an effective strategy for reducing visceral fat, improving metabolic syndrome indicators, and promoting the expression of Omentin-1.

This study provides compelling evidence that five weeks of HIIT results in decreased insulin and blood glucose levels in both training groups. One possible mechanism for this effect is the AMP-activated protein kinase (AMPK) activation that regulates the uptake of glucose in skeletal muscle, following physical activity [32]. Obese individuals often develop T2D due to decreased levels of omentin-1, a factor linked with reduced glucose uptake by insulin-responsive tissues [33]. In line with these findings, Wang *et al*. [32] observed improved glucose control and metabolism in T2D patients after engaging in HIT and HIIT.

Importantly, they also noted that a single or multiple exercise session can have lasting benefits on blood glucose levels for at least 24 hours.

One of the significant findings of this study is the notable reduction in insulin resistance observed in both training groups after engaging in HIT for five weeks. This outcome is in agreement with the study by Sparks *et al*. [34], who characterized exercise as a therapeutic approach for both T2D and Type 1 diabetes (T1D). Exercise plays a crucial role in modulating glucose homeostasis by facilitating the clearance of excess glucose and improving glucose uptake in skeletal muscle, thereby enhancing insulin sensitivity and reducing insulin resistance. These findings are further corroborated by the research conducted by Kumar *et al*. [35], demonstrating the beneficial effects of regular exercise in improving glucose control and reducing insulin resistance. Increased levels of insulin in the bloodstream often precede the development of various metabolic disorders. The involvement of insulin resistance in the development of metabolic syndrome is characterized by impaired insulin sensitivity, further supporting this notion. By addressing insulin resistance through exercise interventions such as HIT, the risk of metabolic disorders can be mitigated, emphasizing the significance of managing insulin resistance for overall metabolic health.

A previous study confirmed that increased production of Omentin is likely to prevent the progression of diabetes among rats [28]. The impact of exercise might be because of omentin modulation, however, there is no clarity on the cause-and-effect relationship. It is further suggested that skeletal muscle and fat tissue are related concerning omentin-1, which appears to influence glucose metabolism, particularly insulin sensitivity. Another study by de Atashak *et al*. [18] reporting that 12 weeks of HIT improved insulin resistance and adipokines (Omentin-1) further supported that HIIT is an effective non-medical therapeutic strategy to minimize cardiovascular risks and other disorders caused due to obesity. One similar study also reported that alterations in Omentin-1 levels induced by aerobic exercise in smokers who are trained in exercise are beneficial as it lowers insulin resistance and improves lipid profiles [14]. On the contrary, Golestani *et al*. [19] examined the impact of spirulina combined with HIITon the levels of Omentin-1, nesfatin-1, and lipid profiles in overweight obese females and reported elevated levels of nesfatin-1 and omentin-1 without affecting the lipid profiles.

The findings of Alizadeh *et al*. [12] revealed a negative correlation between Omentin-1 and blood glucose concentration, insulin resistance, and waist circumference in diabetic rats. However, these results contrast with the findings of our study, which demonstrated a decrease in blood insulin levels, glucose levels, and insulin resistance, in both the HIT diabetic and HIT obese groups. Notably, despite the lack of change in omentin-1 gene expression in the HIT obese group, significant improvements were observed in glucose and insulin parameters. Interestingly, the association between insulin resistance in post-training diabetic individuals and the Omentin-1 gene expression is insignificant in a few of the previous studies [9], [33]. Similarly, the study by Urbanova *et al*. [29] documented significant changes in weight, insulin levels, and insulin resistance, despite the absence of changes in Omentin-1 levels. These findings support the conclusions drawn from our research, suggesting that the regulated levels of glucose and insulin dynamics in response to exercise may involve mechanisms independent of Omentin-1 expression. Overall, while previous studies have reported varying associations between Omentin-1 and metabolic parameters, our study contributes to the previous literature indicating that improvements in glucose control, insulin levels, and insulin resistance can be achieved through exercise interventions, even in the absence of significant changes in Omentin-1 expression.

One of the key findings of this study is the significant decrease in TC, TG, and low-density lipoprotein (LDL) levels in the HIT diabetic group. However, there were significant differences reported in the HIT-obese group. Moreover, the HIT diabetic group exhibited an increase in high-density lipoprotein HDL levels compared to the other groups after five weeks of HIT. The results of the lipid profile analysis indicate a negative relationship between TC, TG, and LDL levels, and the expression of the Omentin-1 gene, while a positive relationship was observed between HDL levels and Omentin-1 gene expression. Physical inactivity, T2D, and obesity, particularly visceral obesity, are known factors contributing to lipid profile disturbances. Zhang *et al*. [36] demonstrated that implementing an exercise program led to a decrease in TC, LDL, and TG levels, and increase in HDL levels in diabetic patients. However, Golestani *et al*. [19] reported no significant changes in LDL, HDL, TC, and TG levels following four weeks of interval training. It is suggested that the duration of four weeks may not be sufficient to influence lipid levels and it is emphasized that exercise intensity and volume play crucial roles in modulating LDL and HDL levels.

5. CONCLUSION

In conclusion, the study provided strong evidence for the effectiveness of HIIT after a 5-week intervention period in rat models with diabetes and obesity. The HIT diabetic group exhibited a significant increase in Omentin-1 gene expression as compared to other groups, indicating a positive impact on

molecular markers. Moreover, both the HIT diabetic and HIT obese groups demonstrated lower levels of glucose, insulin, and insulin resistance, suggesting improved metabolic regulation. The lipid profile analysis further demonstrated the beneficial effects of HIT, revealing diminished levels of TC, TG, and LDL, accompanied by an elevation in HDL levels in the HIT diabetic group. These findings provide evidence supporting the potential of HIIT to induce favorable changes in key metabolic and molecular parameters in the context of diabetes and obesity in the experimental setting.

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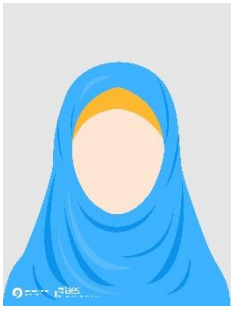
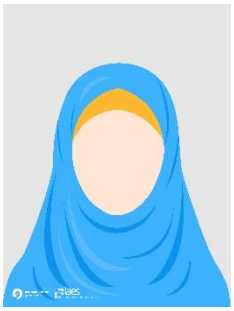
BIOGRAPHIES OF AUTHORS



Noorah Saleh Al-Sowayan a Saudi researcher and academic specializing in physiology, currently holds the position of professor in the Biology Department at the College of Science, Qassim University. In this role, she engages in research activities and educates students in various aspects of life sciences. Her scientific contributions are highly regarded, as evidenced by the publication of numerous research papers in prestigious scientific journals-over 65 papers in total. Professor Al-Sowayan has been honored with international and local awards for her exceptional work in mitigating the detrimental effects of oxidation and body inflammation through the use of natural compounds. Notably, she awarded the Mohammed bin Fahd Award for Best Scientific Production for the year 2024 at the Arab world level, organized by Prince Mohammad Bin Fahd University in collaboration with the League of Arab States. Besides that, she secured first place in both the medicine and health branch, as well as in the nutrition branch, in the Rashid Bin Humaid Award for Culture and Science in the UAE. In addition to her research endeavors, Professor Al-Sowayan has authored the book titled "Amazing Biology", which serves as a valuable resource for students and researchers in the field of life sciences. This comprehensive work delves into topics such as biological diversity, life processes, and evolution, garnering praise from the scientific community. Her commitment extends beyond academia. Professor Al-Sowayan actively fosters knowledge and promotes scientific literacy among students and fellow researchers, with the goal of inspiring them to embark on new intellectual journeys through her research and teaching efforts. She can be contacted at email: nsaoiean@qu.edu.sa.



Aiesha Mohammed Almutawa works as a lecturer in the Biology Department at Qassim University. She is currently a doctoral student at King Saud University. She got a master's degree with a specialization in physiological science, with an excellent grade in 2022. She obtained a bachelor's degree in zoology from Qassim University with an excellent grade and she has scientific publications in her field of specialization. She speaks Arabic and English languages. She can be contacted at email: a.almotawaa@qu.edu.sa.