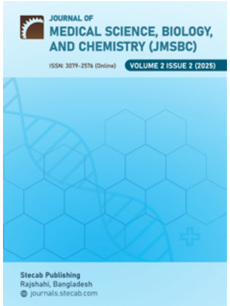

Journal of Medical Science, Biology, and Chemistry (JMSBC)
ISSN: 3079-2576 (Online)
Volume 2 Issue 2, (2025)
https://doi.org/10.69739/jmsbc.v2i2.1222
https://journals.stecab.com/jmsbc

Published by
Stecab Publishing

Research Article

Impact of Cortisol and Sex Hormone Imbalance on Obesity and Insulin Resistance Among Iraqis: A Case-Control Study

*[1]Ali B. Abdulrazzaq

About Article

Article History
Submission: October 14, 2025
Acceptance : November 14, 2025
Publication : November 18, 2025

Keywords
Cortisol, Iraqi Population, Obese Individuals, Sex Hormones

About Author
[1] Department of Biochemistry, Faculty of Medicine, Kufa University, Najaf, Iraq

Contact @ Ali B. Abdulrazzaq
alib.alqureshi@uokufa.edu.iq

ABSTRACT

Obesity is a multifaceted metabolic condition affected by hormonal and environmental elements. There is growing awareness of how dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis and changes in sex hormone levels play a role in insulin resistance linked to obesity. Increased cortisol levels, along with fluctuations in testosterone and estradiol, can interfere with glucose metabolism and fat distribution, leading to various metabolic issues. This research focused on examining the relationship between circulating cortisol and the levels of sex hormones (testosterone and estradiol) in relation to obesity and insulin resistance in adults. A case-control study was carried out with obese and non-obese participants who were matched by age and sex. Key measurements included anthropometric data (such as BMI and waist circumference) and fasting biochemical markers. Serum levels of cortisol, testosterone, and estradiol were analyzed using enzyme-linked immunosorbent assay (ELISA). Insulin resistance was evaluated through the Homeostasis Model Assessment for Insulin Resistance (HOMA-IR). Statistical analyses employed correlation and regression tests to investigate the relationships between hormone levels and metabolic indicators. Obese individuals exhibited notably higher levels of serum cortisol and lower levels of testosterone compared to non-obese controls ($p < 0.001$). Additionally, estradiol levels were significantly increased in obese females. After controlling for BMI, cortisol and testosterone were found to be independently linked to HOMA-IR, suggesting their role in insulin resistance. An imbalance in cortisol and sex hormones is closely linked to obesity and insulin resistance. These changes in hormone levels might act as early warning signs of metabolic risk and could potentially be targeted for therapeutic approaches in addressing obesity-related conditions.

Citation Style:
Abdulrazzaq, A. B. (2025). Impact of Cortisol and Sex Hormone Imbalance on Obesity and Insulin Resistance Among Iraqis: A Case-Control Study. *Journal of Medical Science, Biology, and Chemistry, 2*(2), 262-266. https://doi.org/10.69739/jmsbc.v2i2.1222

1. INTRODUCTION

Obesity is a multifactorial metabolic disorder characterized by the excessive accumulation of body fat due to the imbalance between energy consumed as food and energy expended as physical activity (Friedman *et al.*, 2024). Obesity is highly correlated with conditions such as insulin resistance, dyslipidemia, hypertension, and a higher risk of heart disease (Bastien *et al.*, 2014). Factors such as lifestyle habits and genetic predisposition are known to contribute to this disease. Nevertheless, it is critical to acknowledge the role of hormonal regulation, especially in cortisol and sex steroid hormones, that causes obesity and its comorbidities (Mazza *et al.*, 2024; Sheikh *et al.*, 2017).

Despite extensive global research, the interplay between cortisol dysregulation, sex hormone imbalance, obesity, and insulin resistance has not been adequately examined within the Iraqi population, an important gap given Iraq's distinct sociocultural stressors, high prevalence of obesity-related disorders, and limited endocrine-focused epidemiological data. Addressing this gap is crucial for understanding population-specific biological and environmental contributors to metabolic disease.

2. LITERATURE REVIEW

The understanding of this process is crucial for the management and treatment of obesity. More recently, disturbances in the hypothalamic-pituitary-adrenal axis HPA) and sex steroid dynamics have been identified as critical determinants for visceral fat accumulation, leading to systemic insulin resistance (Janssen, 2022). This is particularly important because of evidence suggesting that hypercortisolism, characterized by elevated 24-h urinary free cortisol and cortisol secretion rates, is a significant determinant of visceral fat and insulin resistance (Min, 2016). In cases of insulin resistance and obesity, plasma cortisol-binding globulin is reduced, resulting in elevated cortisol availability (Bae & Kratzsch, 2015).

Cortisol, the main glucocorticoid secreted from the adrenal cortex, is regulated by the hypothalamic-pituitary-adrenal (HPA) axis and has effects on glucose and lipid metabolism (Beaupere *et al.*, 2021). Elevated cortisol over a prolonged period is linked to central adiposity, liver glucose production, and reduced insulin sensitivity (Anagnostis *et al.*, 2009). On the other hand, sex hormones, such as testosterone and estradiol, play a critical role in systemic composition and energy balance, and 17β-estradiol predominates in women (Bianchi & Locatelli, 2018). Reduced testosterone in men and alterations in estradiol in women are associated with fat accumulation, insulin resistance, and metabolic syndrome (Ciardullo *et al.*, 2023; Mauvais-Jarvis, 2011).

The interaction between cortisol and sex hormones represents an increasingly fragile endoscopic homeostasis that establishes fat tissue distribution and insulin (Yan *et al.*, 2019). However, the relationship between hormonal variations and insulin resistance has not been adequately established, particularly in people with a high prevalence of obesity and diabetes. Thus, this study aims to determine how dysregulation between cortisol and sex hormones: testosterone and 17- β-estradiol influences obesity and insulin resistance; these results may highlight hormonal targets to assess metabolic risk.

3. METHODOLOGY

3.1. Ethical Considerations

The study protocol received approval from the scientific committee of the Department of Biochemistry at the College of Medicine, University of Kufa, Iraq. All participants provided written informed consent prior to their inclusion in the study

3.2. Study Design and Population

A robust case–control study was carried out involving 300 adult participants, consisting of 150 obese individuals and 150 non-obese individuals, all recruited from outpatient clinics and relatives. Obesity was defined precisely according to World Health Organization (WHO) criteria, identifying those with a body mass index (BMI) of ≥ 30 kg/m². The non-obese participants, with BMI values between 18.5 and 24.9 kg/m², served effectively as the control group.

3.3. Inclusion Criteria

- Adults aged 18 years and older
- Both male and female participants
- Individuals who have provided informed consent

3.4. Exclusion Criteria

- A history of endocrine disorders (such as Cushing's syndrome, thyroid disorders, or hypogonadism)
- Current use of corticosteroids or hormone treatments
- Chronic kidney, liver, or heart diseases
- Pregnancy or breastfeeding

3.5. Anthropometric and Clinical Measurements

Height, weight, and waist circumference were assessed in accordance with established measurement protocols. Body Mass Index (BMI) was computed using the formula: weight (kg) divided by height squared (m²). Blood pressure readings were taken following a 10-minute period of rest to ensure accuracy.

3.6. Biochemical Measurements

After a fasting period of 10 to 12 hours, venous blood samples were taken. The serum was then separated and stored at -20°C until it was ready for analysis.

- Fasting blood glucose levels were measured.
- Serum levels of insulin, cortisol, testosterone, and estradiol were assessed using enzyme-linked immunosorbent assay (ELISA) kits, following the manufacturers' instructions.
- The Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) was calculated using the appropriate formula: HOMA-IR = {Fasting Insulin (μIU/mL)} X {Fasting Glucose (mmol/L)} / 22.5.

3.7. Statistical Analysis

Data analysis was conducted using SPSS version 26.0. Continuous variables were reported as mean ± standard deviation (SD). To compare means between groups, the independent t-test was employed. The relationships among hormone levels, BMI, and HOMA-IR were evaluated using the Pearson correlation test. Multiple linear regression was utilized to determine independent predictors of insulin resistance. A p-value of less than 0.05 was deemed statistically significant.

4. RESULTS AND DISCUSSION

4.1. Anthropometric and biochemical parameters of the study population

Demographic, anthropometric and biochemical characteristics of obese and non-obese subjects are shown in Table 1. Data are expressed as mean ± SD. Obese subjects had significantly higher BMI, waist circumference, fasting glucose, insulin and HOMA-IR than non–obese participants (p <0.001). The age was not different between two groups. (p > 0.05).

Table 1. General characteristics of the study population

Variable	Obese group (n=150)	Non-obese group (n=150)	p-value
Age (years)	57.6 ± 10.2	55.7 ± 9.95	0.065
BMI (kg/m²)	32.8 ± 3.6	23.9 ± 2.8	<0.001
Waist circumference (cm)	104.7 ± 8.9	88.2 ± 7.5	<0.001
Fasting glucose (mmol/L)	6.75 ± 1.3	5.1 ± 1.2	<0.001
Fasting insulin (μIU/mL)	14.14 ± 6.44	9.82 ± 4.57	< 0.001
HOMA-IR	2.81 ± 1.27	1.94 ± 0.88	< 0.001

4.2. Hormonal Profile

Mean serum cortisol levels were significantly higher in obese individuals compared to non-obese controls (p < 0.001). Conversely, testosterone levels were significantly lower in obese males, whereas estradiol levels were elevated in obese females (p < 0.01), as shown in Table 2.

Table 2. Comparison of serum hormone levels between obese and non-obese participants

Hormones	Obese group (n=150)	Non-obese group (n=150)	p-value
Cortisol (ng/ml)	18.8 ± 3.6	14.4 ± 3.2	<0.001
Testosterone (ng/ml)	3.2 ± 1.2	4.8 ± 1.2	<0.001
Estradiol (pg/ml)	110.2 ± 21.5	81.4 ± 22.4	<0.001

4.3. Correlation Analysis

Table 3 shows the Pearson correlation coefficients (r) between serum hormone levels and several metabolic parameters such as BMI, waist circumference, fasting insulin and HOMA-IR. Cortisol was significantly positively correlated with BMI, waist circumference, fasting insulin and HOMA-IR (p < 0·001). In contrast, testosterone displayed strong negative correlations with these same factors (p < 0.001). Furthermore, estradiol was positively related to obesity indices and insulin resistance, suggesting that it is involved in the hormonal changes accompanying adiposity.

Table 3. Correlation between hormone levels and metabolic parameters

Parameter	Cortisol (r, p)	Testosterone (r, p)	Estradiol (r, p)
BMI	0.58, <0.001	−0.46, <0.001	0.37, <0.01
Waist circumference	0.54, <0.001	−0.42, <0.001	0.33, <0.01
Fasting insulin	0.61, <0.001	−0.44, <0.001	0.29, <0.05
HOMA-IR	0.63, <0.001	−0.48, <0.001	0.31, <0.05

4.4. Discussion

The current study reveals significant changes in cortisol and sex hormone levels associated with obesity, which correlate strongly with insulin resistance. Notable differences in body mass index (BMI), waist circumference, fasting glucose, fasting insulin, and HOMA-IR between the groups underscore the metabolic dysregulation seen in obesity and insulin resistance. The pronounced differences in cortisol, testosterone, and estradiol levels between obese and non-obese participants further highlight the endocrine disturbances linked to obesity and insulin resistance. These findings suggest that there are complex pathophysiological mechanisms at play, extending beyond mere metabolic dysfunction. The resulting hormonal imbalances contribute to a complicated neuroendocrine environment that perpetuates chronic metabolic disorders among the Iraqi population (Van Hulsteijn *et al.*, 2020).

The study demonstrated that cortisol levels were notably higher in obese individuals compared to healthy controls, with strong positive correlations between cortisol and both HOMA-IR and BMI (Rezaieg, 2021; Abraham *et al.*, 2013). This aligns with existing literature that points to a connection between hypercortisolism and metabolic issues, particularly in relation to glucose homeostasis and insulin resistance (Salehidoost & Korbonits, 2022).

Elevated cortisol has been linked to processes such as increased gluconeogenesis, impaired glucose tolerance, and disruptions in overall glucose metabolism (Salehidoost & Korbonits, 2022). This underscores cortisol's role in influencing insulin sensitivity and its potential impact on the escalation of metabolic disorders (Mazgelytė & Karčiauskaitė, 2024). Moreover, chronic high cortisol levels can lead to shifts in fat distribution, promoting visceral fat accumulation, which is independently associated with increased insulin resistance and cardiovascular risk (Paredes & Ribeiro, 2014). Recent research also found a significant correlation between elevated cortisol levels and increased oxidative stress, which may contribute to insulin resistance through cellular damage and inflammation (Signorello *et al.*, 2024).

Our data also indicated lower testosterone levels in males, which may further exacerbate insulin resistance by reducing lean muscle mass and increasing body fat (Kelly & Jones, 2015). In contrast, elevated estradiol levels in obese females are likely a result of increased aromatase activity in adipose tissue, converting androgens to estrogens (Wang *et al.*, 2013). This hormonal imbalance compounds the metabolic disturbances found in obesity. Our results are congruent with prior studies linking excess cortisol to metabolic syndrome and hypogonadism to obesity (Janssen, 2022; Bianchi & Locatelli, 2018; Abraham *et al.*, 2013). The relationships observed between hormone levels and HOMA-IR imply that both cortisol and sex steroids significantly influence insulin sensitivity.

These findings highlight waist circumference and cortisol as vital factors in insulin resistance, emphasizing the complex interactions between hormonal function, body fat, and metabolic health (Yan *et al.*, 2016). Additionally, some studies suggest that plasma aldosterone concentrations correlate with HOMA indices (Min *et al.*, 2018). This implies that while aldosterone may have a role in metabolic regulation, its direct effects on insulin resistance could be mediated or overshadowed by other hormonal or metabolic factors.

On a mechanistic level, chronic elevated cortisol may disrupt insulin signaling through increased lipolysis and the release of free fatty acids, while low testosterone or altered estrogen levels can influence adipocyte differentiation and glucose uptake (Wawrzkiewicz-Jałowiecka *et al.*, 2021). The collective result fosters a hormonal environment that promotes central obesity and insulin resistance. These outcomes underscore the significance of assessing hormonal profiles in obese patients, as the early detection of cortisol or sex hormone imbalances could help identify individuals at a higher risk for metabolic complications.

5. CONCLUSION

Cortisol and imbalances in sex hormones play a key role in the development of obesity and insulin resistance. Keeping track of these hormonal fluctuations could be helpful in preventing and managing metabolic disorders. The findings of this case-control study indicate that cortisol levels and sex hormone imbalances are associated with obesity and insulin resistance among Iraqi adults. While the observed differences between cases and controls suggest a potential hormonal contribution to metabolic dysfunction, the available analyses do not allow for definitive conclusions regarding the independent effects of each hormone. Further studies incorporating full multivariable regression models are needed to clarify the extent to which these hormonal factors individually predict obesity and insulin resistance. Nonetheless, monitoring hormonal profiles may still offer supportive value in understanding and managing metabolic risks within this population.

REFERENCES

Abraham, S., Rubino, D., Sinaii, N., Ramsey, S., & Nieman, L. K. (2013). Cortisol, obesity, and the metabolic syndrome: A cross-sectional study of obese subjects and review of the literature. *Obesity, 21*(1), E105–E117.

Anagnostis, P., Athyros, V. G., Tziomalos, K., Karagiannis, A., & Mikhailidis, D. P. (2009). The pathogenetic role of cortisol in the metabolic syndrome: a hypothesis. *The Journal of Clinical Endocrinology & Metabolism, 94*(8), 2692–2701.

Bae, Y. J., & Kratzsch, J. (2015). Corticosteroid-binding globulin: modulating mechanisms of bioavailability of cortisol and its clinical implications. *Best Practice & Research Clinical Endocrinology & Metabolism, 29*(5), 761–772.

Bastien, M., Poirier, P., Lemieux, I., & Després, J.-P. (2014). Overview of epidemiology and contribution of obesity to cardiovascular disease. *Progress in Cardiovascular Diseases, 56*(4), 369–381.

Beaupere, C., Liboz, A., Fève, B., Blondeau, B., & Guillemain, G. (2021). Molecular mechanisms of glucocorticoid-induced insulin resistance. *International Journal of Molecular Sciences, 22*(2), 623.

Bianchi, V. E., & Locatelli, V. (2018). Testosterone a key factor in gender related metabolic syndrome. *Obesity Reviews, 19*(4), 557–575.

Ciardullo, S., Zerbini, F., Cannistraci, R., Muraca, E., Perra, S., Oltolini, A., & Perseghin, G. (2023). Differential association of sex hormones with metabolic parameters and body composition in men and women from the United States. *Journal of Clinical Medicine, 12*(14), 4783.

Friedman, M. I., Sørensen, T. I. A., Taubes, G., Lund, J., & Ludwig, D. S. (2024). Trapped fat: Obesity pathogenesis as an intrinsic disorder in metabolic fuel partitioning. *Obesity Reviews, 25*(10), e13795.

Janssen, J. A. (2022). New insights into the role of insulin and hypothalamic-pituitary-adrenal (HPA) axis in the metabolic syndrome. *International Journal of Molecular Sciences, 23*(15), 8178.

Kelly, D. M., & Jones, T. H. (2015). Testosterone and obesity. *Obesity Reviews, 16*(7), 581–606.

Mauvais-Jarvis, F. (2011). Estrogen and androgen receptors: regulators of fuel homeostasis and emerging targets for diabetes and obesity. *Trends in Endocrinology & Metabolism, 22*(1), 24–33.

Mazgelytė, E., & Karčiauskaitė, D. (2024). Cortisol in metabolic syndrome. *Advances in Clinical Chemistry, 123*, 129–156.

Mazza, E., Troiano, E., Ferro, Y., Lisso, F., Tosi, M., Turco, E., … Montalcini, T. (2024). Obesity, dietary patterns, and hormonal balance modulation: gender-specific impacts. *Nutrients, 16*(11), 1629.

Min, L. (2016). Functional hypercortisolism, visceral obesity and metabolic syndrome. *Endocrine Practice: Official Journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists, 22*(4), 506.

Min, S. H., Kim, S.-H., Jeong, I.-K., Cho, H. C., Jeong, J.-O., Lee, J.-H., … Lim, S. (2018). Independent association of serum aldosterone level with metabolic syndrome and insulin resistance in Korean adults. *Korean Circulation Journal, 48*(3), 198-208.

Paredes, S., & Ribeiro, L. (2014). Cortisol: the villain in metabolic syndrome? *Revista Da Associação Médica Brasileira, 60*, 84–92.

Rezaieg, N. S. (2021). Negative associations of diurnal cortisol levels with visceral obesity in adults male and female. *Turkish Journal of Physiotherapy and Rehabilitation, 32*(3).

Salehidoost, R., & Korbonits, M. (2022). Glucose and lipid metabolism abnormalities in C ushing's syndrome. *Journal of Neuroendocrinology, 34*(8), e13143.

Sheikh, A. B., Nasrullah, A., Haq, S., Akhtar, A., Ghazanfar, H., Nasir, A., … Naqvi, S. W. (2017). The interplay of genetics and environmental factors in the development of obesity. *Cureus, 9*(7).

Signorello, M. G., Ravera, S., & Leoncini, G. (2024). Oxidative stress induced by cortisol in human platelets. *International Journal of Molecular Sciences, 25*(7), 3776.

Van Hulsteijn, L. T., Pasquali, R., Casanueva, F., Haluzik, M., Ledoux, S., Monteiro, M. P., … Dekkers, O. M. (2020). Prevalence of endocrine disorders in obese patients: systematic review and meta-analysis. *European Journal of Endocrinology, 182*(1), 11–21.

Wang, F., Vihma, V., Soronen, J., Turpeinen, U., Hämäläinen, E., Savolainen-Peltonen, H., … Jauhiainen, M. (2013). 17β-Estradiol and estradiol fatty acyl esters and estrogen-converting enzyme expression in adipose tissue in obese men and women. *The Journal of Clinical Endocrinology & Metabolism, 98*(12), 4923–4931.

Wawrzkiewicz-Jałowiecka, A., Lalik, A., & Soveral, G. (2021). Recent update on the molecular mechanisms of gonadal steroids action in adipose tissue. *International Journal of Molecular Sciences, 22*(10), 5226.

Yan, H., Yang, W., Zhou, F., Li, X., Pan, Q., Shen, Z., … Majeti, R. (2019). Estrogen improves insulin sensitivity and suppresses gluconeogenesis via the transcription factor Foxo1. *Diabetes, 68*(2), 291–304.

Yan, Y.-X., Xiao, H.-B., Wang, S.-S., Zhao, J., He, Y., Wang, W., & Dong, J. (2016). Investigation of the relationship between chronic stress and insulin resistance in a Chinese population. *Journal of Epidemiology, 26*(7), 355–360.