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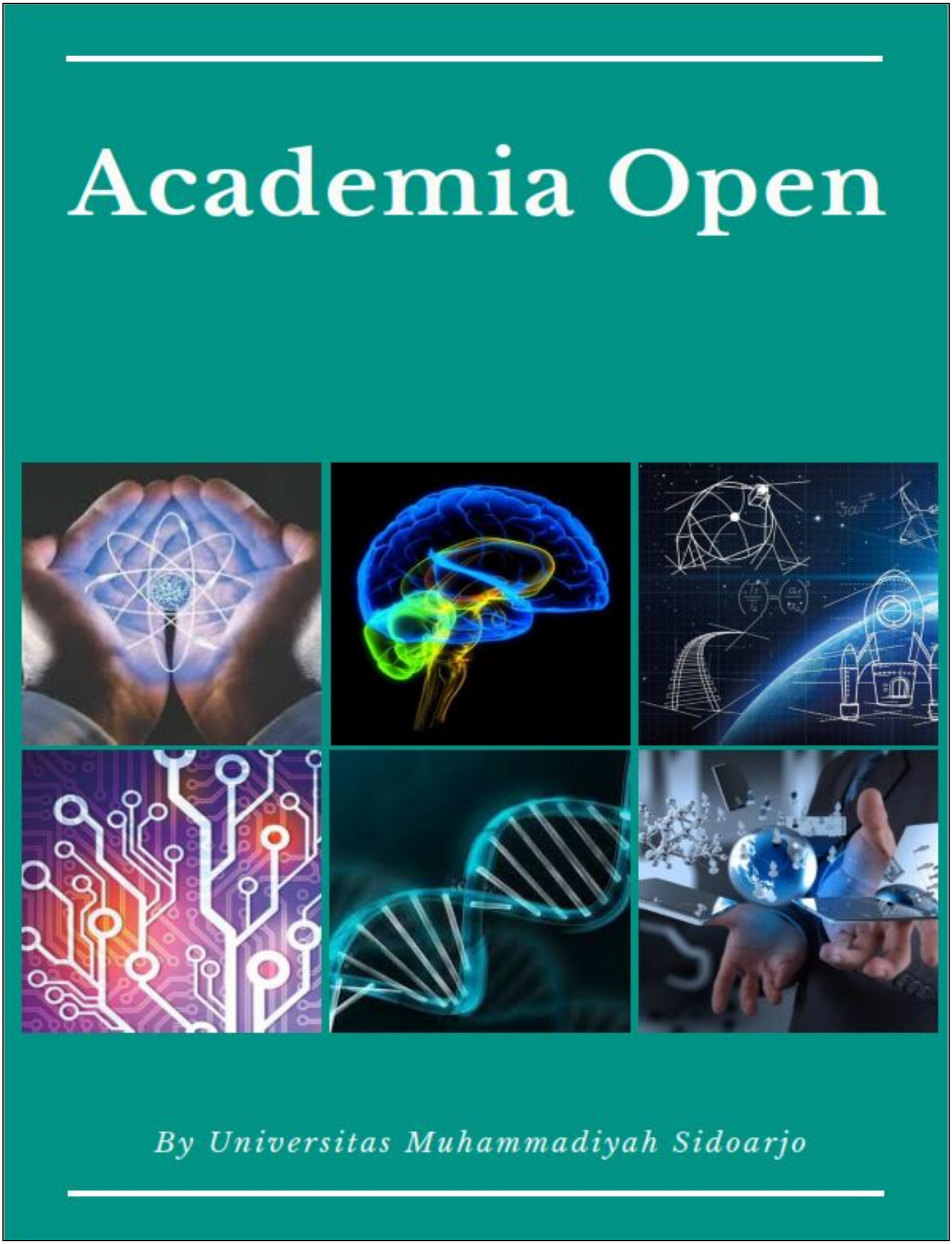

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Exploring the Role of Insulin Resistance in Hormonal imbalance in PCOS patients

Menjelajahi Peran Resistensi Insulin dalam Ketidakseimbangan Hormon pada Pasien PCOS

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Abstract

General Background: Urinary tract infections (UTIs) are a significant concern for transfusion-dependent beta-thalassemia (TDT) patients due to their compromised immune systems and frequent hospital visits. **Specific Background:** Identifying virulence factor genes in bacterial species isolated from UTIs in TDT patients is crucial for understanding pathogenicity and improving treatment strategies. **Knowledge Gap:** Despite the high prevalence of UTIs in TDT patients, limited studies have focused on detecting virulence factor genes in the bacterial isolates from this specific population. **Aims:** This study aims to identify virulence factor genes in bacteria isolated from the urine samples of TDT patients with UTIs. **Results:** Among 173 urine samples, bacterial growth was observed in 38 samples (21.96%), while 135 samples (79.03%) showed no growth. The identified isolates included *Escherichia coli, Enterobacter cloacae,* and *Klebsiella pneumoniae,* confirmed through DNA extraction, universal primers, and partial 16S rRNA sequencing. **Novelty:** This study provides new insights into the molecular characteristics of bacterial pathogens in TDT patients, highlighting the presence of specific virulence factors that contribute to infection severity. **Implications:** The findings enhance our understanding of bacterial virulence in TDT-related UTIs, offering a foundation for targeted therapeutic strategies and improved clinical management.

Highlights:

1. UTI Risk: TDT patients have higher susceptibility due to immune dysfunction.
2. Bacterial Profile: *E. coli, E. cloacae,* and *K. pneumoniae* dominate infections.
3. Clinical Impact: Supports targeted therapy for managing UTIs in TDT patients.

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Introduction

Polycystic ovary syndrome (PCOS) is an endocrine disorder affecting approximately 5–10% of reproductive-age women worldwide [1]. The exact cause of this syndrome remains unclear; however, it is characterized by a set of hormonal imbalances and metabolic disturbances [2]. These hormonal imbalances result in heterogeneous symptoms, morphological, and histological changes in the ovaries, which can be observed through ultrasound imaging. The primary hormonal dysregulation in PCOS involves defect in the hypothalamic-pituitary-ovarian (HPO) axis, leading to an imbalance in gonadotropin secretion. Women with PCOS commonly exhibit elevated luteinizing hormone (LH) levels, reduced follicle-stimulating hormone (FSH) levels, and an increased LH-to-FSH ratio [3]. Consequently, this hormonal dysregulation manifests in symptoms such as anovulation, menstrual irregularities (oligomenorrhea or amenorrhea)

Moreover, studies indicate that women with PCOS often exhibit hyperandrogenism, characterized by elevated testosterone levels, leading to clinical symptoms such as hirsutism (especially facial hair growth), acne, and scalp hair thinning[4]. Since the etiology and exact causes of PCOS is remain unclear insulin resistance (IR) is considered a crucial contributing factor to both hormonal disturbances and metabolic complications associated with the syndrome. These metabolic disturbances include obesity, central adiposity (waist circumference >35 inches), an increased risk of type 2 diabetes, and glucose intolerance[5]. Evidence suggests that 50–70% of women with PCOS experience insulin resistance, which is defined as an impaired cellular response to insulin, resulting in hyperinsulinemia. Hyperinsulinemia reduce the production of sex hormone-binding globulin (SHBG) in the liver, further exacerbating hyperandrogenism and worsening PCOS symptoms[6].

The relationship between insulin resistance and PCOS remains a focal point for research , as understanding this connection is crucial for advancing diagnostic and therapeutic strategies. In this statistical study, we aim to assess the correlation between insulin resistance and key hormonal variables, including LH, FSH, prolactin, and testosterone, among reproductive-aged women in Mosul[7].

Literature Review

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders affecting reproductive-aged women, with a global prevalence ranging between 5% and 10% [1] Despite extensive research, the exact pathophysiology of PCOS remains unclear, making it a complex disorder with multifactorial origins. PCOS is characterized by a spectrum of hormonal and metabolic disturbances, including ovarian dysfunction, hyperandrogenism, and insulin resistance[2].These disturbances contribute to a variety of clinical manifestations, such as irregular menstrual cycles, infertility, hirsutism, and metabolic complications. The heterogeneity of PCOS presentation has ed to challenges in establishing a universal diagnostic criterion, with the Rotterdam criteria being the most widely accepted framework for diagnosis[8].

1 Hormonal Imbalances in PCOS

A key hallmark of PCOS is the dysregulation of the hypothalamic-pituitary-ovarian (HPO) axis, which results in abnormal gonadotropin secretion. Elevated levels of luteinizing hormone (LH) and a reduced follicle-stimulating hormone (FSH) concentration lead to an increased LH-to-FSH ratio, which disrupts ovarian folliculogenesis and contributes to anovulation[3].Additionally, PCOS is often associated with hyperprolactinemia, which can further exacerbate reproductive dysfunction and menstrual irregularities[9]. Hyperandrogenism is another defining feature of PCOS, with increased androgen levels—particularly testosterone—leading to clinical symptoms such as acne, hirsutism, and scalp hair thinning[4]. The impact of these hormonal imbalances extends beyond reproductive health, influencing metabolic processes and increasing the risk of long-term complications, including cardiovascular disease and type 2 diabetes[10].

2 Insulin Resistance and Its Role in PCOS

Insulin resistance (IR) has emerged as a central component of PCOS pathophysiology, affecting up to 50–70% of women with the condition[6]. IR is characterized by a diminished cellular response to insulin, leading to compensatory hyperinsulinemia. This hyperinsulinemia has been shown to amplify ovarian androgen production while simultaneously suppressing hepatic sex hormone-binding globulin (SHBG) synthesis, exacerbating hyperandrogenism[7]. Moreover, the presence of IR in PCOS is closely linked to metabolic disturbances such as obesity, central adiposity, and dyslipidemia, further complicating the clinical picture. While obesity is a common feature among women with PCOS, it is important to note that IR is also prevalent in lean women with the condition[12], suggesting that mechanisms beyond excess weight contribute to metabolic dysfunction in PCOS.

3. Gaps in the Current Literature

Although substantial research has established a connection between insulin resistance and PCOS, there remains a need for a deeper understanding of how IR influences specific hormonal markers in different populations. Most studies have focused on Western populations, while data from Middle Eastern regions, including Iraq, remain limited. Additionally, variations in diagnostic criteria, study methodologies, and population characteristics have led

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to inconsistencies in reported findings. Another gap in the literature is the extent to which insulin resistance affects the secretion patterns of gonadotropins and prolactin, as well as its interaction with androgen levels. Identifying these relationships could provide critical insights into potential therapeutic targets for managing both metabolic and reproductive dysfunction in PCOS patients. This study aims to bridge the existing research gap by examining the correlation between insulin resistance and hormonal markers—including LH, FSH, prolactin, and testosterone—in a sample of reproductive-aged women in Mosul. Understanding these associations may contribute to more targeted diagnostic and treatment strategies, ultimately improving patient outcomes in this population.

Methods

3.1 : Study Design and Participants

This study is a cross-sectional observational study aimed at investigating the relationship between insulin resistance and hormonal imbalances in patients diagnosed with polycystic ovary syndrome (PCOS). The study included 40 female patients, aged 20 to 45 years, recruited from multiple laboratories in Mosul, Iraq. All participants had confirmed insulin resistance, assessed using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR).

3.2 : Data Collection

Blood samples were collected from each participant to measure the levels of the following hormones:

a. luteinizing Hormone (LH)

b. Follicle-Stimulating Hormone (FSH)

c. Thyroid-Stimulating Hormone (TSH)

d. Prolactin

The results were systematically recorded in Microsoft Excel for statistical analysis.

3.3 : Inclusion and Exclusion Criteria

Inclusion criteria: Women aged 20–45 years diagnosed with PCOS and insulin resistance (HOMA-IR positive).

Exclusion criteria: Patients with other endocrine disorders (such as diabetes mellitus or thyroid dysfunction) that could influence hormonal levels.

3.4: Statistical Analysis

Data were analyzed using statistical software to evaluate the correlation between insulin resistance and hormone levels. The analysis included:

Descriptive statistics to summarize the dataset.

Pearson correlation coefficient to assess relationships between variables.

Regression analysis to determine the strength and significance of associations.

patient ID	Age	HOMA-IR	FSH (mIU/mL)	LH (mIU/mL)	Testosterone (ng/dL)	Prolactin (mIU/mL)
1	38	3	2.5	15	35	350
2	30	3	3.6	12.5	20	300
3	36	3.4	3.2	16	35	320
4	30	3.1	3.8	16.2	53.1	142
5	44	3.1	3.2	17.4	43	342
6	24	2.9	3.5	16.4	46	250
7	25	4.4	2.9	18.1	53.9	193
8	33	3.6	3.27	18.32	63.1	177
9	23	3	3.7	13.6	65.4	153
10	42	3.1	4.2	16	40	220
11	27	4.7	3.1	16.8	47.9	185

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12	35	3.3	3	17.1	42	175
13	21	2.7	3.9	11.3	31.8	191
14	33	4.4	3.6	16.4	42	189
15	22	3.7	4.2	14.9	57.7	156
16	27	2.7	4.4	12.6	35	183
17	36	3.5	3.9	17.3	53	176
18	42	4.1	3	17.1	67.8	165
19	26	4.2	4.3	13	32	138
20	35	3.3	4.1	14.9	47.8	164
21	24	4.1	3.9	17.3	47	162
22	34	3.2	4	11.9	37	149
23	27	2.8	4.3	10.3	41	148
24	31	3.3	3.5	17.3	59	159
25	28	3.2	3.5	16	50	168
26	26	3.1	4.3	16.6	63	175
27	45	3.9	3.1	17.4	68	193
28	21	2.9	4.3	16	43	152
29	24	2.7	3.5	14.9	53	144
30	34	3.9	2.9	17.4	58	159
31	29	2.9	3.8	19.3	67.1	146
32	34	3.6	3.7	16.5	69.9	168
33	37	2.7	4.4	13.5	43.1	160
34	28	3.4	4.5	13.1	39	172
35	35	3.1	4.3	10.9	41	322
36	35	2.8	4.5	14.1	59.1	173
37	34	2.6	4.3	10.9	63.2	153
38	28	3.8	4.1	18	61	165
39	33	3.1	4.1	13.3	42	149
40	39	2.8	3.69	16.2	57	162

Table 1. ***Raw Data of Hormonal Measurements***

Table (2)

Hormones	Min	Max	Range
IR	2.6	4.7	2.1
LH	10.3	19.3	9
FSH	2.5	4.5	2
Testosterone	20	69.9	49.9
Prolactin	138	350	212

Table 2.

Summary Statistics Table:

This table presents the minimum (Min), maximum (Max), range, including , insulin resistance (IR), follicle-stimulating hormone (FSH), luteinizing hormone (LH), testosterone, and prolactin. The data provides an overview of the distribution and variation within the sample.

Min (Minimum): The lowest recorded value for each variable.

a. Max (Maximum): The highest recorded value for each variable.

b. Range: The difference between the maximum and minimum values.

Hormones	Average	Median	Variance	Standard Deviation (SD)

IR	3.3275	3.15	0.29487	0.54302
LH	15.2955	16	5.4364	2.33161
FSH	3.7515	3.8	0.27715	0.52645
Testosterone	49.3225	47.85	146.588	12.1074
Prolactin	188.7	168	3279.24	57.2647

Table 3.

Median: The middle value in the dataset when ordered from lowest to highest.

a. Average: The arithmetic mean of the values.

b. SD (Standard Deviation): The measure of the spread of values around the mean.Variance Table:

This table displays the variance (the squared standard deviation) for insulin resistance (IR) and each hormone. Variance provides insight into how much the data for each variable spread out from the mean.

a. Variance (IR): The variance of 0.29487 indicates the spread of insulin resistance values around the mean.

b. Variance (FSH): The variance of 0.27715 shows the spread of FSH values around the mean.

c. Variance (LH): The variance of 5.4364 reflects the variability in LH values.

d. Variance (Testosterone): The variance of 146.588 indicates a large spread in testosterone values within the sample.

Regression Value	Correlation with IR
- 0.3792	- 0.39113
2.028822	0.472498
3.635318	0.123044
- 10.0672	- 0.09546

Table 4.

Correlation Table:

This table illustrates the correlation coefficients between insulin resistance (IR) and different hormones. Correlation coefficients indicate the strength and direction of the linear relationship between two variables.

a. IR and FSH: A negative correlation of -0.39113 suggests a weak inverse relationship between insulin resistance and FSH levels.

b. IR and LH: A positive correlation of 0.472498 suggests a moderate positive relationship between insulin resistance and LH levels.

c. IR and Testosterone: A small positive correlation of 0.123044 indicates a very weak positive relationship between insulin resistance and testosterone levels.

d. IR and Prolactin: A small negative correlation of -0.09546 indicates a weak inverse relationship between insulin resistance and prolactin levels.

Regression Table:

This table shows the regression coefficients for insulin resistance (IR) with respect to each hormone. Regression coefficients indicate how much change in the dependent variable (e.g., FSH, LH, testosterone, prolactin) is expected with a one-unit change in the independent variable (insulin resistance).

a. IR and FSH: A negative regression coefficient of -0.3792 suggests that as insulin resistance increases, FSH levels tend to decrease slightly.

b. IR and LH: A positive regression coefficient of 2.028822 indicates that an increase in insulin resistance is associated with a larger increase in LH levels.

c. IR and Testosterone: A positive regression coefficient of 3.635318 shows that insulin resistance has a significant positive impact on testosterone levels.

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d. IR and Prolactin: A negative regression coefficient of -10.0672 suggests that higher insulin resistance is associated with a decrease in prolactin levels.

Result and Discussion

Results

The statistical analysis conducted on the relationship between insulin resistance (IR) and various hormonal parameters in PCOS patients revealed notable findings. The minimum values recorded were FSH (2.5), IR (2.6), LH (10.3), Testosterone (20), and Prolactin (138), whereas the maximum values reached LH (19.3), FSH (4.5), IR (4.7), Testosterone (69.9), and Prolactin (350). The range for IR was 2.1, while for FSH, LH, Testosterone, and Prolactin, it was 2, 8, 49.9, and 212, respectively.

The correlation analysis indicated a negative correlation between IR and FSH (-0.39113) and Prolactin (-0.09546), while IR showed a positive correlation with LH (0.472498) and Testosterone (0.123044). The regression analysis further demonstrated that changes in IR levels were significantly associated with FSH (-0.3792), LH (2.028822), Testosterone (3.635318), and Prolactin (-10.0672).

Regarding descriptive statistics, the median values for Age, IR, FSH, LH, Testosterone, and Prolactin were 32, 3.15, 3.8, 16, 47.85, and 168, respectively. The mean (average) values for these parameters were 31, 3.3275, 3.7515, 15.2955, 49.3225, and 188.7, respectively. The standard deviation (SD) analysis revealed IR (0.54302), FSH (0.52645), LH (2.33161), Testosterone (12.1074), and Prolactin (57.2647), indicating varying degrees of dispersion among these variables. The variance analysis showed that IR, FSH, LH, and Testosterone had values of 0.29487, 0.27715, 5.4364, and 146.588, respectively.

These findings suggest a complex interplay between insulin resistance and hormonal imbalances in PCOS patients, highlighting the potential role of IR in modulating reproductive hormone levels. The observed correlations and regression values indicate that IR may significantly influence LH and Testosterone levels while exhibiting an inverse relationship with FSH and Prolactin. These results underscore the need for further investigations into the mechanisms linking insulin resistance with hormonal dysregulation in PCOS.

Discussion

This study explores the relationship between insulin resistance (IR) and hormonal imbalances in PCOS patients, revealing key statistical associations between IR and various reproductive hormones. The findings indicate that IR is negatively correlated with FSH (-0.391) and Prolactin (-0.095), while it is positively correlated with LH (0.472) and Testosterone (0.123). These correlations suggest that increased insulin resistance may contribute to an imbalance in gonadotropins and androgens, further complicating the endocrine profile of PCOS patients.

The regression analysis further supports these findings, demonstrating that changes in IR have a notable impact on hormone levels. For example, an increase in IR is associated with a decrease in FSH (-0.3792) and Prolactin (-10.0672), whereas it is linked to an increase in LH (2.0288) and Testosterone (3.6353). These results align with previous studies suggesting that hyperinsulinemia may suppress FSH secretion while stimulating LH production, leading to anovulation and hyperandrogenism in PCOS patients.

Descriptive statistics further highlight the hormonal variations among the studied patients. The mean IR value was 3.3275 ± 0.5430, with a range of 2.1. The LH levels exhibited significant variability (15.29 ± 2.33, range: 8), emphasizing the heterogeneity of hormonal disturbances in PCOS patients. Similarly, the Testosterone levels varied widely (49.32 ± 12.10, range: 49.9), reinforcing the notion that insulin resistance influences androgen excess in PCOS.

These findings are consistent with previous literature, which suggests that insulin resistance plays a central role in the pathophysiology of PCOS by exacerbating hormonal imbalances. However, the study is limited by its sample size and the lack of standardized reference ranges across different laboratories. The variability in measurement techniques and cutoff values for normal hormone levels may have influenced the results.

Future research should focus on larger and more diverse populations to validate these findings. Additionally, standardizing hormonal reference ranges across healthcare institutions would facilitate more accurate comparisons and improve the reliability of statistical analyses in PCOS studies.

Conclusion

In conclusion, this study highlights a significant relationship between insulin resistance (IR) and hormonal imbalances in PCOS patients. The results indicate that IR is positively correlated with LH and Testosterone, while it

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shows a negative correlation with FSH and Prolactin. These findings suggest that insulin resistance may contribute to hormonal dysregulation, potentially exacerbating the reproductive and metabolic complications in PCOS.

The clinical implications of these findings emphasize the importance of insulin-targeted therapies in managing hormonal imbalances in PCOS patients. However, this study has certain limitations, including sample size and regional data collection, which warrant further research. Future studies should explore larger and more diverse populations to better understand the mechanisms linking insulin resistance to endocrine disturbances in PCOS.

Furthermore, it is essential to standardize reference ranges and measurement units across healthcare institutions to ensure consistency in diagnosing and monitoring hormonal imbalances. This standardization would facilitate more accurate statistical analyses and enhance comparability between studies. Additionally, periodic epidemiological and statistical studies on larger populations should be conducted to provide a more comprehensive understanding of the prevalence and progression of PCOS-related hormonal imbalances in the community.

These conclusions align with existing literature that underscores the interplay between insulin resistance and hormonal dysregulation in PCOS patients. Studies have shown that elevated insulin levels can suppress FSH, leading to impaired follicular development and anovulation, while increasing androgen production, which exacerbates hyperandrogenic symptoms (Apollo Fertility, n.d.). Additionally, research indicates that insulin resistance is a driving factor in PCOS pathophysiology, contributing to both reproductive and metabolic disturbances (Elconsolto, 2022).

By acknowledging these findings and advocating for standardized diagnostic criteria and ongoing research, we can enhance our understanding and management of PCOS, ultimately improving patient outcomes.

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