ZITA MEDICAL MANAGEMENT

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PHARMAKEFTIKI, 37, 2S, 2025 | 25-28 RESEARCH

https://doi.org/10.60988/p.v37i2S.135

Hepatocyte nuclear factor-4α and sex hormone-binding globulin levels in overweight polycystic ovary syndrome patients from the Babil Province

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KEY WORDS:
PCOS; SHBG; HNF-α; ELISA; BMI

ABSTRACT

Polycystic ovary syndrome (PCOS) is an endocrine condition that comprises two major elements: metabolic irregularities and elevated male hormone levels. Sex hormone binding-globulin (SHBG) acts as an essential androgen regulator; however, its expression and metabolic functions are controlled by the hepatocyte nuclear factor-4 alpha (HNF-4α). This study has investigated the relationship between the serum levels of SHBG and those of HNF-4α in overweight women with PCOS in the Babil Province of Iraq. To this end, we enrolled 45 women with PCOS (patient group) and a control group consisting of 45 participants. This study was conducted at the Babylon Teaching Hospital for Maternity and Children in Hilla City and at private clinics from May to December 2024. A microplate reader was used in order to determine the serum levels of glycated haemoglobin (HbA1c), SHBG, total testosterone, insulin, and HNF-4α. The PCOS group demonstrated significant elevations of serum HbA1c levels (p<0.05) together with higher serum testosterone (p<0.05), insulin (p<0.05) and HNF-4α (p<0.05) levels, as compared to those of the control group. The SHBG levels displayed a significant relationship with the HNF-4α levels in women with PCOS, thereby indicating that these markers may serve as metabolic regulators. Further studies are required in order to shed more light on both the biological processes and the potential treatment applications of our findings.

ARTICLE INFO:
Received: January 02, 2025
Revised: February 13, 2025
Accepted: February 19, 2025
Available online: October 10, 2025

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1. Introduction

One of the common reproductive disorders that women face is the polycystic ovary syndrome (PCOS). It is a syndrome that oc-

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curs through the convergence of several homogeneous conditions, such as metabolic disorders and reproductive issues, as well as their combination. Most women with PCOS present with higher androgen levels, which is the case behind irregular menstrual cycles, multiple small cysts in the ovaries, and erratic ovulatory functions. It should be emphasized that polarity refers to the presence of cysts; however, for diagnosis purposes, these are not essential[1].

A major factor in the pathophysiology of PCOS is the sex hormone-binding globulin (SHBG); a glycoprotein that is mostly produced in the liver. The SHBG's effect on testosterone and oestradiol levels is critical, because it modulates their levels in circulation. Most of the time, there is a decrease in the levels of SHBG among PCOS patients, which is usually related to coexisting insulin resistance. Insulin resistance worsens metabolic derangements, which are associated with type 2 diabetes and cardiovascular disease[2]. The hepatocyte nuclear factor-4α (HNF-4α) is a key transcription factor that regulates the SHBG expression. Its interaction with distinct promoter regions also modulates the production of hepatic SHBG, thereby impacting glucose and lipid metabolism in the liver. As far as the polycystic ovaries are concerned, the altered regulation of HNF-4α may provide a potential explanation for the metabolic disorders in this condition[3].

Recently, several proteins and peptides have gained increasing attention in energy balance research, classifying them as possible biomarkers for obesity, diabetes, and PCOS. The role of SHBG relative to HNF-4α, particularly in metabolic dysfunction, remains under investigation[4]. This relationship is important for elucidating the mechanisms underlying the pathophysiology of PCOS, and may open up new forms of treatment for the additional metabolic problems associated with PCOS.

Our study has aimed at exploring the relationship between the serum SHBG and HNF-4α levels in patients with PCOS and obesity living in the Babil Province of Iraq.

2. Methodology

The study involved 90 women aged between 19 and 42 years that enrolled in the study; these women were subdivided into two groups: 45 with a diagnosis of PCOS and a control group consisting of 45 healthy women. In the sample of women with PCOS, additional structured interviews were conducted in order to obtain self-reported information on smoking, medical history, family history, and the body mass index (BMI) of each respondent. This study was conducted at the Babylon Teaching Hospital for Maternity and Children in Hilla City and at private clinics from May to December 2024. Verbal consent was obtained from all subjects before sample collection. The specific procedures for the study as well as the information and the informed consent of the participants, were approved by the University of Babylon Medical College's ethics committee (document number: A0012; date: 5/8/2024).

ELISA was used in order to quantify the serum levels of glycated haemoglobin (HbA1c), SHBG, testosterone, insulin, and HNF-α, while we employed a spectrophotometric method for measuring fasting blood glucose. The data were analysed through the employment of Student's *t*-test and linear regression through the use of the SPSS v. 20 analysis software.

3. Results and Discussion

Women with PCOS exhibited significantly higher serum levels of HbA1c, total testosterone, insulin, and HNF-4α compared to controls (Table 1). SHBG levels were found to be significantly lower in patients with PCOS (Table 1). These findings suggest a strong reverse correlation between SHBG and HNF-4α levels in PCOS, potentially contributing to metabolic dysfunction.

PCOS is considered a complicated hormonal imbalance that, along with metabolic disarray and sexual dysfunction, revolves around the reproductive system. A clinical appraisal of women diagnosed with PCOS reveals the presence of insulin resistance, which is key to the pathophysiology of the disease

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Table 1. Hormonal and metabolic profiles of the herein studied patients with polycystic ovary syndrome (PCOS) and of the control group participants. Abbreviations used: BMI, body mass index; FAI, free androgen index; HbA1c, glycated haemoglobin; HNF-α, hepatocyte nuclear factor-alpha; HOMA-IR, homeostatic model assessment of insulin resistance; NS, non-significant; SHBG, sex hormone-binding globulin.

Parameters (mean ± SD)	**PCOS patients** (n=45)	**Control group** (n=45)	***P*-value**
BMI (kg/m^2; range)	28.2 ± 1.3 (26.0–29.2)	27.4 ± 3.5 (25.6–28.2)	>0.05 (NS)
HbA1c (%)	6.4 ± 1.1	5.0 ± 0.4	<0.05
SHBG (nmol/L)	45.1 ± 1.2	52.7 ± 12.6	<0.05
Total testosterone (nmol/L)	0.6 ± 0.1	0.3 ± 0.1	<0.05
FAI	4.5 ± 0.9	1.6 ± 2.2	<0.05
Fasting insulin (mIU/L)	14.7 ± 3.2	4.2 ± 0.6	<0.05
Fasting glucose (mg/dL)	123.1 ± 29.3	80.7 ± 16.9	<0.05
HOMA-IR	6.2 ± 2.0	1.4 ± 0.2	<0.05
HNF-α (pg/mL)	650.7 ± 60.3	77.7 ± 10.3	<0.05

and contributes to hyperandrogenism and metabolic derangement[5]. Supporting this view, we noted significant relationships between SHBG and HNF-4α levels in overweight PCOS women. SHBG is a glycoprotein that is synthesized in the liver and plays a key role in the availability of sex hormones such as androgens and oestrogens[6].

Women with PCOS generally tend to exhibit low SHBG levels, which can lead to elevated free androgen levels that may worsen the features of the syndrome. Our research reflects the work of earlier authors, who have also pointed out that low SHBG levels are markers of metabolic distress or insulin resistance, and are common in this group of women. Moreover, the relationship between insulin and reproductive hormones is further complicated by the presence of the insulin-like growth factor system, which is known to play a role in regulating reproduction. Such a dysfunction can contribute to the derangements in hormonal levels that are seen in PCOS cases, thereby resulting in clinical issues.

Based on the observations made in this study, the menstrual cycle controlled by the hypothalamus provides insight into the neuroendocrine aspects of PCOS[7,8]. Therefore, dietary issues (such as fructose consumption) have been shown to have a negative effect on glucose utilization in insulin-resistant individuals. Hence, it can be inferred that some lifestyle changes that focus on diet could have a positive effect on the management of insulin resistance and, therefore, the metabolic components of PCOS.

Our results on HNF-4α are particularly interesting because this transcription factor is essential for the synthesis of SHBG and participates in the regulation of a variety of metabolic processes. However, the heightened levels of HNF-4α in our PCOS patients may indicate metabolic compensation. In this regard, it seems that clarifying the significance of HNF-4α for SHBG regulation could be helpful in developing therapeutic approaches related to PCOS from both hormonal and metabolic perspectives.

It has also been emphasized in the literature that insulin-sensitizing therapies are important for the treatment of women with PCOS, and some systematic reviews have suggested that an enhanced control of insulin resistance may improve reproductive performance. This combination may increase the effectiveness of treatment and the quality of life in women with PCOS[9].

4. Conclusion

This study highlights the complex and interrelated nature of SHBG, HNF-4α, and insulin resistance in

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women with PCOS. These findings indicate the importance of understanding the bidirectional coupling of the dysregulation of hormonal metabolism that characterizes this syndrome. In future studies, special emphasis must be placed on explaining the mechanisms of action for these relationships, so that interventions of interest toward the improved clinical management of PCOS in women can be initiated.

Acknowledgements

The authors express their gratitude to the College of Pharmacy of the University of Babylon for its support.

Conflicts of interest

None exist.

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References

1. Alshiekh A., Hadakie R., Al Kurdi M.F., Sukkar L., Alhalabi M., Hamed H. Polycystic ovary syndrome negatively affects sexual function and lower urinary tract symptoms in Syrian women: a case-control study. *Sci. Rep.* 15(1), 987, 2025. DOI: 10.1038/s41598-025-85544-8
2. Al-Joda B.M.S., Al-Hindy H.A.M., Mousa M.J. Exploring the role of vitamin D2, parathyroid hormone, and C-peptides as biomarkers in diabetic neuropathy development. *Med. J. Babylon* 21(2), 438–443, 2024. DOI: 10.4103/MJBL.MJBL_1568_23
3. Hussein Z.E., Mohammed R.J., Abdul Wahid H.H. Evaluation of the level of the inflammatory factor interleukin-6 in patients with polycystic ovaries and insulin resistance. *Med. J. Babylon* 20(4), 844–846, 2023. DOI: 10.4103/MJBL.MJBL_651_23
4. Nikolaou E., Tziastoudi M., Gougoura S.G., Filippidis G., Dousdampanis P., Bargiota A., *et al.* Sex hormone binding globulin (SHBG) serum levels and insulin resistance in men on chronic hemodialysis. *Diabetol. Metab. Syndr.* 16(1), 166, 2024. DOI: 10.1186/s13098-024-01406-9
5. Dason E.S., Koshkina O., Chan C., Sobel M. Diagnosis and management of polycystic ovarian syndrome. *CMAJ* 196(3), E85–E94, 2024. DOI: 10.1503/cmaj.231251
6. Zhao H., Zhang J., Cheng X., Nie X., He B. Insulin resistance in polycystic ovary syndrome across various tissues: an updated review of pathogenesis, evaluation, and treatment. *J. Ovarian Res.* 16(1), 9, 2023. DOI: 10.1186/s13048-022-01091-0
7. Franks S. Polycystic ovary syndrome. *N. Engl. J. Med.* 333(13), 853–861, 1995. DOI: 10.1056/NEJM199509283331307
8. Yeh M.M., Bosch D.E., Daoud S.S. Role of hepatocyte nuclear factor 4-alpha in gastrointestinal and liver diseases. *World J. Gastroenterol.* 25(30), 4074–4091, 2019. DOI: 10.3748/wjg.v25.i30.4074
9. Purwar A., Nagpure S. Insulin resistance in polycystic ovarian syndrome. *Cureus* 14(10), e30351, 2022. DOI: 10.7759/cureus.30351

HOW TO CITE:
Abbas S.H., Ali Z.A., Najm Z.M., Alshimary F. Hepatocyte nuclear factor-4α and sex hormone-binding globulin levels in overweight polycystic ovary syndrome patients from the Babil Province. *Pharmakeftiki* 37(2s), 25-28, 2025. https://doi.org/10.60988/p.v37i2S.135