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Assessment of serum insulin in polycystic ovarian syndrome

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Abstract

Background and objective: Polycystic ovarian syndrome (PCOS) is a common endocrinological pathology affecting around 15-20 % women of reproductive age globally. The characteristic features of PCOS are hyperandrogenemia, oligo/anovulation and polycystic ovaries on imaging studies. Serum insulin level is one of the major risk factors. The aim of this study was to show the significance of the insulin level in all phenotypes of the PCOS.

Methods: This cross-sectional study was carried out in the Kurdistan Region of Iraq at the Erbil Maternity Teaching Hospital. It comprised 101 women who had been unequivocally diagnosed with PCOS by laboratory and imaging studies throughout a one-year period beginning on May 2021.

Results: The women's body mass index ranged from 19 to 35, while their ages ranged from 18 to 49.Phenotype A formed the largest group of patients by 39.6% and phenotype D were the smallest group by 14.9% of the total patients with significant difference in the serum insulin level between different phenotypes by *P*-value of (0.035). The mean insulin sensitivity in all phenotypes of PCOS were 31.05 with significance of high serum insulin level by *P*-value of 0.003.

Conclusion: The current study found out that high serum insulin level plays a major role in the development of PCOS.

Keywords: Polycystic ovarian syndrome; Hyperandrogenism; Oligo/anovulation; Reproductive age; Body mass index.

Introduction

Polycystic ovarian syndrome is a common endocrinological pathology affecting young female ladies with different manifestation and clinical presentations.(1) The most widely adopted definition have been released in a meeting between European Society for Human Reproduction and Embryology (ESHRE) and the American society for Reproductive medicine (ASRM) in Rotterdam that defines PCOS as disorder characterized by the presence of two out of three of the following criteria:Hyperandrogenism, characterized by biochemical indicators (elevated free androgen index or testosterone levels) and clinical manifestations (hirsutism or, less frequently, male-pattern alopecia), together with oligo/anovulation and the presence of polycystic ovaries on ultrasonography. The conditions like secreting tumor, Cushing syndrome, congenital adrenal hyperplasia, hyperprolactinemia and thyroid dysfunctions not included.(2) National health institute set the definition of Polycystic ovarian syndrome in 1991 which describes the most severe form of polycystic ovarian syndrome and requires the presence of both oligo/anovulation and hyperandrogenisim.(3)

Insulin resistance is a condition where cells in the body become resistant to the effects of insulin, which may lead to increase in blood sugar level and can eventually result

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in diabetes and other relates issues like cardiovascular disease, PCOS, and obesity. According to a study published in the Journal of Diabetes Research, insulin resistance is a complex condition that involve both genetic and environmental factors including diet and physical actitivty. (4)

Rotterdam criteria have further classified PCOS in to four main phenotypes which are of value in terms of insulin level between four subgroups to be discussed in details later. The groups are divided as following:

PHO phenotype (A): All three diagnostic features are present. HO phenotype (B): Oligo/- amenorrhea and hyperandrogenism. PH phenotype (C): hyperandrogenism and polycystic ovaries on ultrasound, PO phenotype (D): Oligo/-amenorrhea and polycystic ovaries on ultrasound.(5)

Peripheral insulin resistance is defined by the lowering of the glucose-transport at the level of tissues due to dysfunction both at the level of insulin receptor and/or post receptor signaling pathways.(6) normal range of fasting serum insulin is less than 25 u/ml.(7)

In addition to the increased insulin level in patients with PCOS there is defect in secretory function of the B –cell of the pancreas, as a result of the B-cell defect causes increased fasting and post-preprandial insulin secretion results in the incapability of the available insulin to compensate the level of the resistance to its action, the decreased insulin postprandial response in the PCOS women similar to the pathological defect of type 2 DM and more profound in women who have first degree relative with DM type 2.(8)

On the tissue level PCOS women have insulin resistance at the level of the adipose tissue, liver, and the muscles.(9)

It was reported that insulin resistance among different phenotypes of PCOS based on Rotterdam criteria, being 80.4 % in the above mentioned “PHO” and “HO” phenotypes, %65.0 in the PH phenotype, and 38.1% in the norm androgenic phenotype “PO”. This mentioned by a study done in tertiary hospital in Turkey by Eren Ozkaya and his colleagues which found that the number of PCOS individuals with homoeostatic model assessment insulin resistance (HOME-IR) index > 3.8 was markedly higher in androgenic type in comparison with other phenotypes.(10)

The aim of this study is to evaluate the level of the insulin resistance in all phenotypes of PCOS with knowing ratio of each type of the PCOS phenotype in overall sample size with detecting insulin resistance in each type and also knowing the level of insulin resistance in different BMI of PCOS patients. The primary objectives of this research are: to identify insulin resistance in PCOS and to assess the degree of insulin resistance in each PCOS subtype individually.

Methods

This study was conducted in maternity teaching hospital and private clinics in Erbil city. It included 101 women of PCOS with manifestation of amenorrhea/ oligomenorrhea, obesity, hirsutism, with bilaterally enlarged polycystic ovaries in a group of reproductive aged women diagnosed by ultrasound.(2) We used Rotterdam criteria to select the study sample which included presence of two of the following diagnostic criteria (Hyperandrogenism, oligo / anovulation, polycystic ovaries on the ultrasound). The phenotyping of PCOS done on the basis of classification set by Rotterdam criteria.

The diagnosis of hyperandrogenism involves obtaining a medical history and conducting a physical examination, as well as measuring hormonal levels such as luteinizing hormone (LH), follicle-stimulating hormone (FSH), dehydroepiandrosterone sulfate (DHES), and total and free testosterone levels. Clinical evidence of hirsutism and medical imaging of the ovaries and adrenal glands are also used to aid in diagnosis, while other conditions that present similar

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symptoms must be ruled out. Each woman's fasting serum insulin level was measured and recorded on their individual case sheets. The normal range for fasting serum insulin is typically less than 25 u/ml. The collected data was then analyzed using statistical methods.

Inclusion Criteria were women with reproductive age group >18 years diagnosed with PCOS according to Rotterdam criteria. Body mass index 18kg/m^2-35kg/m^2. The exclusion criteria were women who had a BMI greater than 35 Kg/m2, as well as those who had endocrine disorders such as hyperprolactinemia, Cushing's syndrome, hypo- or hyperthyroidism, or who were taking medications that could interfere with hormone levels.

Questionnaire and Data Collection

The investigator questioned the women, and the questionnaire has been completed. A blood sample was obtained from the woman after securing her agreement regarding the purpose of this study, and subsequently, the sample was dispatched to the laboratory for analysis of fasting serum insulin, conducted via enzyme-linked immunosorbent assay (ELISA).

Ethical Approval

Approval from the Ethics Committee of the College of Medicine has been obtained. Informed consent was attained from the participants regarding the goal of our study. They have been assured of the confidentiality and privacy of the information, confirming it will not be utilized for other purposes.

Statistical Analysis

Data were analyzed using the statistical package for social science (SPSS, version 26). One sample T-test (t-test) was conducted to analyze the significance of insulin level in all phenotypes of PCOS collectively and insulin level in each phenotype of PCOS ,and chi-square test used to find significant of serum insulin level between four phenotypes of PCOS. significant *P*-value regarded as ≤0.05 with Mean ± Standard deviation (M± SD), and other statistical variables as shown on the tables and chart.

Results

The mean age of the study sample was 28.7327 with a Median of 28.0, Mode 29.0 and a standard deviation of 7.303 with a range of 18-49 and c classified in to three ranges 65 women were of age range 25-29.9 which constituted 82.2 % of the total ratio, followed by 18 women for each age range of 18-24.9 and 30-49 years that constituted 17.8% of the total ratios, (Table 1).

Table 1 Age Range

Age Group	Frequency	Percent %
18-24.9	18	17.8
25-29.9	65	64.4
30-49	18	17.8
Total	101	100.0

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Phenotypes of PCOS women in this study; Phenotype A formed 40 women which constituted of 39.6% of the total number, followed by phenotype B with 24 women which was 23.8% of the all PCOS women, this followed by phenotype C with 22 women that formed 21.8% of the all women and phenotype D which were 15 women that formed 14.9% of all women, (Table 2). In this study the BMI and overweight one constituted of 65 women which were 64.4% by 65 women, followed by equal number of normal and obese women which constituted 17.8% which were 18 women equally, (Table 3, Figure 1).

Table 2 The Study Sample by the Phenotype Ratio of PCOS women

Phenotype	Frequency	Percent
A	40	39.6
B	24	23.8
C	22	21.8
D	15	14.9
Total	101	100

Table 3 The Study Sample By the Body Mass Index Ratio

BMI kg/m^2	Frequency	Percent
18.5-24.9	18	17.8
25-29.9	65	64.4
30-34.9	18	17.8
Total	101	100

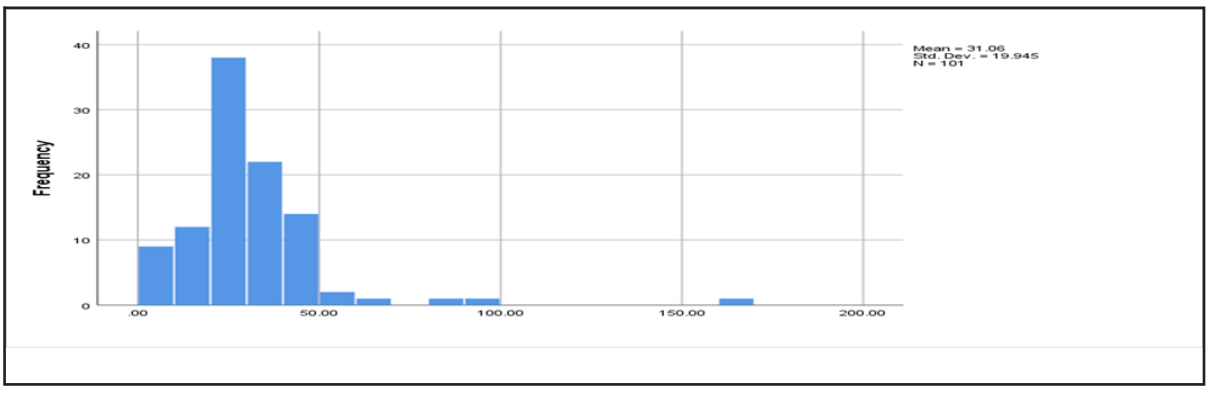

Figure 1 Fasting Serum insulin level in all patients

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The ratio of serum insulin level differs according to the phenotypes, it was observed that high serum insulin level was mostly encountered in phenotype A by 31 women having high serum insulin level (77.5%) with 9 women have normal serum insulin (22.5%) from 40 women , followed by phenotype B with 14 women having high serum insulin level (58.3%) and 10 women with normal serum insulin (41.7%) from 24 women of phenotype B of PCOS. In phenotype C of PCOS women from 22 women the ratio of high serum insulin level was 50% with 11 women and normal serum insulin level 11 women (50%), the least ratio of high serum insulin level observed in phenotype D with only 6 women (35.7%) and 9 women with normal serum insulin level (64.3%), and that was evident by significant difference of insulin level between phenotypes of PCOS which has been revealed by statistical significance of *P*-value of (0.036), (Table 4 and 5).

Table 4 Ratio of Serum Insulin level in Four Phenotypes of PCOS

Phenotypes	HSI	NSI	Total Number	*P - value*
A	31 (77.5%)	9 (22.5%)	40 (100%)	0.036
B	14 (58.3%)	10 (41.7%)	24 (100%)	
C	11 (50.0 %)	11 (50.0 %)	22 (100%)	
D	6 (35.7%)	9 (64.3%)	14.9 (100%)	

HSI: High serum insulin level NSI: Normal serum insulin level

Table 5 Significance of serum insulin level in PCOS patients

One-Sample Statistics					
	N	Mean	Std. Deviation	Std. Error Mean	*P - value*
Serum insulin	101	31.0552	19.94519	1.98462	0.003

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Discussion

Polycystic ovarian syndrome is one of the most common pathologies encountered in women globally, in accordance with that evaluation of their medical profile is much required for the best way of management.[1] Much attention have been paid to the classification of the PCOS after Rotterdam Criteria further classified PCOS into four phenotypes based on the presence of two major different diagnostic criteria required for diagnosis,[2] in this study the ratio of all four phenotypes of PCOS were demonstrated with phenotype A comprising the largest group by more than two third, phenotype B was in one quarter of the study sample and the same for the phenotype C and lastly phenotype D by which forming around one tenth. This first demonstrated by Davis W in 2007 and later confirmed by Guestella E and his colleagues in the later years.[2,11]

Regarding the body mass index of this study sample the vast majority were overweight women which constituted 82.2% and that is have been found by research done by lim SS et al.[12]

Many research has been focused on the pathophysiology of the PCOS in the earlier phases it was regarded as hormonal disturbances with more study there have been more contributing factor as inheritable, environmental and lastly contrasted on the insulin level cause as a major factor in the formation of the PCOS. The serum insulin level in all four phenotypes of PCOS separately and collectively in all women measured in this study , in four phenotypes of PCOS there were different level of serum insulin and the difference of serum insulin level was significant between different phenotypes by *P*-value of (0.003) ,serum insulin level ratio more in the phenotype A and that was found by Mogheti et al which they measured insulin level in women with different phenotypes of PCOS using euglycemic hyper insulinemic clamp they found that women with phenotype A has the highest level of serum insulin level in comparing with other phenotypes.[13]

Analyzing serum insulin level in our local group of PCOS women was main objective in this study, it demonstrated that insulin resistance is a significant in all of the sample and that was in accordance with had been mentioned by other groups beginning from Burghan et al and his colleages.[6,9,14] More recent studies have focused on understanding the underlying mechanisms of high serum insulin in PCOS, such as chronic inflammation, mitochondrial dysfunction, and adipose tissue dysfunction.

These studies have shed light on the complex pathophysiology of PCOS and the multiple factors that contribute to its development. By understanding these underlying mechanisms, it may be possible to develop more targeted and effective treatments for PCOS.[15]

The limitation of our study was limited sample size, many of women refused to participate in this study because of the cost effectiveness of required blood investigations and imaging study.

Conclusion

The results of this study found that elevated serum insulin level have a major role in the development of the PCOS with its clinical and biological consequences. The phenotype A constituted the largest group among other types, in addition to the insulin resistant is more in this group too.

Competing interests

The authors declare that they have no competing interests.

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