Original Article

Assessment of Insulin Resistance in Polycystic Ovary Syndrome Patients

Bimol Kumar Agarwala[1*], Ratan Kumar Agarwala[2], Nausher Azimul Huq[3], Shyamal Chandra Banik[4], Shahin Ibn Rahman[5]

[1]Associate Professor (cc), Department of Endocrinology, Dhaka National Medical College, Dhaka, Bangladesh, [2]Senior Consultant, Department of Gynecology and Obstetrics, Maternal and Child Health Training Institute, Mirpur, Dhaka, Bangladesh,[3]Professor (cc), Department of Endocrinology, Dhaka National Medical College, Dhaka, Bangladesh,[4]Associate Professor, Department of Physiology, Dhaka National Medical College, Dhaka, Bangladesh,[5]Registrar, Department of Endocrinology, BIRDEM General Hospital, Dhaka, Bangladesh.

Abstract

Background: Polycystic Ovarian Syndrome (PCOS) is a common Gynecological condition marked by anovulation and hyperandrogenism, affecting 7-8% of reproductive-age women. It's a leading cause of treatable infertility. Many PCOS patients also show metabolic syndrome signs like insulin resistance, obesity, and dyslipidemia.

Objective: To assess the insulin resistance in polycystic ovary syndrome patients.

Methods: This was a case-control study that was conducted in the Department of Obstetrics & Gynecology, Dhaka Medical College Hospital, Dhaka, Bangladesh from January 2015 to December 2016. This study included 51 women aged 20-35 with polycystic ovary syndrome (PCOS). Data analysis was performed with MS Office tools and SPSS Version 23.0.

Results: Among the total participants, the mean s. testosterone was 1.8±0.9 ng/ml and D2 s. LH was 12.7±6.7 mIU/mL; the difference was statistically significant ($p<0.05$). PCOS patients with HOMA-IR >3.2 had higher testosterone, LH, and insulin levels compared to those with HOMA-IR <3.2. FSH levels did not differ significantly ($p>0.05$). Insulin resistance analysis revealed mean fasting insulin of 27.3 ± 10.7 μU/ml, fasting blood sugar of 5.1 ± 0.8 mmol/L, and HOMA-IR at 4.1 ± 1.3. These values were statistically significant ($p<0.05$).

Conclusion: The probability of developing insulin resistance is significantly greater in women with Polycystic Ovary Syndrome (PCOS) compared to women without PCOS. PCOS patients with insulin resistance are at increased risk of long-term complications like type 2 diabetes mellitus, hypertension, dyslipidemia, CAD, and gestational diabetes mellitus.

Keywords: Insulin Resistance, Polycystic Ovary Syndrome, HOMA-IR.

Introduction

Polycystic ovary syndrome (PCOS) is recognized as one of the most common endocrine disorders affecting females. Its etiology is influenced by a combination of genetic and environmental factors, resulting in a complex interplay. PCOS patients can exhibit a range of symptoms, but the primary clinical features typically include irregular menstruation and/or oligo/anovulation, hyperandrogenism, and the presence of polycystic ovaries. The prevalence of PCOS varies across different populations, influenced by geographic location and ethnicity. Additionally, the utilization of various diagnostic criteria contributes to observed differences in prevalence among different demographic groups. The widely adopted Rotterdam criteria diagnose PCOS in approximately 8-13% of females.[1] In Western countries, polycystic ovarian syndrome (PCOS) exhibits a prevalence ranging from 4% to 12%, making it the most common endocrine disorder affecting women of reproductive age.[2] European countries report a prevalence of 6.5% to 8%.[3] Clinical manifestations of PCOS encompass menstrual irregularities, hirsutism, and frequently, issues related to infertility or subfertility. Menstrual irregularities commonly observed in PCOS patients include prolonged erratic menstrual bleeding, amenorrhea, and oligomenorrhea.[4] On the other hand, some females with PCOS may have normal menstrual cycles, either with or without anovulation.[5] Notably, the majority of females with oligomenorrhea and about half of those with amenorrhea will be diagnosed with PCOS upon presentation.[6] Additionally, most females displaying

***Correspondence:**
Dr. Bimol Kumar Agarwala, Associate Professor (cc) Department of Endocrinology Dhaka National Medical College,Mobile:01711682364
Email:drbimol68@gmail.com

Received: 16.11.2023 **Accepted:** 04.01.2024

clinical features of androgen excess will ultimately receive a PCOS diagnosis.[7] Ramanand et al. conducted a study[8] in which 44.16% of women were clinically diagnosed with hirsutism. Interestingly, while a higher percentage of obese women presented with hirsutism, there was no significant correlation between hirsutism and obesity. Acne was observed in 20% of the patients, while baldness was less common at 6.66%. A significant 44.16% of patients exhibited acanthosis nigricans (AN), which serves as a surrogate marker for insulin resistance.[8] PCOS is associated with a range of other medical conditions. Often, fat accumulation leading to overweight and obesity precedes the clinical manifestations of PCOS. Research has shown that adopting a healthy lifestyle involving dietary modifications and exercise therapy can lead to weight reduction, improved insulin resistance, reduced abdominal fat, decreased testosterone levels, and improved features of hyperandrogenism in females with PCOS.[9] PCOS patients with insulin resistance have an increased risk of developing metabolic syndrome, reproductive dysfunction, and epilepsy.[10]

Materials & Methods

This case-control study was conducted in the Department of Obstetrics & Gynecology at Dhaka Medical College Hospital, Dhaka, Bangladesh, spanning from January 2015 to December 2016. The study participants included 51 women aged between 20-35 years with polycystic ovary syndrome (PCOS) in the case group. Other 51 women without PCOS were recruited in the control group for comparison. Sample selection was carried out using a purposive sampling technique. Ethical approval for the study was obtained from the hospital's ethical committee and informed written consent was collected from all participants before data collection. The inclusion criteria for this study encompassed patients with oligomenorrhea (menstrual cycle interval > 35 days), amenorrhea (absence of menstruation for six months or more), clinical and/or biochemical signs of hyperandrogenism, and the presence of polycystic ovaries as confirmed by ultrasound examination. Patients exhibiting at least two out of these three features were considered to have PCOS. Furthermore, the PCOS patients were categorized into subgroups based on their BMI, with divisions into two groups: 18.5-24.9 kg/m² and ≥25 kg/m². Conversely, the exclusion criteria for this study included patients with a known history of diabetes mellitus, hyperprolactinemia, hypothyroidism, hyperthyroidism, and patients with cardiac or renal dysfunction. The demographic and clinical information of all participants was recorded, and data analysis was conducted using MS Office and the SPSS version 23.0 program, as needed.

Results

In this study, as the age distribution of the study patients, it was observed that the mean age was found 25.0±32 years in the case group and 26.5±4.7 years in the control group (Table I). The difference was statistically not significant between the two groups. Regarding the distribution of BMI levels of the study patients, it was observed that the mean BMI was found 27.0±3.1 kg/m2 in the case group and 26.1±2.1 kg/m2 in the control group (Figure I). The difference was statistically not significant ($p>0.05$) between the two groups. Among participants with normal insulin resistance (Insulin resistance <0.2), the mean waist circumference was 82.4 cm (±6.7), the mean hip circumference was 99.4 cm (±4.6), and the mean W/H ratio was 0.80 (±0.38). In contrast, in participants with high insulin resistance (Insulin resistance >3.2), these measurements were notably higher. Specifically, the mean waist circumference was 86.6 cm (±3.9), the mean hip circumference was 101.4 cm (±5.6), and the mean W/H ratio was 0.83 ±0.18 (Table II). In PCOS patients, those with HOMA-IR >3.2 exhibited more severe symptoms of hirsutism, acanthosis nigricans, and oligomenorrhea compared to patients with HOMA-IR levels <3.2 (Table III). Among the control patients with insulin resistance, 3 out of 4 (75.0%) had acanthosis nigricans and hirsutism, while 2 out of 4 (50.0%) had acne. The mean serum testosterone was found 1.8±0.9 ng/ml in the case group and 0.9±0.2 ng/ml in the control group. The mean D2 serum FSH was found 5.7±2.0 IU/L in the case group and 5.1±1.3 IU/L in the control group. The mean D2 serum LH was found 12.7±6.7 mIU/mL in the case group and 5.9±1.4 mIU/mL in the control group (Table IV). Individuals with insulin resistance (HOMA-IR >3.2) had significantly higher serum testosterone levels (2.8 ± 0.8 ng/ml) compared to those with HOMA-IR <3.2 (2.2 ± 1.0 ng/ml) with a p-value of 0.021. D2 serum FSH levels showed no significant difference between the two groups ($p = 0.483$). However, D2 serum LH levels were notably higher in insulin-resistant patients (14.5 ± 5.0 mIU/mL) compared to those without (11.2 ± 3.3 mIU/mL), with a statistically significant difference ($p = 0.006$). Fasting insulin levels were also significantly elevated in

individuals with insulin resistance (32.8 ± 8.3 µU/ml) compared to those without (26.8 ± 12.1 µU/ml) with a p-value of 0.041 (Table V). The mean serum testosterone level and D2 serum LH level were statistically significant ($p<0.05$) between the two groups. The mean fasting insulin was found 27.3±10.7 µU/ml in the case group and 14.3±6.0 µU/ml in the control group. Serum fasting blood sugar was found 5.1±0.8 (mmol/L) in the case group and 4.6±0.6 (mmol/L) in the control group. The mean HOMA IR was found 4.1±1.3 in the case group and 2.4±1.2 in the control group (Table VI). The mean fasting insulin, fasting blood sugar, and HOMA IR were statistically significant ($p<0.05$) between the two groups. In this study, when analyzing the serum LH/FSH ratio in the study participants, it was observed that the serum LH/FSH ratio was increased in 30 (58.8%) of the cases in the case group, while it was only seen in 4 (7.8%) of the control group (Table VII). The difference in LH/FSH ratio between the two groups was statistically significant ($p<0.05$). In the case group, the mean fasting insulin was notably higher at 27.3±10.7 µU/ml, compared to the control group with a mean of 14.3±6.0 µU/ml. Likewise, fasting blood sugar levels were significantly elevated in the case group, with a mean of 5.1±0.8 mmol/L, whereas the control group exhibited a lower mean fasting blood sugar of 4.6±0.6 mmol/L. Furthermore, when assessing insulin resistance using the Homeostatic Model Assessment of Insulin Resistance (HOMA IR), the case group displayed a considerably higher mean value of 4.1±1.3 compared to the control group, which had a mean HOMA IR of 2.4±1.2. These differences in mean fasting insulin, fasting blood sugar, and HOMA IR were all statistically significant ($p<0.05$) between the two groups. In the current study, when analyzing the fasting lipid profile of the study patients, it was observed that 54.90% had HDL levels less than 40, while 54.10% had HDL levels greater than 40. In terms of total cholesterol and triglycerides, 83.40% had levels below 200, and 17.60% had levels above 200. Moreover, the Scatter diagram showed a positive correlation ($r= -0.357$; $p=0.009$) between HOMA-IR level and serum testosterone (Figure II). On the other hand, another Scatter diagram showed a positive correlation ($r= -0.275$; $p=0.048$) between HOMA-IR level and serum LH (Figure III).

Table-I: Age distribution of study participants. (N=10)

Age (Years)	Case (n=51)		Control (n=51)	
	n	%	n	%
20-25	29	56.9%	24	47.1%
26-30	18	35.3%	17	33.3%
31-35	4	7.8%	8	15.7%
36-40	0	0.0%	2	3.9%

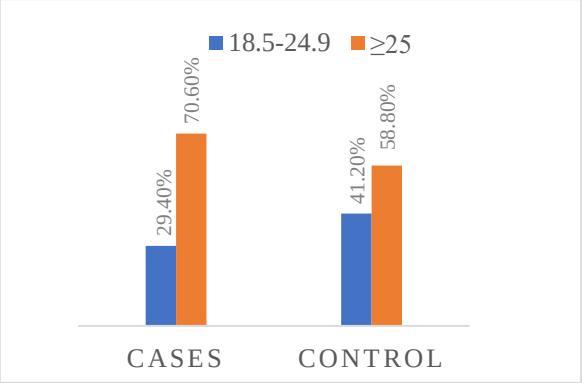

Figure-I: BMI status of the study participants

Table-II: Comparing waist circumference, hip circumference, and W/H ratio to insulin resistance in participants. (n=51)

Variables	Insulin resistance	
	<.2 (normal) (n=23)	>3.2 (high) (n=28)
	Mean ±SD	Mean ±SD
WC (cm)	82.4±6.7	86.6±3.9
Hip circumference	99.4±4.6	101.4±5.6
W/H Ratio	0.80±0.38	0.83±0.18

Table-III: Comparison between clinical parameters of PCOS patients with IR and non-IR. (n=51)

Clinical parameters	**HOMA-IR level**				**P value**
	<3.2 (n=23)		>3.2 (n=28)		
	n	%	n	%	
Case group					
Hirsutism	11	47.8	22	78.6	0.022
Acne	4	17.4	6	21.4	0.051
Acanthosis nigricans	10	43.5	20	71.4	0.043
Oligomenorrhoea	14	60.9	24	85.7	0.042
Amenorrhea	5	21.7	8	28.6	0.577
Hypertension	4	17.4	6	21.4	0.5
Control Group					
Hirsutism			3	75	0.076
Acne			2	50	0.538
Acanthosis Nigricans			3	75	0.033

Table-IV: Laboratory findings in study participants. (N=102)

Parameter	Cass		Control		P-value
	(n=51)		(n=51)		
	n	%	n	%	
Serum testosterone (ng/ml)					
0.5-1.2 (normal)	29	56.90%	47	92.20%	
>1.2	22	43.10%	4	7.80%	
Mean ±SD	1.8±0.9		0.9±0.2		0.001[s]
D2 Serum FSH (IU/L)					
2.8-8.6 (normal)	43	84.30%	46	90.20%	
>8.6	8	15.7	5	9.80%	
Mean ±SD	5.7±2.0		5.1±1.3		0.075[ns]
Serum LH (mIU/mL)					
2.8-13.7	22	43.10%	46	90.20%	
> 13.7	29	56.90%	5	9.80%	
Means ±SD	12.7±6.7		5.9±1.4		0.001[s]

Table-V: Hormone profile variation in patients with insulin resistance. (n=51)

Variables	<3.2	>3.2	P value
	(n=23)	(n=28)	
	Mean ±SD	Mean ±SD	
Serum testosterone (ng/ml)	2.2±1.0	2.8±0.8	0.021
D2 serum FSH (IU/L)	4.8±1.9	5.2±2.1	0.483
D2 serum LH (mIU/mL)	11.2±3.3	14.5±5.0	0.006
Fasting insulin (µU/ml)	26.8±12.1	32.8±8.3	0.041

Table-VI: Distribution of the study participants by insulin resistance. (N=102)

Variables	Cass		Control		P value
	(n=51)		(n=51)		
	n	%	n	%	
Fasting insulin ((µU/ml)	21	41.20%	47	92.20%	
>25	30	58.80%	4	7.80%	
Mean +SD	27.3+10.7		14.3+6.0		0.001s
Serum fasting blood sugar (mmol/L)					
3.6-6.1 (Normal)	29	56.90%	46	90.20%	
6.1-6.9	22	43.20%	5	9.80%	
Mean ±SD	5.1+0.8		4.6+0.6		0.005[s]
HOMA IR					
<3.2	23	45.10%	47	92.20%	
>3.2	28	54.90%	4	7.80%	
Mean ±SD	4.1+1.3		2.4+1.2		0.001[s]

Table-VII: Serum LH/FSH ratio in study participants. (N=102)

LH/FSH ratio	Case		Control		P value
	(n=51)		(n=51)		
	n	%	n	%	
<2	21	41.2	47	92.2	0.001
>2	30	58.8	4	7.8	

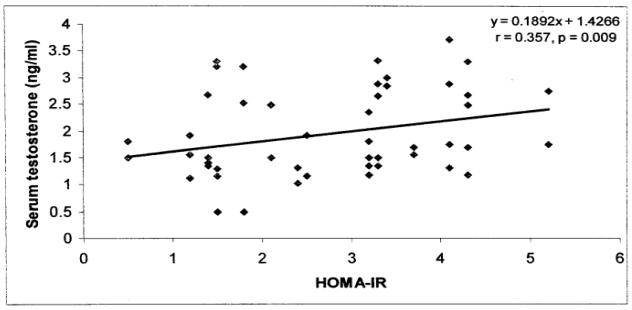

Figure-II: Scatter diagram showed positive correlation (r= -0.357; p=0.009) between HOMA-IR level and serum testosterone

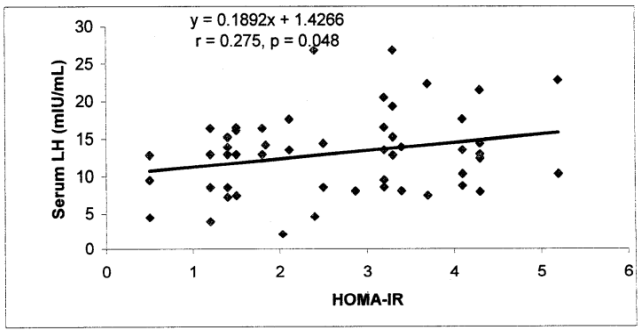

Figure-III: Scatter diagram showing positive correlation (r= -0.275; p=0.048) between HOMA-IR level and serum LH

Discussion

This study aimed to assess the insulin resistance in patients with polycystic ovary syndrome. In this study, regarding the age distribution of the study participants, the mean age was determined to be 25.0±32 years in the case group and 26.5±4.7 years in the control group. The observed difference between the two groups was statistically nonsignificant. These findings are consistent with the results of Amisi et al.[11], who reported similar age distributions in PCOS cases and the control group. The majority of study participants in this research belonged to the 20-30 year's age group, highlighting the higher prevalence of PCOS in younger women. Additionally, concerning the distribution of BMI levels among the study participants, the mean BMI was determined to be 27.0±3.1 kg/m^2 in the case group and 26.1±2.1 kg/m^2 in the control group. The observed difference between the two groups was statistically nonsignificant (p>0.05). These results align with the findings of Yildir et al.[12], who reported comparable BMI values in the case and control groups. In terms of waist, hip circumference, and the W/H ratio related to insulin

resistance, 23 cases had measurements within the normal range, including a mean waist circumference of 82.4 ± 6.7 cm, hip circumference of 99.4 ± 4.6 cm, and a W/H ratio of 0.80 ± 0.38. However, 28 cases showed higher values, with a mean waist circumference of 86.6 ± 3.9 cm, hip circumference of 101.4 ± 5.6 cm, and a W/H ratio of 0.83 ± 0.18, indicating insulin resistance. A study by Cakir et al.[13] found a mean W/H ratio of 0.84 ± 0.5 in the case group and 0.81 ± 0.06 in the control group, consistent with these findings. Among the total women in the study, the mean serum testosterone was 1.8±0.9 ng/ml in the case group and 0.9±0.2 ng/ml in the control group. The mean D2 serum FSH was 5.7±2.0 IU/L in the case group and 5.1±1.3 IU/L in the control group. The mean D2 serum LH was 12.7±6.7 mIU/mL in the case group and 5.9±1.4 mIU/mL in the control group. Both the mean serum testosterone level and D2 serum LH level were statistically significant ($p<0.05$) between the two groups. Dipankar et al.[14] reported that PCOS patients with fasting hyperinsulinemia had high serum testosterone levels and an elevated LH: FSH ratio. Their study found a mean insulin level of 30.18 ± 13.47 mIU/ml, serum testosterone at 1.91 ± 0.21 ng/ml, and LH: FSH ratio >2.5, which aligns with the findings of this study. In this study, the distribution of the participants by insulin resistance revealed several notable findings. The mean fasting insulin was 27.3±10.7 μU/ml in the case group and 14.3±6.0 μU/ml in the control group. Serum fasting blood sugar was 5.1±0.8 mmol/L in the case group and 4.6±0.6 mmol/L in the control group. The mean HOMA IR was 4.1±1.3 in the case group and 2.4±1.2 in the control group. All three parameters, fasting insulin, fasting blood sugar, and HOMA IR, were statistically significant ($p<0.05$) between the two groups. These findings align with another research. Lunger et al. reported that 43.5% of PCOS patients exhibited elevated fasting insulin levels. Sun et al.[15] observed higher fasting insulin levels in PCOS patients compared to the control group, with values of 16.4 ± 9.15 μU/ml in the case group and 7.63 ± 3.42 μU/ml in the control group. Similarly, Begum[16] found that the mean fasting serum insulin level was 32.15 ± 12.13 μU/ml in some cases and 11.32 ± 10.02 μU/ml in the control group. Dipankar et al.[14] conducted a study on PCOS patients and found high insulin levels in 38.6% of cases. In this study, PCOS patients with HOMA-IR >3.2 exhibited more severe symptoms of hirsutism (78.60%), acanthosis nigricans (71.40%), and oligomenorrhea (85.70%) compared to those with HOMA-IR <3.2, where hirsutism (47.80%), acanthosis nigricans (43.50%), and oligomenorrhea (60.90%) were less severe. Patients with insulin resistance (IR) in PCOS had more severe symptoms of hirsutism, acanthosis nigricans, and oligomenorrhea than those without IR. Haq et al.[17] found that PCOS patients with impaired glucose tolerance had more severe symptoms of oligomenorrhea, hirsutism, and acanthosis nigricans, similar to the results of this study. In the current study, fasting lipid profile results showed that 54.90% had HDL levels below 40, while 45.10% had HDL levels above 40. For total cholesterol, 83.40% had levels below 200, and 17.60% had levels above 200. Various studies have demonstrated increased insulin resistance (IR) in PCOS women using HOMA-IR. Cakir et al.[13] reported IR in 45.5% of PCOS patients, Yildir et al.[12] found IR in 64.7%, and Begum[16] identified IR in 42.3% in the case group and 12.0% in the control group. However, Enzevaie et al.[18] reported relatively less IR, found in 22.7% of 75 PCOS patients based on HOMA-IR. Amisi et al.[11] also detected IR in 39.3% of PCOS women using HOMA-IR.

Conclusion

In the context of Polycystic Ovary Syndrome (PCOS), women affected by this condition face a notably elevated risk of developing insulin resistance in comparison to their counterparts without PCOS. Importantly, PCOS patients who grapple with insulin resistance confront a heightened susceptibility to long-term complications that encompass type 2 diabetes mellitus, hypertension, dyslipidemia, coronary artery disease (CAD), and gestational diabetes mellitus. These findings underscore the critical importance of recognizing and addressing insulin resistance in PCOS patients, as it represents a pivotal factor in the increased risk of various significant health issues and underscores the need for proactive management and monitoring in this patient population.

Conflict of interest: None

References

1. Bozdag G, Mumusoglu S, Zengin D, Karabulut E, Yildiz BO. The prevalence and phenotypic features of polycystic ovary syndrome: a systematic review and meta-analysis. Hum Reprod. 2016; 31(12):2841–55.
2. Azziz R, Woods KS, Reyna R, Key TJ, Knochenhauer ES, Yildiz BO. The prevalence and features of the polycystic ovary syndrome in an unselected population. J Clin Endocrinol Metab. 2004; 89(6):2745–2749.
3. Asunción M, Calvo RM, San Millán JL, Sancho J, Avila S, Escobar-Morreale HF. A prospective study of the prevalence of the

polycystic ovary syndrome in unselected Caucasian women from Spain. J Clin Endocrinol Metab. 2000; 85(7):2434–2438.
4. Mohd, Maqsood, et al. "Polycystic ovary syndrome, a modern epidemic: an overview." Journal of Drug Delivery and Therapeutics 9.3 (2019): 641-644.
5. Balen AH, Conway GS, Kaltsas G, Techatrasak K, Manning PJ, West C, et al. Polycystic ovary syndrome: the spectrum of the disorder in 1741 patients. Hum Reprod. 1995; 10(8):2107-11.
6. Hart R, Hickey M, Franks S. Definitions, prevalence and symptoms of poly-cystic ovaries and polycystic ovary syndrome. Best Pract Res Clin Obstet Gynaecol. 2004; 18(5):671–83.
7. Azziz R, Sanchez LA, Knochenhauer ES, Moran C, Lazenby J, Stephens KC, et al. Androgen excess in women: experience with over 1000 consecutive patients. J Clin Endocrinol Metab. 2004; 89(2):453–62.
8. Ramanand, Sunita J., et al. "Clinical characteristics of polycystic ovary syndrome in Indian women." Indian journal of endocrinology and metabolism 17.1 (2013): 138.
9. Salehi M, Bravo-Vera R, Sheikh A, Gouller A, Poretsky L. Pathogenesis of polycystic ovary syndrome: what is the role of obesity? Metab Clin Exp. 2004; 53:358–76.
10. Dunaif A, Segal KR, Futterweit W, Dobrjansky A. Profound peripheral insulin resistance, independent of obesity, in polycystic ovary syndrome. Diabetes. 1989; 38(9):1165–74.
11. Amisi, C., et al. "Biological insulin resistance in Congolese woman with polycystic ovary syndrome (PCOS)." Gynecologie, Obstetrique & Fertilite 41.12 (2013): 707-710.
12. Yildir, Ismail Cem, et al. "Insulin resistance and cardiovascular risk factors in women with PCOS who have normal glucose tolerance test." Gynecological endocrinology 29.2 (2013): 148-151.
13. Cakir, Evrim, et al. "Insulin-like growth factor 1, liver enzymes, and insulin resistance in patients with PCOS and hirsutism." Turkish Journal of Medical Sciences 44.5 (2014): 781-786.
14. Dipankar B, Kumar MS, Satinath M, Mamata P, 'Clinical correlation with biochemical status in polycystic ovarian syndrome', J Obstet Gynecol India, 2005; 55: (1):67-71.
15. Sun, Xianchang, et al. "Evaluation of apelin and insulin resistance in patients with PCOS and therapeutic effect of drospirenone-ethinylestradiol plus metformin." Medical science monitor: international medical journal of experimental and clinical research 21 (2015): 2547.
16. Begum F, 'Clinical and Hormonal Profile of Polycystic Ovary Syndrome', South Asian Federation of Obstetrics and Gynecology 2009; 1(2):22-25.
17. Haq, Fauzia, Omar Aftab, and Javed Rizvi. "Clinical, biochemical and ultrasonographic features of infertile women with polycystic ovarian syndrome." Journal of the College of Physicians and Surgeons Pakistan 17.2 (2007): 76.
18. Enzevaei, Anahita, et al. "Subclinical hypothyroidism and insulin resistance in polycystic ovary syndrome: is there a relationship." Iranian journal of reproductive medicine 12.7 (2014): 481.