"To Study The Association Of Leptin As A Predictive Marker In Obese And Non-Obese Women With Polycystic Ovary Syndrome Patients."

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Abstract

Background: Polycystic ovary syndrome(PCOS) is a common endocrine problem where Leptin, an adipocyte-derived hormone encoded by *'ob'* gene, has been proposed as the peripheral signal indicating the adequacy of nutritional status for reproductive functions. Circulating leptin correlates strongly with obesity, which is frequently associated with polycystic ovarian syndrome (PCOS). However, the changes in serum leptin levels in patients with PCOS and its predictive value for PCOS remain obscure. We intend to analyze the association of serum Leptin levels as a predictive marker in obese and non-obese women with Polycystic Ovary Syndrome Patients.

Material and Methods: The study comprised of 85 patients with PCOS and 75 controls without PCOS.Each group was analysed for the following parameters as TSH, Prolactin, FSH, LH,AMH, Totalcholesterol,Systolic/diastolic(BP),BMI,Leptin,MDA(Malondialdehyde) and SOD(Superoxide dismutase).The validity of leptin toward the diagnosis of PCOS or leptin combined with these parameters was estimated by Descriptive and inferential statistical analysis at 5% level of significant.

Results: The results of the present study indicated that an increased level of leptin among women with PCOS positively associated with FSH, LH, TSH, Total cholesterol, MDA in PCOSpatients. However, there was no statistical significant correlation between Insulin and the Body Mass index.

Conclusion: Higher leptin levels were independently associated with the risk of PCOS. However, there was no significant correlation between insulin and BMI. Elevated leptin levels may contribute to etiology of PCOS but further, well-designed prospective studies are still needed to elucidate the precise association between leptin and PCOS.

Keywords: Thyroid stimulating hormone, Follicle stimulating hormone, Luteinizing hormone, Antimullerian hormone

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a complex condition characterized by elevated androgen levels, menstrual irregularities, and/or small cysts on one or both ovaries [1]with aworldwide prevalence rate of 5 to 20% [2]. Clinical signs of PCOS include elevated luteinizing hormone (LH) and gonadotropin–releasing hormone (GnRH) levels, whereas follicular-stimulating hormone (FSH) levels are muted or unchanged. As a result of the increase in GnRH, stimulation of the ovarian the cells, in turn produces more androgens. Follicular arrest can be corrected by elevating endogenous FSH levels or by providing exogenous FSH [3].

Abdominal obesityis a feature of overweight, endocrine disorders which may influence women more prevalent to PCOS women than in normal reproductive age [4]. Leptin is a major adipokine that regulates weight balance and energy homeostasis. Leptin, a product of OB gene, is produced in adipose tissues and has a long list of endocrine functions besides being responsible for causing obesity [5].

Leptin and adiponectin, adipocyte-secreted hormones, have important effects on the reproductive axis. However, the relationship between these adipokines and polycystic ovarian syndrome (PCOS) has not been fully evaluated. Approximately 25% of patients with PCOS have elevated prolactin levels. Additionally, higher and lower levels of leptin are also related with infertility but the mechanism of involvement is still undiscovered [6,7].

PCOS patients may serve as a reliable model to assess the relationship of hyperinsulinemia and androgen excess with leptin concentrations beyond the association of leptinand obesity [6,8].

Therefore the present study was undertaken to study the inter-relationship between serum leptin level with body mass indexin obese and non obese women with Polycystic ovary syndrome patients.

MATERIAL AND METHODS:

This was a case control study carried out in the Department of Biochemistry for the period of 1 yeari.e, March 2019 to March 2020at RMCH& RC, Mandhana. The Ethical clearance was obtained from the Ethical Committee of RMCH&RC, Mandhana Kanpur. Women diagnosed clinically of PCOS, aged between 20 to 40 years, negative for serum Hepatitis B virus (HBV), Hepatitis C virus (HCV) and HIV were included in the study and women aged from 20 to 40 years, normal fertile women without a history of PCOS were inclusion for the controls. Women had any other reproductive disorder, were aged below 20 or above 40-years, had a known history or acquired thrombophilia or tumors in any part of the body were excluded from the study and those. The 5ml of the venous blood sample was collected under aseptic precaution and transferred in the serum separator tubes. The serum was separated within an hour and stored at -20^0 C until analysis. Leptin levels were assayed by human sensitive leptin double-antibody sandwich enzyme-linked immunosorbent one step process assay (QAYEE-BIO Life Science) according to the manufactures's guidelines. The study comprised of 85 patients with PCOS and 75 controls without PCOS. In the present study a total of 85 patients with PCOS and 75 controls without PCOS were studied. Based on the present study for an outcome variable on LH with difference of 1.6 and common standard deviation of 4.5 for two groups (cases vs controls) comparison, to attain significant for present study with Type I error of 5% and Type II error of 10%, 90% statistical power, the sample size estimated to be 160 (85 vs 75) is adequate after adjusting for lost- to-follow-up, drop-out rate and non-response rate at 95% confidence interval.

Each group was stratified as either normal- or hyper-fasting serum insulin (FSI), lean or overweight/obese (BMI) and systolic / diastolic (BP).

Statistical Methods: Data were collected and entered in MS Excel worksheets and the sample size calculated was 85. Descriptive statistics were used to represent the baseline variables, number, and percentage for the categorical variables and mean and standard deviation for the continuous variables.

Student t test (two tailed, independent) has been used to find the significant of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Leven`s test for homogeneity of variance has been performed to assess the homogeneity of variance.

Chi-square/ Fisher Exact test has been used to find the significant of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis. Fisher Exact test used when cell samples are very small.

Figure 1: The Qayee Bio Kit

Figure 2: The Qayee Bio Kit Reagents

RESULTS

During the study period a total of 85 patients attending OPD of Gynecology department and 75 controls were recruited from RAMA Medical College, Kanpur were studied. Each group was analysed for the following parameters as TSH, Prolactin, FSH, LH, AMH, Total cholesterol, systolic / diastolic (BP), BMI, Leptin, MDA and SOD.

Table 1: Age in years- Frequency distribution in two groups of patients studied

Age in Years	PCOS	CONTROL	Total
<20	3(3.5%)	1(1.3%)	4(2.5%)
20-30	67(78.8%)	70(93.3%)	137(85.6%)
>30	15(17.6%)	4(5.3%)	19(11.9%)
Total	85(100%)	75(100%)	160(100%)
Mean ± SD	26.66±4.37	25.79±3.02	26.25±3.81

Samples are age matched with P=0.150, student t test

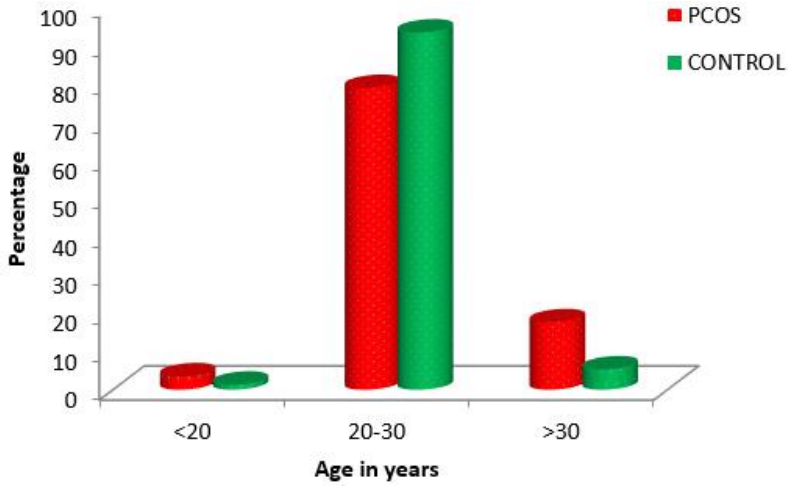

Figure 3: Age in years- Frequency distribution in two groups of patients studied

In the present study it was observed that there was no statistical significant between the mean age of the two groups with PCOS cases and other without PCOS as controls listed above in [Table 1].

Table 2: Residence- Frequency distribution in two groups of patients studied

Residence	PCOS	CONTROL	Total
Rural	15(17.6%)	15(20%)	30(18.8%)
Urban	70(82.4%)	60(80%)	130(81.3%)
Total	85(100%)	75(100%)	160(100%)

P=0.862, Not Significant, Chi-Square Test

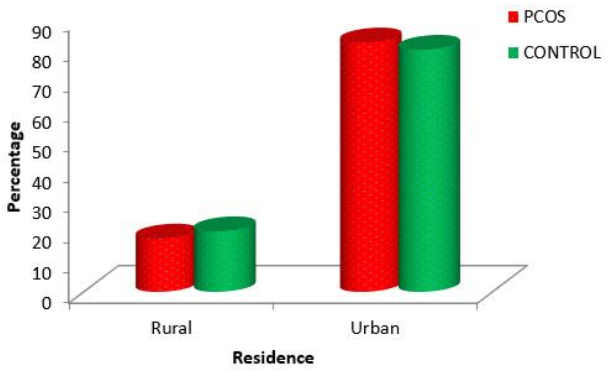

Figure 4: Residence- Frequency distribution in two groups of patients studied

From the above [Table 2] it was clear that there was no statistical significant between the residence of both the groups one with PCOS and the other as controls (without PCOS).

Table 3: Lifestyle- Frequency distribution in two groups of patients studied

Lifestyle	PCOS	CONTROL	Total
Moderate	75(88.2%)	69(92%)	144(90%)
Sedentary	10(11.8%)	6(8%)	16(10%)
Total	85(100%)	75(100%)	160(100%)

P=0.596, Not Significant, Chi-Square Test

Figure 5: Lifestyle- Frequency distribution in two groups of patients studied

Table3 observed that there was no statistical significant between the lifestyle of both the groups one with PCOS and the other as controls (without PCOS).

Table4: Oligomenorrhea- Frequency distribution in two groups of patients studied

Oligomenorrhea	PCOS	CONTROL	Total
No Oligomenorrhea	34(40%)	58(77.3%)	92(57.5%)
Oligomenorrhea	51(60%)	17(22.7%)	68(42.5%)
Total	85(100%)	75(100%)	160(100%)

P≤0.001**, Significant, Chi-Square Test

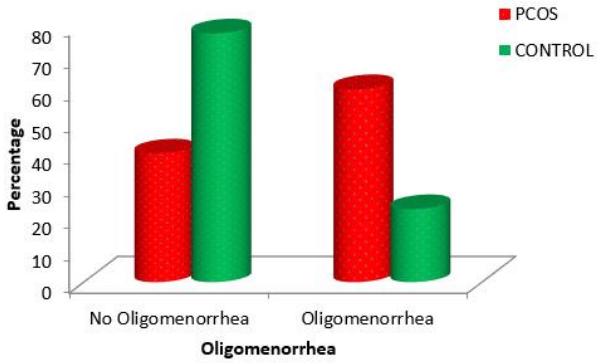

Figure 6: Oligomenorrhea - Frequency distribution in two groups of patients studied

From the above Table 4 observed for Oligomenorrhea that there was a Statistical significant between PCOS and the control group as there was increased cases of Oligomenorrhea in PCOS cases compared to the (control group) without PCOS .

Table 5: Diabetics/Hypertension - Frequency distribution in two groups of patients studied

Variables	PCOS	CONTROL	Total	P Value
DIABETES				
• 0	85(100%)	75(100%)	160(100%)	1.000
• 1	0(0%)	0(0%)	0(0%)	
HYPERTENSION				
• 0	81(95.3%)	72(96%)	153(95.6%)	1.000
• 1	4(4.7%)	3(4%)	7(4.4%)	
Total	85(100%)	75(100%)	160(100%)	

Chi-Square Test/Fisher Exact Test

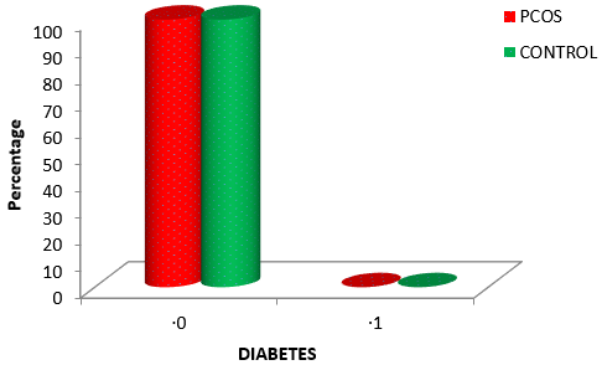

Figure 7: Diabetes- Frequency distribution in two groups of patients studied

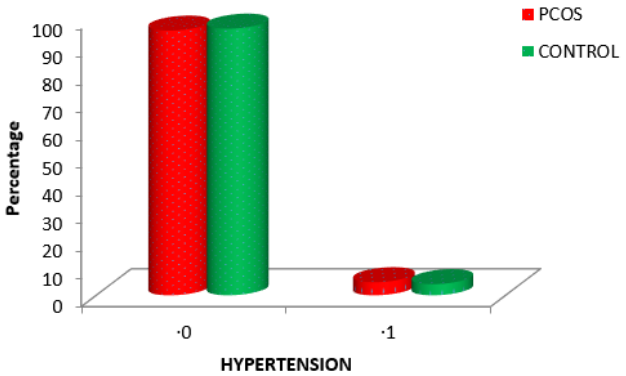

Figure 8: Hypertension- Frequency distribution in two groups of patients studied

The Diabetes and Hypertension was found to have no statistical significant between PCOS and the (control) group without PCOS [Table 5].

Table 6: BMI_2 - Frequency distribution in two groups of patients studied

BMI (kg/m2)	PCOS	CONTROL	Total
Non obese	27(31.8%)	33(44%)	60(37.5%)
Obese	58(68.2%)	42(56%)	100(62.5%)
Total	85(100%)	75(100%)	160(100%)

P=0.152, Not Significant, Chi-Square Test

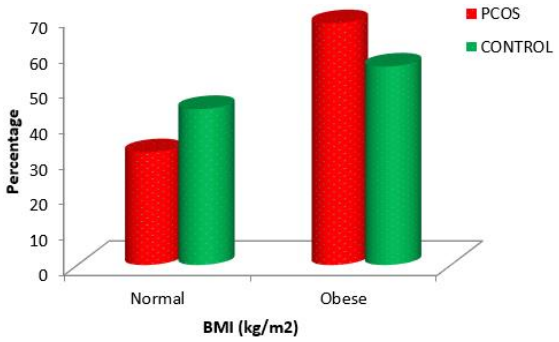

Figure 9: BMI- Frequency distribution in two groups of patients studied

In the present study the PCOS was not statistical significant to the BMI for both the groups of PCOS and the other (control) group without PCOS.

Table 7: HIRUTISM- Frequency distribution in two groups of patients studied

HIRUTISM	PCOS	CONTROL	Total
Hirutism	41(48.2%)	13(17.3%)	54(33.8%)
No Hirutism	44(51.8%)	62(82.7%)	106(66.3%)
Total	85(100%)	75(100%)	160(100%)

P≤0.001**, Significant, Chi-Square Test

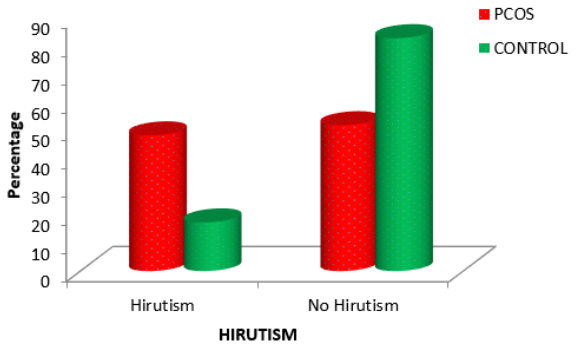

Figure 10: Hirutism- Frequency distribution in two groups of patients studied

The Hirutism studied showed the statistical significant for both the groups of PCOS and the other (control) group without PCOS, where in case of PCOS the increase cases of hirutism was observed as compared to the cases without PCOS [Table 7].

Table 8: Study/Outcome variables –Comparison in two groups studied

Variables	PCOS	CONTROL	Total	P Value
TSH	5.1±4.34	3.32±2.05	4.27±3.56	0.005
PROLACTIN	13.52±7.89	13.09±3.77	13.33±6.41	0.761
LH	7.61±3.13	6.01±5.18	6.82±4.33	0.043*
FSH	5.79±1.49	6.89±2.06	6.29±1.85	<0.001**
AMH	8.08±5.95	6.34±4.97	7.27±5.56	0.087+

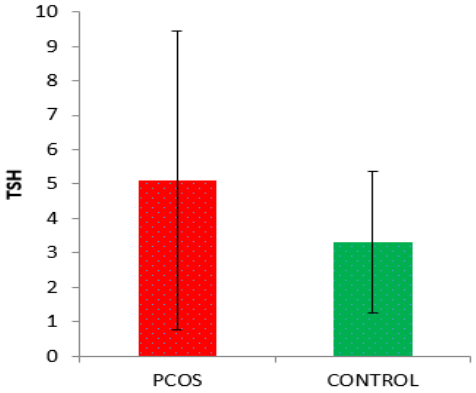

Figure 11: TSH- Frequency distribution in two groups of patients studied

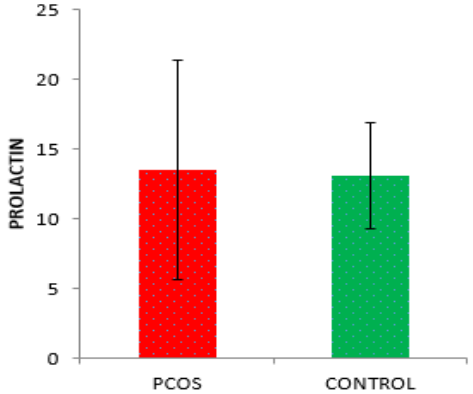

Figure 12: Prolactin –Frequency distribution in two groups of patients studied

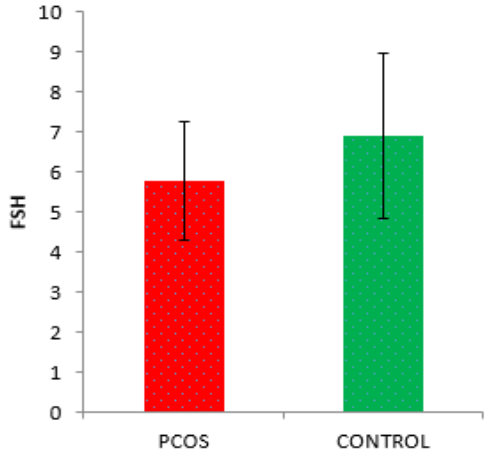

Figure 13: FSH –Frequency distribution in two groups of patients studied

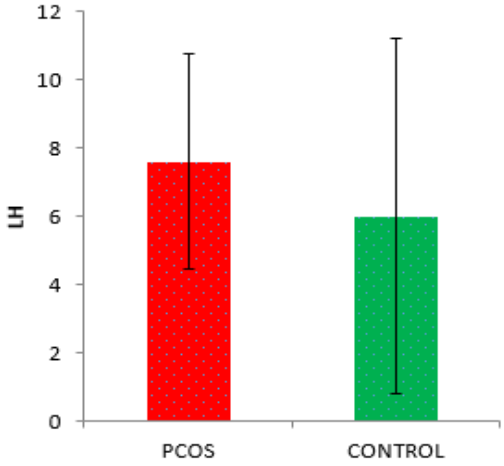

Figure 14: LH-Frequency distribution in two groups of patients studied

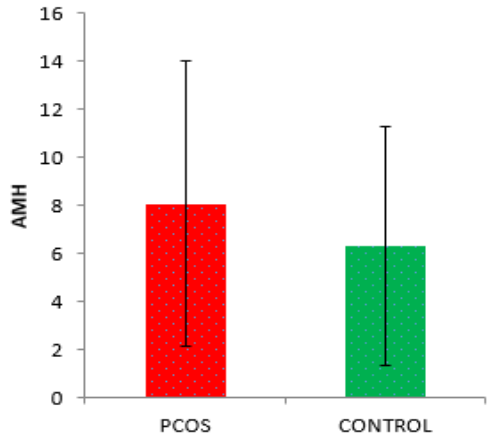

Figure 15: AMH- Frequency distribution in two groups of patients studied

In the present study the TSH, LH and FSH was found to be statistical significant, in which our statistical analysis demonstrated that LH: FSH ratio is statistically significantly higher in the women with PCOS (1:47) as compared to controls (1:2) with the mean difference of 0.27.

Table 9: Study/Outcome variables- Comparison in two groups studied

Variables	PCOS	CONTROL	Total	P Value
TOTALCHOLESTEROL(MGDL)	176.17±15.56	168.47±21.07	172.69±18.58	0.020*
SYSTOLIC BP	123.26±7.21	123.03±3.42	123.15±5.74	0.799
DIASTOLIC BP	76.71±7.26	76.35±6.63	76.54±6.95	0.745
BMI (KGM2)	26.08±4.83	24.74±4.2	25.45±4.58	0.063+
LEPTIN	14.28±7.32	10.14±6	12.34±7.02	<0.001**
MDA	4.1±1.54	3.47±1.3	3.79±1.46	0.009**
SOD	104.86±64.39	100.54±63.48	102.87±63.79	0.683

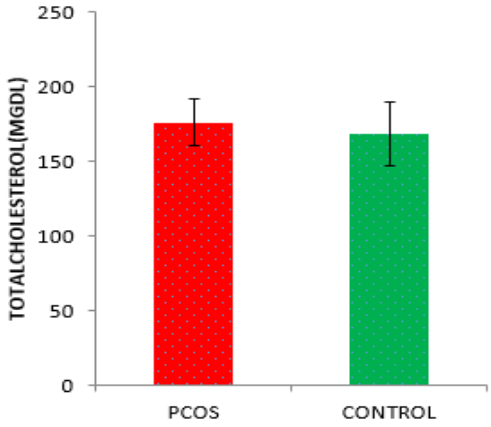

Figure 16: Total Cholesterol –Frequency distribution in two groups of patients studied

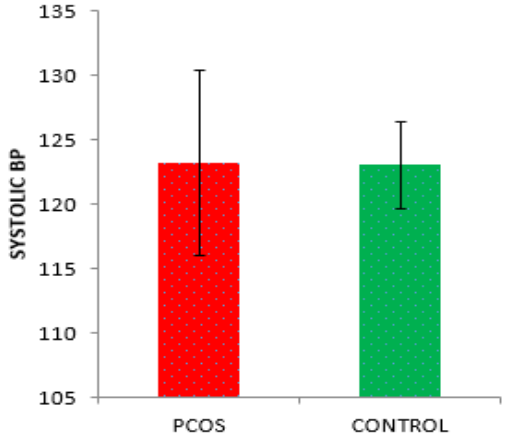

Figure 17: Systolic BP-Frequency distribution in two groups of patients studied

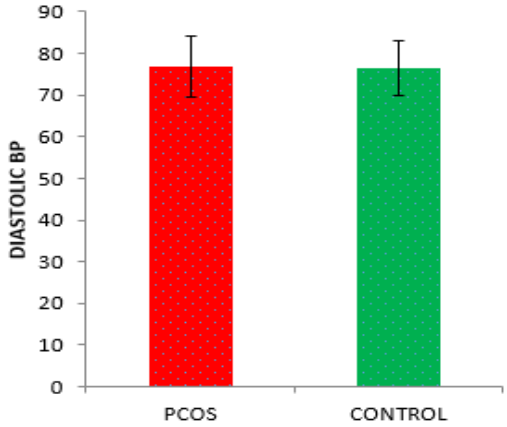

Figure 18: Diastolic BP-Frequency distribution in two groups of patients studied

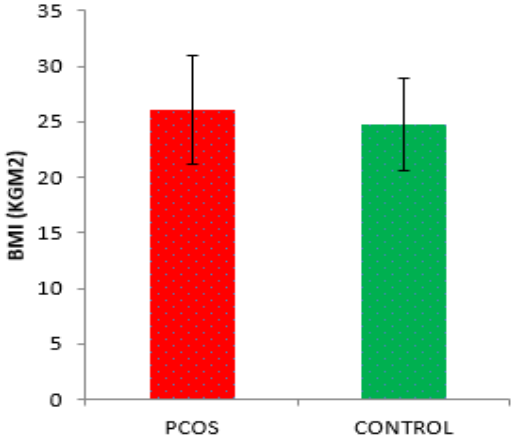

Figure 19: BMI-Frequency distribution in two groups studied

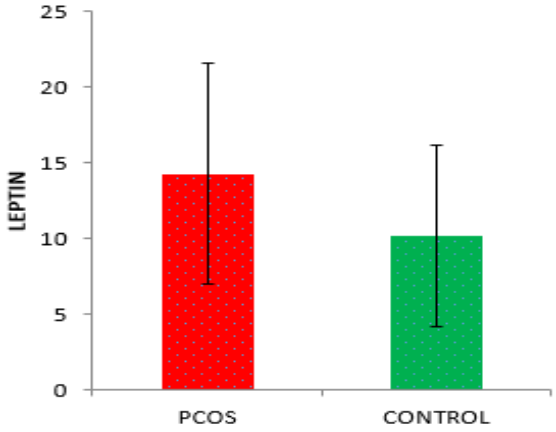

Figure 20: Leptin-Frequency distribution in two groups studied

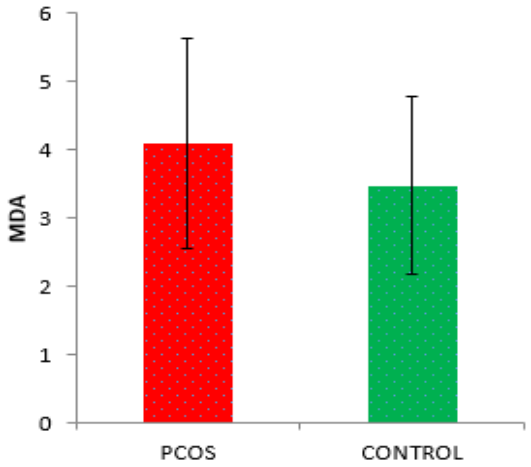

Figure 21: MDA-Frequency distribution in two groups studied

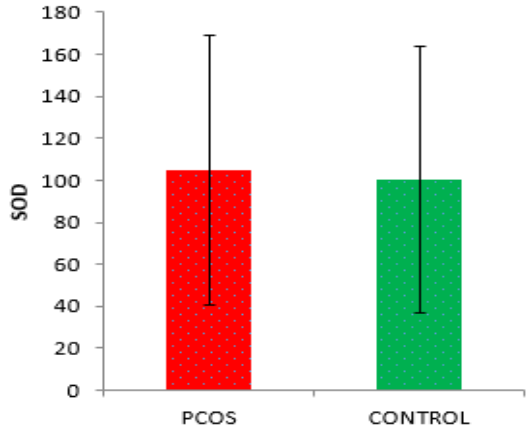

Figure 22: SOD-Frequency distribution in two groups studied

In the present study it was observed that Total Cholesterol, Leptin and MDA was found to be statistical significant. The higher level of serum leptin in women with PCOS (14.28±7.32) as compared to controls (10.14±6) with P <0.001. Similarly, PCOS women had statistically significantly raised total cholesterol level (176.17±15.56) as compared to controls ((168.47±21.07) with p=0.020 [Table 9].

DISCUSSION:

PCOS is the common dysovulatory infertility, which is characterizedby the chronic anovulation and hyperandrogenemia [9]. These features manifest with advancement of age and gradual increase of adipose tissue [10] which are often linked to leptinand its receptor.

In the present study the maximum number of cases was recorded in the age group of 20-30 years of age with the mean age of 26.66±4.37 and for the controls 25.79±3.02 and the minimum in the age group below 20 years of age. This finding was in support with the study performed by the Yuanyuan Peng et al.,[11]where, the mean age for the controls was 31.00 (29.00-33.00and PCOS group was 32.00 (30.00-33.00). The study performed by Mukhtiar Baig[12] also correlated to our study.

In the current study there was no statistical significant between the residence and the lifestyle of both the groups one with PCOS and the other as controls (without PCOS).This study correlates with the another study where there was no statistical significant in the residence or life style[13][14]. It was also observed that for Oligomenorrhea there was a statistical significant between PCOS and the control group as there was increased cases of Oligomenorrhea in PCOS cases compared to the (control group) without PCOS. In the current study the diabetes and hypertension was found to have no statistical significant between PCOS and the (control) group without PCOS. This study was parallel to the study conducted by Nomair A [15] in Taif where there was no statistical significant between the insulin levels and hypertension with obese and non obese cases. The Hirutism studied showed the statistical significant for both the groups of PCOS and the other (control) group without PCOS, where in case of PCOS the increase cases of hirutism was observed as compared to the cases without PCOs

Leptin is mainly produced by the adipocytes and considered as a polypeptide hormone for the regulation of normal body weight. Several studies have observed a strong association of circulating leptin with obesity, which has also been associated with PCOS, a major form of diovulatory infertility in women[14]. In the current study there was aelevation of serum leptin in women with PCOS. This finding is comparable with the study of Mohiti-Ardekani and Taarof, which showed elevated level of serum leptin in 27 Iranian women with PCOS[16].

Our results indicate that serum leptin is significantly higher in PCOS women compared with controls. This result also supports the findings of other studies which showed elevation of serum leptin in women with PCOS [17,18].

In the present study, the possibility of a relationship between leptin and BMI in women with PCOS was investigated where it was observed that PCOS was not statistically significant to the BMI for both the groups of PCOS and the other (control) group without PCOS. However, there are many studies reported that have no statistical significant in serum leptin levels of PCOS women with insulin and BMI-matched controls [19,20].
Baig*et al*. in their study revealed, compared to controls, PCOS women had higher serum leptin levels but it was not statistically significant[21].

Leptin seems to be directly related to obesity by maintaining energy homeostasis with decreased food intake and increased energy expenditure [16]. But in our study there was no statistical significant in serum leptin levels ofPCOS subjects with BMI matched controls. There are many other studies performed by different authors where Leptin seems to be related with BMI and controls. This study was in support with the study by NasrinJalilian [13] where, serum leptin level is significantly correlated with BMI in PCOS women and this results correlates with other studies [22,23].

In the present study Total cholesterol, Leptin and MDA were found to be statistically significant but it was also observed that blood Pressure and superoxide dismutase were not statisticaly significant in PCOS patients. Moreover, in our study, no association was found between leptinlevel and insulin level which was parallel to the study by NasrinJalilian [13].Leptin reduces glucose-mediated insulin secretion through its receptorsin the hypothalamus and also reduces its action at the cellular level [24].
In the present study the TSH, LH and FSH was found to be statistical significant, in which our statistical analysis demonstrated that LH: FSH ratio is statistically significantly higher in the women with PCOS (1:47) as compared to controls (1:2) with the mean difference of 0.27, but AMH and Prolactin does not show any correlation with the PCOS patients. This study was in support with the study by Mohiti-Ardekani and Taarof [16]where there is a significant positive relationship between leptin and LH.But in contrast with the study by Sir-Petermannet al. [[25]where no correlation between leptin secretion pulses and LHwere observed.
The Total Cholesterol, Leptin and MDA was found to be statistical significant. The higher level of serum leptin in women with PCOS (14.28±7.32) as compared to controls (10.14±6) with P <0.001. Similarly, PCOS women had statistically significant raised total cholesterol level (176.17±15.56) as compared to controls ((168.47±21.07) with p=0.020.
Leptin is considered to play a role in conservation of energy and maintenance of body weight by neuroendocrine mechanisms. Thus, PCOS patients may serve as a reliable model to assessthe relationship of hyperinsulinemia and androgen excess with leptin concentrations beyond the association of leptinand obesity.

CONCLUSION:

The results of the present study indicated an increased leptinlevel among women with PCOS that positively associated with FSH, LH and TSH. Substantially elevated serum leptin is significantly associated Total cholesterol, MDA in PCOS patients. However, there was no significant correlation between leptin with BMI, diabetes, hypertension, Prolactin, AMH and SOD. These findings warrant as a further investigations into the function of leptin in the pathogenesis of PCOS patients.

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Conflict of Interest: None

REFERENCES

1. Rotterdam ESHRE/ASRM-sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. FertilSteril. 2004; 81:19-25.
2. Marx TL, Mehta AE. Polycystic ovary syndrome: Pathogenesis and treatment over the short and long term. Cleve Clin J Med. 2003; 70(1):31–33. 36–41, 45.
3. A. Usmani, R. Rehman, and Z. Akhtar, "Association of body mass index and dietary habits with ovarian and uterine morphology with subfertile polycystic ovarian syndrome," Journal of Postgraduate Medical Institute. 2014; vol. 28, no. 2, pp. 133–138.
4. J. Chakrabarti, "Serum leptin level in women with polycystic ovary syndrome: correlation with adiposity, insulin, and circulating testosterone," Annals of Medical and Health Science Research. 2013; 3(2):191–196, 2013.
5. A. Barash, C. C. Cheung, D. S. Weigle et al., "Leptin is a metabolic signal to the reproductive system," Endocrinology. 1996;137(7):3144–3147.
6. P. R. Brzechffa, A. J. Jakimiuk, S. K. Agarwal, S. R. Weitsman, R. P. Buyalos, and D. A. Magoffin, "Serum immunoreactive leptin concentrations in women with polycystic ovary syndrome," The Journal of Clinical Endocrinology & Metabolism. 1996; 81(11): 4166–4169.
7. V. R. Drel, N. Mashtalir, O. Ilnytska et al., "The leptin-deficient (ob/ob) mouse: a new animal model of peripheral neuropathy of type 2 diabetes and obesity," Diabetes. 2006; 55(12):3335–3343.
8. Umland EM, Weinstein LC, Buchanan EM. Menstruation-related disorders. In: DiPiro JT, Talbert RL, Yee GC, et al., editors. Pharmacotherapy: A Pathophysiologic Approach. 8th ed. New York: McGraw-Hill. 2011. p. 1393
9. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, et al. The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: The complete task force report. FertilSteril. 2009; 91:456-88.
10. Arikan S, Bahceci M, Tuzcu A, Kale E, Gökalp D. Serum resistin and adiponectin levels in young non-obese women with polycystic ovary syndrome. Gynecol Endocrinol 2010; 26:161-6.
11. Yuanyuan Peng1 et al. Elevated Serum Leptin Levels as a Predictive Marker for Polycystic Ovary Syndrome. 2022; doi: 10.3389/fendo.2022.845165
12. MukhtiarBaig, RehanaRehman, Saba Tariq, and SyedaSadia Fatima. Serum Leptin Levels in Polycystic Ovary Syndrome and Its Relationship with Metabolic and Hormonal Profile in Pakistani Females. International Journal of Endocrinology. 2014; 132908.
13. NasrinJalilian, Lida Haghnazari1, Samira Rasolinia. Leptin and body mass index in polycystic ovary syndrome. Indian Journal of Endocrinology and Metabolism. 2016; 20:324-8.
14. Chakrabarti J. Serum leptin level in women with polycystic ovary syndrome: Correlation with adiposity, insulin, and circulating testosterone. Ann Med Health Sci Res 2013; 3:191-6.
15. Nomair A, Aref N, Rizwan F, Ezzo O, Hassan N. Serum Leptin levels with polycystic ovary syndrome, and its relation to insulin resistance.Asian Pacific journal of reproduction. 2014; 3(4):288-294.
16. Mohiti-Ardekani J, Taarof N. Comparison of leptin blood levels and correlation of leptin with LH and FSH in PCOS patients and normal individuals. JSSU 2010;17:353-7
17. Gorry A, White DM, Franks S. Infertility in polycystic ovary syndrome: Focus on low-dose gonadotropin treatment. Endocrine. 2006; 30:27-33.
18. Mantzoros CS, Cramer DW, Liberman RF, Barbieri RL. Predictive value of serum and follicular fluid leptin concentrations during assisted reproductive cycles in normal women and in women with the polycystic ovarian syndrome. Hum Reprod. 2000; 15:539-44.
19. Bideci A, Camurdan MO, Yesilkaya E, Demirel F, Cinaz P. Serum ghrelin, leptin and resistin levels in adolescent girls with polycystic ovary syndrome. J ObstetGynaecol Res 2008;34:578-84.
20. S. J. Ramanand, J. B. Ramanand, S. S. Jain et al., "Leptin in non PCOS and PCOS women: a comparative study," International Journal of Basic and Clinical Pharmacology. 2014; vol. 3, no. 1, pp. 186–193.
21. Baig M, Rehman R, Tariq S, Fatima SS. Serum leptin levels in polycystic ovary syndrome and its relationship with metabolic and hormonal profile in Pakistani females. Int J Endocrinol 2014;2014:132908.
22. Rotterdam ESHRE/ASRM-sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. FertilSteril. 2004;81:19-25.
23. El-Gharib MN, Badawy TE. Correlation between insulin, leptin and polycystic ovary syndrome. J BasiClinReprod Sci. 2014;3:49-53.
24. Dagogo-Jack S, Fanelli C, Paramore D, Brothers J, Landt M. Plasma leptin and insulin relationships in obese and nonobese humans. Diabetes. 1996; 45:695-8
25. Sir-Petermann T, Recabarren SE, Lobos A, Maliqueo M, Wildt L. Secretory pattern of leptin and LH during lactational amenorrhoea in breastfeeding normal and polycystic ovarian syndrome women. Hum Reprod. 2001; 16:244-9.