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Research Article

**SERUM CCL 18 LEVELS IN WOMEN WITH POLYCYSTIC
OVARIAN SYNDROME****Dr. Rabbia Shahzadi¹, Dr. Natasha Wafa¹, Dr. Faiza Maqsood¹, Dr. Saiqa Ilyas¹, Dr.
Khurram Khaliq Bhinder²**¹Sir Gangaram Hospital, Lahore²DHQ Teaching Hospital, Gujranwala**Article Received:** September 2020**Accepted:** October 2020**Published:** November 2020**Abstract:**

Introduction: The CC chemokine ligand 18 (CCL18) is a chemokine highly expressed in the lung and in antigen-presenting cells such as M2 macrophages and dendritic cells, which can act as a chemoattractant for both lymphocytes and immature dendritic cells. **Objectives:** The main objective of the study is to analyse the serum CCL 18 levels in women with polycystic ovarian syndrome. **Material and methods:** This cross sectional study was conducted in Sir Gangaram Hospital, Lahore during June 2019 to March 2020. The data was collected from 90 female patients which was suffering from PCOS. The data was collected into two groups, one was control group and one was selected patients. **Results:** The data was collected from 90 patients. 45 patients in group A and 45 patients in group B. The mean age was 25.4 ± 5.67 years. The mean serum CCL 18 levels in the PCOS group were 28.32 ± 4.17 ng/mL with the levels in the control group being 11.90 ± 4.91 ng/mL. **Conclusion:** It is concluded that serum CCL 18 were considered to be the basic marker for PCOS. There is also a significant difference in serum CCL 18 levels in PCOS subjects with age and BMI matched healthy controls.

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INTRODUCTION:

The CC chemokine ligand 18 (CCL18) is a chemokine highly expressed in the lung and in antigen-presenting cells such as M2 macrophages and dendritic cells, which can act as a chemoattractant for both lymphocytes and immature dendritic cells. In cultured monocytes, CCL18 stimulates the expression of other chemokines (eg, CCL2, CCL3) and induces an M2-like macrophage phenotype [1]. In nonadipose tissues, CCL18 has mainly been associated with conditions involving fibrosis and inflammation. For example, CCL18 induces pulmonary fibrosis by stimulating alveolar fibroblasts to produce collagen, and plasma CCL18 levels are a marker of disease activity. CCL18 has also been implicated in chronic inflammatory conditions such as atopic dermatitis, asthma, and arthritis, although its exact role in influencing pro- and anti-inflammatory pathways remains to be defined. Mechanistic studies of CCL18 have been hampered by the fact that there is no murine orthologue and that the signaling receptors are not known [2].

Polycystic ovarian syndrome (PCOS) is one of the most common metabolic disorders. Globally, the prevalence of PCOS varies from 2.2% to 26%, while in India, the prevalence ranges from 9.13% to 36%. Severe degree of insulin resistance or impaired glucose tolerance (IGT) is more common in obese PCOS [3]. About two-thirds of females with PCOS are insulin resistant and the degree of insulin resistance exceeds that of women without PCOS matched for body mass index (BMI) or the degree of adiposity. Studies have reported the prevalence of insulin resistance in Indian women with PCOS to be 75% and also more severe than their white counterparts. There is consistent evidence that a large proportion of women with PCOS develop diabetes mellitus later in life [4]. IGT or frank diabetes is evident in approximately 45% of women with PCOS by their fourth decade. Both insulin resistance and type 2 diabetes mellitus are linked to disturbances in white adipose tissue (WAT) with mechanisms involving altered secretion of adipokines, peptides, which exert autocrine, paracrine, and or endocrine effects on metabolism [5].

CC chemokine ligand 18 (CCL18) is a chemokine constitutively expressed in the lung and is endowed

with chemotactic properties. The main producers of CCL18 are antigen-presenting cells like alveolar macrophages and follicular dendritic cells in vivo and in vitro, several human cells “spontaneously” secrete CCL18, such as monocyte-derived dendritic cells. Using gene microarray data from subcutaneous WAT of obese and nonobese women, it was shown that CCL18 expression was significantly increased in obesity and decreased upon weight loss [6].

Objectives

The main objective of the study is to analyse the serum CCL 18 levels in women with polycystic ovarian syndrome.

MATERIAL AND METHODS:

This cross sectional study was conducted in Sir Gangaram Hospital, Lahore during June 2019 to March 2020. The data was collected from 90 female patients which was suffering from PCOS. The data was collected into two groups, one was control group and one was selected patients. A complete clinical examination which included anthropometric indices like, height, weight, waist circumference, waist-hip ratio was obtained. Blood pressure measurement and modified FG scoring, acne, acanthosis nigricans, skin tags were also examined. Patients were called on a separate day and 2 mL of a blood sample, after an overnight fast for 8 h, was collected from all the subjects, sera separated and stored at -80°C . Serum testosterone levels, HbA1c (HPLC), and ultrasound examination of abdomen and pelvis for ovaries and adnexa were done as part of routine evaluation. CCL 18 level was estimated by the ELISA method.

Statistical analysis

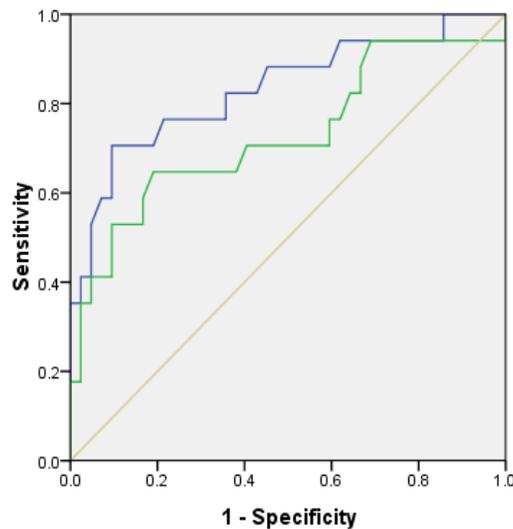
The data was collected and analysed by using SPSS version 19. All the values were expressed in mean and standard deviation.

RESULTS:

The data was collected from 90 patients. 45 patients in group A and 45 patients in group B. The mean age was 25.4 ± 5.67 years. The mean serum CCL 18 levels in the PCOS group were 28.32 ± 4.17 ng/mL with the levels in the control group being 11.90 ± 4.91 ng/mL.

Table 01: Baseline characteristics of cases and controls

Parameters	Group A	Group B	P
Age (years)	25.4±5.67	25.18±4.01	0.195
Weight (kg)	74.18±9.52	73.59±8.20	0.875
BMI (kg/m ²)	28.82±4.78	27.55±2.72	0.77
SBP (mmHg)	120.62±5.78	115.96±6.775	0.001
DBP (mmHg)	80.44±3.01	78.53±4.77	0.026
HbA1C (%)	5.64±0.33	5.10±0.91	0.100
Fasting Insulin (mIU/L)	12.12 (12.45)	7.72 (4.97)	0.017
CCL 18 (ng/mL)	27.31±5.17	12.76±4.91	<0.001
Serum testosterone (ng/dL)	44 (31.07)	13.5 (14.75)	<0.001



In the present study, a cutoff for HOMA IR is 1.98, which has been calculated by applying the Receiver Operating Characteristic (ROC) curve. It was noted that serum CCL 18 levels (OR 1.71, 95% CI 1.09–2.67) were found to be the independent factor for predicting PCOS after adjusting for other factors.

DISCUSSION:

Studies undertaken previously on serum CCL 18 levels were mainly in inflammatory conditions, and a positive relation has been established between the two. However, recently the role of serum CCL 18 levels as a marker of white adipose tissue inflammation is gaining importance [7]. On reviewing the literature, the present study is the first to examine the relationship between serum CCL 18 levels and insulin resistance in PCOS. The finding of the significant difference in the serum CCL 18 levels between PCOS women and normal controls is in agreement with the study done by Eriksson Hogling *et al.*, where it was demonstrated that the mean serum CCL 18 levels were 63.5 ng/mL in insulin-resistant subjects and 41.0 ng/mL in the insulin-sensitive cases, whereas in our study, the mean serum CCL 18 levels were 28.32 ng/mL and 11.90 ng/mL in cases and controls, respectively [8]. The relationship between BMI and serum CCL 18 levels

has been disputed with studies showing conflicting relationships.

In our study, the relationship between serum CCL 18 and BMI was not significant, whereas a significant relationship was shown between serum CCL 18 and waist circumference and waist-hip ratio. The waist circumference in the study done by Eriksson Hogling *et al.* showed a significant difference in the insulin-resistant group and insulin-sensitive group, and a similar difference was present in our study also [9]. We feel that the greater waist circumference, a marker of insulin resistance, seen in the earlier study, as well as in our study, could be responsible for the greater serum CCL 18 levels. Serum CCL 18 was shown to be a marker of WAT inflammation and alternatively activated M2 macrophages, which are abundant in fibrotic areas of insulin-resistant subjects, act as a source of CCL 18. This could account as a

possible mechanism for the significant relationship between insulin resistance and serum CCL18 levels in PCOS subjects as a majority of them have insulin resistance [10].

CONCLUSION:

It is concluded that serum CCL 18 were considered to be the basic marker for PCOS. There is also a significant difference in serum CCL 18 levels in PCOS subjects with age and BMI matched healthy controls.

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