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THE CORRELATION BETWEEN THE BLOOD AND HORMONAL DISORDERS WITH SYNDROME OF POLYCYSTIC OVARIES IN WOMEN OF THE BAGHDAD CITY

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ABSTRACT

Polycystic ovary syndrome (PCOS) is an endocrine and metabolic disorder affecting around 8-10% of women characterized mainly by hyperandrogenism and chronic anovulation associated with other variable manifestations such as insulin resistance, dyslipidemia and hirsutism. Thirty female patients with PCOS together with twenty healthy volunteer females included as controls. Serum levels of hormones such as FSH, LH, testosterone and prolactin were tested in the two groups. Blood parameters (RBC count, WBC count, PCV, Hb, platelet count, MCV, MCHC and RDW were evaluated in this study in addition to the estimate the correlation between blood parameters and hormonal level be a part of the correlation. Hormonal parameters of patients of PCOS showed a statistically highly significant ($P < 0.0001$) decrease in follicular stimulating hormone (FSH) levels (4.01 ± 0.33) compared to control group (6.91 ± 0.35) whereas the luteinizing hormone (LH) of patients showed highly significant increase ($P < 0.0001$) in their level (11.56 ± 0.60) as compared with control group(3.86 ± 0.38). The statistical analysis of results for blood parameters showed that there is highly significant difference ($P < 0.0001$)in WBC, RBC, Hb, MCV, MCH, MCHC, RDW-CV and platelet for PCOS patients when compared with control group. an intermediate positive correlation and significantly difference ($P < 0.05$) was found between WBC count and testosterone level in the blood of PCOS patients group, meanwhile a strong positive correlation and highly significant difference ($P < 0.01$) was found between the RBC count and testosterone level (r=0.47).

KEYWORDS: PCOS, Blood parameters, hormonal parameters, Baghdad city.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is an endocrine and metabolic disorder affecting around 8-10% of women in their reproductive age characterized mainly by hyperandrogenism and chronic anovulation associated with other variable manifestations such as insulin resistance, dyslipidemia and hirsutism (Najem *et al.,* 2012). Numerous inflammatory markers has been described in women with PCOS, some of them are elevated white blood cell (WBC) count and C-reactive protein (CRP) concentrations with other manifestations of chronic inflammation such as increased oxidative stress and endothelial dysfunction (González, 2012).

Obesity is more common in women with PCOS, and it can lead to severe hyperandrogenism. Obesity is more common in women with PCOS and it can lead to severe hyperandrogenism (Maturana *et al.* 2008).Women who suffer from PCOS have high insulin hormone as hormone resistance and cause an increase in the male testosterone hormone secreted from the ovary, Which lead to cardiovascular disease because of a defect in fat distribution, as well as to the occurrence of cervical cancer also elevation of testosterone hormone lead to obesity, acne and coarse hair (Rjeffrey, 2000). The research indicated that the menstrual cycle disorder at the age of adolescence (16 years and above) leads to increased risk for PCOS, especially in obese girls, or when an increase in LH hormone level where the disease is at the top of picking between the ages (18-30 years old) (Lo *et al*., 2006).

where the incidence of PCOS in the early ages and lack of ovulation for a long time leads to delayed childbearing and if pregnancy is got it causes spontaneous abortion or accompanied by infection with early diabetes (Marilym and Richardson, 2003). Beyond these factors, there is strong evidence that polycystic ovarian syndrome in young women is associated with vascular endothelial dysfunction9-11 and platelet hyperaggregability (Orio *et al*., 2004).

Aim of the research was to study the correlation between the Blood and hormonal disorders with syndrome of polycystic ovaries in women of the Baghdad city.

MATERIALS AND METHODS

1-Patients and Healthy women

A total of 30 premenopausal women between the ages of 19-35 years, who presented with the clinical features of the PCOS were assessed, while control group were healthy volunteers with a normal menstrual cycle and with no clinical or biochemical features of hyperandrogenism. PCOS was defined as an ovarian ultrasound diagnosis, with a history of menstrual disturbance (amenorrhoea/ oligomenorrhoea), in association with elevated of serum testosterone and LH, and low or normal FSH hormone (Franks, 1998).

Survey was made for each women suffering from PCOS which comprised age, Social status, Irregular menstrual cycle, education. The abnormal hair growth in the face and neck area was taken into account the mind.

2-Included Criteria

POCS patients were chosen according to the presence of polycystic ovary morphology and anovulation, while healthy women were chosen according to the regular menstrual cycle and normal endocrinal hormones.

3-Blood sampling

Three ml of blood was collected from each patients and control, placed in EDTA K3 tube and used for hematological assessments such as WBC count, RBC count, Hb value, PCV value, MCV, MCH, RDW and Platelet count that measured by equipment Bc-333plus auto hematology analyzer USA.

4-Hormonal assay

Blood sample was collected and placed into a plain tube and centrifuged at 6000 rpm/min for 5 min. The serum samples were collected into Eppendorf tube followed by labeling and eventually frozen under – 28 C to be used for hormonal assays including follicular stimulating hormone, luteinizing hormone, testosterone and prolactin. Hormonal assays were quantitative measured using enzyme immunoassay technique (mini VIDAS Biomerieux manufacturer, Italia).

5-Statistical Analysis

The Statistical Analysis System- SAS (2012) program was used to effect of difference factors in study parameter. Least significant difference –LSD test (T-test) was used to significant compare between means. Estimate of Spearman's correlation coefficient (Spearman's, r) between means in this study.

RESULTS

Hormonal parameters of patients of PCOS showed a statistically highly significant ($P < 0.0001$) decrease in follicular stimulating hormone (FSH) levels (4.01 ± 0.33) compared to control group (6.91 ± 0.35) whereas the luteinizing hormone (LH) of patients showed highly significant increase ($P < 0.0001$) in their level (11.56 ± 0.60) as compared with control group (3.86 ± 0.38). PCOS patients showed highly significant increase ($P < 0.0001$) in testosterone level (0.984 ± 0.04) when compared with control group (9.31 ± 0.67). Also, highly significant increase ($P < 0.05$) in prolactin hormone was observed in patients (20.94 ± 0.86) as compared with the control (9.31 ± 0.67) (Table 1).

Table (1) Correlation in hormonal parameters between two groups.

Parameters	Control	Case	P value
FSH (miu/ml)	6.91 ± 0.35	4.01 ± 0.33	0.0001 **
LH (miu/ml)	3.86 ± 0.38	11.56 ± 0.60	0.0001 **
Test. (ng/ml)	0.668 ± 0.02	0.984 ± 0.04	0.0001 **
PRT (ng/ml)	9.31 ± 0.67	20.94 ± 0.86	0.0001 **

Data are mean ±S.E. **: Highly significant.

The statistical analysis of results for blood parameters showed that there is highly significant difference ($P < 0.0001$) in WBC, RBC, Hb, MCV, MCH, MCHC, RDW-CV and platelet for PCOS patients when compared with control group. The results of PCV parameter for PCOS patients (38.19 ± 0.76) showed non-significant difference as compared with control group (36.65 ± 0.66) (Table 2).

Table (2). Comparison in blood parameters between study groups

Parameters	Control	Case	P value
WBC (*10^9/L)	6.56 ± 0.34	8.94 ± 0.33	0.0001 **
RBC (*10^{12}/L)	4.43 ± 0.11	4.92 ± 0.07	0.0005 **
Hb (g/dL)	13.81 ± 0.29	11.09 ± 0.27	0.0001 **
PCV (%)	36.65 ± 0.66	38.19 ± 0.76	0.1696 NS
MCV (fL)	83.25 ± 0.37	78.11 ± 0.39	0.0001 **
MCH (pg)	30.63 ± 0.26	22.75 ± 0.22	0.0001 **
MCHC (g/dL)	37.01 ± 0.30	29.34 ± 0.29	0.0001 **
RDW-CV (%)	12.57 ± 0.22	14.40 ± 0.21	0.0001 **
PLT (*10^9/L)	262.42 ± 18.58	370.19 ± 14.45	0.0001 **

Data are mean ±S.E. **: Highly significant, NS: Non-significant.

The result in table (3) showed that there is an intermediate positive correlation and significantly difference (P < 0.05) was found between WBC count and testosterone level in the blood of PCOS patients group, meanwhile a strong positive correlation and highly significant difference (P < 0.01) was found between the RBC count and testosterone level (r=0.47). also there is an intermediate positive correlation (r=0.37) and significantly difference (P < 0.05) was found between PCV and LH level in the blood of PCOS patients group.

A weak positive correlation but not statistically significant (r=0.17,P> 0.05) was observed in the PCOS patient group between WBC count and FSH level and between Platelet count and testosterone level, also between WBC count and prolactin level(r=0.16). The there is a negative but significantly difference (r=-0.36, P> 0.05) was found between MCH and prolactin. While the other results in the same table showed that there is a negative correlation and non-significant difference between the other parameters.

Table(3). Correlation between blood parameters and hormonal tests of PCOS patients group

Parameters	FSH	LH	Testosterone	Prolactin
WBC	0.17 NS	-0.15 NS	0.35 *	0.16 NS
RBC	-0.05 NS	-0.09 NS	0.47 **	0.11 NS
Hb	0.15 NS	-0.09 NS	0.03 NS	-0.31 NS
PCV	0.16 NS	0.37 *	0.21 NS	-0.25 NS
MCV	-0.02 NS	0.11 NS	-0.30 NS	-0.12 NS
MCH	-0.09 NS	-0.15 NS	-0.15 NS	-0.36 *
MCHC	-0.09 NS	-0.19 NS	-0.05 NS	0.13 NS
RDW-CV	0.11 NS	0.01 NS	-0.01 NS	-0.12 NS
PLT	-0.05 NS	0.01 NS	0.17 NS	-0.05 NS

Data are r value
* (P<0.05), ** (P<0.01), NS: Non-significant.

DISCUSSIONS

Polycystic ovary syndrome is a common reproductive and cosmetic disorder of young women that may cause psychological disorders (Roberts *et al.*, 2000). PCOS is associated with the early appearance of multiple risk factors for cardiovascular disease, such as abdominal obesity (Vryonidou *et al.*, 2005). It is undoubtedly one of the most confusing diseases, probably due to various manifestations of the disorder and lack of uniformly accepted diagnostic criteria (Amin *et al.,* 2003).

Results of the present study showed that the hormonal profile of PCOS patient a significant decrease in FSH level and significant increase in LH level this due to altered in LH/FSH ratio. This results are agree with other study that confirmed LH/FSH ratio prevents follicular maturation during follicular phase (Cook *et al.*, 2002).

The results appear that the mean serum LH was significantly higher than mean serum FSH in PCOS women compared with control group. The ratio is more than 2. This has been also seen in other studies such as Banaszewaska, *et al.* (2003) and Anlakesh, *et al.* (2007).

Disturbed pulsatile release of gonadotrophin releasing hormone (GnRH) results in the relative increase in LH to FSH release due to Hypothalamic-pituitary-ovarian or adrenal axis abnormality (Radosh, 2009). The increase in LH level is due to inability of ovarian to secretion of Gonadotropin reproductive hormones such as estrogen by negative feedback nutrition that fall under the control of pituitary axis hypothalamic (Louck *et al.*, 2000).

Also, the result showed that there is highly significant increase in testosterone and prolactin level in PCOS

patients as compared with control, this results agree with result of Luboshitzky *et al.*, (2001) who showed that the PCOS women have an increase in testosterone level, FSH /LH ratio and insulin as compared with healthy women.

Another source for increasing of Testosterone in blood in addition to ovary is the obesity which play a key role in the functional and reproductive changes that are connected to each other and which is one of the most important characteristics of PCOS disease, adipose tissue has the ability to manufacture the active androgens in the body so when increasing of obesity this lead to increase of androgen because cholesterol was converted to testosterone by a series of metabolic processes (Valkenburg *et al.*, 2008; Recabarren *et al.,* 2008). Conway, (2000) showed the increase in testosterone was due to elevated of insulin in obesity that stimulates the of ovaries for production of testosterone.

The additional finding in this study was high prolactin level in PCOS patients, there is no causative relationship between PCOS and hyperprolactinemia and the reason for this state could be hypothyroidism (Abdelsalam and Ibrahim, 2015). The high level of prolactin may be due to the obesity, This finding agreed with Shibli-Rahhal and Schlechte (2009) who described an association between prolactin and obesity. Likewise, Filho *et al.*, (2007) stated that hyperprolactinemia is not a laboratory manifestation of PCOS. Kanagavalli *et al.,* (2013) found in their study that mean Prolactin levels in PCOS patients were within normal range.

The present study revealed highly significant difference (P < 0.0001) in WBC, RBC, Hb, MCV, MCH, MCHC,

RDW-CV and platelet for PCOS patients when compared with control group. The increase in the inflammatory parameter including total WBC count among PCOS patients group compared to healthy subjects regardless of their normal ranges. This indicates persistence of low grade chronic inflammation exerting a direct influence on anovulation (Ali *et al.,* 2015). The oxidative stress is involvement in initiating and progressing PCOS pathogenesis, the reactive oxygen species are produced in response to hyperglycemia and hypertriglyceridemia (features of PCOS) (Kurdoglu *et al*., 2012). The impact of oxidative stress on ovarian functions may be due to its direct influence on ovulation through decreasing granulosa cells luteinization and oocyte maturation which eventually leads to anovulation (Rodrigues *et al.,* 2010).

Also, other studies emphasized our results regarding elevated total leukocyte count and concluded that WBC count is slightly elevated in PCOS patients although they were within the normal range (Fransesco *et al*., 2005).

Other studies stated that obesity (PCOS features) seem to play a key role in initiation of the inflammatory immune response because they result in accumulation of free fatty acids which leads to nuclear factor kB (NF kB) activation and subsequently release of inflammatory cytokines including IL-6 and TNFα. (Jardena *et al.,* 2005). Testosterone stimulates the hematopoiesis in the bone marrow and, consequently, increases the hematocrit (Shahidi, 1973).

The increased of plasminogen activator inhibitor type I the cause in the elevation of Platelet and clot formation in PCOS women (Sampson *et al.,* 1996). Ishibashi*et al*., (2000) found that the elevated of platelet count in PCOS women may be due to increasing of interlukin-6 which work on platelet production from Megakaryocytes in bone marrow. To explain the decline in Hb concentration of PCOS patient to the possibility of a decrease in the iron and as a result cause anemia or due to a shortfall in the level of ferritin in serum knowing that he is the main reservoir of iron within the body (Al-Jabery *et al.,* 2011). Researches points to a link between prolactin and platelet activation, In women with PCOS, elevated PRL levels may increase the risk of developing atherothrombotic events via the activation of platelets (Yilmaz *et al*., 2015). Tsompos *et al.,* (2015) Tshowed that there is an increase in RDW level of the PCOS group than control group and found that there is a link between RDW and PCOS this may be due to an underlying chronic inflammation in subjects with PCOS where the RDW levels were useful as a diagnostic marker for PCOS.

REFERENCES

1. Abdelsalam, K. E. A. and Ibrahim, W. (2015). Relationship between TSH, T4, T3 and Prolactin in overweight and lean Sudanese PCOS Patients. International Journal of Biomedical Research. 6(02): 108-112.
2. Al-Jabery, K.M.; Al-Dujaily, A.N. and Al-Kafagey, Z.H. (2011).Changes in some physiological criterioi and relation with pationswomens of polycystiv ovary syndrome. Al-Kufa J. for biological sciences. 3(1): 1-12.
3. Ali, H.A.; Ali, I.H.M.1 and Ibrahim, Sh.A. (2015). The role of inflammation and oxidative stress in the pathogenesis of polycystic ovary syndrome. World Journal of Pharmacy and Pharmaceutical Sciences. 4(05): 316-323.
4. Amin, M.; Abdel-Kareem, O.; Takekida, S.; Moriyama, T.; Abd el-Aal, G. and Maruo, T. (2003). Up-date management of non-responder to clomiphene citrate in polycystic ovary syndrome. Kobe J Med Sci. 49: 59–73.
5. Anlakashm A.H. (2007). Polycystic ovarian syndrome-the correlation between LH/FSH ratio and disease manifestation. Middle East Fertil Soc J. 12: 35–40.
6. Banaszewska, B.; Spaczyński, R.Z.; Pelesz, M.; Pawelczyk, L. (2003). Incidence of elevated LH/FSH ratio in polycystic ovary syndrome women with normo-and hyperinsulinemia. RoczAkad Med Bialymst. 48: 131–4.
7. Conway, G. (2000). "The Polycystic Ovary Syndrome" Department of Endocrinology. The Middle sex Hospital Mortimer Street London W1N8AA. January.
8. Cook, C.L.; Siow, Y.; Brenner, A.G. and Fallat, M.E. (2002). Relationship between serum mullerian-inhibiting substance and other reproductive hormones in untreated women with polycystic ovary syndrome and normal women. Fertil Steril, 77: 141–146.
9. Filho, R.B.; Domingues, L.; Naves, L.; Ferraz, E.; Alves, A. and Casulari, L.A. (2007). Polycystic ovary syndrome and hyperprolactinemia are distinct entities. Gynecological endocrinology: the official journal of the International Society of Gynecological Endocrinology. 23(5): 267- 72.
10. Franks S. (1998). Polycystic ovary syndrome. J R Coll Physicians Lond. 32: 111–13.
11. Fransesco, O.; Stafano, P.; Annamaria, C. and Gaetano, L. (2005). The increase in leukocyte as a new putative marker of low grade chronic inflammation and early cardiovascular risk in polycystic ovary syndrome. J Clin Endocrin Metab. 90: 2-5.
12. González F. (2012). Inflammation in polycystic ovary syndrome: under pinning of insulin resistance and ovarian dysfunction. *Steroids*. 77: 300–305.
13. Ishibashi, T.; Kimura, H.; Shikama, Y.; Uchida, T.; Kariyone, S.; Hirano, T.; Kishimoto, T.; Takatsuki, F. and Akiyama, Y.: (2000). Interleukin 6 is a potent thrompoietic factor in vivo in mice. *Blood*, *74*: 1241-1244.
14. Jardena, J.; Sabina, V.; Marius, K.; Christina, G.; Ulrich, K. and Beat, M. (2005). Central fat excess in polycystic ovary syndrome: relation to low grade

inflammation and insulin resistance. J Clin Endocrin Metab. 90(11): 6014-6021.

15. Kanagavalli, P., Muraliswaran, P., Sathisha, T.G., Thirunaaukarasu, D. and Lakshmi, K. (2013). A Study to Assess the Hormonal Profile of Polycystic Ovarian Syndrome in a Tertiary Care Hospital in Puducherry. Research Journal of Pharmaceutical, Biological and Chemical Sciences (RJPBCS). 4(2): 1223-1228.

16. Kurdoglu, Z.; Ozkol, H.; Tuluce, Y. and Koyuncu, I. (2012). Oxidative status and its relation with insulin resistance in young non-obese women with polycystic ovary syndrome. J Endocrinol Invest. 35(3): 317-21.

17. Lo, J.C.; Feigenbaum, S.L. and*et al.* (2006). "Epidemiology and adverse cardiovascular risk profile of diagnosed Polycystic Ovary Syndrome" J. Clin. Endocrinol. Metab. 91(4): 1357-63.

18. Louck, T.L.; Talbott, E.O. *et al*. (2000). "Do polycystic -appearing ovaries affect the risk of cardiovascular disease among women with Polycystic Ovary Syndrome?" Fertile. Sterile. 74(3): 547-52.

19. Luboshitzky, R..; Quota, G.; *et al*. (2001)."Increased 6-sulfatoxymelatonin excretion in women with Polycystic Ovary Syndrome"29: Fertile. Sterile. 76(3): 506-10.

20. Marilym, R. and Richardson, M.D. (2003). "Current perspective in Polycystic Ovary Syndrome" University of Kansas Medical Center, American Family Physician. 68(4): 697-700.

21. Maturana, M.A.; Breda, V.; *et al.* (2008). "Relationship between endogenous testosterone and cardiovascular risk in early Postmenopausal woman" Metabolism. 2008; 57(7): 961-5.

22. Najem F, Elmehdawi R and Swalem A. (2012). Clinical and biochemical characteristics of polycystic ovary syndrome; a retrospective study. LJM, 2012; 80: 71-74.

23. Orio F Jr, Palomba S, Cascella T, et al. (2004). Early impairment of Endothelial structure and function in young normal-weight women with Polycystic ovary syndrome. J Clin Endocrinol Metab. 89(9): 4588-4593.

24. Radosh L. (2009). Drug Treatments for Polycystic Ovary Syndrome. Am Fam Physician. 79(8): 671-676.

25. Recabarren, S. E.; Smith, R.; *et al*. (2008). "Metabolic profile in sons of women with Polycystic Ovary Syndrome" J. Clint. Endocrinal. Metal. 93(5): 156-81.

26. Rjeffrey, M.D, (2000). Long term consquences at polycytic Ovary syndrome Joint ASRM/ESHRE. Repraluctive Endocrinol congress, Coarse 1.

27. Roberts, R.E.; Kaplan, G.A.; Shema, S.J. and, Strawbridge, W.J. (2000). Are the obese at greater risk for depression? Am. J. Epid. 152: 163–170.

28. Rodrigues, J.K.; Dib, L.A.; Ferriani, R.A.; Jordão Junior, A.A. and Navarro, P.A. (2010). Serum markers of oxidative stress and assisted reproduction procedures results in infertile patients with polycystic ovary syndrome and controls. Rev Bras GinecolObstet, 32(3): 118-25.

29. Sampson, M.; Kong, C.; Patel, A.; Unwin, R. and Jacob, H. S. (1996). Ambulatory blood pressure profiles and plasmogen activator inhibitor (PAI-) activity in lean women with and without Polycystic ovary syndrome. Gynecol, Obstet, Invest, 53: 157: 62.

30. Shahidi, N. T. (1973). "Androgens and erythropoiesis," New England Journal of Medicine. 289(2): 72–80.

31. Shibli-Rahhal, A and Schlechte, J. (2009). The effects of hyperprolactinemia on bone and fat. Pituitary. 12(2): 96-104.

32. Tsompos, C.; Panoulis, C.; Toutouzas, K. Zografos, G. and Papalois, A. (2015). The acute effect of the antioxidant drug u-74389G on red blood cell distribution width levels during hypoxia reoxygenation injury in rats. Folia Medica. 57(3&4): 235-242.

33. Valkenburg, O.; Steegers-Theunissen, R.P.; *et al.* (2008). " A more atherogenic serum Lipoprotein Profile is Present in women with Polycystic Ovary Syndrome: a case-control study" J. Clin. Endocrinol. Metab. 93(2): 470-6.

34. Vryonidou, A.; Papatheodorou, A.; Tavridou, A. Terzi, T.; Loi, V.; Vatalas, I.A. et al. (2005). Association of hyperandrogenemic and metabolic phenotype with carotid intima-media thickness in young women with polycystic ovary syndrome. The Journal of clinical endocrinology and metabolism. 90(5): 2740-6.

35. Yilmaz, Ö.; Calan, M.; Kume, T.; Temur, M.; Yesil, P. and Senses, M. Y. (2015). The effect of prolactin levels on MPV in women with PCOS. clinical endocrinology, 82(5): 747–752.