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The relationship between male testosterone hormone and some female hormones in women with polycystic ovary syndrome (PCOS)

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Objectives This study was designed to determine the levels of hormones insulin, testosterone and some female hormones in some male and female hormones in patients with polycystic ovary syndrome (PCOS) and find the relationship between the male testosterone hormone and female hormones in patients with PCOS and to know the reasons for these changes in view of the prevalence of PCOS and its importance as a major problem affecting the health of women and her fertility.
Methods The hormones included LH, FSH, PRL, estradiol (E2), progesterone (P4) and LH/FSH ratio in patients with PCOS compared with control group, and to find the relationship between male testosterone hormone and female hormones under the study in patients with PCOS. Fifty-five female patients with PCOS in reproductive age with body mass index (BMI) (25.01 ± 1.70 kg/m^2), aged 15–46 years old and who recalculated fertility centre of teaching Al-Sadr hospital in Al-Najaf Al-Ashraf Governorate from 1/9/2013 to 1/10/2014, compared with 20 non-patients women with PCOS with BMI (23.87 ± 2.66 kg/m^2) and age 17–47 years old as control group.
Results The results showed that there was a significant increasing ($p < 0.05$) in insulin, testosterone, LH, PRL and LH/FSH ratio in patients with PCOS compared with control group, while there was a significant decreasing ($p < 0.05$) in FSH, E2 and P4 in patients with PCOS compared with non-patients women.
Conclusion As the results have shown that there was a positive significant relationship between testosterone and LH, PRL and LH/FSH ratio while the relationship was negative significant between testosterone and FSH, E2 and P4 in patients with PCOS.
Keywords polycystic ovary syndrome (PCOS), testosterone, LH, FSH, progesterone (P4)

Introduction

Polycystic ovary syndrome (PCOS) was first described in 1935 by Stein and Leventhal therefore is known Stein-Leventhal syndrome,[1] PCOS is one of gynaecological very common in reproductive age and it occurs in about 5–10% of women reproductive age in the world.[2,3] PCOS is a disease that infected the ovaries which may be associated with a number of clinical symptoms and hormonal disorders; therefore, PCOS is not one disease, but a group of related diseases together, which may lead, in the end to infertility resulting from chronic anovulation.[4–6] In some cases of PCOS did not have any pathogenic symptoms except there are several small cysts in size in the ovaries, which can be observed when vaginal examination by ultrasound,[7,8] but in most cases, this syndrome is accompanied by several clinical symptoms, which can be diagnosed in the PCOS such as menstrual cycle disorders (amenorrhea or oligomenorrhoea), anovulation, infertility, hirsuitism, acne and obesity[9–11] and these symptoms often are produced by hyperandrogenism that caused by insulin resistance and hyperinsulinemia,[12,13] also PCOS can be diagnosed through some laboratory tests such as measuring hormones levels especially insulin, LH, FSH and male hormones (androgens) especially testosterone hormone[14–16] and these symptoms may be shown individually or jointly, but did not require their presence together to diagnose PCOS.[17,18]

The studies also showed that insulin resistance and hyperinsulinaemia in PCOS may also cause hyperlipidemia and diabetes mellitus type 2 (NIDDM),[19–21] early arteriosclerosis[22] and thyroid dysfunction,[23] in addition to a number of complications on the long extent such as chronic cardiovascular diseases,[24] hypertension,[25,26] cervical cancer, nerve system diseases and stroke.[27,28] Researches indicated that infection in the pregnant women with PCOS may cause abortion, early birth, hypertension and diabetes associated with pregnancy.[29,30] The real reasons of PCOS are unknown yet, several theories were put to explain mechanisms of PCOS, but the recent studies suggested that there are new evidences pointed to transmit this syndrome genetically by gene of prevailing type has not been detected to present time,[31–33] the treatment of PCOS focuses on treating the different symptoms and disorders accompanying of PCOS.[34,35]

The aim of present study is to examine changes in some male and female hormones in patients with PCOS and find the relationship between the male testosterone hormone and female hormones in patients with PCOS and to know the reasons for these changes in view of the prevalence of PCOS and its importance as a major problem affecting the health of women and her fertility.

Materials and Methods

Subjects

This study was conducted on 75 women of reproductive age. Among them 55 women with pcos with body mass index (BMI; 25.01 ± 1.70), aged 15–46 years who recalculated Fertility Center of teaching Al-Sadr hospital in Al-Najaf Al-Ashraf Governorate from 1/9/2013 to 1/10/2014 and diagnosed in brief by the doctor of the fertility center through clinical and biochemical signs of hyperandrogenism as hirsutism, acne and obesity or oligo and/or anovulation that is menstrual disturbance or appearance of the polycystic ovarian on ultrasound, while 20 healthy women with BMI (23.87 ± 2.66) and

age 17–47 years as control group, their fertility have been confirmed and they have no other diseases like artery diseases, thyroid gland diseases, diabetes mellitus and blood pressure.

Count BMI

Weight and height of the body were measured, BMI was calculated by dividing by the weight square of the height (kg/m^2).[64]

Hormone Assays

Venous blood samples of PCOS patients and non-patients were collected in third and fourth day of menstrual cycle (follicular phase) after 12 h overnight fasting for the estimation of the hormones, serum levels of LH, FSH, testosterone, PRL and estradiol (E2) were measured by specific electro chemiluminescence immunoassay (Elecsys 2010 Cobas, Roche Diagnostics, Mannheim, Germany), insulin hormone was measured using chemiluminescence (Siemens Medical Solutions Diagnostics, CA, USA), and progesterone (P4) levels were determined using chemiluminescence (Advia Centaur, Siemens healthcare Diagnostics, UK).

Statistical Analysis

Results were entered to SPSS version 17, mean and standard deviation (mean ± SD) were also calculated, statistical analysis was done using the Student's *t* test of confirmation of the normal distributed. The correlation among the hormones was performed by Pearson correlation test and *p* value $P < 0.05$ was considered statistically significant.

Results

Comparison of the Hormone Concentrations between Patients with PCOS and Control Group

The results (Table 1) show a significant increase ($P < 0.05$) in concentrations of hormones insulin (14.84 ± 7.80), LH (9.87 ± 1.94) testosterone (0.88 ± 1.56) and PRL (26.59 ± 7.75) and LH/FSH ratio (2.8 ± 1.57) in patients women with PCOS compared with control group (12.50 ± 5.33), (6.88 ± 1.94), (0.47 ± 0.31), (15.60 ± 3.17) and (0.88 ± 0.34) respectively, while there was a significant decreasing ($P < 0.05$) in hormones levels FSH, estradiol (E2) and progesterone (P4) in women patients with PCOS (3.86 ± 1.39, 58.14 ± 8.56, 1.85 ± 0.34) when compared with non-patients women with PCOS (8.34 ± 1.51, 75.35 ± 5.9, 0.87 ± 0.6) respectively (Table 1).

Table 1. **Comparison of hormone concentrations between patients with PCOS and control group**

Hormonal parameters	Patients with PCOS $n = 55$	Non-patients with PCOS (control group) $n = 20$	$P < 0.05$
	Mean ± SD	Mean ± SD	
Fasting insulin, IU/ml	14.84 ± 7.80	12.50 ± 5.33	P < 0.05
Testosterone, ng/ml	0.88 ± 1.56	0.47 ± 0.31	P < 0.05
LH, IU/ml	9.87 ± 1.79	6.88 ± 1.94	P < 0.05
FSH, IU/ml	3.86 ± 1.39	8.34 ± 1.51	P < 0.05
LH/FSH	2.82 ± 1.57	0.88 ± 0.34	P < 0.05
P R L, ng/ml	26.59 ± 7.75	15.60 ± 3.17	P < 0.05
Estradiol (E2), pg/ml	58.14 ± 8.56	75.35 ± 5.9	P < 0.05
Progesterone (P4), ng/ml	1.85 ± 0.34	0.87 ± 0.6	P < 0.05

Correlation between Male Testosterone Hormone and Female Hormones in Patients Women with PCOS

A significant positive correlation was found between the testosterone and LH ($P < 0.05$, $R = 0.93$) and LH/FSH ratio ($P < 0.05$, $R = 0.87$) and PRL ($P < 0.05$, $R = 0.79$) in patients with PCOS (Figs. 2–4), while there was a significant negative correlation between testosterone and FSH, E2 and P4 ($P < 0.05$, $R = -0.98$, $R = -0.89$, $R = -0.96$) respectively in patients with PCOS (Figs. 1, 5, 6).

Discussion

PCOS is a group of disorders in the reproductive and metabolism function of the body, and the mechanism of PCOS is unknown so far, but may cause in it one or more of the

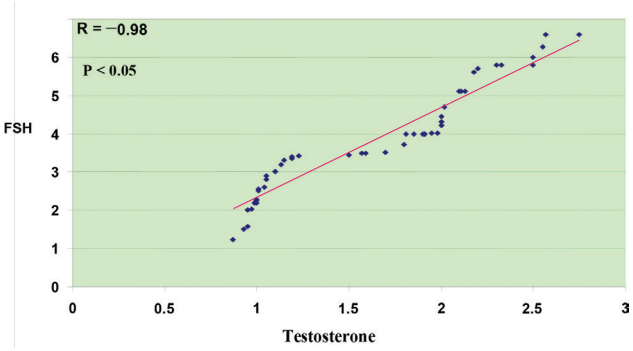

Fig. 1 **Relationship between testosterone and FSH.**

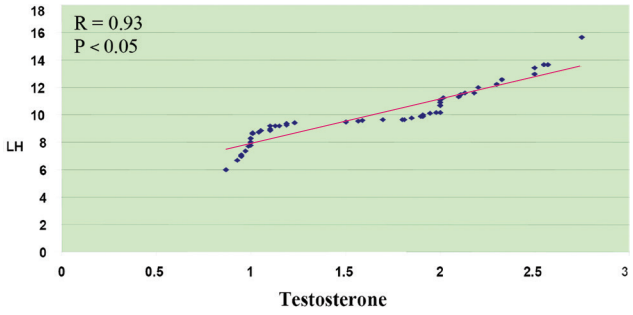

Fig. 2 **Relationship between testosterone and LH.**

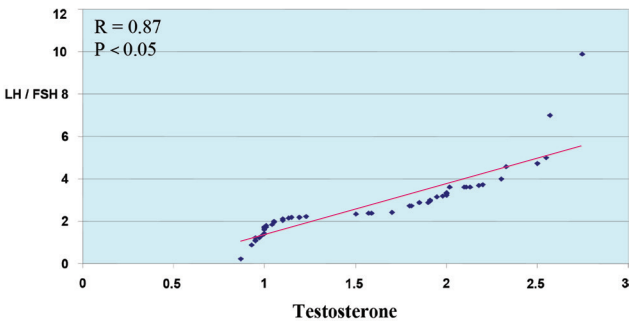

Fig. 3 **Relationship between testosterone and LH/ FSH ratio.**

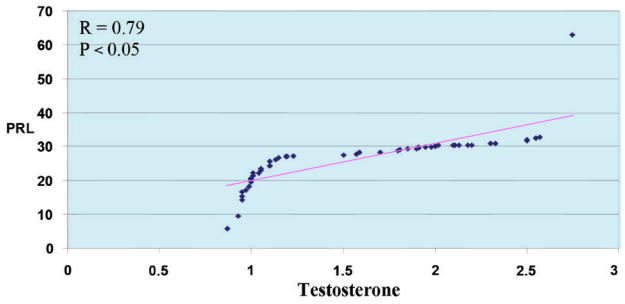

Fig. 4 **Relationship between testosterone and PRL.**

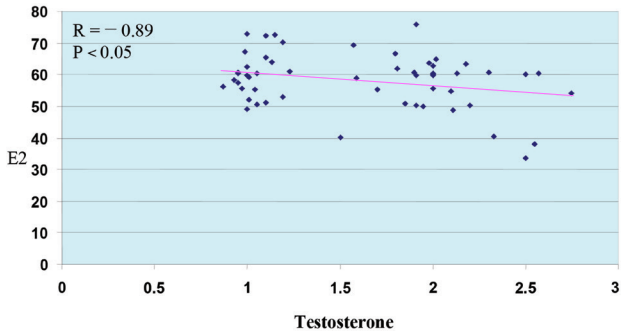

Fig. 5 **Relationship between testosterone and estradiol (E2).**

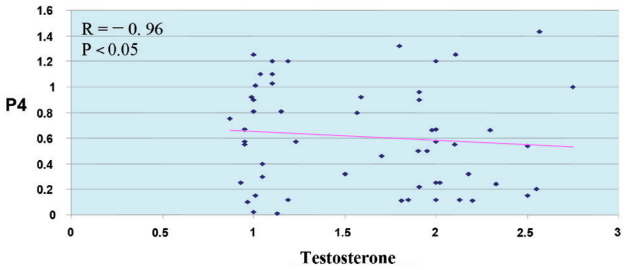

Fig. 6 **Relationship between testosterone and progesterone (P4).**

genetic defects but not the point that starts from and causes rest disorders[36,37] is not known. However, recent studies indicate that the resistance of insulin which leads to hyperinsulinemia due to a malfunction in the effectiveness of the insulin hormone receptors on the cell membrane, leading to the inability of insulin to carry glucose particles from blood to the cells and this situation gives a prompt to pancreas to secret increasing of insulin to compensate the lack of effectiveness, causing higher insulin[20,38] and this is indicated by our current study which agreed with other results of many studies.[39,40] As the results showed that there is a significant increase in the concentration of testosterone in patients with PCOS compared with control group, and this due to either an increase in insulin and growth factor-like insulin I (GFI) from the ovary in women with PCOS, which causes damage non-mature follicles and anovulation and appearance acne and hirsutism[41,42] or due to initial enzymatic defect in adrenal glands[43,44] and this result has agreed with results of many studies.[45,46] And the results also indicated a significant increase in LH and LH/FSH ratio, and a significant positive relationship between LH, LH/FSH ratio and testosterone hormone, while FSH has been decreased significantly in patients with PCOS compared with healthy controls, which was its relationship significantly negative with the testosterone hormone in patients with PCOS, the studies have pointed that hyperinsulinemia may affect the system hypothalamic-pituitary system, causing an increase in LH through either the increased frequency pulsating of GnRH[47] or by increasing sensitivity of the pituitary gland to GnRH hormone, or increase stimulation of the gland because of disorder feed back mechanism between the pituitary gland and ovary steroids[48,16] and hyperandrogenism caused abnormal secretion of the gonadotrophins with relatively high on levels of LH to FSH, which lead to stop growth development of the follicles and production the androgen and the excess of it turns into excess of terminal tissue to estrogen causing abnormal production of the steroids of the ovaries which leads to the continuation of abnormal secretion of gonadotrophins.[49,50] Also studies have demonstrated that any disorder in the level of LH leads to disorder in the level of FSH because of the pituitary gland disorder or not to respond to GnRH hormone, as each increased the LH may decrease FSH and this leads to height rate of LH/FSH and this rate increases with secretion increased the androgens in women with PCOS[51,52] and this is indicated by many studies.[53–55] And the results of our study also showed a significant increase in the level of PRL in patients with PCOS compared with non-patients, and the relationship was significant positive between PRL and the testosterone hormone, and the reason may be due to hyperinsulinemia, which causes hyperandrogens in the body that affects prolactin-releasing hormone (RPH) which is generated by the hypothalamus causing increased hormone,[56] or may be due to the disorders in the body of patients with PCOS, especially high level of androgens which may lead to a number of neuroendocrine changes such as decreasing level of the dopamine hormone, which is the prolactin inhibiting factor (PIF) causing a high level of prolactin hormone[57,58] thus, hyperandrogenism in the body increases the level of prolactin hormone, and this result was consistent with the results of many studies.[59–61]

The study showed that there was a significant decrease in levels of E2 and P4 hormones in patients with PCOS compared with control group, and there was a significant negative relationship between E2 and P4 and testosterone hormone in women with PCOS, and result of this study agreed with results of many researches, which demonstrated the inability of the ovary to form ovarian hormones (estradiol and progesterone) by granulosa cells[62,63] and this would lead to a reduction in levels of these hormones in blood serum against an increase in the levels of androgenic hormones that produce from the ovary which increase secretion of LH which inhibited aromatase enzyme and this reduces transformation the androgen to estradiol.[64,65] A few of the FSH leads to low level of estradiol because FSH, the main hormone in the stage of follicular phase of the menstrual cycle, operates on the composition and maturity of ova and thus estrogen hormone secretion of mature ovum[66] and the high level LH causes damage to the premature follicles and anovulation and thus, non formation of yellow body in the second half of menstrual cycle, leading to lack of progesterone that works with the estradiol on metamorphosis of the endometrium last stages of the menstrual cycle in recent menstrual cycle of the cession endometriosis in the normal case.[67] But in patients with PCOS, the secretion of estradiol

from the ovary stimulates growth of the endometrium to become thick and with no enough progesterone leads to severe bleeding or intermittently for a long time and this may cause carcinoma of uterus.[68,69] Therefore, high secretion of LH increases the secretion of androgens whenever there is a decreased secretion of progesterone and estradiol, this result agreed with the findings of many studies.[70,71]

Conclusion

As the results have shown that there was a positive significant relationship between testosterone and LH, PRL and LH/FSH ratio while the relationship was negative significant between testosterone and FSH, estradiol (E2) and progesterone (P4) in patients with PCOS.

References

1. Stein IF, Leventhal ML. Amenorrhea associated with bilateral polycystic ovaries. Am J Obstet Gynecol. 1935;29:181.
2. Franks S. Polycystic ovary syndrome. Endocrinol Metab Clin North Am. 1995;28(2):379–408.
3. Dahiya K, Sachdeva A, Singh V, Dahiya P, Singh R, Dhankhar R, et al. Reproductive hormone and thyroid hormone profile in polycystic ovarian syndrome. Endocrinol. 2012;3(6):41–43.
4. Speroff L, Glass RH, Kase NG. Anovulation and polycystic ovary. Clinical Gynaecologic. Endocrinology and Infertility. In: Speroff LG, Kase NG, (eds). Baltimore: Lippincott Williams & Wilkins; 1999. pp. 487–521.
5. Ehrmann D. Polycysticovarysyndrome. N Eng J Med. 2005;352:1223–1236.
6. Vause TD, Cheung AP, Sierra S, Claman P, Graham J, et al. Ovulation induction in polycystic ovary syndrome. J Obstet Gynaecol Can. 2010;32: 495–502.
7. Parisi L, Framonti M, Casciano S, Zurli A, Gazzarrini O. The role of ultrasound in the study of polycystic ovarian disease. J Clin Ultrasound. 1982;10(14): 167–172.
8. Balen AH, Laven JS, Tan SL, Dewailly D. Ultrasound assessment of the polycystic ovary international consensus definitions. Hum Reprod Update. 2003;9:505–514.
9. Theresa L, Marx MD, Mehta MD. Polycystic ovary syndrome: pathogenesis and treatment over the short and long term. Cleveland Clin J Med. 2003;70(1):31–41.
10. Alhalby A, Abdel-Salam OA, Ahmed ZM. Weight reduction aids antiepileptic therapy to restore ovarian functions of epileptic polycystic ovary women. J Neurol Psychol. 2014;2(1):1–6.
11. Shah D, Rasool S. PCOS and metabolic syndrome: the worrisome twosome. Endocrinol Metab Syn. 2015;4:2.
12. Burghen CA, Givens JR, Kitabchi AE. Correlation of hyperandrogenism with hyperinsulinemia in polycystic ovarian disease. J Clin Endocrinol Metab. 1980;50:113–116.
13. Schuring AN, Schulte N, Sonntag B, Kiesel L. Androgens and insulin: two key players in polycystic ovary syndrome. Gynecol Geburtshilfliche Rundsch. 2008;48:9–15.
14. Lewandowski KG, Cajdler-Luba A, Salata I, Bienkiewicz M, Lewinski A. The utility of the gonadorophin releasing hormone (GnRH) test in the diagnosis of polycystic ovary syndrome (PCOS). Endocrinol Pol. 2011;62(2):120–128.
15. Kanagavalli P, Muraliswaran P, Sathisha TG, Thirunaaukarasu D, Lakshmi K. A study to assess hormonal profile of polycystic ovarian syndrome in a tertiary care hospital in Puducherry. Res J Pharm Bio Chem Sci. 2013;4(2):1223–1228.
16. Fulghesu AM, Cucinelli F, Pavone V, Murgia F, Guido M, Caruso A, et al. Changes in luteinizing hormone and insulin secretion in polycystic ovarian syndrome. Hum Reprod. 1999;14(3):611–617.
17. Melissa H, Hunter MD, James J, Sterrett J, Pharm D. Polycystic ovary syndrome: it´s not just infertility. American Academy of Family Physicians. 2000.
18. Marcondes JA, Hayashida SA, Barcellos CR, Rocha MP, Maciel GA, Baracat EC. Metabolic syndrome in women with polycystic ovary syndrome: prevalence, characteristics and predictors. Arq Bras Endocrinol Metab. 2007;51(6):972–979.
19. Holte J, Bergh T, Berne C, Lithell H. Serum lipoprotein lipid profile in women with the polycystic ovary syndrome: relation to anthropometric, endocrine and metabolic variables. Clin Endocrinol (OXF). 1994;41:463–471.
20. Dunaif A. Insulin resistance and the polycystic ovary syndrome: mechanisms and implications for pathogenesis. Endocrinol Rev. 1997;18: 774–800.
21. Azziz R, Wood 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;89:2745–2749.
22. Kelly C, Speirs A, Gould GW, Petrie JR, Lyall H, Connell JM. Altered vascular function in young women with polycystic ovary syndrome. J Clin Endocrinol Metab. 2002;87:742–746.
23. Cakir E, Sahin M, Topaloglu O, Colak NB, Karbek B, Gungunes A, et al. The relationship between LH and thyroid volume in patients with pcos. J Ovarian Res. 2012;5:43. doi: 10.1186/1757-2215-5-43 PMID: 23231775
24. Orio FJ, Palomba S, Spinelli L, Cascella T, Tauchmanovà L, Zullo F, et al. The cardiovascular risk of young women with polycystic ovary syndrome: an observational analytical, prospective case: control study. J Clin Endocrinol Metab. 2004;89:3696–3701.
25. Chen MJ, Yang WS, Yang JH, Chen CL, Ho HN, Yang YS. Relationship between androgen levels and blood pressure in young women with polycystic ovary syndrome. Hypertension. 2007;49:1442–1447. PMID: 17389259
26. Joham AE, Boyle JA, Zoungas S, Teede HJ. Hypertension in reproductive-aged women with polycystic ovary syndrome and association with obesity. Am J Hypertens. 2015;28:847–51. doi: 10.1093/ajh/hpu251 PMID: 25542625
27. Rosenfield RL. Current concepts of polycystic ovary syndrome. Baillieres Clin Obstet Gynecol. 1997;11(2):307–333.
28. Wild S, Pierpoint T, Mckeigue P, Jacobs H. Cardiovascular disease in women with polycystic ovary syndrome at long-term follow-up: retrospective Cohort study. Clin Endocrinol (OXF). 2000;52(5):595–600. PMID: 10792339
29. Jakubowicz DJ, Iuomo MJ, Jakubowicz S, Roberts KA, Nestler JE. Effects of Metfomin on early pregnancy loss in the polycystic ovary syndrome. J Clin Endocrionol Metab. 2002;87:524–529.
30. Milosavljevic M, Stefanovic M, Kutlesic R, Vukomanovic P, Andric A. Pregnancy outcomes among infertile patients with polycystic ovary syndrome treated with Metformin. Med Biol. 2006;13(3):172–176.
31. Legro RS. The genetics of polycystic ovary syndrome. Am J Med. 1995;98(1A):9S–16S.
32. Urbanek M. The genetics of the polycystic ovary syndrome. Nat Clin Pract Endocrinol Metab. 2007;3:103–111.
33. Koracs GT, Norman R. Polycystic ovary syndrome. 2nd. Cambridge University; 2007.
34. Badawy A, Elnashar A. Treatment options for polycystic ovary syndrome. Int J Womens Health. 2011;3:25–35.
35. Asimi ZV. Evaluation of endocrine changes in women with the polycystic ovary syndrome during Metformin treatment. Bosn Basic Med Sci. 2013;13(3):180–185.
36. Perricone R, Pasetto N, Dencarolis E, Vaquero E, Noccioli G, Panerai A, Fontana L. Cystic ovaries in women affected with hereditary angioedema. Clin Ex Immunol. 1992;90(3):401–404.
37. Dunaif A, Segal KR, Futterweit W, Dobrjansky A. Prefound peripheral insulin resistance, independent of obesity, in polycystic ovary syndrome. Diabetes. 1989;38:1165–1174.
38. Pasquali R, Gambineri A, Pagotto U. The impact of obesity on reproduction in women with polycystic ovary syndrome. BJOG. 2006;13:1148–1159.
39. Poretski L, Piper B. Insulin resistance, hypersecretion of LH and a dual defect hypothesis for the pathogenesis of PCOS. Obstet Gynecol. 1994; 84:613–621.
40. Pagotto U, Gambineri A, Vicennati V, Heiman ML, Tschöp M, Pasquali R. Plasma ghrelin, obesity and polycystic ovary syndrome: correlation with insulin resistance and androgen levels. J Clin Endocrinol Metab. 2002;87:5625–5629. PMID: 12466363
41. Pasquali R, Gambineri A. Insulin-sensitizing agents in polycystic ovary syndrome. Eur J Endocrinol. 2006;154:763–775.
42. Duleba AJ, Spaczynski RZ, Olive DL. Insulin and insulin-like growth factor I stimulate the proliferation of human ovarian theca-interstitial cells. Fertil Steril. 1998;69:335–340.
43. Barbieri RL, Makris A, Randall RW, Daniels G, Kistner RW, Ryan KJ. Insulin stimulates androgen accumulation in incubations of ovarian stroma obtained from women with hyperandrogenism. J Clin Endocrinol Metab. 1986;62:904–910.
44. Yildiz BO, Azziz R. The adrenal and polycystic ovary syndrome. Rev Endocrinol Metab Disord. 2007;8:331–342.

45. Gil Junior AB, Rezende AP, Carmo AV, Duarte EI, de Medeiros MM, de Medeiros SF. Adrenal androgen participation in the polycystic ovary syndrome. Rev Bars Ginecol Obstet. 2010;32(11):541–548. PMID: 21271165
46. Feuser CS, Barbosa JS, da Silva EB, de Medeiros F. Current insights into gonadotropic pituitary function in the polycystic ovary syndrome. Asian Pacific J Reprod. 2014;3(1):64–70.
47. McCartney CR, Eagleson CA, Marshall JC. Regulation of gonadotropin secretion: implications for polycystic ovary syndrome. Semin Reprod Med. 2002;20(4):317–326.
48. Adashi E, Hsueh A, Yen SS. Insulin enhancement of LH and FSH levels by cultured pituitary cells. Endocrinol. 1981;108:1441–1449.
49. Ropelato MG, Rudaz MG, Escobar ME, Bengolea SV, Calcagno ML, Veldhuis JD, et al. Acute effects of testosterone infusion on the serum luteinizing hormone profile in eumenorrheic and polycystic ovary syndrome adolescents. J Clin Endocrinnol Metab. 2009;94(9):3602–3610.
50. Dunaif A. Do androgens directly regulate gonadotropin secretion in the polycystic ovary syndrome? J Clin Endocrinol Metab. 1986;63(1):215–221.
51. Banaszewska B, Spaczynski RZ, Pelesz M, Pawelczyk L. Incidence of elevated LH/FSH ratio in polycystic ovary syndrome women with normo- and hyperinsulinemia. Rocz Akad Med Bialymst. 2003;48:131–4.
52. Cho LW, Jayagopal V, Kilpatrick ES, Holding S, Atkin SL. The LH/FSH ratio has little use in diagnosing polycystic ovarian syndrome. Ann Clin Biochem. 2006;43(3):217–219.
53. Adams J, Frank S, Polson DW. Multifollicular ovaries: clinical and endocrine feature and response to pulsatile gonadotrophin releasing hormone. Lancet. 1985;1375–1378.
54. Kazer RR, Kassel B, Yen SS. Circulating latinizing hormone pulse frequency in women with polycystic ovary syndrome. J Clin Endocrinol Metab. 1987;65:233–236.
55. Taylor AE, Mccourt B, Martin KA, Anderson EJ, Adams JM, Schoenfeld D, et al. Determinants of abnormal gonadotropin secretion in clinically defined women with polycystic ovary syndrome. J Clin Endocrinol Metab. 1997;82:2248–2256. PMID: 9215302
56. Chaudhuri S, Maiti BR. Effect of gonadotropin and prolactine on ovarian activity of a wide ovarian species, the tree pie Dendrocitta vagabura. Indian J Exp Biol. 1998;36(8):790–795. PMID: 9838881
57. Zumoff B, Freeman R, Coupey S, Saenger P, Markowitz M, Kream JA. A chronobiologic abnormality in luteinizing hormone secretion in teenage girls with the polycystic ovary syndrome. N Engl J Med. 1983;309:1206–1209.
58. Liu JH, Park KH. Gonadotrophin and prolaction secretion increases during sleep during the puerperium in nonlactating women. J Clin Endocrinol Metab. 1988;66:839–845.
59. Falsetti L, Eleftheirou G. Hyperinsulinemia in the polycystic ovary syndrome: a clinical endocrine and echographic study in 240 patients. Gynaecol Endocrinol. 1996;10:319–326.
60. Scott MG, Ladson JH, Green ED, Gast MJ. Hormonal evaluation of female infertility and reproductive disorders. Clin Chem. 1989;35:620–629. PMID: 2522836
61. Michelmore KF, Balen AH, Dunger DB, Vessey MP. Polycystic ovaries and associated clinical and biochemical features in young women. Clin Endocrinol (Oxf). 1999;51:779–86.
62. Mason HD, Willis DS, Beard RW, Winston RM, Margara R, Franks S. Estradiol production by granulosa cells of normal and polycystic ovaries: relationship to menstrual cycle history and to concentrations of sex steroids in follicular fluid. J Clin Endocrinol Metab. 1994;79:1355–1360. PMID: 7962330
63. Wickenheisser JK, Quinn PG, Nelson VL, Legro RS, Strauss JF, McAllister LM. Differential activity of the cytochrome P450 17α-hydroxylase and steroidogenic acute regulatory protein gene promoters in normal and polycystic ovary syndrome theca cells. J Clin Endocrinol Metab. 2000;85:2304–2311.
64. Urban RJ, Veldhuis JD, Dufau ML. Estrogen regulates the gonadotrophin releasing hormone-stimulated secretion of biologically active Luteinizing hormone. J Clin Endocrinol Metab. 1991;72:660–668.
65. Greespan G, Gardner D. Basic and clinical endocrinology. J Endocrinol Inverst. 2001;24:491–498.
66. Vale W, Wiater E, Gray P, Harrison C, Bilezikjian L, Choe S. Actives and inhibins and their signaling. Ann Acad Sci. 2004;1038:142–147. PMID: 15838109
67. Batista MC, Cartledge TP, Zellmer AW, Nieman LK, Merriam GR, Loriaux DL. Evidence for a critical role of progesterone in the regulation of the midcycle gonadotrophin surge and ovulation. J Clin Endocrin Metab. 1992;74(3): 565–570.
68. Lasley BL, Wang CF, Yen SS. The effects of estrogen and progesterone on the functional capacity of the gonadotrophs. J Clin Endocrinol Metab. 1975;41:820–826.
69. Conway G. The polycystic ovary syndrome having identifiable infirmity. Department of Endocrinology. The middle sex Hospital Mortimer Street London. W1N8AA; 2000.
70. Pastor CL, Griffin-Korf ML, Aloi JA, Evans WS, Marshall JG. Polycystic ovary syndrome: evidence for reduced sensitivity of the gonadotropin-releasing hormone pulse generator to inhibition by estradiol and progesterone. J Clin Endocrinol Metab. 1998;83(2):582–590.
71. de Medeiros SF, Gil-Junior AB, Barbosa JS, Isaias ED, Yamamoto MM. New insights into steroidogenesis in normo- and hyperandrogenic polycystic ovary syndrome patients. Arq Bras Endocrinol Metab. 2013;57:437–444.