Comparison of Androgen Levels, Endocrine and Metabolic Indices, and Clinical Findings in Women with Polycystic Ovary Syndrome in Uygur and Han Ethnic Groups from Xinjiang Province in China

Authors' Contribution:
Study Design **A**
Data Collection **B**
Statistical Analysis **C**
Data Interpretation **D**
Manuscript Preparation **E**
Literature Search **F**
Funds Collection **G**

BCE 1 **Hongli Zhao***
CG 2 **Xiangxin Song***
ABEF 3 **Li Zhang**
ADF 4 **Yancheng Xu**
BCF 5 **Xinling Wang**

1 Department of Endocrinology, People's Hospital of Xinjiang Uygur Autonomous Region, Urumqi, Xinjiang, P.R. China
2 Department of Endocrinology, People's Hospital of Xinjiang Uygur Autonomous Region, Urumqi, Xinjiang, P.R. China
3 Department of Medicine, Xinjiang Altay Region People's Hospital, Altay, Xinjiang, P.R. China
4 Department of Endocrinology, Zhongnan Hospital, Wuhan University, Wuhan, Hubei, P.R. China
5 Department of Endocrinology, People's Hospital of Xinjiang Uygur Autonomous Region, Urumqi, Xinjiang, P.R. China

Corresponding Authors:
Source of support:

* Hongli Zhao and Xiangxin Song are contributed equally to this work
Yancheng Xu, e-mail: yingfang09747@163.com; Xinling Wang, e-mail: xjwangxinling@vip.163.com
Departmental sources

Background: The aim of this study was to compare androgen levels, endocrine and metabolic indices, and clinical findings in women with polycystic ovary syndrome (PCOS) in Uygur and Han ethnic groups from Xinjiang Province, China.

Material/Methods: Between January 2016 to May 2017 clinical data were collected from Uygur (N=82) and Han (N=100) women diagnosed with PCOS, including age, body mass index (BMI), the Ferriman-Gallwey (mFG) hirsutism score, and waist-to-hip ratio (WHR). Blood samples obtained from all study participants were used to measure androgenic steroid levels, including androgen, androstenedione, dehydroepiandrosterone (DHEA), dihydrotestosterone (DHT), and the free androgen index (FAI). Endocrine indices measured included sex-hormone binding globulin (SHBG), luteinizing hormone (LH), follicle-stimulating hormone (FSH), estradiol (E2), and prolactin (PL). Metabolic indices measured included insulin, glucose, total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL), triglyceride (TG), and low-density lipoprotein (LDL).

Results: The FAI in Uygur women with PCOS (4.89) was significantly increased compared with Han women with PCOS (2.78) (p<0.05); androgen levels were significantly correlated with the FAI, glucose, insulin, TC, HDL, and LDL (p<0.05); androstenedione levels were positively correlated with glucose and insulin levels (p<0.05). In Han women with PCOS, androgen levels were negatively correlated with TG levels and positively correlated with TC levels (p<0.05); the FAI was positively correlated with glucose and insulin levels (p<0.05).

Conclusions: There were significant differences in androgen levels, endocrine, and metabolic indices in women with PCOS between the Uygur and Han ethnic groups from Xinjiang Province in China.

MeSH Keywords: Enteroendocrine Cells • Hyperandrogenism • Internationality • Metabolism

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/909715

📄 2216   ▦ 6   📊 1   📖 25

Background

Polycystic ovary syndrome (PCOS) is the most common endocrine disease in women of childbearing age and is associated with metabolic changes. The clinical manifestations of PCOS include menstrual disorders, amenorrhea, hirsutism, obesity, and infertility, all of which seriously affect the quality of life.

The incidence of PCOS accounts for between 6–8% of clinical disorders in women of childbearing age and is the main reason for female infertility [1,2]. PCOS is also associated with a variety of clinical complications that mainly involve the endocrine system, including an increased incidence of diabetes mellitus, and the cardiovascular system, including hyperlipidemia [3,4]. The pathogenesis of PCOS is complex and is associated with genetic factors, environmental factors, and social factors [5,6]. Previously published studies have shown that clinical factors associated with PCOS include adrenergic hyperthyroidism, increased pulse frequency of release of hypothalamic gonadotropin-releasing hormone and luteinizing hormone (GnRH-LH), and ovarian autocrine and paracrine abnormalities [7,8]. Among the factors associated with PCOS, hyperandrogenism is considered to be the most important characteristic involved in the pathological and physiological basis for PCOS [9]. Hyperandrogenism can be diagnosed and treated in the clinic by measurement of levels of androgen, androstenedione, dehydroepiandrosterone (DHEA), and dihydrotestosterone (DHT) in routine blood samples [9]. The clinical features of hyperandrogenism are reduced ovulation, anovulation, alopecia, acne, hirsutism, and the development of masculine characteristics [10,11]. Three-dimensional (3D) ultrasound in PCOS shows increased numbers of follicles and enlarged follicular size.

The incidence, age of onset, and clinical associations of PCOS differ between different regions and races, and the incidence and severity of hyperandrogenism have also been reported to show geographic and ethnic differences [12,13]. The reason for these geographic and ethnic differences may be related to eating habits, age, and living and working environment [14]. China is a large and multi-ethnic country with many provinces that include cities and rural areas. Therefore, the occurrence and clinical manifestations of PCOS in different ethnic groups in China are also different [15,16]. There are a large number of ethnic minorities with different living habits in Xinjiang Province, which includes the Uygur and Han ethnic groups.

Therefore, the aim of this study was to compare androgen levels, endocrine and metabolic indices, and clinical findings in women with polycystic ovary syndrome (PCOS) in Uygur and Han ethnic groups from Xinjiang Province, China.

Material and Methods

Ethical approval and patient consents

This study was approved by the Medical Ethics Committee of Zhongnan Hospital, Wuhan University, China. All patients who participated in the study signed informed consent to participate in the study.

Diagnosis of polycystic ovary syndrome (PCOS) and study inclusion criteria

Patients were enrolled in the study who were diagnosed with polycystic ovary syndrome (PCOS) at Zhongnan Hospital, Wuhan University between June 2016 to December 2017. The study included 182 women, including Uygur (N=82) and Han (N=100) women diagnosed with PCOS. Inclusion criteria were reduced menstruation or amenorrhea with fewer than eight menstruation cycles with one year or a menstrual cycle of more than 35 days. Other study inclusion criteria included meeting the clinical and/or biochemical criteria for hyperandrogenism, with ovarian polycystic changes including the number of ovarian follicles between 2–9 mm in diameter located at least one side of the ovary, and an ovarian volume >10 ml.

Study exclusion criteria include pregnancy, lactation, the presence of ovarian cancer, hormone therapy within the previous three months, functional hypothalamic amenorrhea, congenital adrenal hyperplasia or androgen-secreting adrenal tumors, premature ovarian failure, hyperprolactinemia, primary ovarian dysfunction, Cushing's syndrome, or thyroid dysfunction [16].

Patients clinical data

Clinical data collected for each study participant included age, body mass index (BMI), the Ferriman-Gallwey (mFG) hirsutism score, and waist-to-hip ratio (WHR).

Blood sample collection

Blood samples were collected from all study participants. Peripheral venous blood was collected on the morning of the third to the fifth day of menstrual cramps or bleeding in the patients with oligomenorrhea or amenorrhea using progestin withdrawal therapy.

Measurement of androgenic steroid levels

A chemiluminescence method was used to determine the androgen indices using an automatic chemiluminescence analyzer (Model: AU5800) (Beckman, Germany). Levels of androgenic steroids measured included androgen, androstenedione, dehydroepiandrosterone (DHEA), and dihydrotestosterone (DHT).

Table 1. General information comparison between PCOS women from Uygur and Han.

Index	Uygur PCOS group	Han PCOS group
Age (year)	28.2±4.1	27.6±5.2
BMI (kg/m²)	25.1±3.5*	21.3±2.4
Menstrual cycle (d)	40.0±4.5	42.0±3.5
WHR	0.91±0.05	0.89±0.07

* $P<0.05$, compared with Han PCOS group.

Table 2. Androgen index analysis between PCOS women from Uygur and Han.

Index	Uygur PCOS group	Han PCOS group
T (nmol/L)	1.72±0.61 *	1.21±0.47
A4 (nmol/L)	10.78±0.78*	5.35±0.91
DHEAS (µg/dl)	272.38±24.28*	180.11±35.89
DHT (µg/dl)	329.21±42.16	378.66±29.88
m-FG	2.12±0.35	2.35±0.24

* $P<0.05$, compared with Han PCOS group.

Measurement of endocrine indices

Endocrine indices measured included sex-hormone binding globulin (SHBG), luteinizing hormone (LH), follicle-stimulating hormone (FSH), estradiol (E2), prolactin (PL), and insulin. The free androgen index (FAI) was calculated as the level of androgen/sex hormone binding globulin (SHBG).

Measurement of metabolic indices

Metabolic indices measured included insulin, glucose, total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL), triglyceride (TG), and low-density lipoprotein (LDL). Glucose levels were determined by the oxidative enzymatic method. Levels of TC, TG, HDL, TG, and LDL were measured using the enzymatic degradation method and the automatic biochemical analyzer (Model: AU640) (Olympus, Japan).

Statistical analysis

Data analysis were performed by using SPSS version 16.0 software (SPSS, Inc., Chicago, IL, USA). Measurements were presented as the mean ± standard deviation (SD) and compared by using one-way analysis of variance (ANOVA). Correlation analysis was performed using Pearson's correlation coefficient. A p-value <0.05 was regarded as representing statistical significance.
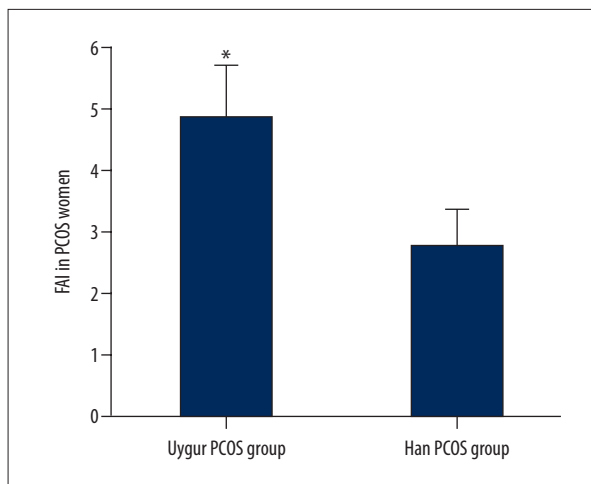

Figure 1. Comparison of the free androgen index (FAI) between women with polycystic ovary syndrome (PCOS) in Uygur and Han ethnic groups from Xinjiang Province, China. * $P<0.05$, compared with the group of Han women with polycystic ovary syndrome (PCOS).

Results

Comparison of clinical and demographic data between women with polycystic ovary syndrome (PCOS) from Uygur and Han

There were no statistical differences between the two groups of women with polycystic ovary syndrome (PCOS) from Uygur and Han for age, waist-to-hip ratio (WHR), and menstrual cycle (p>0.05). However, the body mass index (BMI) in the group of women with PCOS from Uygur was significantly increased compared with the group of women with PCOS from Han (p<0.05) (Table 1).

Comparison of androgenic steroid levels between women with PCOS from Uygur and Han

The levels of androgen, androstenedione, and dehydroepiandrosterone (DHEA) were significantly increased in the group of women with PCOS from Uygur compared with the group of women with PCOS from Han (p<0.05) (Table 2). However, no statistical difference was found between the two groups for dihydrotestosterone (DHT) and the Ferriman–Gallwey (mFG) hirsutism score (p>0.05) (Figure 1).

Correlation analysis of androgen indices between women with PCOS from Uygur and Han

Correlation analysis of androgen results showed that there was a positive correlation between levels of androstenedione and androgen, DHEA, DHT, and free androgen index (FAI) in women with PCOS from Uygur (p<0.05). There was also a correlation among these androgen levels in women with PCOS from

Table 3. Correlation analysis of androgen index between PCOS women from Uygur and Han.

Group	T	A4	DHEAS	DHT	m-FG
Uygur					
T	/	0.61**	0.21	0.11	0.21
A4	0.61**	/	0.72**	0.57*	0.12
DHEAS	0.31	0.72**	/	0.23	0.09
DHT	0.11	0.57*	0.23	/	0.10
FAI	0.09	0.75**	0.15	0.16	0.08
Han					
T	/	0.59*	0.75**	0.69**	0.17
A4	0.59*	/	0.81**	0.65*	0.16
DHEAS	0.75**	0.81**	/	0.53*	0.06
DHT	0.69**	0.65*	0.53*	/	0.09
FAI	0.59*	0.71*	0.83**	0.56*	0.11

*$P < 0.05$; ** $P < 0.01$

Table 4. Metabolic and endocrine index analysis between PCOS women from Uygur and Han.

Index	Uygur PCOS group	Han PCOS group
FSH (IU/L)	5.72±0.49	5.89±0.72
LH (IU/L)	8.61±2.31	9.05±1.47
E2 (pmol/L)	142.71±52.21	138.22±41.38
PRL (mIU/L)	372.44±34.28	380.55±38.18
INS (mU/L)	11.23±2.16	12.66±2.81
GLU (mmol/L)	11.81±1.21	10.98±1.67
TC (mmol/L)	4.39±0.28	4.51±0.37
TG (mmol/L)	1.31±0.19	1.28±0.11
HDL (mmol/L)	1.24±0.29	1.22±0.25
LDL (mmol/L)	2.78±0.36	2.56±0.29

Han ($p < 0.05$). However, the androgen levels in both groups were not correlated with the m-FG score ($p > 0.05$) (Table 3).

Comparison of metabolic and endocrine levels between women with PCOS from Uygur and Han

There were no significant differences between of metabolic and endocrine indices between the two groups, of women with PCOS from Uygur an Han, including follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), prolactin (PL), insulin, glucose, total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) ($p > 0.05$) (Table 4).

Correlation analysis of androgen and metabolic indices between women with PCOS from Uygur and Han

In the group of women with PCOS from Uygur, each androgen and metabolic index exhibited a stronger correlation between androgen and the free androgen index (FAI) with glucose, insulin, TC, HDL, and LDL, respectively ($p < 0.05$), while androstenedione levels were positively correlated with glucose and insulin ($p < 0.05$). However, there was no significant correlation between each androgen index and the metabolic parameters in the group of women with PCOS from Han, but androgen levels were negatively correlated with TG and positively correlated with TC in this group ($p < 0.05$), the FAI was positively correlated with glucose and insulin ($p < 0.05$), but there were no significant correlations between androgen and other metabolic indices ($p > 0.05$) (Table 5).

Correlation analysis of androgen and endocrine indices between women with PCOS from Uygur and Han

In the group of women with PCOS from Uygur, the correlation between the androgen and endocrine indices was weak. Androgen, androstenedione, and the FAI were positively correlated with LH and E2, but not with the FSH. In the group of women with PCOS from Han, there was a significant correlation between each of the androgen and endocrine indices, with androstenedione negatively correlated with FSH, positively correlated with PL, but not correlated with LH, and androgen and DHEA were negatively correlated with FSH and FAI ($p < 0.05$) (Table 6).

Table 5. Correlation analysis of androgen and metabolic index analysis between PCOS women from Uygur and Han.

Group	GLU	INS	TC	TG	HDL	LDL
Uygur						
m-FG	0.31	0.17	0.21	0.19	0.11	0.25
T	0.58*	0.62**	0.66**	0.41	0.59*	0.61*
A4	0.65**	0.49*	0.25	0.37	0.16	0.08
DHEAS	0.29	0.22	0.19	0.13	0.19	0.08
DHT	0.21	0.07	0.20	0.18	0.15	0.24
FAI	0.72**	0.75**	0.61*	0.39	0.58*	0.62*
Han						
m-FG	0.09	0.15	0.18	0.17	-0.09	-0.12
T	0.14	0.17	0.61*	-0.63*	0.21	0.13
A4	0.18	0.10	0.06	0.15	0.06	0.11
DHEAS	0.03	0.11	0.07	0.14	0.05	0.10
DHT	0.05	0.02	0.02	0.06	0.08	0.03
FAI	0.73**	0.69**	0.21	0.19	0.15	0.17

* $P<0.05$; ** $P<0.01$.

Table 6. Correlation analysis of metabolic and endocrine index analysis between PCOS women from Uygur and Han.

Group	FSH	LH	E2	PRL
Uygur				
m-FG	−0.11	0.17	0.15	−0.22
T	−0.17	0.71**	0.62**	0.18
A4	−0.13	0.58*	0.60*	0.15
DHEAS	−0.07	0.23	0.18	0.19
DHT	−0.13	−0.04	−0.06	0.09
FAI	−0.05	0.68**	0.74**	0.03
Han				
m-FG	−0.04	0.02	0.05	0.07
T	−0.62**	0.11	0.12	0.08
A4	−0.53*	0.16	0.19	0.75**
DHEAS	−0.63**	0.09	0.11	0.01
DHT	−0.19	0.16	0.16	0.09
FAI	−0.59*	0.02	−0.12	−0.10

* $P<0.05$; ** $P<0.01$.

Discussion

Due to reduced ovulation or anovulation, polycystic ovary syndrome (PCOS) may lead to irregular thickening of the endometrium. Therefore, PCOS is associated with an increased risk of endometrial disease, including endometrial cancer. Also, PCOS can be associated with abnormalities of the endocrine and metabolic systems, resulting in the increased risk of clinical conditions that include hypertension and diabetes [17,18]. In the process of estrogen synthesis in women, pregnenolone in the ovary and adrenal gland can synthesize androgens, including testosterone, androstenedione, dehydroepiandrosterone (DHEA), dihydrotestosterone (DHT), and the free androgen index (FAI).

Among the androgen precursors is DHEA, the intermediate product of androstenedione, and the final effective androgen synthesis process includes both androgen and DHT [19]. In PCOS, androgen synthesis is increased in theca cells, resulting in hyperandrogenism and its associated clinical effects. Therefore, the androgenic index is of significance in the occurrence and development of PCOS and in the diagnosis and monitoring of its progression or response to treatment. Because the pathogenesis and clinical manifestations of PCOS in different ethnic groups differ, the aim of this study was to analyze whether there were any differences in the androgenic, endocrine, and metabolic characteristics between the two groups of women with PCOS from Uygur and Han.

In this study, comparison of the two groups of women with PCOS from Uygur and Han, the body mass index (BMI) in the group from Uygur was significantly greater when compared with the Han group. Increased BMI might be involved in the pathogenesis of PCOS and also affect the effects of treatment, as obesity can cause hyperinsulinemia, dyslipidemia, hyperglycemia, increased secretion of inflammatory cytokines, hypertension, and diabetes mellitus, all of which might explain the clinical presentation in the group from Uygur [20,21]. One of the clinical manifestations of hyperandrogenism is hirsutism. However, the results of the present study found no significant difference in the Ferriman-Gallwey (mFG) hirsutism score between the two groups, which supported the relative independence of clinical symptoms and biochemical indicators in PCOS. Androgen, androstenedione, DHEA, and FAI in the group of women with PCOS from Uygur were significantly increased compared with the levels in the Han group, but DHT levels were not significantly different between the two groups. In the group of women with PCOS from Uygur, levels of androstenedione were significantly correlated with levels of androgen, DHEA, DHT, and the FAI. The correlation between the androgen indices in the Han PCOS group was significant, which might indicate a correlation between the androgen metabolic pathways in the Han group of women with PCOS, and any

differences between the Uygur group of women with PCOS might be explained by difference in the activity of metabolic enzymes between these two groups [22].

In the present study, a further separate analysis was performed to evaluate the correlation between androgen and endocrine and metabolic indices between the two ethnic groups. The results of this analysis confirmed that there was an increased correlation between each of the androgen indices and the metabolic indices in the Uygur study group. In the Han study group, the correlation between the androgen indices and the metabolic indices were not significant.

The correlation trends between the androgen and endocrine indices in the present study is supported by previously published studies that have shown that the androgen receptor might have an effect on apoptosis of ovarian granulosa cells apoptosis, granulosa cell death, reducing antral follicles, led to ineffective effects on the ovary by pituitary gonadotropin secretion, and leading to premature ovarian senility [23,24]. This study also showed that there was a correlation between androgen levels, the FAI, androstenedione, luteinizing hormone (LH), estradiol (E2), and follicle-stimulating hormone (FSH) in two study groups, indicating that androgens can affect follicular development. The FAI has previously been reported to evaluate the activity of androgens, and to be a better method of evaluation of the significance of the effects of hyperandrogenism [25].

In the present study, androgenic indices measured showed a stronger correlation with metabolic indices in women with PCOS from Uygur, and their BMI levels were significantly increased compared with women with PCOS from Han, indicating that women from Uygur with PCOS were more likely to accumulate visceral fat, and have an increased risk of developing metabolic syndrome and cardiovascular disease.

Although the aim of this study was to investigate androgen levels, endocrine and metabolic indices, and clinical findings in women with PCOS in Uygur and Han ethnic groups to determine whether any differences might affect diagnosis or clinical management, the study had several limitations. The study sample size was limited as the study was undertaken from a single center and during a limited time. Further large-scale, multi-center studies within regions are recommended to further evaluate regional differences in androgen, endocrine, and metabolic indices in Chinese women with PCOS.

Conclusions

The findings of this study showed that there were significant differences in androgen levels, endocrine, and metabolic indices

in women with polycystic ovary syndrome (PCOS) between the Uygur and Han ethnic groups from Xinjiang Province in China. In particular, there were significant differences in androgen levels between the two ethnic groups, indicating that further studies should include evaluation of androgenic steroid indices, including the free androgen index (FAI).

Conflict of interest

None.

References:

1. Lambertini L, Saul SR, Copperman AB et al: Intrauterine reprogramming of the polycystic ovary syndrome: evidence from a pilot study of cord blood global methylation analysis. Front Endocrinol. 2017; 8: 352

2. Kuyucu Y, Celik LS, Kendirlinan Ö et al: Investigation of the uterine structural changes in the experimental model with polycystic ovary syndrome and effects of vitamin D treatment: An ultrastructural and immunohistochemical study. Reprod Biol, 2018; 18(1): 53–59

3. Jamilian M, Shojaei A, Samimi M et al: The effects of omega-3 and vitamin E co-supplementation on parameters of mental health and gene expression related to insulin and inflammation in subjects with polycystic ovary syndrome, J Affect Disord, 2017; 229: 41–47

4. Szczuko M, Malarczyk I, Zapałowska-Chwyć M: Improvement in anthropometric parameters after rational dietary intervention in women with polycystic ovary syndrome as the best method to support treatment. Rocz Panstw Zakl Hig, 2017; 68: 409–17

5. Reddy TV, Govatati S, Deenadayal M et al: Impact of mitochondrial DNA copy number and displacement loop alterations on polycystic ovary syndrome risk in south Indian women. Mitochondrion, 2017 [Epub ahead of print]

6. Seyyed Abootorabi M, Ayremlou P, Behroozi-Lak T, Nourisaeidlou S: The effect of vitamin D supplementation on insulin resistance, visceral fat and adiponectin in vitamin D deficient women with polycystic ovary syndrome: a randomized placebo-controlled trial. Gynecol Endocrinol, 2017 [Epub ahead of print]

7. Cakiroglu Y, Doger E, Vural F et al: Impact of insulin resistance and obesity on intracytoplasmic sperm injection outcomes in young women with polycystic ovary syndrome. North Clin Istanb, 2017; 4(3): 218–24

8. Okamura Y, Saito F, Takaishi K et al: Polycystic ovary syndrome: Early diagnosis and intervention are necessary for fertility preservation in young women with endometrial cancer under 35 years of age. Reprod Med Biol, 2016; 16(1): 67–71

9. Kazemi Jaliseh H, Ramezani Tehrani F, Behboudi-Gandevani S et al: Polycystic ovary syndrome is a risk factor for diabetes and prediabetes in middle-aged but not elderly women: A long-term population-based follow-up study. Fertil Steril, 2017; 108(6): 1078–84

10. Ding Y, Xia BH, Zhang CJ, Zhuo GC: Mitochondrial tRNA(Leu(UUR)) C3275T, tRNA(Gln) T4363C and tRNA(Lys) A8343G mutations may be associated with PCOS and metabolic syndrome. Gene, 2018; 642: 299–306

11. Harris HR, Babic A, Webb PM et al: Polycystic ovary syndrome, oligomenorrhea, and risk of ovarian cancer histotypes: Evidence from the Ovarian Cancer Association Consortium. Cancer Epidemiol Biomarkers Prev, 2018; 27(2): 174–82

12. Jamilian M, Maktabi M, Asemi Z: A trial on the effects of Magnesium-Zinc-Calcium-Vitamin D co-supplementation on glycemic control and markers of cardio-metabolic risk in women with polycystic ovary syndrome. Arch Iran Med, 2017; 20: 640–45

13. Henes M, Jurow L, Peter A et al: Hyperandrogenemia and ovarian reserve in patients with Mayer-Rokitansky-Kuster-Hauser syndrome type 1 and 2: Potential influences on ovarian stimulation. Arch Gynecol Obstet, 2018; 297(2): 513–20

14. Zhang HY, Guo CX, Zhu FF et al: Clinical characteristics, metabolic features, and phenotype of Chinese women with polycystic ovary syndrome: A large-scale case-control study. Arch Gynecol Obstet, 2013; 287: 525–31

15. Feng JG, Guo Y, Ma LA et al: Prevalence of dermatologic manifestations and metabolic biomarkers in women with polycystic ovary syndrome in north China. J Cosmet Dermatol, 2017 [Epub ahead of print]

16. Bishop CV, Mishler EC, Takahashi DL et al: Chronic hyperandrogenemia in the presence and absence of a western-style diet impairs ovarian and uterine structure/function in young adult rhesus monkeys. Hum Reprod, 2018; 33: 128–39

17. Liao Y, Huang R, Sun Y et al: An inverse association between serum soluble receptor of advanced glycation end products and hyperandrogenism and potential implication in polycystic ovary syndrome patients. Reprod Biol Endocrinol, 2017; 15(1): 9

18. Skarra DV, Hernández-Carretero A, Rivera AJ et al: Hyperandrogenemia induced by letrozole treatment of pubertal female mice results in hyperinsulinemia prior to weight gain and insulin resistance. Endocrinology, 2017; 158(9): 2988–3003

19. True CA, Takahashi DL, Burns SE et al: Chronic combined hyperandrogenemia and western-style diet in young female rhesus macaques causes greater metabolic impairments compared to either treatment alone. Hum Reprod, 2017; 32(9): 1880–91

20. Czyzyk A, Latacz J, Filipowicz D et al: Severe hyperandrogenemia in postmenopausal woman as a presentation of ovarian hyperthecosis. Case report and mini review of the literature. Gynecol Endocrinol, 2017; 33(11): 836–39

21. Mishra JS, More AS, Hankins GDV, Kumar S: Hyperandrogenemia reduces endothelium-derived hyperpolarizing factor-mediated relaxation in mesenteric artery of female rats. Biol Reprod, 2017; 96(6): 1221–30

22. Borghi L, Leone D, Vegni E et al: Psychological distress, anger and quality of life in polycystic ovary syndrome: associations with biochemical, phenotypical andsocio-demographic factors. J Psychosom Obstet Gynaecol, 2018; 39(2): 128–37

23. Alexiou E, Hatziagelaki E, Pergialiotis V et al: Hyperandrogenemia in women with polycystic ovary syndrome: Prevalence, characteristics and association with body mass index. Horm Mol Biol Clin Investig, 2017; 29(3): 105–11

24. Atanasova Boshku A, Zafirova Ivanovska B, Jovanovska Mishevsk S: Hormonal and adiposity state of women with polycystic ovary syndrome: Implication of adipocytokines. Atherosclerosis, 2017; 263: e250–51

25. Maredia H, Lambert-Messerlian GM, Palomaki GE et al: Cut-off levels for hyperandrogenemia among Samoan women: An improved methodology for deriving normative data in an obese population. Clin Biochem, 2016; 49: 782–86