

## Hyperandrogenia and Visceral Obesity in Women

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### ABSTRACT

The purpose of the present work was study of clinical peculiarities of insulin-resistant metabolic syndrome and secretion of insulin and free testosterone (Free T) regarding to visceral obesity. With the use of prospective investigation a total of 108 patients aged 16 to 40 years with polycystic ovary (PCO) and 23 healthy volunteers (women) were studied. Anamnesis, objective and clinical investigations, detection of immunoreactive insulin (IRI) and Free T in blood serum was carried out. The obtained data were analyzed statistically using the Student's t test. Investigations have shown that in patients with the same body mass during visceral obesity, the more is I L/F (when the visceral type obesity is well expressed), the frequently are detected increased values of the IRI and the Free T, and the more prominently and clearly are expressed clinical manifestations of the hyperandrogenia. According to the carried out investigations the positive correlation between insulin and I L/F was revealed ( $r=0,5$ ) as well.

**KEYWORDS:** *polycystic ovary, metabolic syndrome, insulinresistance, visceral obesity, hyperandrogenia*

In the late years the great attention is applied to the pathogenetic role of hyperinsulinemia in formation of polycystic ovary [3,4].

During hyperinsulinemia/insulinresistance (HI/IR) obesity or excess body weight is frequently manifested. Noteworthy that type of distribution of the adipose tissue is of great value and it is much more important than the total body weight. J. Vague (1956, 1976) distinguished two main types of excess body weight: Android (visceral, male type, upper, Cushing's type) and Gynoid (lower, female) [1,7].

In case of visceral type of obesity adipose tissue mainly is redistributed into the scapular region, posterior surface of the neck and anterior wall of the abdomen. In case of the gynoid type of obesity adipose tissue is redistributed into the buttocks and lower limbs. Morphologically the visceral adipose tissue is characterized by hypertrophy of adipocytes, whereas gynoid type is characterized by increased quantity of adipocytes. That's why, in the other words the visceral adipose tissue is called as hypertrophied and gynoid - as hyperplasic. Unlike the gynoid adipose tissue the visceral adipose tissue mainly develops in the period of sexual maturity, therefore this adipose tissue is also called as obesity of adults.

Nowadays for detection of obesity type the index of ratio of lumbar and femoral circumferences (I L/F) is used. If this index is more than 0,8, type of obesity is visceral and when index is less than 0,8, obesity is of gynoid type [2,6].

J. Vagne, M. Pouliot, et al. consider that in case of visceral obesity the hyperinsulinemia is most expressed that is determined by the biochemical peculiarities of the visceral adipose tissue. Hyperinsulinemia in turn, according to various authors, contribute to increased synthesis of androgens due to various mechanisms. Concretely, inhibits sexsteroidbinding protein concentration in liver, thereby increasing fraction of functional free androgens. In the ovarian teca cells and stroma increases synthesis of

luteinizing dependent androgens. Along with that, it activates enzyme cytochrom P450C17 $\alpha$  hydroxylase, which plays an important role in the metabolism of androgens. All of the above-mentioned processes lead to the expressed hyperandrogenia [5,8].

According to the aforesaid, we were aimed to investigate the peculiarities of clinical indices of insulinresistant metabolic syndrome, insulin and free T secretions in relation to increased intensity of the visceral adipose tissue.

### MATERIAL AND METHODS

A total of 108 patients aged 16 to 40 years with insulin resistant metabolic syndrome and secondary polycystic ovary were under observation. The same program was used for investigation of all of the patients. Anamnesis and nature of menstrual disorders were studied. The special emphasis was laid on the period of the weight gain and appearance of pathological hairiness.

Evaluation of the hirsutism was performed according to Feriman-Galvey's scheme. With the use of Gray's formula the body mass index (BMI) was determined, and using the index of lumbar and femoral ratio (I L/F) the type of obesity was established.

The serum level of the immunoreactive insulin (IRI) and the free testosterone (Free T) were tested by the immuno-fermentation method.

In order to detect the relation of the hyperinsulinemia (HI) and hyperinsulinemia-related hyperandrogenia to the type of adipose tissue distribution, the patients were divided into two major groups according to the body mass index (BMI).

Group I - individuals with normal body weight, BMI < 25 and Group II - patients with excess body mass, BMI >25. In turn the mentioned groups according to the I L/F were subdivided into gynoid >0,8, and

visceral <0,8 excess body weight, visceral obesity subgroup - II b according to the I L/F quality was divided again into two subgroups: I L/F from 0,8 to - 0,87 IIb1 and IIb2 I L/F above the 0,87.

In all groups the indices of IRI, free T and clinical manifestations of the hyperandrogenia were studied.

The received data were analyzed using the Student's test.

## RESULTS AND DISCUSSION

A total of 25 patients with normal body weight were involved in the group I. 13 patients (52%) with I L/F <0,8 were placed in the group Ia, and the group Ib involved 12 patients (48%) with the I L/F ≥0,8 (Tab.1).

The patients from the group Ia were distinguished by the lowest characteristics of the hirsutism and hyperandrogenic dermatopathy. The mean value of the hirsutic number was 15,30±1,71; the man-type hair loss on the head was not detected in this group. *Acantosis nigricans* of the perineal region was expressed in 2 patients. The menstrual disorders predominantly by the type oligomenorrhea were revealed in 8 cases (61%), by the type secondary amenorrhea - in 2 cases, and on the background of the rhythmic menstruation, the anovulation and lutein phase insufficiency - in 3 cases.

In the subgroup Ia the IRI and Free T mean values were significantly increased compared to the control group IRI 29,46±1,20 lu/ml (P<0,001), Free T 6,85±0,57 pg/ml (P<0,001).

In the subgroup Ib the mean value of the hirsutic number increases 19,58±1,33 and the skin dermatopathy - *acantosis nigricans* of the perineal region was detected in 10 patients. The man-type hair loss on the head was not detected in this group as well. The oligomenorrheal type menstrual disorders were manifested in 5 cases, the secondary amenorrheal type - in 6 cases, and on the background of the rhythmic menstruation, the anovulation and lutein phase insufficiency - in 1 cases.

In the subgroup Ib the IRI and Free T mean values were significantly increased compared to the control group, IRI 33,98±19,6 lu/ml (P<0,001), Free T 7,56±0,80 pg/ml (P<0,001). Increase was not statistically significant compared to group Ia data (P>0,05; P>0,20).

As it has shown in the subgroup Ib in patients with normal body mass during redistribution of existed adipose tissue into visceral type the IRI and associated Free T mean values are higher than in case of adipose tissue redistribution into the gynoid type in the subgroup Ia. The clinical manifestation of the hyperandrogenia increases respectively.

A total of 83 patients with excess body weight were involved in the group II. In the subgroup IIa the I L/F <0,8 (gynoid type obesity) were only 5 patients (6%), and in the subgroup IIb the I L/F >0,8 (visceral type obesity) - 78 patients (94%).

In the subgroup IIa the mean value of the hirsutic number was 19,60±2,44; The man-type hair loss on the head was not detected in this group. *Acantosis nigricans* of the perineal region was expressed in 2 patients; the menstrual disorders by the type oligomenorrhea were revealed in 4 cases, by the type secondary amenorrhea - in 1 case.

In the subgroup IIa the IRI and Free T mean values were significantly increased compared to the control group. IRI 28,42±1,27 lu/ml (P<0,001), the Free T 7,01±0,57 pg/ml (P<0,001).

In the subgroup IIb clinical features characteristic for hyperandrogenia exacerbate. The mean value of the hirsutic number was 20,32±0,58. The man-type hair loss on the head was detected in 6 cases. *Acantosis nigricans* of the perineal region was expressed almost in all patients and on the posterior surface of the neck and under the mammary glands - in 24 cases. The menstrual disorders by the oligomenorrheal type were manifested in 43% of cases, by the secondary amenorrheal type - in 32% of cases and on the background of the rhythmic menstruation, the anovulation and lutein phase insufficiency - in 25% of cases.

In the subgroup IIb the IRI mean value was significantly increased compared to both control group and gynoid type obesity group IIa 36,50±1,26 lu/ml (P<0,001). The mean value of the Free T 7,51±0,32 pg/ml was statistically reliably increased compared to the control group (P<0,001).

Noteworthy the data obtained after division of the subgroup IIb (Tab.2). The subgroup IIb1 (I L/F=0,8-0,87) involved 40 patients. The mean value of the hirsutic number - 20,1±0,82.

The man-type hair loss on the head was detected in 1 case. *Acantosis nigricans* of the perineal region was expressed almost in all patients and on the posterior surface of the neck and under the mammary glands - in 5 cases. The oligomenorrheal type menstrual disorders were manifested in 47% of cases, the secondary amenorrheal type - in 20% of cases.

The mean value of the IRI was 33,1,73 lu/ml (P<0,001), the Free T mean value - 6,66±0,43 pg/ml (P<0,001).

A total of 38 patients were in the subgroup IIb2 (I L/F >0,87). The clinical picture of the hyperandrogenia was expressed most sharply in this subgroup. The mean value of the hirsutic number was 21,53±0,8. The man-type hair loss on the head was detected in 5 cases. *Acantosis nigricans* of the posterior surface of the neck and under the mammary glands was expressed in 19 cases. The menstruation was disordered predominantly by the type amenorrhea in 42% of cases, by the oligomenorrheal type - in 33% of cases and on the background of the rhythmic

menstruation, the anovulation and lutein phase insufficiency - in 25% of cases.

The mean values of the IRI and the Free T were significantly increased compared to both control and IIb1 groups' data. The IRI  $40,19 \pm 1,65$  Iu/ml ( $P < 0,001$ ;  $P < 0,005$ ), the free T  $8,41 \pm 0,45$  pg/ml ( $P < 0,001$ ;  $P < 0,01$ ).

Thus, the results of the present study have shown that in patients with the same body mass during visceral obesity,

the more is I L/F (when the visceral type obesity is well expressed), the frequently are detected increased values of the IRI and the Free T, and the more prominently and clearly are expressed clinical manifestations of the hyperandrogenia. According to the carried out investigations the positive correlation between insulin and I L/F was revealed ( $r=0,5$ ) as well.

	Group I BMI < 25		Group II BMI > 25		The control group
	Ia I L/F < 0,8	Ib I L/F > 0,8	IIa I L/F < 0,8	IIb I L/F > 0,8	
IRI Iu/ml	$29,42 \pm 1,2$	$33,98 \pm 1,06$	$28,42 \pm 1,07$	$36,50 \pm 1,26$	$10,93 \pm 1,14$
Free T pg/ml	$6,85 \pm 0,57$	$7,56 \pm 1,96$	$7,01 \pm 0,57$	$7,51 \pm 0,32$	$1,36 \pm 0,12$
P <sub>contr</sub> IRI	$P < 0,001$	$P < 0,001$	$P < 0,001$	$P < 0,001$	
P <sub>contr</sub> Free T	$P < 0,001$	$P < 0,001$	$P < 0,001$	$P < 0,001$	
P <sub>Ia-Ib</sub> IRI	$P > 0,05$				
P <sub>Ia-Ib</sub> Free T	$P > 0,2$				
P <sub>IIa-IIb</sub> IRI			$P < 0,001$		
P <sub>IIa-IIb</sub> Free T			$P > 0,20$		

P - statistical significance

**Tab.1** The IRI and Free T secretion indices during the insulinresistant metabolic syndrome in correlation with gynoid and visceral adiposity

	Excess body mass IIb > 0,8		The control group
	IIb I L/F = 0,8 - 0,87	IIb2 I L/F > 0,87	
IRI Iu/ml	$33,0 \pm 1,73$	$40,19 \pm 1,65$	$10,93 \pm 1,14$
Free T pg/ml	$66,6 \pm 0,43$	$8,41 \pm 0,45$	$1,36 \pm 0,12$
P <sub>contr</sub> IRI	$P < 0,01$	$P < 0,001$	
P <sub>contr</sub> Free T	$P < 0,001$	$P < 0,001$	
P <sub>IIa-IIb</sub> IRI	$P < 0,005$		
P <sub>IIa-IIb</sub> Free T	$P < 0,01$		

P - statistical significance

**Tab.2** The IRI and Free T secretion indices during the insulinresistant metabolic syndrome in correlation with increased intensity of visceral adipose tissue.

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## **Гиперандрогения и висцеральное ожирение среди женщин**

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### **Р Е З Ю М Е**

Цель исследования – изучить динамику клинических показателей, уровня ИРИ и Free T при нарастании интенсивности висцерального ожирения при инсулинорезистентном метаболическом синдроме. Обследовано 108 пациенток с поликистозом яичников и 23 практически здоровых женщин в возрасте от 16 до 40 лет. Статистическую обработку полученных результатов проводили вариационным методом с использованием критериев t Стюдента. Результаты исследования показали, что при нарастании висцерального ожирения усиливается гиперинсулинемия, гиперандрогения и обусловленная этими сдвигами клиническая картина.

**КЛЮЧЕВЫЕ СЛОВА:** поликистоз яичников, метаболический синдром, инсулинорезистентность, висцеральное ожирение, гиперандрогения