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Polycystic Ovary Syndrome and the Relation with 5alpha-Reductase

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Abstract: ***Introduction: The Polycystic ovary syndrome (PCOS) is generally characterized by the presence of polycystic ovaries, hyperandrogenism, by clinical and / or biochemical androgen excess. 5α-reductase activity might be important during the development of PCOS by increasing the conversion of testosterone (TT) to dihydrotestosterone (DHT). Methods: In 70 cases diagnosed as PCOS, based on Rotterdam criteria we measured the serum levels of luteinizing hormone (LH), follicle stimulating hormone (FSH), total testosterone (TT) and DHT . TT/DHT ratio was calculated in order to reflect 5alpha-reductase activity. Results: In 70 cases of PCOS patients we measured the level of TT (0.87±0.79) (ng/ml), DHT (29.9±11.8)(ng/dl), FSH (5.7±2.06)(UI/L), LH (12.7±10.2)(UI/L). We calculate LH/FSH ratio (2.3±1.2) and TT/DHT ratio (3.1±1.7). PCOS patients showed significantly higher levels of TT than control group. The TT/DHT ratio was significantly higher in PCOS patients (P <.005). No difference was found for total DHT levels. Conclusion: Testosterone, LH, LH/FSH ratio, TT/DHT ratio raised in women with PCOS .Our data show that PCOS is a condition accompanied by high level of TT and a higher TT/DHT ratio in serum of patients , Increased 5alpha-reductase activity could contribute to the development of PCOS by amplifying androgen action.***

Keywords: DHT, TT, 5alpha-reductase activity, PCOS

1. Introduction

Polycystic ovary syndrome is one of the most common endocrine pathologies in fertile women. PCOS is an endocrine disorder characterized by disorders of the reproductive and metabolic systems that include hyperandrogenism, ovarian dysfunction and morphological changes in the ovaries (cysts) and other clinical and biochemical symptoms such as hirsutism, hyperinsulinemi, hyperprolactimeni. It is estimated that this pathology affects 4-12% of women of childbearing age.

This pathology is characterized by a lack of follicular maturation and stromal hyperplasia accompanied by hypersecretion of androgens. This production is assessed by high-dose LH dosing.

This pathology may appear in the form of Stein-Leventhal syndrome (OPK type I) or in the form of macrofollicular dystrophy (OPK type II).

- Stein-Leventhal syndrome (OPK type I) is clinically associated with primary oligomenorrhea, overweight, ovaries are large with painless microfollicles.

In the hormonal context we notice anomaly of gonadotropin secretion hypersecretion of LH and FSH insufficiency characterized by an LH / FSH ratio> 2.Testosterone and androstenedione are in increased values.In the ultrasound of microcervical ovaries.

- OPK type II is characterized by secondary oligomenorrhea. The ovaries are large, painful, varying in size from one cycle to the next.

In the hormonal context we notice an increase in androgens and LH disorders, FSH less sensitive than in the case of OPK type I.

The most common causes are overweight, hyperthyroidism, hyperprolactinemia, insulin resistance or iatrogenic causes. The diagnosis of polycystic ovary is made on the basis of Rotterdam criteria which include the following criteria:
1) oligo- or anovulation,
2) Clinical and / or biochemical signs of hyperandrogenism
3) Polycystic ovary (more than 12 cysts)

In a woman with PCOS we have high levels of FSH and LH which stimulate the production of androgens by the ovaries. This is accompanied by increased production of total testosterone which through 5 alpha reductase is converted to dehydrotestosterone (DHT) responsible for the morphological and functional changes of the ovaries and as metabolic disorders of the organism. The activity of 5 alpha reductase plays a key role in the formation of DHT which has a higher affinity for androgenic receptors in the periphery and is responsible for secondary androgenic sexual clinical signs such as hirsutism, morphological and functional changes of the ovaries and metabolic disorders. Therefore, total serum levels of Testosterone (TT), DHT, and evaluation of 5 alpha reductase activity through the TT / DHT ratio are considered diagnostic indicators for androgenic activity responsible for biochemical, clinical disorders in PCOS.

Assessment of the hyperandrogenic state by assessing the level of androgenic hormones as well as increased activity of 5 alpha reductase that accompanies hormonal imbalance with increasing DHT effect in the periphery is accused of causing the pathogenesis of PCOS and hirsutism.

2. Material and Methods

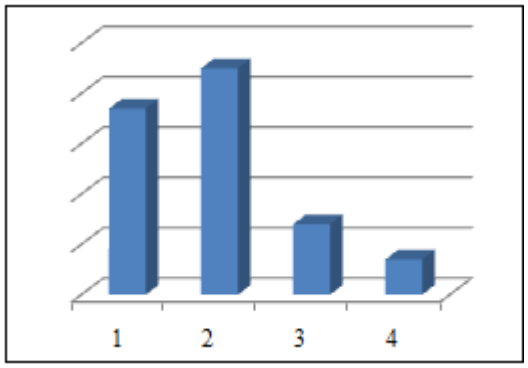
The study included 70 cases of fertile women, aged 16-40 years, diagnosed with polycystic ovaries, according to Rotterdam criteria, accompanied by clinical, biochemical and hormonal examinations that included examinations with ovarian echo, weight, biochemical examinations (glycemia,

cholesterol, triglycerid and hormonal examinations involving FSH, LH, estradiol, prolactin, insulin, Testosterone, dehydrotestosterone, as well as the TT / DHT ratio for evaluating the activity of 5α reductase.

The study also included 30 cases of control of women of childbearing age, clinically and metabolically normal.

3. Results

Based on the collected data, the distribution of the polycystic ovary according to age groups is presented in the graph below where the largest percentage is occupied by the age of 20-30 years:

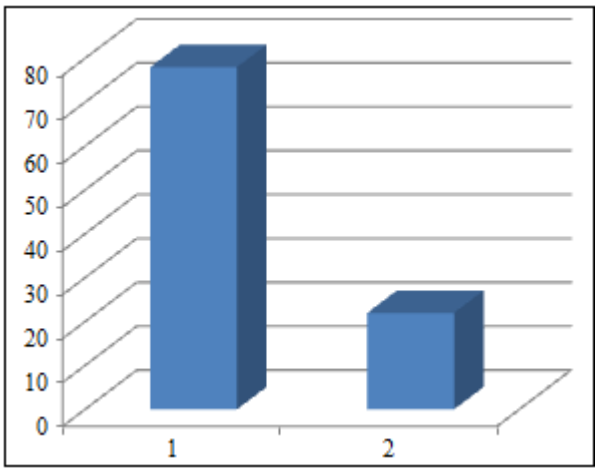


Graph 1: PCOS distribution by age: 16-20 years old 37%, 21-30 years old 45%, 31-35 years old 14%, 35-40 years old 7%

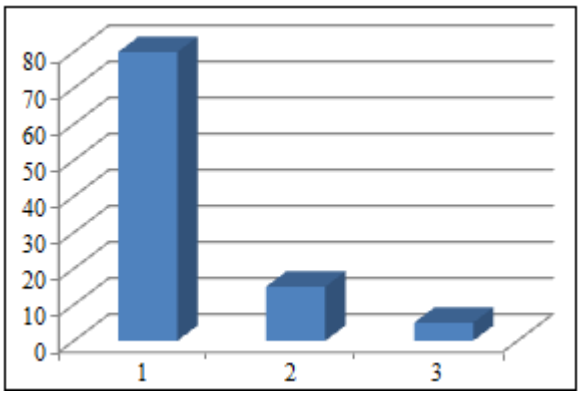
The distribution of clinical manifestations was observed in patients with PCOS presented in Table No. 1.

Clinical manifestations	No of case	%
Manifestations of hyperandrogenism		
Hirsutism	52	78
Manifestations of ovarian dysfunction		
Oligomenorrhea	56	80
Amenorrhe	11	15
Normal cycle	3	5
PCOS in Echo	62	89
Obesitet	38	54

Clinical manifestations in polycystic ovary



Graph 2: Presence of hirsutism in patients with PCOS



Graph 3: Manifestations of ovarian dysfunction

Biochemical manifestations in patients with polycystic ovaries are shown in Table 2

Table 2

	Group		
	PCOS	Controll	P value
Glucose	90.2±1.8	87.1±1.4	0.5
TG (mg/dL)	140.6±70	140±35	0.6
COL (mg/dL)	185±33	1190±45	0.6
HDL (mg/dL)	43.3±7.2	43±5.3	0.8
LDL (mg/dL)	115±24	120±27	0.5

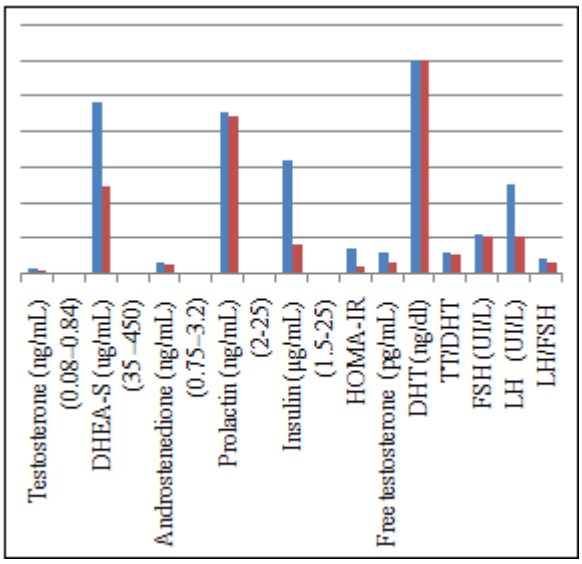
In this case, no significant association was observed between the control group and patients with polycystic ovaries.

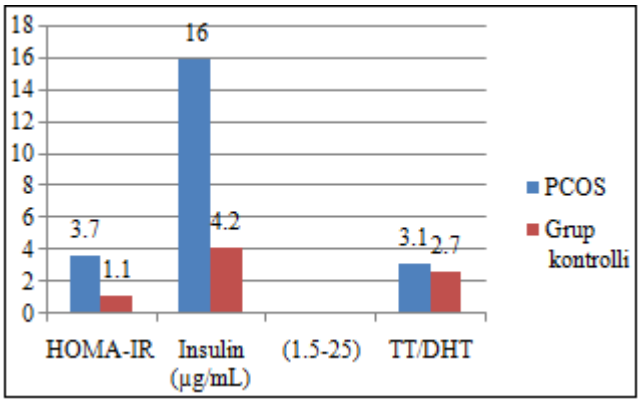
Hormonal manifestations in patients with polycystic ovaries appear in Table No.3.

Table 3

	Group		
	PCOS	Controll	P value
Testosterone (ng/mL) (0.08–0.84)	0.87±0.89	0.62±0.08	0.7
DHEA-S (ug/mL) (35 –450)	259 ±110	124 ±131	0.001*
Androstenedione (ng/mL) (0.75–3.2)	1.7±0.4	1.5±0.4	0.3
Prolactin (ng/mL) (2-25)	22.8±12	22.1±2.2	0.7
Insulin (µg/mL) (1.5-25)	2±12.7	18.4±2.8	0.001
HOMA-IR	3.7±3.3	1.1±0.9	0.001
Free testosterone (pg/mL)	3.2±0.1	1.6±0.1	0.05
DHT (ng/dl)	29.9±11.8	30±10	0.7
TT/DHT	3.1±1.7	2.7±1.3	0.05
FSH (UI/L)	5.7±2.06	5.3±1.6	0.51
LH (UI/L)	12.7±10.2	5.37±1.4	0.4
LH/FSH	2.3±1.2	1.6±1.2	0.001

In this case a significant association was observed between the control group and Patients with PCOS in the case of insulin ($p < 0.001$), HOMA-IR ($P < 0.001$). In the case of androgens, a significant relationship was observed in the case of the TT / DHT ratio ($P < 0.01$) Free Testosterone ($P < 0.05$) as well as the LH / FSH ratio ($p < 0.001$).





The relationship between TT / DHT ratio, HOMA-IR, insulin between PCOS patients and the control group

4. Conclusion

This study aims to show the relationship that exists between the TT / DHT ratio and the polycystic ovary as well as the anthropometric, metabolic and hormonal changes that occur in it.

PCOS is a complex disease but hyperandrogenism is one of its key factors. However, high androgen values are found in women who do not have PCOS, so hyperandrogenism alone should not be taken as a determinant of PCOS. Total testosterone is considered to be the main marker for the growth of androgens in PCOS since it is produced directly by the ovaries or by its direct precursors in tissues.

Testosterone itself is converted to DHT by 5 α reductase, so the TT / DHT ratio assesses the activity of this enzyme in PCOS.

In patients with PCOS, an increase in TT / DHT ratio was observed and correlation of this ratio with other hormonal and metabolic parameters was observed.

In patients with PCOS alone, an increase in TT / DHT was observed in obese patients (BMI> 30).

A decrease in DHT levels was also observed in obese patients. From here we estimate that an increase in TT / DHT can serve as a risk for metabolic syndrome in patients with PCOS.

The increase in TT / DHT has a positive correlation with glucose metabolism because a significant statistical relationship was observed between glucose intolerance, insulin resistance, HOMA and other metabolic factors such as triglycerides, cholesterol, From here we conclude that the TT / DHT ratio can serve as an indicator of the risk of metabolic syndrome and insulin resistance in PCOS patients.

References

[1] J Münzker [1], D Hofer, C Trummer, M Ulbing, A Harger, T Pieber, L Owen, B Keevil, G Brabant, E Lerchbaum, B Obermayer-Pietsch Testosterone to Dihydrotestosterone Ratio as a New Biomarker for an Adverse Metabolic Phenotype in the Polycystic Ovary Syndrome J Clin Endocrinol Metab 2015 Feb;100(2):653-60.