ECRONICON OPEN ACCESS

EC GYNAECOLOGY
Research Article

Lifestyle Changes Impact on Metabolic Risk in Women with PCOS

Andreea Borlea[1], Laura Cotoi[1]*, Yousra Annabi[2], Dan Bogdan Navolan[3] and Dana Stoian[4,5]

[1]PhD Student, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania

[2]Medical Student, "Victor Babes" University of Medicine and Pharmacy Timisoara, Romania

[3]Department of Obstetrics-Gynecology, "Victor Babes" University of Medicine and Pharmacy Timisoara, Romania

[4]Discipline of Endocrinology, 2nd Department of Internal Medicine, "Victor Babes" University of Medicine and Pharmacy Timisoara, Romania

[5]Dr. D Medical Center for Endocrinology, Timisoara, Romania

***Corresponding Author:** Laura Cotoi, PhD Student, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania.

Received: September 07, 2019; **Published:** September 23, 2019

Abstract

Polycystic ovary syndrome (PCOS) is a frequently diagnosed endocrinopathy among women in childbearing age, characterized by androgen excess, polycystic ovaries and ovulatory dysfunction. Women with PCOS are at greater risk of developing long-term metabolic complications, infertility and cardiovascular disease. Excess body weight exacerbates PCOS features and narrows treatment efficacy. Lifestyle modifications involving behavioural interventions and weight management aim to alleviate the severity of the syndrome.

The study aimed to detect clinical and hormonal parameters improvement in PCOS patients after sustained long-standing intervention to reduce weight and to observe the correlations between these parameters.

Initially, 148 women known with PCOS in the age group 16 - 40 years old were included in the study, of which 47 entered and followed the program and 101 were controls. Clinical and biochemical evaluation was performed initially and at 6 and 12 months after entering the program. Weight loss was noted in the study group, along with reduced degree of hirsutism and the hormonal parameters such as testosterone, LH:FSH ratio. Significant positive correlations were seen between weight and LH:FSH and testosteone, between BMI and LH:FSH ratio and testosterone, and between FG score and LH:FSH ratio, testosterone, DHEAS and 17 OH-progesterone.

In conclusion, sustained weight loss did help develop notable changes in the clinical and hormonal profiles of women with PCOS. This entails that lifestyle intervention implying weight loss could play a major role in alleviating the features of the syndrome and restoring the reproductive function. The study of an optimal diet and exercise plan for PCOS patients could be of interest for future applications.

Keywords: *Weight Loss; Lifestyle; Obesity; Hyperandrogenism*

Abbreviations

DM: Diabetes Mellitus; IR: Insulin Resistance; MetS: Metabolic Syndrome; HA: Hyperandrogenism; OCPs: Oral Contraceptive Pills; OA: Oligomenorrhea; PCOM: Polycystic Ovary Morphology; PCOS: Polycystic Ovary Syndrome

Introduction

Polycystic ovary syndrome (PCOS) is a complex disorder affecting women in fertile age, defined by androgen excess and ovarian dysfunction [1].

The etiology of the syndrome is still ambiguous. Its diverse implications involve insulin resistance (IR) up to type 2 diabetes mellitus (DM), increased cardiovascular risk, reproductive and psychological features. It is a heterogeneous syndrome generating different phenotypes, depending on individual and environmental factors, with a notable familial aggregation [2,3].

Obesity is becoming a leading worldwide public health issue. PCOS has a particular connection with the growing prevalence of obesity-related insulin resistance, as obesity does not cause but it worsens PCOS characteristics while PCOS patients are more susceptible to be overweight. Compared to women with PCOS and normal weight, the obese category tends to associate a more severe ovarian dysfunction and difficulty for conception, even a 5% weight loss has proven to help recover normal menses and ovulation [2-5].

High levels of steroid hormones reinforce obesity. Increased estrogens arise not only from ovaries, but also visceral and subcutaneous adipose tissue and excess androgen production serves as substrates for non-ovarian aromatization, resulting in a vicious cycle of hyperestrogenemia-hyperandrogenemia in obese PCOS women [6,7].

Metabolic syndrome (MetS) has a higher prevalence in PCOS women compared to general population, insulin resistance being often greater than expected based on the amount of adipose tissue. About 33% of adolescent girls and up to 50% of adult women with PCOS associate MetS. IR and hyperinsulinism are important contributors to ovarian alterations [8,9].

PCOS treatment targets weight loss, normalizing hormonal parameters and reproductive disturbances, psychological aspects and long-term metabolic complications prevention. Lifestyle changes represent first-line approach for PCOS patients that are overweight, but which type of diet is better for these cases is still debatable. For most cases pharmacological intervention is needed. Oral contraceptive pills (OCPs) are used with success in women with hyperandrogenism (HA) and oligomenorrhea (OA), metformin is recommended for patients that associate metabolic disease, inositols may ameliorate HA and metabolic features of PCOS and Letrozole is used as first-line treatment to achieve fertility [2,5,10-13].

Materials and Methods

The study aims to evaluate how sustained lifestyle intervention influences the evolution of PCOS parameters and which patients benefited most from the program. It intends to analyse changes of clinical (BMI, FG score) and biochemical parameters (hormonal values) in patients with PCOS at baseline, detecting possible changes after lifestyle intervention, consisting of sustained weight loss, at 6 and 12 months.

The prospective study included 148 women in the reproductive age group, between 16 - 40 years old, the recruitment period starting January 2015 in Dr. D Medical Center, Timisoara. Inclusion criteria were represented by confirmed PCOS cases, with the exclusion of other causes of HA, or the use of OCPs in the past year, patients willing to be evaluated and to enter the lifestyle modification program, encompassing consistent physical activity and healthy eating. Forty-seven patients entered the program and have been compliant to it. The control group comprised 101 cases that did not enroll for the program or did drop out during the 12 months follow up.

All participants gave written informed consent and the study was approved by our ethics committee.

Initial clinical evaluation included hirsutism assessment using the Ferriman Gallwey score (0-36), weight, height, BMI and months of amenorrhea. Hormonal measurements comprised FSH, LH, LH:FSH ratio, total testosterone, free testosterone, DHEA-S, 17-OH progester-

one. Transvaginal ultrasound was performed for each patient at the time of inclusion, polycystic ovaries morphology (PCOM) was defined as ≥ 12 follicles per ovary, peripherally arranged and/or ovarian volume ≥ 10 cm^3. PCOS diagnosis was confirmed based on the ESHRE/ASRM Rotterdam criteria: minimum two out of the three: OA/ovulatory dysfunction (OD), clinical or biochemical evidence of HA and PCOM [11].

Statistical analysis

The statistical analysis was performed using SPSS, data was expressed as mean and standard deviation. The parameters for the study group and the controls were compared using the unpaired t-test. To compare the parameters at three different times (baseline, 6 months and 12 months after intervention), the paired t-test was used. A threshold value for probability (p) < 0.05 (5%) was considered to be statistically significant as in to reject the null hypothesis. Pearson's r was calculated to measure the linear interdependence between clinical and hormonal parameters initially, at 6 and 12 months after entering the program [14].

Results

Out of the total of 148 patients on whom the study was conducted, 47 PCOS patients followed the weight-loss program and were considered the study group; the 101 remaining patients were considered controls. How hormonal parameters for the study group changed after 6 and 12 moths respectively after starting the program is presented in table 1 and 2 and figure 1.

After entering the program to reduce their weight, the evolution of the 47 patients was with significant changes in their clinical and hormonal parameters at 6 and 12 months respectively, as presented below. Initially the mean weight was 83.65 ± 16.54, significantly lower at 6 months 75.98 ± 16.24 and at 12 months 71.31 ± 15.72. Initially the mean BMI was 30.85 ± 5.29 kg/m^2, going down to 28.1 ±

Parameters	Initial	6 months	p (two-tailed)
Weight (kg)	83.65 ± 16.54	75.98 ± 16.24	< 0.0001
BMI (kg/m^2)	30.85 ± 5.287	28.1 ± 5.280	< 0.0001
FG score	12.02 ± 3.103	11 ± 2.484	< 0.0001
LH:FSH ratio	2.27 ± 0.419	1.85 ± 0.238	< 0.0001
Testosterone (mUI/ml)	0.0415 ± 0.0037	0.0116 ± 0.0033	< 0.0001
DHEAS (mg/dl)	408.7 ± 60.348	386.8 ± 54.784	< 0.0001

Table 1: *Clinical and hormonal parameter evolution of the study group initially and at 6 months after intervention.*

Parameters	Initial	12 months	p (two-tailed)
Weight (kg)	83.65 ± 16.54	71.31 ± 15.72	< 0.0001
BMI (kg/m^2)	30.85 ± 5.287	26.38 ± 5.178	< 0.0001
FG score	12.02 ± 3.103	9.95 ± 1.910	< 0.0001
LH:FSH ratio	2.27 ± 0.419	1.69 ± 0.212	< 0.0001
Testosterone (mUI/ml)	0.0415 ± 0.0037	0.0238 ± 0.1590	< 0.0001
DHEAS (mg/dl)	408.7 ± 60.348	379.12 ± 46.556	< 0.0001
17 OH-progesterone (ng/ml)	2.12 ± 0.752	1.81 ± 0.379	< 0.0001

Table 2: *Clinical and hormonal parameter evolution of the study group initially versus at 12 months.*

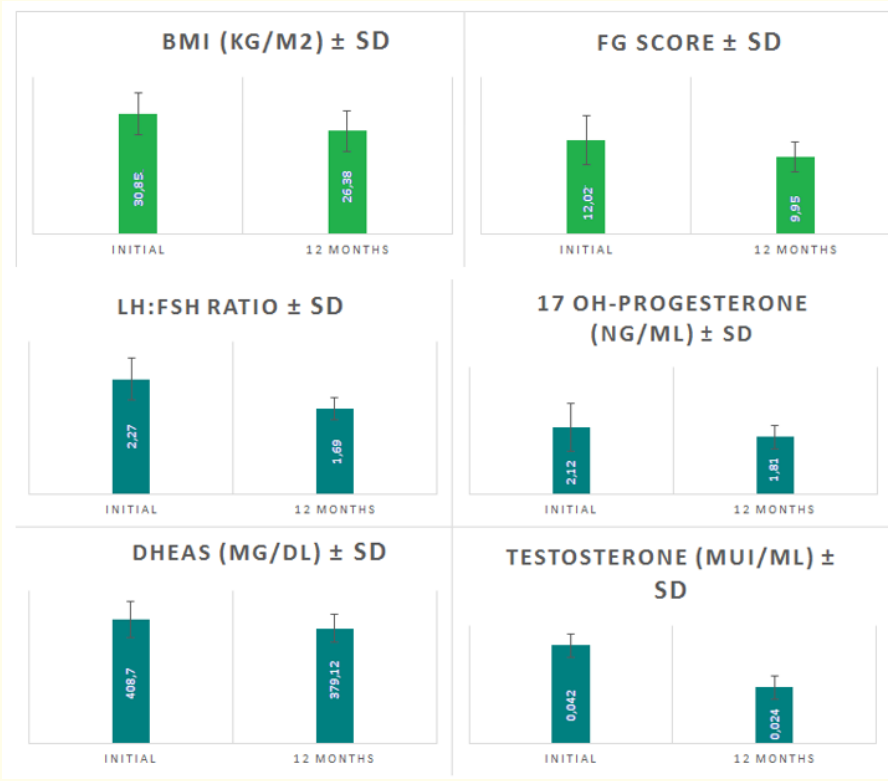

Figure 1: *Graphic representation of parameter evolution of the study group initially versus at 12 months.*

5.28 kg/m^2 at 6 months and 26.38 ± 5.18 kg/m^2 at 12 months. The mean FG score also improved from 12.02 ± 3.1 at baseline to 11 ± 2.48 at 6 months and 9.95 ± 1.91at 12 months.

Hormonal parameters also showed significant improvements. The initial mean LH:FSH ratio initially was 2.27 ± 0.42 going down at 6 months to 1.85 ± 0.23 and continuing to decrease at a slower pace until at 1.69 ± 0.21 at 12 months post-intervention. Testosterone was 0.014 ± 0.0037 initially, then lowering to a mean of 0.011 ± 0.0033 at 6 months and 0.023 ± 0.16 at 12 months. Initially the mean DHEAS value was 408.7 ± 60.35, at 6 months 386.8 ± 54.78 and at 12 months it was 379.12 ± 46.56. OH-progesterone went from a baseline 2.12 ± 0.75 down to 1.81 ± 0.38 after 12 months of lifestyle modifications.

The comparison between the clinical and hormonal parameters of the study group at 6 and 12 months and those of the controls using the Student's t-test is presented below in table 3. For FG score, LH:FSH ratio, testosterone levels and DHEAS statistically significant changes were noted at 6 months. All parameters continued to improve at 12 months and statistically significant changes were found when comparing the two groups, except for testosterone.

Pearson's correlation coefficient was calculated to see the correlation between clinical and hormonal parameters in the study group initially, at 6 and at 12 months respectively and numbers are presented in figure 2. Positive correlations were seen between weight and

Parameters	Initial vs. 6 months		Initial vs. 12 months	
	p (two-tailed)	Std. Error Difference	p (two-tailed)	Std. Error Difference
Weight	0.1696	2.635	0.0018	2.604
BMI	0.3542	0.907	0.0051	0.901
FG score	< 0.0001	0.356	< 0.0001	0.320
LH:FSH ratio	< 0.0001	0.050	< 0.0001	0.048
Testosterone	< 0.0001	0.001	0.1105	0.001
DHEAS	< 0.0001	9.646	< 0.0001	9.211
17 OH-Progesterone	-	-	0.0007	0.063

Table 3: *T-Test results for 12 months parameters of the study group vs. the control group parameters.*

LH:FSH ratio (r = 0.306, p = 0.0344), between weight and testosterone (r = 0.283, p = 0.0509), BMI and LH:FSH ratio (r = 0.287, p = 0.0050), BMI and Testosterone (r = 0.319, p = 0.0017), FG score and testosterone (r = 0.003, p = 0.9732), FG score and DHEAS (r = 0.380, p = 0.0002), FG score and LH:FSH ratio (r = 0.511, p = 0.0001), FG score and OH-Progesterone (0.230, p = 0.0254).

Discussions

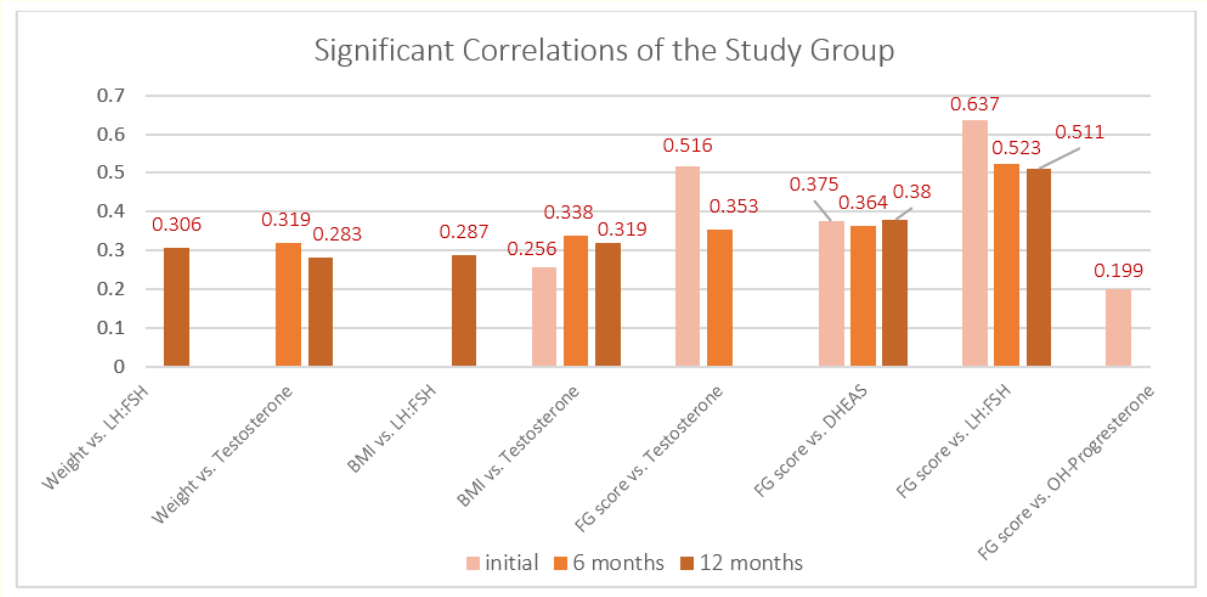

Figure 2: *Graphic representation of correlations that have been found statistically significant in the study group.*

Excess body weight in PCOS patients aggravates clinical symptoms and hormonal disturbances and treatment outcomes are poorer in this case even with pharmaceutical intervention. A weight reduction program was implemented in PCOS patients in this study and possible clinical and hormonal changes were observed.

Clinical and hormonal parameters of the 148 women included in the study were evaluated. Out of 101 controls, 27 (26.73%) women were normal weight, 35 (34.65%) were overweight, 27 (26.73%) were obese class I, 9 (8.9%) were obese class II and 3 (2.97%) were obese class III. Regarding the FG score in the controls, 94 (93.06%) had a normal score for hirsutism, while 7 (6.93%) women had mild hirsutism. The LH:FSH ratio was around 1.1 in 33 (32.67%) women with the rest being 68 (67.63%) women had higher values. The values of DHEAS depend on the age as the following: 75% of 8 girls aged 15-19 years, 8.33% of 12 women aged 20-24 years, 17.65% of 51 women aged 25-34 years, 10% of 30 women aged 35-44years had higher values than normal of DHEAS. Concerning the 17 OH-Progesterone hormone 68.32% had high values.

Regarding the study group (47 cases), distribution was as following: 6 (12.76%) women had normal weight, 16 (34.04%) were overweight, 15 (31.91%) were obese class I, 8 (17.02%) were obese class II and 2 (4.25%) were obese class III. As to the FG score, 8 (17.02 %) women had no hirsutism while 38 (80.85%) had mild hirsutism and only 1 (2.13%) had moderate hirsutism. The LH:FSH ratio was around 1.1 in only 3 (6.38%) women while the rest which is 44 (93.61%) women had higher values. Regarding the DHEAS values depend on age; 100% of 3 girls aged 15-19 years, 74% of 6 women age group 20 - 24, 93.33% of the 30 women age group 25 - 34 and 66.66% out of the 6 women aged 35 - 44 years had higher DHEAS values than normal. 85.10% of women had high values of 17 OH-Progesterone.

In the group that entered and completed the weight reduction program (47 cases), we noticed that the normal weight group increased to 14 (29.79%) patients after 6 months and to 18 (38.40%) patients after 12 months. Still, the number of overweight women changed just slightly at 6 months, coming back around the initial value at 12 months. The obesity group went through some impressive changes as follows: women with class I obesity went down to 11 (23.40%) after 6 months and to 9 (19.15%) after 12 months, class II obesity group dropped to 3 (6.38%) women after 6 months and remained so at 12 months, while there were no class III obese at 12 months. Worth mentioning that after 12 months, 1 (2.13%) woman became underweight. To summarize, the initially 53.19% obese group decreased at 12 months to 25.53%, which shows the study intervention remarkable effectiveness in reducing the weight in the study group. This may be partially explained by the patients' wish to conceive or the wish to increase their self-esteem by obtaining a better body image.

Most of the studies on lifestyle intervention in PCOS patients proved similar results. The 2018 ESHRE/ASRM Evidence-Based International Guideline supports healthy lifestyle behaviors, as they are recommended for all PCOS patients in order to improve all syndrome parameters. Recent research also suggests that weight reduction from the first 2 months is a good indicator for good outcomes at 1 year of lifestyle changes, but results may not come so easily for these patients, given associated insulin resistance and lazy metabolism. One trial by Moran., *et al*. tried to evaluate impact of energy-restricted diet together with physical activity in 28 PCOS patients with obesity during 12 weeks; they achieved a 7.5% average weight loss and fertility improved. Huber., *et al*. demonstrated that implementing a healthy lifestyle that does not lead to rapid weight reduction, but to a rather slow decrease of abdominal obesity will improve insulin resistance and with it restore ovulation and fertility [11,15-17].

FG score in our study group diminished and at 6 months there were no cases of moderate hirsutism, but a little increase in the mild hirsutism category to 82.97%. Testosterone, LH:FSH ratio, DHEAS and 17-OH progesterone levels decreased in all cases. When the two groups were compared, initial weight of the study group vs. initial weight of controls ($p = 0.1302$) and 6 months vs. controls ($p = 0.1696$) were not statistically significant, however the weight at 12 months vs. controls ($p = 0.0018$) was considered to be statistically very significant. Initial BMI of study groups vs. controls BMI ($p = 0.0492$) was considered to be statistically significant, 12 months BMI of study group vs. controls BMI ($p = 0.0051$). The rest of the results were all considered statistically significant ($p < 0.0001$) except for BMI at 6 months vs. controls ($p = 0.3542$) and Testosterone at 12 months vs. controls ($p = 0.1105$).

When comparing parameter values for study group initially and at a period of 6 and 12 months, all of them were extremely significant ($p < 0.0001$), DHEAS at 6 months vs. DHEAS at 12 months ($p = 0.0026$) was considered to be very statistically significant. These important

results for FG score correlate with a study done by Kiddy., *et al*. that concludes that >5% weight loss results in a 40% reduction of hirsutism. Linderbaum similarly suggested that weight reduction in obese PCOS patients ameliorated some hyperandrogenic symptoms such as hirsutism and acne [18,19].

Pearson's correlation coefficient was used to examine the strength and the direction of the linear relationship between weight and LH:FSH ratio, weight and testosterone, BMI and LH:FSH ratio, BMI and testosterone, FG score and all the hormones evaluated, initially, at 6 and 12 months. A weak uphill (positive) relationship and correlation was found statistically significant between BMI and testosterone initially ($r = 0.0256$, $p = 0.0126$) and between FG score and 17 OH-Progesterone at 12 months ($r = 0.230$, $p = 0.0254$), very statistically significant between BMI and LH:FSH ratio at 12 months ($r = 0.287$, $p = 0.0050$). A moderate uphill (positive) relationship and correlation was found statistically significant between weight and LH:FSH ratio at 12 months ($r = 0.306$, $p = 0.0344$) and between weight and testosterone at 6 months ($r = 0.319$, $p = 0.0271$), very statistically significant between BMI and testosterone at 12 months ($r = 0.319$, $p = 0.0017$) and extremely statistically significant between BMI and testosterone at 6 months ($r = 0.338$, $p = 0.0008$), between FG score and testosterone at 6 months ($r = 0.353$, $p = 0.00050$), between FG score and DHEAS initially ($r = 0.375$, $p = 0.0002$), between FG score and DHEAS at 6 months ($r = 0.364$, $p = 0.0003$), between FG score and DHEAS at 12 months ($r = 0.380$, $p = 0.0002$), between FG score and testosterone initially ($r = 0.516$, $p < 0.0001$), between FG score and LH:FSH ratio initially ($r = 0.637$, $p < 0.0001$), between FG score and LH:FSH ratio at 6 months ($r = 0.523$, $p < 0.0001$), and between FG score and LH:FSH ratio at 12 months ($r = 0.511$, $p < 0.0001$).

Our correlations concord with Pasquali., *et al*. findings, who found that 5 - 10% of initial weight loss was likely to reverse the PCOS hormonal disturbances with the improvement of menstrual pattern, fertility and pregnancy rates, insulin resistance and androgen levels. Likewise Escobar-Moreale., *et al*. found supporting evidence in morbidly obese PCOS women, weight loss correlates with a decrease in the degree of hirsutism, testosterone levels, which resulted in improvement of insulin resistance and restoration of ovulatory cycle [20-22].

Limitations of the current study were mainly represented by the high dropout rates from the weight reduction program, resulting in a smaller group of study than initially anticipated and an exact fertility assessment has not been made. One study strength was given by the different severities of excess weight of women who were included, as well as the length of the study program.

Conclusion

To conclude, the overall significant data obtained in this study indicated that sustained weight loss promoted by lifestyle intervention in PCOS women developed notable changes on their clinical and hormonal profiles. To be more precise, a lower LH:FSH ratio and testosterone values were associated with weight loss and reduced BMI. Furthermore, reduction of LH:FSH ratio and testosterone levels were particularly associated with a lower degree of hirsutism. These findings may allow us to presume that weight loss is associated with a lower hirsutism degree. Also, an association between decreased DHEAS and improvement in hirsutism degree was noted but to a lesser degree. Lower 17 OH-progesterone poorly correlated with the degree of hirsutism. This entails that lifestyle changes and weight reduction play a major role in alleviating the major syndrome characteristics: insulin resistance, hirsutism, ovulatory dysfunction, with an important role in restoring fertility. Future research should focus on establishing ideal dietary plans and individualized lifestyle strategies for the increasing number of PCOS patients.

Bibliography

1. Escobar-Morreale and Héctor F. "Polycystic Ovary Syndrome: Definition, Aetiology, Diagnosis and Treatment". *Nature Reviews Endocrinology* 14.5 (2018): 270-284.

2. Teede H., *et al*. "Polycystic Ovary Syndrome: A Complex Condition with Psychological, Reproductive and Metabolic Manifestations That Impacts on Health across the Lifespan". *BMC Medicine* 8 (2010): 41.

3. Naderpoor N., *et al*. "Obesity and Polycystic Ovary Syndrome". *Minerva Endocrinologica* 40.1 (2015): 37-51.

4. Badawy Ahmed and Abubaker Elnashar. "Treatment Options for Polycystic Ovary Syndrome". *International Journal of Women's Health* 3 (2011): 35-45.

5. LJ Moran., *et al*. "Lifestyle Changes in Women with Polycystic Ovary Syndrome". *Cochrane Database of Systematic Reviews* 2 (2011): CD007506.

6. Dumitrescu R., *et al*. "The Polycystic Ovary Syndrome: An Update on Metabolic and Hormonal Mechanisms". *Journal of Medicine and Life* 8.2 (2015): 142-145.

7. Rojas Joselyn., *et al*. "Polycystic Ovary Syndrome, Insulin Resistance, and Obesity: Navigating the Pathophysiologic Labyrinth". *International Journal of Reproductive Medicine* (2014): 719050.

8. Yao Kui., *et al*. "Association of Polycystic Ovary Syndrome with Metabolic Syndrome and Gestational Diabetes: Aggravated Complication of Pregnancy". *Experimental and Therapeutic Medicine* 14.2 (2017): 1271-1276.

9. HJ Teede., *et al*. "Recommendations from the International Evidence-Based Guideline for the Assessment and Management of Polycystic Ovary Syndrome". *Human Reproduction* 33.9 (2018): 1602-1618.

10. Bajuk Studen Katica., *et al*. "Cardiovascular Risk and Subclinical Cardiovascular Disease in Polycystic Ovary Syndrome". *Frontiers of Hormone Research* 40 (2013): 64-82.

11. Teede Helena., *et al*. "International Evidence-Based Guideline for the Assessment and Management of Polycystic Ovary Syndrome 2018". National Health and Medical Research Council (NHMRC) (2018).

12. Sm Sirmans and Pate Ka. "Epidemiology, Diagnosis, and Management of Polycystic Ovary Syndrome". *Clinical Epidemiology* 6 (2014): 1-13.

13. Bednarska Sylwia and Agnieszka Siejka. "The Pathogenesis and Treatment of Polycystic Ovary Syndrome: What's New?" *Advances in Clinical and Experimental Medicine* 26.2 (2017): 359-367.

14. Kissling Grace E. "Statistical Methods". The Clinical Chemistry of Laboratory Animals, Third Edition (2017).

15. Unick Jessica L., *et al*. "Evaluation of Early Weight Loss Thresholds for Identifying Nonresponders to an Intensive Lifestyle Intervention". *Obesity (Silver Spring, Md.)* 22.7 (2014): 1608-1616.

16. Moran LJ., *et al*. "Dietary Composition in Restoring Reproductive and Metabolic Physiology in Overweight Women with Polycystic Ovary Syndrome". *The Journal of Clinical Endocrinology and Metabolism* 88.2 (2003): 812-819.

17. Huber-Buchholz MM., *et al*. "Restoration of Reproductive Potential by Lifestyle Modification in Obese Polycystic Ovary Syndrome: Role of Insulin Sensitivity and Luteinizing Hormone". *The Journal of Clinical Endocrinology and Metabolism* 84.4 (1999): 1470-1474.

18. Kiddy DS., *et al*. "Improvement in Endocrine and Ovarian Function during Dietary Treatment of Obese Women with Polycystic Ovary Syndrome". *Clinical Endocrinology* 36.1 (1992): 105-111.

19. Lindenbaum Cheryl. "Polycystic Ovarian Syndrome. Where Genetics and Environment Collide". *Advance for Nurse Practitioners* 18.2 (2010): 20-27.

20. Pasquali Renato., *et al*. "PCOS Forum: Research in Polycystic Ovary Syndrome Today and Tomorrow". *Clinical Endocrinology* 74.4 (2011): 424-433.

21. Pasquali Renato Carla Pelusi., *et al*. "Obesity and Reproductive Disorders in Women". *Human Reproduction Update* 9.4 (2003): 359-372.

22. Escobar-Morreale Hector F., *et al*. "The Polycystic Ovary Syndrome Associated with Morbid Obesity May Resolve after Weight Loss Induced by Bariatric Surgery". *The Journal of Clinical Endocrinology and Metabolism* 90.12 (2005): 6364-6369.

Volume 8 Issue 10 October 2019