



## RESEARCH PAPER

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## Nutritional and lifestyle modifications of polycystic ovary syndrome (pcos) in obesity

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### Abstract

Polycystic ovary syndrome (PCOS) is an endocrine-metabolic disorder characterized by polycystic ovaries, chronic anovulation and hyper-androgenism leading to signs of menstrual irregularity, infertility and hirsutism. Insulin resistance, obesity and high levels androgens are linked with PCOS. The contributory factors include lazy standards of living, dietary dissimilarities, lack of exercise and anxiety etc. There appears to be an epidemic of both obesity and polycystic ovary syndrome (PCOS) in the world today. Obesity is not a cause of PCOS, as the high prevalence of PCOS among relatively thin populations demonstrate. However, obesity does worsen many aspects of the phenotype, especially cardiovascular risk factors such as glucose intolerance and dyslipidemia. It is also associated with a poor response to infertility treatment and likely an increased risk for pregnancy complications in those women who do conceive. Although most treatments of obesity, with the exception of bariatric surgery, achieve modest reductions in weight and improvements in the PCOS phenotype, encouraging weight loss in the obese patient remains one of the front-line therapies plus life style modification is also very encouraging. However, new studies are required to identify the best interventions, and the role of lifestyle therapies in women of normal weight with PCOS is uncertain.

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## Introduction

Polycystic ovary syndrome is abbreviated as PCOS, is an endocrine disorder associated with hyperandrogenism, ovarian dysfunction and polycystic ovarian morphology. PCOS is characterized by chronic anovulation and include hyperinsulinemia, insulin resistance, type 2 diabetes mellitus, dyslipidemia, CVD, and infertility (Silfen *et al.*, 2003).

National Institute of Child Health Development defined polycystic ovary syndrome as indications of hormonal imbalance in reproductive age of women. PCOS may alter menstrual cycle fluctuations, skin changes such as facial and body hair and acne, tumors in the ovaries, and infertility. The problems in metabolism also occurs (Palomba *et al.*, 2009).

The etiology of PCOS remains unclear. Different physiological changes of puberty and the pathological features of the syndrome have been observed, such as the hyper pulsatile secretions through gonadotropic hormone, increased ovarian and adrenal steroid genesis, menstrual abnormalities, reduced levels of SHBG and IGFBP-1, hyperinsulinemia, and insulin resistance that progress in both conditions (Witchel SF, 2006).

Polycystic ovary syndrome (PCOS) is the most common disorder affecting 10% reproductive aged women. Overweight and have an increased risk of metabolic disorder, type 2 diabetes and cardiovascular disease are more common in these women. Dietary restriction and increased physical activity are some factors that helps in reducing weight for overweight and obese women with PCOS (Azziz R, 2004).

18% of reproductive aged women are affected with PCOS (Mohammad and Seghinsara, 2017). Women suffering with PCOS determine obvious medical heterogeneity; the commonly accompanying features of unwanted hair growth (hirsutism), acne, nodules, overweight, and acanthosis nigricans are not universal (Chen *et al.*, 2006; Chittenden *et al.*, 2009).

Increased BMI is a common feature in women with PCOS. 30–70% PCOS women have increased BMI apart from anovulation and is related with reproductive (hyperandrogenism, menstrual irregularity, anovulation, infertility, and pregnancy complications), metabolic (high risk factors for type 2 diabetes mellitus and CVD disease) and psychological features degraded aspects of life and high incidence of anxiety and depression (Tang *et al.*, 2006; Burchall *et al.*, 2011; Sirmans and Pate, 2014).

The incidence of polycystic ovarian syndrome (PCOS) differs depending upon diagnosis standards, but when different societies of the world including the European Society for Human Reproduction and Embryology\American Society for Reproductive Medicine standards are used is as high as 15-20% (Ali *et al.*, 2018). In Iraq about 69.8% of overweight women with PCOS were noted. Occurrence of PCOS was observed more in younger women  $\leq 35$  years of age than older (Al-Tu'ma *et al.*, 2017).

Elevated level of PCOS was found with obese women 42.28% (with BMI 30 -34.9 kg/m<sup>2</sup>). In this category, obesity and the deviation of lipid profile parameters in women were expressive for the increased risk of developing metabolic significances and cardiovascular diseases (Al-Tu'ma *et al.*, 2017). PCOS administration should focus on dietary interventions, education and required more importance on healthy routine, with targeted medical therapy as required (Stepto *et al.*, 2013). First line therapy for PCOS involves lifestyle interventions, including nutritional education and exercise training in order to prevent the risk of diabetes by supporting weight loss and improved glucose metabolism that helps in stabilization distressing disorders related to the condition of PCOS (Vause *et al.*, 2010).

Obesity and PCOS are interlinked and mostly morbidly overweight women progress this disorder. Study revealed that hyperandrogenemia degrade central obesity and androgen results in visceral fat deposition in women with PCOS (Moran *et al.*, 2010). 35 – 60% of patients of PCOS are noted with

obesity and specifically central obesity (Badawy and Elnashar, 2011). It worsens the reproductive, metabolic and psychological factors linked with insulin resistance (Al-Tu'ma *et al.*, 2017; Thomson *et al.*, 2011). Changes of both synthesis and metabolic clearance rates of sex hormones and reduced serum sex hormone-binding globulins (SHBG) levels are linked with abdominal obesity. Insulin resistance further results in obesity and overweight in women with PCOS. Non-esterified fatty acids released from the muscle in insulin resistance state and adipose tissues provide substrate for triglyceride invention in the liver (Chang *et al.*, 2015). Cravings of carbohydrates are the results of high blood androgens, which is shown by a study indicating high intake of specific glycemic-index foods which includes white bread and potatoes by women with PCOS as compare to healthy women without PCOS (Douglas *et al.*, 2006). A study revealed that there is also twice the risk of metabolic disorder in adult woman with PCOS than general healthy population and its common features like insulin resistance, dyslipidemia, glucose intolerance, central obesity and hypertension are more frequent in PCOS (Coviello *et al.*, 2006; Rautio *et al.*, 2006). Anovulation, miscarriage, or late pregnancy complications such as pre-eclampsia and gestational diabetes are also interlinked with obesity (Rautio *et al.*, 2006).

Many researchers notify that overweight is not only a risk factor of type 2 diabetes, arterial hypertension, cancer, liver and bile duct diseases or osteoarthritis but also worsely effects regulation of menstrual cycle, ovulation and consequently, delays fertility and getting pregnant (Smyka *et al.*, 2017). Due to the various phenotypes of the patients with polycystic ovary syndrome, they suffer from different clinical symptoms and require an individual approach. The treatment based on a change of lifestyle, an appropriate diet and physical activity, is the effective way to overcome overweight, obesity, metabolic and hormonal disturbances as well as ovulation and menstrual cycle disorders (Shi, Y *et al.*, 2007). Nutritional therapy with adequate diet is effective to recover metabolic disorders in obese PCOS women.

High fiber and less trans-fatty acid consumptions are primary predictors of metabolic improvement and weight management (Nybacka *et al.*, 2017). Lifestyle interventions strategies are considered consistently to be a best alternative to drug therapy for overweight women with an ovulatory infertility (Cussons *et al.*, 2005; Pasquali *et al.*, 2011). Various clinicians and recent plans regard lifestyle interventions as the primary treatment in overweight and obese women with PCOS (Moran *et al.*, 2010). Lifestyle modification is regarded as rehabilitation of excellent for both PCOS and metabolic disorder. Weight management in obese PCOS women is associated with a decrease of androgens hormone and normalization of menstrual cycles (Lass *et al.*, 2011).

Minimum 30 minutes adequate physical activity 3-5 days in a week and behavior.

Adaptation strategy is required. A broad lifestyle modification program including modified diet with moderate energy control based on basic healthy eating principles. Hypocaloric diets and carbohydrate modifications have found to be effective. Selection of suitable foods among low glycemic load (GL) and high fiber foods and choosing substitute fats with polyunsaturated fats may be a supportive policy in PCOS patients (Kamran *et al.*, 2017).

Due to the association of obesity and insulin resistance with PCOs, dietary interventions, increased physical exercise and management of weight is suggested as initial intervention for female with PCOS (Rutter *et al.*, 2005; Bates and Legro, 2013).

## Materials and methods

### *Polycystic ovary syndrome (PCOS) and Obesity*

#### *Diagnosis and treatment*

This study was based on the diagnosis and management of polycystic ovary syndrome (PCOS). The results showed that establishing an analysis of PCOS is difficult especially in adolescents and menopausal women. Assessment of PCOS in women should eliminate substitute androgen-excess disorder and risk factors for endometrial cancer, mood

disorders, obstructive sleep apnea, and diabetes especially type 2 diabetes mellitus and CVD's. Hormonal contraceptives and metformin are the two treatment options in adolescents with PCOS. Life style modification is beneficial in overweight and obese patients for various other health benefits (Lliodromiti *et al.*, 2013).

#### *Obesity and PCOS*

This study was conducted on the relation between obesity and PCOS. As the high prevalence of PCOS among relatively thin population establishes so this study obesity is not considered as a cause of PCOS. However, obesity worsen many aspects of the phenotype, especially CVD risk factors such as glucose intolerance and dyslipidemia. It is also linked with a poor response to infertility management and high risk for pregnancy complications in those women who do conceive. Although most interventions and managements of obesity, excluding of bariatric surgery, achieve modest loss in weight and improvements in the PCOS phenotype, cheering weight loss in the obese patient remains one of the most important feature (Legro, 2012).

#### *Association of gene with obesity*

This study was about the large effects on BMI and insulin resistance (IR) of fat mass and obesity linked with gene variations in patients with polycystic ovary syndrome (PCOS). A study was conducted in 386 patients with PCOS. They use single nucleotide polymorphisms in or in proximity to the fat mass and obesity linked gene (FTO). Results of the study revealed that the FTO risk allele was linked with IR traits and measures of increased body weight or obesity. In addition, the TCF7L2 SNP was linked to body weight traits/characteristics (Tan *et al.*, 2010).

#### *Ovarian function and obesity*

This study is based on the functions of ovaries and obesity. Effect on women's reproductive lifespan and treatment strategies were studied. Insulin resistance is a significance of obesity and in women it is often intimately associated with ovarian function leading to clinical reproductive manifestations. The decrease in

estrogen production after menopause may results in weight gain and variations in adipose tissue distribution may occur. This study showed that the reproductive obese women have complications including PCOS, and recognized as specific high-risk subgroups for further advancement through to prediabetes, type 2 diabetes mellitus and potentially CVD disease (Thomson *et al.*, 2010).

#### *Exercise*

Quality of life can be improved through lifestyle management and depression or anxiety in overweight and obese women with PCOS. The purpose of this research was to check the effect of adding exercise to dietary restriction on depressive symptoms and health-associated value of life in women with PCOS. The results indicated that 49 women successfully finished the intervention (14= diet only, 15= diet and aerobic exercise, 20= diet and combined aerobic-resistance exercise). By week 20 all groups were successful in losing weight and showed improvements in depression and PCOS-specific HRQOL scores, excluding body hair domain score (Thomson *et al.*, 2010).

#### *Exercise and Hypocaloric diet*

A six-week research was conducted by Palomba *et al.* The purpose of the research was to enhance the probability of ovulation in overweight and obese patients with polycystic ovary syndrome after clomiphene with controlled exercise teaching and hypocaloric diet. It was a cohort study of 69 CC-resistant PCOS patients that were enrolled in 3 treatments; 32 women were in each Groups A, B and C. The three interventions include in such a way that Group A: hypocaloric diet for 6 weeks, Group B: one cycle of CC therapy for the 2 weeks of observation, Group C: SET plus hypocaloric diet for 6 weeks. No ovarian response was noticed in any of the patients in 3 groups and all patients and protocol was continued. The ovulation rate was significantly ( $P=0.008$ ) higher in Group C [12/32 (37.5%)] than in Groups A [4/32 (12.5%)] and B [3/32 (9.4%)] with relative risks of 3.9 [95% confidence interval (CI) 1.1–8.3;  $P=0.035$ ] and 4.0 (95% CI 1.2–12.8;  $P=0.020$ ) compared with

Groups A and B, respectively after 6 weeks. When it was compared with baseline, in groups A and C, an improvement in clinical and biochemical androgen and insulin sensitivity indexes were noticed. Only 1 patient from group C became pregnant. Multiple follicles were observed in 5 patients. In groups A and C, the insulin sensitivity index was significantly ( $P, 0.05$ ) better than that in Group B (Palomba *et al.*, 2010).

#### *Comparison of Low GI and conventional diet*

This study was based on the impact of a low glycemic index diet compared with a conventional healthy diet on polycystic ovary syndrome. They allotted to consume either an ad libitum low-GI diet or a macronutrient healthy diet to overweight and obese premenopausal women with PCOS for 12 months or until they loss 7% weight. Comparison of changes in whole-body insulin sensitivity changes were observed, and was evaluated by the insulin sensitivity index derived from the oral-glucose-tolerance test. Results concluded that the Attrition value was elevated in both groups (49%). Among completers, ISIOGTT improved more with the low-GI diet than with the conventional healthy diet (mean 6 SEM: 2.2 6 0.7 compared with 0.7 6 0.6, respectively;  $P = 0.03$ ). There was a greater improvement in ISIOGTT due to metformin interaction ( $P = 0.048$ ), in women recommended both metformin and the low-GI diet (Marsh *et al.*, 2010).

#### *Comparison of different diets*

This research was conducted to compare different diets for Polycystic Ovary Syndrome patients. The purpose of the study was to compare the consequence of different diet structures on different parameters including anthropometric, reproductive, metabolic and psychological effects in PCO's. PCO's women not consuming anti-obesity drugs or maintenance diets comparing different dietary compositions were included in inclusive criteria category. In this training, there were delicate alterations between diets, with high weight loss for a monounsaturated fat-enriched diet, better menstrual regularity for a low-GI diet, high carbohydrate diet, greater decline in insulin

resistance, fibrinogen, total and high-density lipoprotein cholesterol for a low-carbohydrate or low-GI diet, improved depression or anxiety and self-esteem for a high-protein diet. Results concluded that weight loss should be achieved in all overweight PCO's women through lowering caloric intake with adequate nutritional consumption and healthy diet selection irrespective of diet composition (Moran *et al.*, 2013).

#### *Association of diet and BMI*

Following research was conducted in Australia in 1996. The data was collected through 13-year follow-up from 1973-1978. This was a population-based observational study which includes Australian women. At Survey 5, the dietary questionnaire was used for Epidemiological Studies in 2009 for self-reported dietary intake data. 7466 responded to the questionnaire out of 8200 participants; 409 self-reported a diagnosis of PCOS and 7057 showed diagnosis of polycystic ovary syndrome. The results indicated higher mean BMI PCOS women as compared with non-PCOS (29.3+7.5 versus 25.6+5.8 kg/m<sup>2</sup>,  $P, 0.001$ ). The reason concluded that women with PCOS informed a better consumption of diet and better micronutrient intake and low saturated fat and GI consumption but improved energy intake on the other hand the women with no PCOS had more sitting time and no changes in total physical activity. Many other factors were also associated with BMI including PCOS status, higher energy intake and glycaemic index and lower physical activity, age, smoking, alcohol consumption, occupation, education status and area of birth. The disadvantage of this training includes the self-reported diagnosis of PCOS, and some women didn't report PCOS. Confusion factor either lifestyle modification contributed to the PCOS diagnosis or were changed in answering to diagnosis (Teede *et al.*, 2011).

#### *Lifestyle intervention*

Lifestyle mediation is considered as method of choice for both PCOS and metabolic disorder/syndrome. Decline in androgens and regularization of menstrual cycle is associated with losing weight in obese women.

**Table 1.**

Titles	Study Design	Subjects	Interventions	Duration	Results	References
Studies on the quality of Nutrition in women with Polycystic Ovary Syndrome (PCOS)	Qualitative assessment	54 PCOS women with avg age and more BMI	HDI BT-K BMI Circumference	3-day food diaries, food records of the last 24-hour dietary interview.	Risk of metabolic syndrome ↑BMI PCOS irregularities related with diet quality.	(Szczukoet al., 2017)
A ketogenic diet may restore fertility in women with Polycystic Ovary Syndrome: A Case Series	Case Study	4 women with PCOS	Ketogenic diet	Once monthly in a shared medical appointment setting for total of 6 months	Free fatty acids↓ glucose production during the first 2 week of diet. ↓ghrelin level ↑amylin, leptin and glucose ↑more moderate carbohydrate diet. restore ovulation for second pregnancy	(Alwahabet al., 2018)
Significant Improvement Selected Mediators of Inflammation in Phenotypes of Women with PCOS after Reduction and Low GI Diet.	Screening Tests	36 Atherosclerotic women with polycystic ovary syndrome	Comparison of Eicosanoids (HETE and HODE) biochemical phenotypes of women with PCOS. HPLC	3 months	Significant difference in mediators except lipoxins. According to the phenotype there was no differences. Diet repair mechanism, diet ↑SFA and ↓PUFA and MUFA. ↓lipoxins showed that 3 months was a short duration to suppress the inflammatory mediators	(Szczukoet al., 2017)
How do we Manage Obese PCOS Infertile Patients?	Review Paper	Obese PCOS Infertile Patients	Lifestyle interventions Bariatric Surgery	8 months	60% of PCOS were obese. Life style interventions, role of bariatric surgery, ovulation induction agents with clomiphene citrate and letrozole, role of metformin. Gonadotrophins, IVF, electroacupuncture.	(Ali et al., 2018)
Dietary Options in Polycystic Ovary Syndrome (PCOS)	Review article	Obese and overweight PCOS females	Relationship of Obesity and PCOS Weight Management in PCOS Role of Diet in Management of PCOS Hypocaloric Diet High-Protein Diet Low Carbohydrate, Low-GI, Low-GL, High Fiber Diet Omega-3 Polyunsaturated Fatty Acids (n-3 PUFAs) Low Fat Diet	8 months	30 min regular exercise for 3 days for weight loss. Hypocaloric diet and Calorie restricted diet also helpful. ↓ Carbohydrate diet and Keto-genic diet showed improvement in weight loss, hormones imbalance and fasting insulin. ↑ Protein diet and ↓fat diet had improvements in weight reduction and maintenance, Insulin resistance. A greater ↓ in LDL cholesterol and	(Kamran et al., 2017)

					beneficially effect HDL. Use of supplements of omega-3 was useful in reducing BMI and SHBG levels.	
The Effect of Diet and Exercise on Serum Lipids in Overweight and Obese Women with Polycystic Ovary Syndrome in Mosul city	Interventional study	200 Infertile obese and over-weight PCOS female	Anthropometric, blood sugar, hormonal, and lipid profile measurement specific dietary advice and fitness program to the interventional group	6 months	Interventional group had significant improvements in all the tests taken and laboratory tests. The results showed the significant difference in hirsutism, scalp hair loss and acne in intervention group compared to the other one. Conception rate increased 10%. No significant difference appeared in non-interventional group.	(Ali <i>et al.</i> , 2018)
The role of lifestyle changes in the treatment of polycystic ovary syndrome	Review Paper	PCOS females of reproductive age	Lifestyle modification, well-balanced diet including appropriate calorie requirements, Vitamin D and low glycemic index foods and physical activity.	7 months	Balanced diet. BMI and circumferences calculation. ↓glycemic index food was helpful in fat burning. Vitamin D deficiency could lead to insulin resistance, inflammation, dyslipidemia and also effect on calcium metabolism, menstruation and ovulation. Physical activity proper diet= ↓body fat.	(Smyka <i>et al.</i> , 2017)
Diagnosis and Treatment of Polycystic Ovary Syndrome: An Endocrine Society Clinical Practice Guideline	Review paper	Adolescents and menopausal women	Hormonal contraceptives Clomiphene metformin lifestyle interventions	2 years	Evaluation of women with PCOS should exclude alternate androgen-excess disorder and risk factors for endometrial cancer, mood disorders, obstructive sleep apnea, diabetes and CVD's. Hormonal contraceptives and metformin are the treatment options in adolescents with PCOS. Life style intervention is beneficial in overweight/obese patients.	(Iliodromitiet <i>al.</i> , 2013)
The contribution of diet, physical activity	Populationbased	Australian	Lifestyle factor s such as	13 year follow-up	↑Mean BMI women with PCOS reported a better	(Moran <i>et al.</i> ,



and sedentary behavior to body mass index in women with and without polycystic ovary syndrome	observational study	women born in 1973–1978	dietary intake, physical activity or sedentary behaviour	dietary intake and ↓ saturated fat and glycaemic index intake but improved energy intake. Women with no PCOS had increased sitting time and no modification in total physical activity. Many other factors are PCOS status, ↑energy intake and glycaemic index and ↓ physical activity, age, smoking, alcohol intake, occupation, education and country of birth.	2013)
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Polycystic ovarian syndrome (PCOS) is associated with cardiovascular risk factors. The basic purpose of the study was to examine the effect of lifestyle intervention on menses irregularities, hyperandrogenemia, CVD risk factors, and intima-media thickness (IMT) in teen-age girls with PCOS. This study includes 59 obese aged 12-18 years girls with PCOS. It was a 12 month life style intervention based on nutrition counseling, exercise training, and behavior rehabilitation. Menses cycles, IMT, waist circumference, blood pressure (BP), fasting lipids, insulin, glucose, testosterone, dehydroepiandrosteronesulfate, and rostenedione, and SHBG were evaluated. BMI was reduced in 26 girls during the life style intervention (by a mean of  $-3.9\text{kg/m}^2$ ) improved most CRF and reduced their IMT (by a mean of  $-0.01\text{ cm}$ ). Testosterone value reduced (by a mean of  $-0.3\text{ nmol/liter}$ ) and SHBG concentrations increased (by a mean of  $+8\text{ng/ml}$ ) considerably in girls with a reduction in weight as compared to girls with high weight. There was a reduction in prevalence of amenorrhea ( $-42\%$ ) and oligoamenorrhea ( $19\%$ ) in the girls with weight loss. The changes in insulin in the 1-year follow-up were significantly correlated to changes in testosterone ( $r=0.38$ ;  $P=0.002$ ) and SHBG ( $r=-0.35$ ;  $P=0.048$ ). A linear regression model with changes in IMT as dependent variable demonstrated a significant linked with changes in BP and weight status but not with changes in testosterone. They concluded their study in such a way that lifestyle intervention is effective to manage menses irregularities, regulate androgens, and improve CRF and IMT in obese teenage girls with PCOS (Lass *et al.*, 2011).

#### *Association of diet and exercise on Serum lipids*

Impact of diet and exercise on serum lipids in 200 overweight women with PCOS was studied. Two groups were made named interventional and non-interventional. In their first visit they took all the measurements like Bp, hormonal, blood sugar, Anthropometric measurements and laboratory tests included total cholesterol, Triglyceride, High density lipoprotein, Low density lipoprotein, very low-density lipoprotein and repeated after every three months. They gave specific diet plan and exercise program to intervention group only and nothing to the second group. Diet included low fat, lean protein sources, reduced their dairy products and foods with low glycemic index. An energetic walk for 30 minutes, 5 days in a week. Interventional group had significant improvements in all the tests taken. The results showed the significant difference in hirsutism, scalp hair loss and acne in intervention group compared to the other one. Conception rate increased  $10\%$ . No significant difference appeared in non-international group (Ali BM *et al.*, 2018).

#### *Dietary Options, hypocaloric diet*

Acne, male pattern baldness and hirsutism was always diagnosis criteria of PCOS. The study indicates criteria of diagnosis in 3 features polycystic ovary seen in ultrasound, oligomenorrhea and hyperandrogenism in biochemical tests. Androgen excess can lead to increase of visceral fat. PCOS always linked with obesity. Carbohydrates cravings increased with raised androgen in the blood. Metabolic syndrome risk incredibly increased in PCOS. Obesity can lead to late pregnancy,



miscarriages, pre-eclampsia and pregnancy induced diabetes. Initial management for PCOS were to modify their diet and exercise to manage insulin resistance. 30 minutes regular exercise for 3 days in a week said to be good for weight loss. Physical activity results in improvements in PCOS symptoms. Studies revealed diet with low fat for a little duration will lead to weight loss and metabolic improvements. Hypocaloric diet was a good option for weight loss in PCOS can reduce 7-10% of weight in 6-12 months. Calorie restricted diet *also* helped in reducing other symptoms of PCOS. Low carbohydrate diet gave great improvement in weight and in all symptoms of PCOS. Keto-genic diet reduced body weight hormones imbalance and fasting insulin. Fibers also effected on hormones also reduce the insulin secretion. Low glycemic load foods found effective in weight loss but not on androgenism. High protein diet had great effects in weight loss and also improves glucose metabolism. Hypocaloric diet with protein supplements had effects in weight loss also more changes occurred in androgen levels and insulin sensitivity. Protein intake produced a long satietogenic effects then sugar. Low fat diet had improvements in weight reduction and maintenance, Insulin resistance. A greater decrease in LDL cholesterol and beneficially effect HDL. Low fat diet was good for weight loss but it didn't affect the PCOS linked symptoms. Omega-3 polyunsaturated fatty acids found in fish, nuts and seed oils are very helpful in managing PCOS in obese or non-obese. Found important in reducing hypertension, hepatic lipogenesis etc. Long chain fatty acids found in fish oil increase beta oxidation in liver and skeletal muscles. Use of supplements of omega-3 was useful in reducing BMI and SHBG levels. PCOS always face obesity, that linked with all symptoms and made them more complicated hence weight management was must, but it was difficult in obese with PCOS. So, with a moderate diet like hypocaloric with modify carbs, poly unsaturated fats and 30 minutes moderate physical activity can be effective (Kamran *et al.*, 2017).

#### *Lifestyle modification in women with PCOS*

Lifestyle changes in PCOS with obesity required a

balanced diet including fats, carbohydrates and protein. Weight should be calculated by BMI and circumferences. Energy requirements measured through the resting metabolic rate. This study includes the patients who were under treatment and require monitoring because it could lower the basal energy. Low glycemic index food was helpful in fat burning. Vitamin D deficiency could lead to insulin resistance, inflammation, dyslipidaemia and also effect on calcium metabolism. Also influence the menstruation and ovulation. More fat in body less will be the vitamin D. Best way to take vitamin D always from ultraviolet radiation in dermal synthesis. But in PCOS it was not enough they also need supplementation depending upon the body mass. Inositol and the isomers Myo-inositol and D-chiro-inositol helpful in hormonal disturbance in PCOS. Reduced the prolactin and LH concentrations. Myo inositol with metformin effected the menstruation, body mass and ovulation but only myo inositol effected on HOMA index and cause no side effects.

It was proved through study that physical activity with proper diet can lower the body fat. More active females had lower BMI, lower body mass, more concentrations of sex hormones binding proteins and less depression. Lifestyle modification was more helpful in diabetes exercise for 30 minutes, most important as more the physical activity more of the store glycogen will use. Physical activity was according to the body weight of the person. Also, in the beginning exercise sessions started from short time and only willing exertion was helpful for long lasting effects (Smyka *et al.*, 2017).

#### *Quality of nutrition*

Quality of nutrition with in group of 54 PCOS women with average age and more BMI was studied. Circumference of the women that were above the limitations was also measured because of mistaken diets. Rotterdam's criteria were used to evaluate the link between diet and PCOS. According to the tests taken in women majority was on the risk of metabolic syndrome. Because of higher BMI that was due to wrong foods taken by the PCOS women.

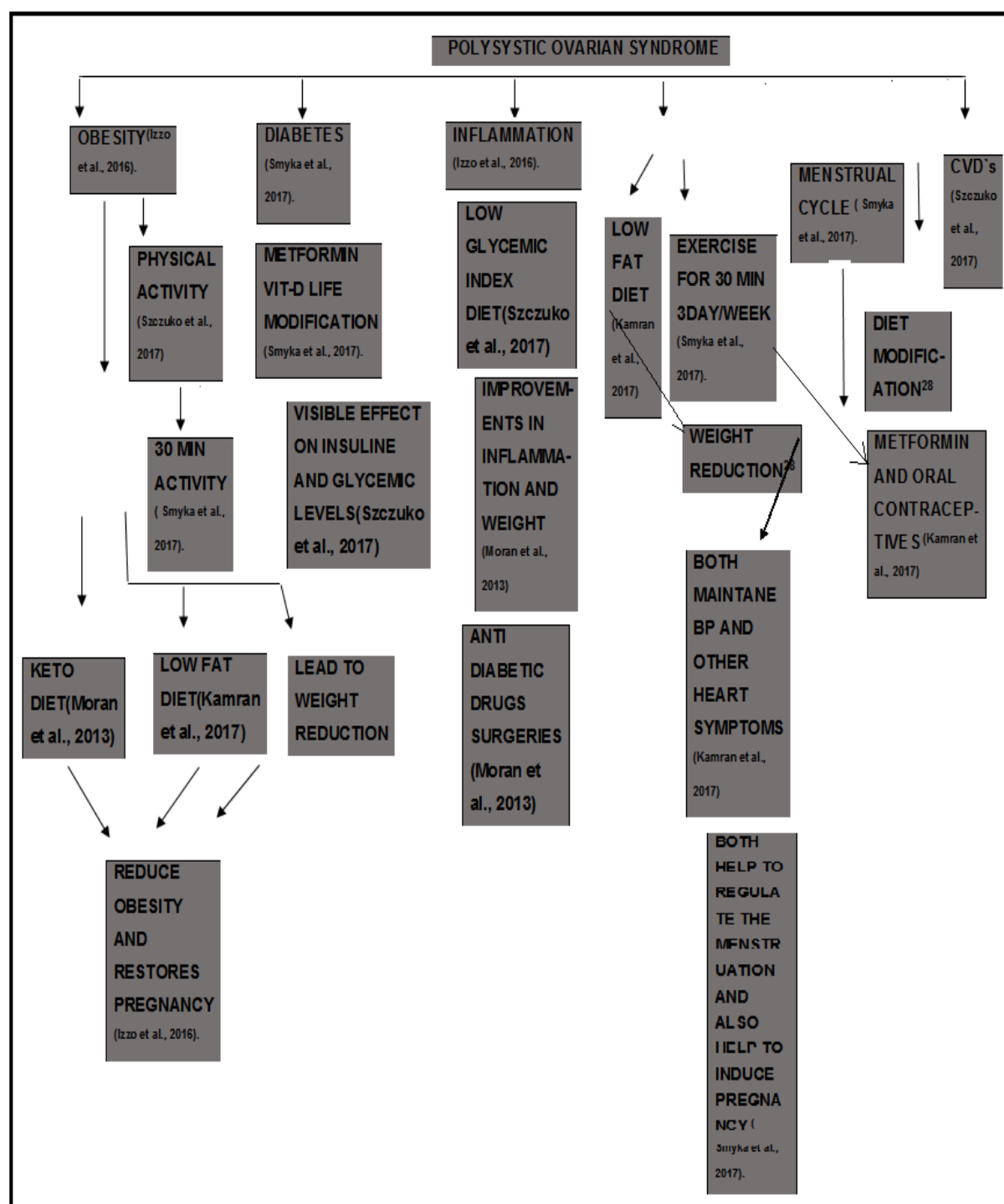


Fig. 1.

All the qualitative tests such as HDI and BT-K, could be used to assess the quality of food in PCOS. In all the woman had PCOS irregularities related with diet quality was observed, that was because of inappropriate diet in women according to the Rotterdam's criteria. In the treatment of PCOS woman correct nutrition and diet was necessary (Szczuko et al., 2017).

#### *Lifestyle medication versus medical treatment*

This study was on the assessment of lifestyle medication versus medical treatment with clomiphene citrate, metformin and clomiphene citrate-metformin in patients with polycystic ovary syndrome. The aim of this study was to compare the effect of clomiphene citrate, metformin and lifestyle modifications on treatment of patients with PCOS.

The result showed that the clinical pregnancy rate was 12.2% in clomiphene group, 14.4% in metformin group, 14.8% in clomiphene + metformin group and 20% in lifestyle modification group (Tabrizi *et al.*, 2014).

#### *Animal study*

This study was about benefits of a drug named metformin in the polycystic ovary syndrome. Different experimental studies on human being's muscle cell cultures and rat adipocytes revealed that metformin acts by improving glucose uptake through the glucose transport system. In fact, it enables the translocation of glucose transporters (GLUTs) from intracellular sites to the plasma membrane. The PCOS related insulin-resistant state is linked both with less ability of insulin to stimulate glucose disposal into target cells and with reduced glucose response to a given amount of insulin. An experimental study demonstrated that a 6-month metformin trial induces a considerable progress of the GLUT-4 mRNA expression in the adipose tissue of PCOS patients, demonstrating that metformin action recovers the peripheral insulin signal transduction. Besides its impact on glucose metabolism, metformin may also act on the insulin levels and, specifically, on insulin receptor (Palomba *et al.*, 2008).

#### *Lifestyle modification*

Effect of lifestyle modification on PCOS was studied. By reducing fats intake with proper physical activity gave improvements in metabolic disturbance. In comparison of two groups one with diet and exercise failed to increase their exercise habits because of their upper body strength. In case of only exercise group hsCRP decreased. Diet in more fibers and low fats, with exercise or with-out exercise always effected the metabolic complications. By changing the diet in groups with more fibers and low fats was observed that all store fats and lipids of the body started using up and decreased, BMI reduced and waistline also decreased, except in exercise group. However, the patients showed an increase HOMA and insulin resistance decreased also improvements in cardiac issues. In exercise group upper body fat decreased.

Lifestyle modification in PCOS obese lead to fat reduction and all other symptoms related to obesity and PCOS such as blood pressure, metabolic disturbance and insulin resistance but diet should contain more fibers, low fats and low refined carbohydrates (Nybacka *et al.*, 2017).

#### *Ketogenic diet*

Clinical data of the women had PCOS related conceiving issues also their reproduction and fertility changes during the PSMF diet was reviewed. All the study showed that small amount of carbohydrates in diet can reverse the insulin resistance. This diet could help not only in weight loss but restored the ovulation cycle. Patients also increased their ghrelin levels during first week. However, appetite control in PCOS was the good option to lose weight, but in case of pregnancy onset that would not be a good idea. That's why ketogenic diet was given to the patients by Alwahaab and his coworkers. Free fatty acids may decrease the food intake glucose production, during the first 2 week of diet ghrelin level decrease and amylin, leptin and glucose were higher. After 6 months they switched to more moderate carbohydrate diet. Ketogenic diet with metformin could restore ovulation for second pregnancy. Other ways such as pills for contraception may lead to more related issues in PCOS such as venous thrombosis. There was a lack of lab data of pre and post keto diet these additional informations were necessary to describe the underlying mechanism this needed to be overcome in future (Alwahabet *et al.*, 2018).

#### *Mediators of Inflammation*

Lipid mediators could provide helpful information about PCOS. When 5-LOX increased also effect the insulin resistance, obesity also increase the synthesis of inflammatory mediators. But in other case it was contrary that PCOS had lower levels of inflammatory mediators, as mediators used in repair system and become dormant. It had discussed that dormant repair system involve cell mediated, hemostatic, vascular and cell mediated response, lead to more androgen and such woman were more prone to damage the blood vessels and atherosclerosis. 9-

HODE and 13 HODE are linked with TSH which made atherosclerosis intense. Also decreased the attachment of platelets to the endothelium wall. Comparing the level of inflammatory mediators in PCOS and control group there was significant difference in mediators except lipoxins. But when divided according to the phenotype there was no differences. Diet mostly effected the repair mechanism, diet rich in SFA and low in PUFA and MUFA. Low level of lipoxins showed that 3 months was a short duration to suppress the inflammatory Mediators (Szcukoet *al.*, 2017).

#### *Diets along with medication*

Treatment of obese PCOS infertile women through diet and different drugs, in PCOS BMI and insulin resistance effect the ovulation. Low carbohydrate diet effect on insulin sensitivity, basal beta cell response and circulating testosterone. To remove fat when diet was not working bariatric surgery was done in PCOS patient and found 100% conception rate with improvements in linked signs like menstrual irregularities and hirsutism. But in case of drugs there was a variety like CC is an estrogen receptor is always first choice that work antagonist by increasing serum FSH. In overages obese limitations remained because it effected the endometrium and poor cervical mucus. But by using letrozole and tamoxifen in patients with CC resistance, effects of letrozole were more effective. But it needed careful monitoring even during IUI because in a review sextuplets got born after 3<sup>rd</sup> cycle of letrozole. Letrozole with CC effected on patients found helpful in live births, ovulation, pregnancy loss and malformations. When dexamethason was given with DHEAS to the females with CC resistance in high dose because they failed to ovulate, its prolonged use effect the insulin resistance. Metformin which is a hypoglycemic drug was helpful in menstruation and ovulation. Metformin also corrected the steroid synthesis from ovary and adrenal glands. In increasing the dose from 500mg to 2000mg some side effects appeared like nausea vomiting. The drugs like troglitazone helped to reduce visceral fat mass. Rosiglitazone enhance ovulation in PCOS. Metformin with rosiglitazone can decreased BMI and pregnancies

achieved. CC with rosiglitazone induced ovulation compare to the alone CC. Rosiglitazone and pioglitazone both had no adverse effects on pregnancy. IPG these are mediators of insulin action, deficiency of IPG in PCOS may be on the basis of IR. In obese PCOS 8 weeks Myo treatment decreased the BMI and RI ad also LH and FSH.

In DCI administration in obese PCOS, BMI reduced and also improvements appeared in insulin sensitivity. By giving only myoinositol to the PCOS ovarian activity improved and BMI also decreased. Last way to achieve pregnancy till term is IVF. By using different protocols PCOS fertilization rate was lower in IVF and higher in ICSI, but no difference in stimulation protocols. Good pregnancy rate appeared in lean PCOS females then in obese. Two groups named EA group and Medication group, both methods equally effected the fertilization, high quality production of embryos studies of oocytod from severely obese compared to the normal had more spindles and were disorganized. Topiramate and exenatide were use in obese cases. It was reported in 2013 in FDA, topiramate during pregnancy can cause orofacial cleft in infants. In case of phentermine/Intake women should do negative pregnancy tests first to decrease the abnormalities in infants (Izzo *et al.*, 2016).

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