DOI : 10.35124/bca.2019.19.1.787

Biochem. Cell. Arch. Vol. 19, No. 1, pp. 787-792, 2019 | www.connectjournals.com/bca | *ISSN 0972-5075*

STUDY OF SOME BIOCHEMICAL PARAMETERS ASSOCIATED WITH POLYCYSTIC OVARY SYNDROME IN TYPE2 DIABETIC WOMEN

Faten Khudhair Abbas Al-Husaini and Ahmed Aboud Khalifa

Department of Biology, College of Science, Misan University, Iraq.
e-mail: alhashimim220@ yahoo.com

(Accepted 12 March 2019)

ABSTRACT : The present study was attempted to study some biochemical parameters associated with polycystic ovary syndrome in type 2 diabetic women in Misan province. The current study included one hundred twenty premenopausal women with age ranged (35-45) years divided into four groups and each group has 30 women as the following: group (1) control group, group (2) women with PCOS, group (3): women with type 2 diabetic mellitus (T2DM) and group (4): women with PCOS and T2DM. The results of fasting blood glucose (FBG), glycated hemoglobin (HBA1c), insulin and homeostasis model assessment of insulin resistance (HOMA-IR) exposed that the second, third and fourth groups was significantly raised ($p \leq 0.05$) in comparison with the first group. The results of cholesterol, triglyceride (TG) and very low density lipoprotein (VLDL) exposed that the second, third and fourth groups was significantly raised ($p \leq 0.05$) in comparison with the first group. While the results of high density lipoprotein (HDL) and total protein exposed that a non-significant difference ($p \leq 0.05$) in the second, third and fourth groups in comparison with the first group. The results of low density lipoprotein LDL exposed that a non-significant difference ($p \leq 0.05$) in the second group in comparison with the first group. While the third and fourth groups significantlyincreased ($p \leq 0.05$) in comparison with the first and second group. The results of c-reactive protein (CRP) and microalbuminuria (MAU) exposed that the second, third and fourth groups significantly raised ($p \leq 0.05$) in comparison with the first group.

Increased CRP in the women with PCOS and T2DM is a sign of severity of inflammation because of adverse clinical of both diseases, leading to cardiovascular disease (CVD).

Key words : MAU, insulin resistance, PCOS.

INTRODUCTION

Infertility is one of the major challenge affecting the lives of every men and women among the worldwide. It is defined as the inability of the couple to realize pregnancy during an average stage of one year despite regular competence (3-4 times per week) unprotected intercourse (Cooper *et al*, 2010). Besides many environmental factors there are many causes leading to this phenomenon in women like endometriosis, early ovarian failure, pelvic inflammatory disease, fibroids and polycystic ovary syndrome (PCOS) (Eniola *et al*, 2017). Polycystic ovary syndrome is one of the main causes of ovarian infertility, in 1935, this syndrome first described by Stein and Leventhal, additionally referred to as Stein-Leventhal syndrome, PCOS is a complicated endocrine metabolic disorder that disturbs between 5–17% of women international (Dumesic *et al*, 2015; Azziz, 2016). Recent epidemiological data observed a strongly relationship between PCOS and metabolic syndrome that 75% of PCOS females are insulin resistance,practically, the symptoms of PCOS can be recognized in all fertility women with IR and Mes (Jukic *et al*, 2016; Pal *et al*, 2016). Furthermore, the occurrence of metabolic syndrome in PCOS women's is 2-4 times greater in comparison with thecommon population, and this occurrence be high by 50% during 30-40 years old age (Apridonidze *et al*, 2005). Metabolic syndrome includes the following diseases: cardiovascular risk, hypertension, endothelial dysfunction and insulin resistance, and about 50%-60% of women with PCOS infects with IR that its prevalence in the general public between 10% and 25% depending on method of evaluation and mean body weight (Jensterle *et al*, 2008; Baptiste *et al*, 2010). Insulin resistance is a main risk component for the advance of type 2diabetes mellitus in early age (Niswender *et al*, 2013; Pala *et al*, 2014; Li and Baek, 2015). The present study was attempted to study some biochemical parameters associated with polycystic ovary syndrome in type 2 diabetic women in Misan province.

MATERIALS AND METHODS

Subjects

The current study involved 120 premenopausal women at the age of 35-45 years. Then, these women are divided into four groups and each group have 30 women at the following:

- First group (control group) health women.
- Second group women with polycystic ovary syndrome(PCOS).
- Third group women with type2 diabetes mellitus T2DM.
- Fourth group women with PCOS and T2DM.

Women with PCOS have been checked medically by ultrasound waves to confirm that they have PCOS by radiologist. The practical part was carried out in AL-Sader Teaching Hospital, addition to dejla private laboratory of Misan province.

Blood sampling

About 7 ml of venous blood was withdrawn by a medical syringe on the follicular phase (2-3) day of the menstrual cycle at 9 a.m. of each subject (patients and controls). The blood sample was divided into: (2 ml) put in EDTA tubes after being gently shaken to prevent blood clotting and used to analyze HbA1c and (5 ml) put in gel tube for 20 minutes at room temperature for clotting. Then, centrifuge at 3000 rpm for 10 minutes to collect the serum, then it used for the purpose of biochemical tests including fasting blood glucose tests, lipid profile and CRP within 24 hours. Insulin resistance was measured through the HOMA-IR index, as follows:

HOMA-IR = fasting Insulin (mg/dl) × fasting glucose (mg/dl) /405.

Urine sample

Urine samples (5 ml) of all participants (patients and control) were obtained in a suitable plastic tube for urine collection. The centrifuge was then centrifuged at 3000 rpm for 10 minutes after it was analyzed.

Statistical analysis

The results are expressed as Mean ± Standard Division (SD). Students ANOVA test and Duncan's were used to analyze results by using Statistical Package for SPSS, P-value ≤ 0.05 was measured significant.

RESULTS

The results of fasting blood glucose (FBG), glycated hemoglobin (HBA1c), insulin and homeostasis model assessment of insulin resistance (HOMA-IR) revealed that the second, third and fourth groups were increased significantly ($p \leq 0.05$) in comparison with the first group as shown in Table 1 and Fig. 1. The results of cholesterol, triglyceride (TG) and very low density lipoprotein (VLDL) revealed that the second, third and fourth groups were increased significantly ($p \leq 0.05$) in comparison with the first group as shown in Table 2 and Fig. 2. While the results of high density lipoprotein (HDL) and total protein revealed that a non-significant difference ($p \leq 0.05$) in the second, third and fourth groups in comparison with the first group.

The results of low density lipoprotein LDL revealed that a non-significant difference ($p \leq 0.05$) in the second group in comparison with the first group. While the third and fourth groups increased significantly($p \leq 0.05$) in comparison with the first and second group. The results of C-reactive protein (CRP) and microalbuminuria (MAU) revealed that the second, third and fourth groups increased significantly ($p \leq 0.05$) in comparison with the first groupas shown in Table 3 and Fig. 3.

DISCUSSION

Insulin resistance was defining as a decreased sensitivity of target organ tissues to the action of insulin, also IR is known as a reduced glucose response to a given amount of insulin, or IR is described as decreased insulin-mediated glucose uptake, hyperinsulinism is defined as a state of elevated insulin clinically or biochemically (hyperinsulinemia) (Essah and Nestler, 2006). IR is measured by several tests, some of these measures are very dependable but a complex like the hyperinsulinemic glycemic glucose clamp and others less exact, but easier like HOMA-IR, insulin resistance is a prevalent in PCOS women's independently of obesity and play critical role in the reproductive and metabolic complications of the syndrome (Polak *et al*, 2017). Appiah (2016) observed that the abnormalities in insulin action in a variety of tissues from PCOS women's, and that may be explained the multi-organ involvement of this syndrome. Baranova *et al* (2011) reported that about 50%-80% of PCOS women's have insulin resistance. IR with compensatory hyperinsulinemia, is one causes of the pathogenesis of PCOS and it lead to development of complications related to PCOS (Diamanti-Kandarakis and Dunaif, 2012).

Janus *et al* (2016) reported that the main actions of insulin are stimulating glucose uptake in adipocytes and skeletal muscles, suppressing hepatic glucose production to maintain blood glucose homeostasis also acts to stimulating glycogen synthesis in skeletal muscles, and preventing lipolysis in adipocytes.and these our results agree with the study of Aljoda (2016), Smaism *et al* (2016). Patients with PCOS have a high level of FBG

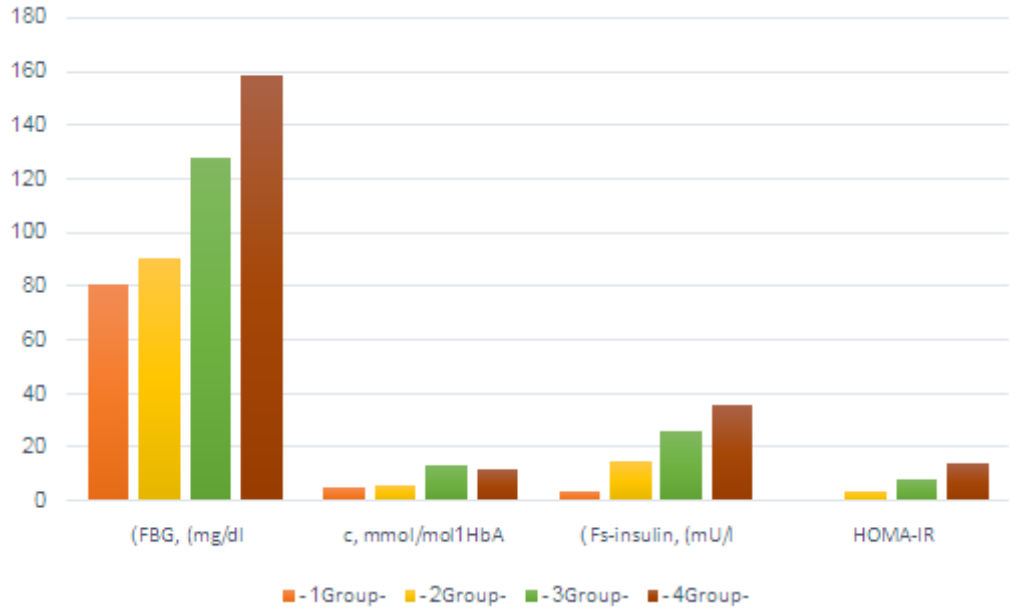

Fig. 1 : Serum levels of FBG, HbA1c, Fs-insulin and HOMA-IR associated with PCOS in diabetic women (type 2).

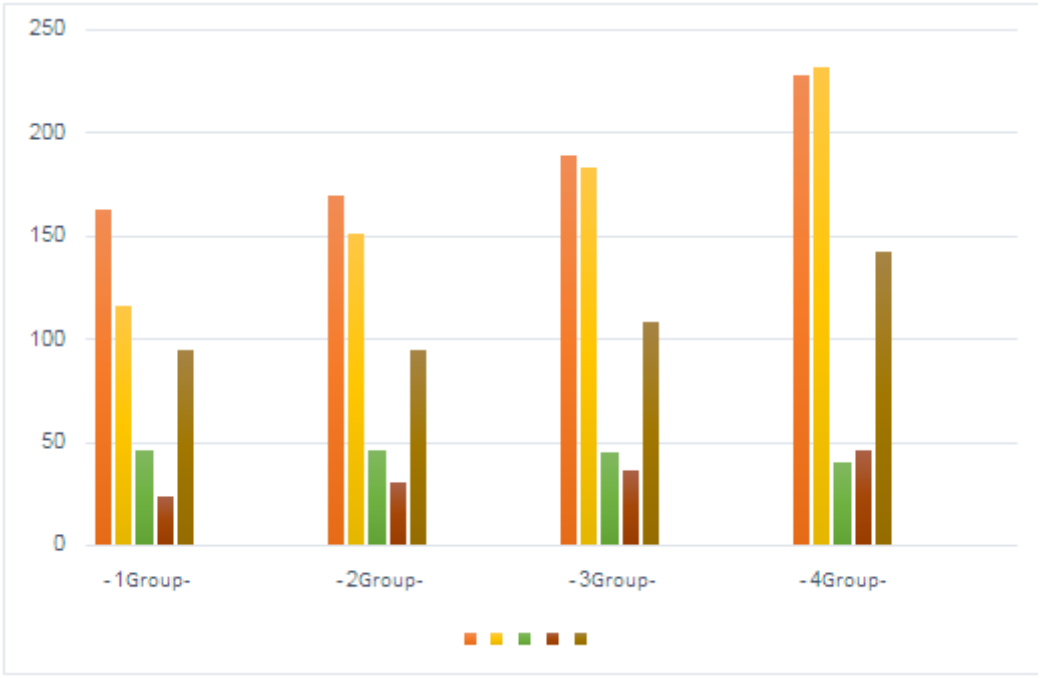

Fig. 2 : Serum levels of lipid profile associated with PCOS in diabetic women (type 2).

may be as a result of insulin resistance to these patients' and these our results agree with the studies of Abbas *et al* (2013), Rodríguez Blanco *et al* (2014), Smaism *et al* (2016).

HbA1C is reflect the average glucose concentration over the past three months (Aljoda, 2016). The glycosylated hemoglobin levels are determined by two factors: the red blood cell life span and the average glucose concentration (AL-mashhadani *et al,* 2009). In women with PCOS and T2DM have a high level of HBA1c may be as a result of insulin resistance. Kim (2012) observed that a high prevalence of increased HbA1c in PCOS Patient's so, it refers to that PCOS itself associated with the abnormal HbA1c status. Dyslipidemia is a type of qualitative and progressive lipid disorders that reflect structural disorders, metabolism, and biological activities of both arterial lipoproteins, which include decreased levels of anti-sclerosis, high-density lipoprotein (HDL) cholesterol and increased levels of lipoprotein B, TGs, VLDL and LDL cholesterol (Kaur, 2014). Women with PCOS and T2DM have a high level of TC, TG, VLDL and LDL, while these women have a low level of HDL, as a result of hyperinsulinemia and hyperandrogenism

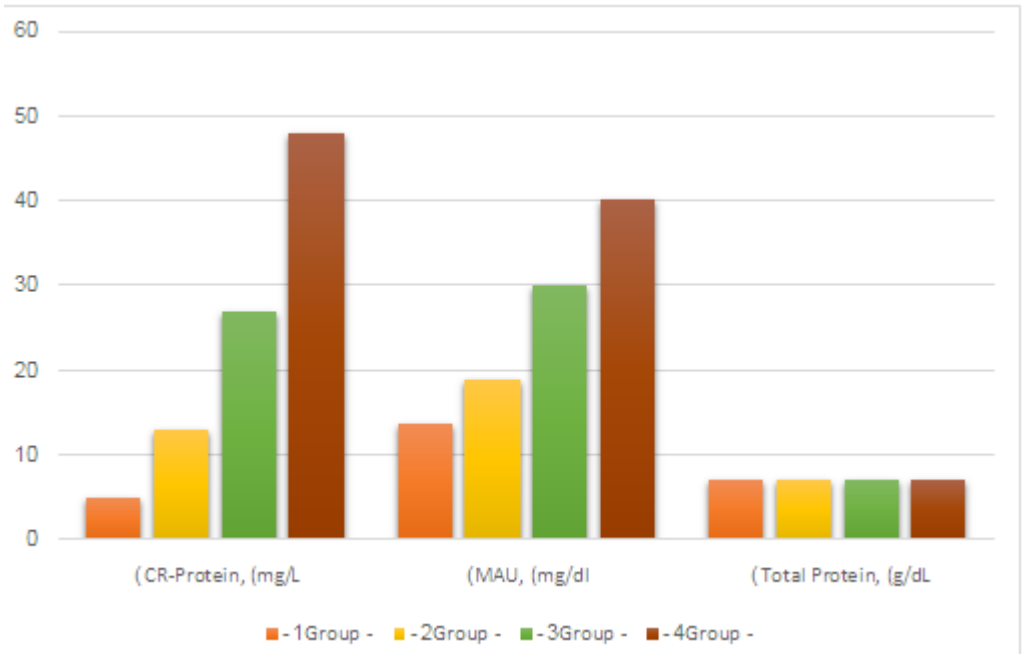

Fig. 3 : Serum levels of CRP, MAU and total protein associated with PCOS in diabetic women (type 2).

Table 1 : The HbA1c, FBG, Fs-insulin and HOMA-IR associated with PCOS in diabetic women (type 2).

Groups	FBG, (mg/dl)	HbA1c (mmol/mol)	Fs-insulin, (mU/l)	HOMA-IR
Group-1-	**80.666±3.447a**	**4.975±0.456a**	**3.726±1.192a**	**0.758±0.275a**
Group-2-	**90.533±3.257b**	**5.520±0.614b**	**14.602±1.944b**	**3.264±0.457b**
Group-3-	**128.133±3.319c**	**13.398±0.727c**	**25.893±1.32 3c**	**8.184±0.308c**
Group-4-	**158.266±2.211d**	**11.751±0.765d**	**36.081±1.726d**	**14.093±0.558d**

- Values exemplify mean ± SD.
- Bold letters refer to significant difference at p ≤ 0.05.
- Similar letters refer to non-significant differences.

Table 2 : The lipid profile associated with PCOS in diabetic women type 2.

Groups	Cholesterol (mg/dl)	Triglycerides (mg/dl)	HDL-cholesterol (mg/dl)	VLDL-cholesterol (mg/dl)	LDL-cholesterol (mg/dl)
Group-1-	**162.266±2.211 a**	**115.733±3.433a**	**45.733±2.211a**	**23.146±0.686 a**	**94.04±3.958a**
Group-2-	169.066±3.885 b	150.466±4.216b	45.733±2.211a	30.093±0.843 b	94.106±4.339a
Group-3-	**188.9±3.565c**	**183.066±2.958c**	**44.4±2.540a**	**36.48±0.474 c**	**108.02±4.296b**
Group-4-	227.733±4.126 d	231.566±2.860d	39.533±3.036a	46.313±0.572 d	141.806±6.306c

- Values exemplify mean ± SD.
- Bold letters refer to significant difference at (p ≤ 0.05).
- Similar letters refer to non-significant differences.

leading to lipid abnormalities. A hyperandrogenism may possibly lead to the abnormalities in lipoprotein profile via working directly on liver, or it may change the body composition by favoring central adiposity (Echiburú *et al*, 2012).

The results of CRP revealed that the second, third and fourth groups increased significantly (p ≤ 0.05) in comparison with the first group. C-reactive protein (CRP) is an acute-phase protein released by the liver during chronic inflammatory disorders and in response to infection as a result, CRP is in widespread clinical use as a marker of inflammation (Newling *et al*, 2018). Nehir Aytan *et al* (2016) mentioned that in the clinical studies, PCOS women had significantly higher levels of plasma inflammatory markers such TNFá and as C-reactive protein (CRP) in comparison to women without PCOS also, anti-inflammatory cytokines including interleukin-37, interleukin-35 and interleukin-27, were all declined in these PCOS women. González *et al* (2014), suggested that the diet may be also contribute to inflammation in women with PCOS, on the other hand glucose intake stimulates the oxidative stress and release of CRP, TNF-á and IL-6, so, inflammation could also explain why women with PCOS are a higher risk of cardiovascular disease and dyslipidemia. In PCOS, high level of androgen

Table 3 : The MAU, total protein and CRP associated with PCOS in diabetic women (type 2).

Groups	CR-Protein (mg/L)	MAU (mg/dl)	Total protein (g/dL)
Group -1-	**5.018±0.695a**	**13.783±1.532a**	**7.010±0.411a**
Group -2-	13.029±0.645b	18.844±2.977b	6.990±0.690a
Group -3-	**26.855±0.544c**	**29.977±2.225c**	**7.073±0.614a**
Group -4-	47.978±1.0863d	40.2±1.765d	6.966±0.482a

- Values exemplify mean ± SD.
- Bold letters refer to significant difference at ($p \leq 0.05$).
- Similar letters refer to non-significant differences.

may be lead to stimulating the bone marrow to produce white blood cells and these cells due to the severity of inflammation, especially in women with high value of CRP and these our results agree with the studies of Kelly *et al* (2001), Hoffman *et al* (2004). The increased levels of CRP in women with T2DM due to insulin resistance. Microalbuminuria (albumin level increased in urine) is defined as a urine albumin-to-creatinine ratio (UACR) which is range between (30–300 mg/dl) and is used as an early marker of endothelial damage of renal glomeruli (Ekblad *et al*, 2018). Women with PCOS have higher level of MAU may be due to high level of androgens in this women lead to insulin resistance. Overall, there is a paucity of data concerning the relationship between PCOS and microalbuminuria (Patel *et al*, 2008; Duleba and Ahmed, 2010; Caglar *et al*, 2011). Women with T2DM have a higher level of MAU as a result of insulin resistance probability that considered as one of the most component of metabolic syndrome. The results of total protein concentration revealed that slightly reduced in the second, third and fourth groups in comparison with the first group. Women with PCOS, T2DM or both have a low level of total protein concentration due to the elevation of insulin that inhibits hepatic synthesis of SHBG in these women, that lead to decrease total protein.

CONCLUSION

- Increased CRP in the women group with PCOS and T2DM is a sign of severity of inflammation because of adverse clinical of both diseases, leading to cardiovascular disease (CVD).
- Increased lipid profile (TC, TG, LDL, VLDL) in a group of women with PCOS and T2DM leads to dyslipidemia and arteriosclerosis.
- A high level of MAU in women with PCOS and T2DM are an initial indicator of metabolic and kidney disorders.

REFERENCES

Abbas A H, Salloom D F and Aboud R S (2013) Detection of Type 2 Diabetes Mellitus in Serum from Women with Polycystic Ovarian Syndrome. *Baghdad Science Journal* **10**(2), 324-330.

Aljoda B M S (2016) Novel Biomarker in Polycystic ovary syndrome (PCOS) infertile females with Diabetes Mellitus prone to atherosclerosis. *Iraqi National Journal of Chemistry* **16**(1), 1-12.

AL-Mashhadani Z I, AL-Sarrag N F and Al-Ubaidy T A (2009) Insulin effect on inflammatory response compared to sulfonylurea in diabetes mellitus patients. *Journal of Research Diyala humanity* **39**, 38-53.

Appiah E (2016) Effect of insulin resistance in polycystic ovary syndrome and impact on pregnancy.

Azziz R (2016) Introduction: Determinants of polycystic ovary syndrome. *Fertility and Sterility* **106**(1), 4-5.

Baptiste C G, Battista M C, Trottier A and Baillargeon J P (2010) Insulin and hyperandrogenism in women with polycystic ovary syndrome. *The Journal of steroid biochemistry and molecular biology* **122**(1-3), 42-52.

Baranova A, Tran T P, Birerdinc A and Younossi Z M (2011) Systematic review: Association of polycystic ovary syndrome with metabolic syndrome and non-alcoholic fatty liver disease. *Alimentary Pharmacology and Therapeutics* **33**(7), 801-814.

Cooper T G, Noonan E, Von Eckardstein S, Auger J, Baker H W, Behre H M, Haugen T B, Kruger T, Wang C, Mbizvo M T and Vogelsong K M (2010) World Health Organization reference values for human semen characteristics. *Human Reproduction Update* **16**(3), 231-245.

Dumesic D A, Oberfield S E, Stener-Victorin E, Marshall J C, Laven J S and Legro R S (2015) Scientific statement on the diagnostic criteria, epidemiology, pathophysiology, and molecular genetics of polycystic ovary syndrome. *Endocrine Reviews* **36**(5), 487-525.

Caglar G S, Oztas E, Karadag D, Pabuccu R and Eren A A (2011) The association of urinary albumin excretion and metabolic complications in polycystic ovary syndrome. *European Journal of Obstetrics and Gynecology and Reproductive Biology* **154**(1), 57-61.

Diamanti-Kandarakis E and Dunaif A (2012) Insulin resistance and the polycystic ovary syndrome revisited: an update on mechanisms and implications. *Endocrine Reviews* **33**(6), 981-1030.

Duleba A J and Ahmed I M (2010) Predictors of urinary albumin excretion in women with polycystic ovary syndrome. *Fertility and Sterility* **93**(7), 2285-2290.

Echiburú B, Pérez-Bravo F, Maliqueo M, Ladrón de Guevara A, Gálvez C, Crisosto N and Sir-Petermann T (2012) CAG repeat polymorphism of androgen receptor gene and X-chromosome inactivation in daughters of women with polycystic ovary syndrome (PCOS): relationship with endocrine and metabolic parameters. *Gynecological Endocrinology* **28**(7), 516-520.

Eniola O W, Adetola A A and Abayomi B T (2017) A review of Female Infertility; important etiological factors and management. *Journal of Microbiology and Biotechnology Research* **2**(3), 379-385.

Ekblad L L, Toppala S, Johansson J K, Koskinen S, Sundvall J, Rinne J O, Puukka P, Viitanen M and Jula A (2018) Albuminuria and Microalbuminuria as Predictors of Cognitive Performance in a General Population: An 11-Year Follow-Up Study. *Journal*

of Alzheimer's Disease **62**(2), 635-648.

Essah P A and Nestler J E (2006) Insulin Resistance and Hyperinsulinism in the Polycystic Ovary Syndrome. In Androgen Excess Disorders in Women (pp. 273-281). Humana Press.

González F, Sia C L, Bearson D M and Blair H E (2014) Hyperandrogenism induces a proinflammatory TNFα response to glucose ingestion in a receptor-dependent fashion. *The Journal of Clinical Endocrinology and Metabolism* **99**(5), E848-E854.

Hoffman M, Blum A, Barunch R, Kaplan E and Benjamin M (2004) Leukocytes and coronary heart disease. *Aterioscler* **172**, 1-6.

Jensterle M, Weber M, Pfeifer M, Prezelj J, Pfutzner A and Janez A (2008) Assessment of insulin resistance in young women with polycystic ovary syndrome. *International Journal of Gynecology and Obstetrics* **102**(2), 137-140.

Jukic A M Z, Upson K, Harmon Q E and Baird D D (2016) Increasing serum 25-hydroxyvitamin D is associated with reduced odds of long menstrual cycles in a cross-sectional study of African American women. *Fertility and sterility* **106**(1), 172-179.

Janus A, Szahidewicz-Krupska E, Mazur G and Doroszko A (2016) Insulin resistance and endothelial dysfunction constitute a common therapeutic target in cardiometabolic disorders. *Mediators of Inflammation*.

Kaur J (2014) A comprehensive review on metabolic syndrome. *Cardiology Research and Practice* **2014**, 1–21.

Kelly C C, Lyall H, Petrie J R, Gould G W, Connell J M and Sattar N (2001) Low grade chronic inflammation in women with polycystic ovarian syndrome. *The Journal of Clinical Endocrinology & Metabolism* **86**(6), 2453-2455.

Kim J J, Choi Y M, Cho Y M, Jung H S, Chae S J, Hwang K R, Hwang S S, Ku S Y, Kim S H, Kim J G and Moon S Y (2012) Prevalence of elevated glycated hemoglobin in women with polycystic ovary syndrome. *Human Reproduction* **27**(5), 1439-1444.

NehirAytan A, Bastu E, Demiral I, Bulut H, Dogan M and Buyru F (2016) Relationship between hyperandrogenism, obesity, inflammation and polycystic ovary syndrome. *Gynecological Endocrinology* **32**(9), 709-713.

Newling M, Sritharan L, Everts B, de Boer L, Zaat S, Baeten D and den Dunnen J (2018) SAT0012 C-reactive protein: not only a marker, but also a cause of inflammation through metabolic reprogramming of human macrophages.

Niswender K, Pi Sunyer X, Buse J, Jensen K H, Toft A D, Russell Jones D and Zinman B (2013) Weight change with liraglutide and comparator therapies: an analysis of seven phase 3 trials from the liraglutide diabetes development programme. *Diabetes, Obesity and Metabolism* **15**(1), 42-54.

Li L and Baek K H (2015) Molecular genetics of polycystic ovary syndrome: an update. *Current Molecular Medicine* **15**(4), 331-342.

Pal L, Zhang H, Williams J, Santoro N F, Diamond M P, Schlaff W D, Coutifaris C, Carson S A, Steinkampf M P, Carr B R and McGovern P G (2016) Vitamin D status relates to reproductive outcome in women with polycystic ovary syndrome: secondary analysis of a multicenter randomized controlled trial. *The Journal of Clinical Endocrinology and Metabolism* **101**(8), 3027-3035.

Pala L, Barbaro V, Dicembrini I and Rotella C M (2014) The therapy of insulin resistance in other diseases besides type 2 diabetes. *Eating and Weight Disorders-Studies on Anorexia, Bulimia and Obesity* **19**(3), 275-283.

Patel A, Bloomgarden Z and Futterweit W (2008) Premicroalbuminuria in women with polycystic ovary syndrome: a metabolic risk marker. *Endocrine Practice* **14**(2), 193-200.

Polak K, Czyzyk A, Simoncini T and Meczekalski B (2017) New markers of insulin resistance in polycystic ovary syndrome. *Journal of Endocrinological Investigation* **40**(1), 1-8.

Rodríguez Blanco S, Almeida Gómez J and Pérez Guerra J C (2014) Multivessel coronary artery disease, angioplasty and endothelial dysfunction in diabetes mellitus. *Case Report. CorSalud (Revista de EnfermedadesCardiovasculares)* **6**(1), 110-118.

Smaism M F, Gatea A K and Ejam Z Y (2016) Evaluation of Insulin, Insulin Resistance LH, and FSHin Women with Polycystic Ovary Syndrome and Diabetic Mellitus Type 2. *Medical Journal of Babylon* **13**(1), 73-78.