Levels of Some Pro-inflammatory Cytokines in Pregnant Women with Polycystic Ovary Syndrome

Mohammed A.Taher and Aminah A. Al-Juboori

Department of Clinical Laboratory Sciences, College of Pharmacy, University of Baghdad.

الخلاصة:

الهدف من هذه الدراسةِ هو لقياس مستويات بعض السايتوكينات السابقة للألتهاب (انترلوكين 12 ومستقبلات انترلوكين 2 الذائبة) في النساءِ الحوامل المصابات بمتلازمة المبيض متعدد الأكياس وكذلك لتعين حادثة الاجهاض التلقائي أثناء الأشهر الثلاثة الأولى في الحوامل المصابات بمتلازمة المبيض متعدد الأكياس مقارنة مع النساءِ الحوامل غيرالمصابات بمتلازمة المبيض متعدد الأكياس.

أجريت هذه الدراسةِ على (93) شخصا،والتي تَضمّنتْ:

1 - (63) من النِساء الحوامل أثناء الأشهر الثلاثة الأولى, والتي تَضمّنتْ:

أ– (33) من النِساء الحوامل المصابات بمتلازمة المبيض متعدد الأكياس واللواتي شُخّصَن قبل الحملِ, قسّمَن إلى المجموعاتِ التاليةِ: (20) نساء بحمل ناجح مع متلازمة المبيض متعدد الأكياس, (7) نساء عانين من البيضةَ الكاذبة مع متلازمة المبيض متعدد الأكياس و (6) نساء عانين من الاجهاض المنسي مع متلازمة المبيض متعدد الأكياس.

ب– (30) من النِساء الحوامل غيرمصابات بمتلازمة المبيض متعدد الأكياس،والتي تَضمّنَت: (27) نساء حوامل كمجموعة سيطرة و (3) نِساء حوامل غيرمصابات بمتلازمة المبيض متعدد الأكياس سُحِبتْ مِنْ هذه الدراسةِ بسبب إجهاضِهِن في الأشهر الثلاثة الأولى.

2 - (30) إمرأةٍ غير حامل قسّمَن إلى المجموعاتِ التاليةِ: (18) نساء غير حوامل مع متلازمة المبيض متعدد الأكياس و (12) نساء غير حوامل كمجموعة سيطرة.

أجري فحص السونار و سُحِبتْ عيناتَ دمّ وريديةَ مِنْ كُلّ النساء لقيَأس مستويات الهرمون اللوتيني (LH), الهورمون الذكري التيستوستيرون ومستويات بعض السايتوكينات السابقة للألتهاب (انترلوكين 12 ومستقبلات انترلوكين 2 الذائبة) في المصل.

حادثة الإجهاضِ التلقائيِ في الأشهر الثلاثة الأولى مِنْ الحملِ لـ (33) من النساء الحوامل المصابات بمتلازمة المبيض متعدد الأكياس واللواتي شُخّصَن قبل الحملِ كَانَت (39.4 %){المنسي (18.2 %) والبيضةَ الكاذبةَ (21.2 %)} والتي هي 3.9 مرة أعلى مِنْ حـادثةِ الإجهاضِ التلقائيِ في الأشهر الثلاثة الأولى مِنْ الحملِ لـ (30) من النِساءِ الحوامل غيرالمصابات بمتلــازمة المبيض متعدد الأكياس بنسبة (10 %){المنسي (3.3 %) والبيضةَ الكاذبة (6.7 %)}.

مستويات الهورمون اللوتيني(LH) كَانتْ تَزيدُ بشكل معنوي (الاحتمالية >0.05) في مجموعةِ غير الحوامل المصابات بمتلازمة المبيض متعدد الأكياس عندما قورن بمجموعة السيطرة غير الحوامل. مستويات التيستوستيرونَ كَانتْ تَزيدُ بشكل معنوي (الاحتمالية >0.05) في كُلّ المجاميع الأربعة المصابات بمتلازمة المبيض متعدد الأكياس عندما قورن بمجموعتي السيطرة (حامل وغير حامل). مستويات انترلوكين –12 ارتفعتْ في كُلّ المجاميع الأربعة المصابات بمتلازمة المبيض متعدد الأكياس عندما قورن بمجموعتي السيطرة (حامل وغير حامل). مستويات مستقبلات انترلوكين 2 الذائبة (sIL–2) كَانتْ تَزيدُ بشكل معنوي (الاحتمالية >0.05) في مجموعتي الإجهاضِ التلقائيِ المصابة بمتلازمة المبيض متعدد الأكياس (المنسي والبَيضةَ الكاذبة) وفي مجموعةِ النساء غير الحوامل مع متلازمة المبيض متعدد الأكياس عندما قُورن بمجموعة السيطرة للنساء الحوامل. نتيجةً لذلك أرتفاع حادثة الإجهاضِ التلقائيِ أثناء الأشهر الثلاثة الأولى بالنساء الحوامل المصابات بمتلازمة المبيض متعدد الأكياس قَدْ يُنْسَبُ لإرتِفاع مستويات السايتوكينات السابقة للألتهاب (انترلوكين 12 ومستقبلات انترلوكين 2 الذائبة) بسبب حالاتٍ شذوذ إفرازيةٍ ويتعلق مباشرة بمستويات التيستوستيرونِ العاليةِ. إرتفاع مستويات السايتوكينات السابقة للألتهاب (انترلوكين 12 ومستقبلات انترلوكين 2 الذائبة) في مجموعة النساء غير الحوامل مع متلازمة المبيض متعدد الأكياس قَدْ يُنْسَبُ إلى التفاعلاتِ بين الافرازات العصبية (neuroendocrine) ونظام المناعة.

Abstract:
The objective of this study is to determine levels of some pro-inflammatory cytokines (IL-12 and SIL-2R) in pregnant women with polycystic ovary syndrome (PCOS) and also to determine incidence of spontaneous abortion during first trimester in pregnant women with PCOS compared with non-PCOS pregnant women. This Study was performed on (93) women, consisted of:

1. (63) pregnant women during the first trimester, which included:A- (33)PCOS pregnant women and subdivided into the following groups: (20) successful pregnant PCOS, (7) blighted Ovum PCOS and (6) missed abortion PCOS. B- (30) non-PCOS pregnant women, which included: (27) successful pregnant control and (3) non-PCOS pregnant women were withdrawn from this study because of their abortion in first trimester.
2. (30) non-pregnant subjects, which subdivided into the following groups: (18) non-pregnant PCOS and (12) non-pregnant control.

Serum luteinizing hormone (LH), testosterone hormone levels and serum pro-inflammatory cytokines [IL-12 and sIL-2R] levels were measured in all subjects. It is found that the incidence of spontaneous abortion {missed(18.2%) and blighted ovum(21.2%)} in first trimester of pregnancy for 33 women which was (39.4%) and it is 3.9 fold higher than incidence of spontaneous abortion {missed(3.3%) and blighted ovum (6.7%)} for 30 non-PCOS pregnant women which was (10%). The LH levels were increasing significantly (P<0.05) in

non-pregnant PCOS group when compare with non-pregnant control group. The testosterone levels were increasing significantly (P<0.05) in all four PCOS groups when compared with two control groups (pregnant and non-pregnant). The IL-12 levels were elevated in all four PCOS groups when compared with two control groups. The sIL-2R levels were increasing significantly (P<0.05) in spontaneous abortion PCOS group and in non-pregnant PCOS group when compared with pregnant control group. In conclusion rise of some pro-inflammatory cytokines (IL-12 and sIL-2R) levels in pregnant women with PCOS during the first trimester may be attributed to an endocrine abnormalities and related directly to high levels of testosterone. The rising pro-inflammatory cytokines (IL-12 and sIL-2R) levels of non-pregnant PCOS may be attributed to interactions between the neuroendocrine and immune systems.
Key words: pro-inflammatory cytokines, polycystic ovary syndrome.

Introduction:

The factors that explain the immunological relationship between mother and fetus which included Th1/Th2 balance[1].The exact mechanism by which abnormal immune factors cause recurrent miscarriage is uncertain, but there is a suggestion that this may involve modulation or imbalance between the various cells of the immune systems, especially the T cell subgroups, as indicated by the cytokine secretion profile. Thomas Wegmann, who proposed the original immunotrophic hypothesis, focused attention on the role of cytokines in the feto-maternal dialogue[2]. He hypothesized that (successful allo-pregnancy is a Th2 cytokine phenomenon) and demonstrated a Th2 cytokine profile response in normal pregnancy[3]. This Th2 response allows the production of blocking antibodies to mask fetal trophoblast antigens from immunological recognition by maternal Th1 cell-mediated/cytotoxic response which is responsible for rejection of allograft/semi-allografts[4]. The precise effects of progesterone hormone on foetal tolerance have been also described, at high concentrations, progesterone is a potent inducer of Th2-type cytokines by T cells also regulated genes in the uterus first of these molecules is Glycodelin (Gd) a 24-kDa glycoprotein also called; placental protein 14 (PP14)[5]. Second of these molecules is Progesterone-induced blocking factor (PIBF) a 34-kDa synthesize by activated human lymphocytes, especially γδT cells[6]. Soluble interleukin-2 receptor (sIL-2R) also known as the sTac (Soluble T cell activation) detection and quantitation provides clinicians with a useful and simple means of assessing immune function in vivo as part of the investigation, management and prognosis of a broad spectrum of human diseases[7]. Interleukin-12p70 heterodimer(IL-12) have been found to play distinct cellular and functional roles in Th1 development[8].

Complex endocrine abnormalities as possible risk factors, hypersecretion of LH, hyperandrogenaemia and hyperinsulinaemia have all been investigated as possible causes of PCOS. It is likely that these factors are interlinked and

together might result in disordered ovarian and endometrial function[9]. The chronic anovulation and infertility associated with PCOS can usually be treated; however, overall pregnancy rates are not high[10]. Successful folliculogenesis occurs in 80% of treated women, yet the ultimate pregnancy rate is only 40–50%, even when other factors are excluded. Furthermore, spontaneous miscarriages also occur frequently in this group[11]. Similarly, women with recurrent spontaneous miscarriages are often diagnosed with PCOS[11,12].

Materials and Methods:

This study was conducted in Baghdad city in Kamal-Alsamaree Hospital, from which four PCOS study groups (non-pregnant PCOS, successful pregnant PCOS, missed abortion PCOS and blighted ovum PCOS) were recruited consecutively whereas pregnant control group were recruited from Al-Elwia Maternity Teaching Hospital (antenatal care unit), additionally, non-pregnant control group came from different residence from October-2009 till August-2010.

This Study was performed on (93) women, which included:

1- (63) pregnant women during the first trimester, which included:

A- (33) PCOS pregnant women who subdivided into the following groups:
- (successful pregnant PCOS): (20) pregnant women with PCOS completed their pregnancy to delivery, included as study group.
- (blighted Ovum PCOS): (7) pregnant women with PCOS who were diagnosed blighted ovum during first trimester of pregnancy, included as study group.
- (missed Abortion PCOS): (6) pregnant women with PCOS who were diagnosed missed abortion during the first trimester of pregnancy, included as study group.

All of these pregnant women with PCOS received clomiphene citrate or gonadotropin stimulation and use human chorionic gonadotropin for ovulation induction to achieve pregnancy, and on progesterone therapy during the first trimester period.

B- (30) non-PCOS pregnant women, which included:
- (successful pregnant control): (27) non-PCOS healthy pregnant women completed to delivery, included as control group.(3) non-PCOS pregnant women were withdrawn from this study because of their abortion in first trimester.

2- (30) non-pregnant subjects, which subdivided into the following groups:
- (non-pregnant PCOS): (18) non-pregnant PCOS patients who were diagnosed newly and not taking any medication that affect the reproductive or metabolic function, included as study group.
- (non-pregnant control): (12) non-pregnant healthy subjects with normal ovulatory and menstrual cycles, included as control group.

The study excluded the patients with diabetes mellitus, hypertention, autoimmune diseases, rubella virus, cytomegalovirus (CMV), herpes simplex virus (HSV), hepatitis, toxoplasma gondii, bacterial infection (eg. niesseria gonorrhea ,and Chlamydia trachomatis), solid malignancies and hematological neoplasms, organ transplantation, chronic renal failure or on dialysis.

In this study, the diagnosis of PCOS depended on AES (Androgen Excess Society) 2006 criteria[13] to include all of the following:hyperandrogenism (hirsutism and/or hyperandrogenemia), ovarian dysfunction (oligo-anovulation and/or polycystic ovaries), exclusion of related disorders such as hyperprolactinemia, thyroid disorders and congenital adrenal hyperplasia.
Pregnancy was diagnosed Clinically by ultrasonography between five and six weeks after the last menstrual period[14].

Anembryonic pregnancy was diagnosed by sonography which failed to show a fetal pole[14].

Missed abortion was diagnosed by ultrasonography shows disappearance of previously detected embryonic or fetal cardiac activity[15].

Venous blood samples were drawn from non-pregnant women (PCOS and control) at the day (2) of menstrual cycle while from non-PCOS and PCOS pregnant women at (8-12) week of gestation to measure serum luteinizing hormone (LH) , testosterone levels and serum pro-inflammatory cytokines [IL-12 and sIL-2R] levels. The study also included the measurement of body mass index (BMI) of the subjects using standard formula: BMI =Weight (Kg) / Height (m^2)[16]. Obese subjects were defined as having BMI$\geq$ 30 and overweight subjects were defined as having BMI (25.0-29.9) [17,18].

Hormonal and Cytokine analysis:

Serum LH levels were determined using a commercial kit obtained from Veda.Lab, using the ELISA method[19]. Serum testosterone levels were determined using a commercial kit obtained from DRG, using the ELISA method[20]. Serum IL-12 levels were determined using a commercial kit obtained from Quantikine, R&D systems, using the ELISA method[21]. Serum sIL-2R levels were determined using a commercial kit obtained from Demeditec, using the ELISA method[22].

Statistical analysis:

Data were analyzed by one-way analysis of variance with ANOVA- test. Data are presented as means ± SE. The level of significance was $P < 0.05$ was used for analysis of variance test (ANOVA)[23].

Results:

Table-1 showed that the mean value of age and BMI (Kg/m^2) were not changed significantly between all groups enrolled in this study. The most non-pregnant PCOS group of this study with oligomenorrhea (61.1%). Mean value of weeks of gestation was not changed significantly between all pregnant and spontaneous abortion groups enrolled in this study. There were 9 of 20

successful pregnant PCOS (45%), 4 of 6 missed abortion PCOS (66.7%) and 5 of 7 blighted ovum PCOS (71.4%) have had previous abortion and the total of previous abortion were 18 of 33 pregnant women with PCOS (54.5%). Incidence of spontaneous abortion {missed(18.2%) and blighted ovum(21.2%)} in first trimester of pregnancy for 33 women with PCOS who were diagnosed before pregnancy was (39.4%) which 3.9 fold higher than incidence of spontaneous abortion {missed(3.3%) and blighted ovum (6.7%)} in first trimester of pregnancy for 30 non-PCOS pregnant women which was (10%).However the percentage of successful pregnancies in PCOS women were 60.6% while in non-PCOS women were 90%.

Subjects (n=93)	Pregnant women (n=63)						Non-pregnant women (n=30)	
	Non-PCOS pregnant women (n=30) (%)			PCOS pregnant women (n=33) (%)				
Groups Characters	Pregnant control (n=27) (%)	Missd abortion (n=1) (%)	Blighted ovum (n=2) (%)	Successful pregnant PCOS (n=20) (%)	Missed abortion PCOS (n=6) (%)	Blighted ovum PCOS (n=7) (%)	Non-pregnant PCOS (n=18) (%)	Non-pregnant control (n=12) (%)
Age(year) (mean±SE)	A 29.75±3.176	_	_	A 28.764±6.768	A 33.0±1.581	A 29.33±6.658	A 30.41±4.05	A 29.92±3.58
BMI kg/m^2 (mean±SE)	A 26.53±3.92			A 31.68±1.41	A 31.72±2.00	A 28.08±1.78	A 32.03±3.09	A 26.00±8.18
Obesity (BMI≥30Kg/m^2)	9/27 (33.3%)	_	_	14/20(70%)	4/6 (66.7%)	2/7 (28.6%)	14/18 (77.8%)	2/12 (16.7%)
Overweight (BMI 25-29.9 Kg/m^2)	18/27 (66.7%)	_	_	6/ 20 (30%)	2/6 (33.3%)	5/7 (71.4%)	4/18 (22.2%)	10/12 (83.3%)
Amenorrhea (absences of menstruation > 6 months)	–	–	–	–	–	–	3/18 (16.7%)	–
Oligomenorrhea (less than 8 cycle/year)	–	–	–	–	–	–	11/18 (61.1%)	–
Regular cycle	–	–	–	–	–	–	4/18 (22.2%)	12/12 (100%)
Weeks of gestation (mean±SE)	A 11.958±1.835	_	_	A 10.076±1.441	A 10.0±1.581	A 10.0±2.00	–	–
Previous abortion	–	–	–	9/20 (45%)	4/6 (66.7%)	5/7 (71.4%)	–	–
Total of Previous abortion	–			18/ 33 (54.5%)			–	
−Spontaneous abortion	3/ 30 (10%)			13/ 33 (39.4%)			—	—
. Missed abortion	1/ 30 (3.3%)			6/ 33 (18.2%)			—	—
. Blighted ovum	2/ 30 (6.7%)			7/ 33 (21.2%)			—	—
−Pregnancies	27/ 30 (90%)			20/ 33 (60.6%)			—	—

Table-1: Demographic data of 90 subjects

Identical subscript (A) among different groups considered non significant difference. n = number of subjects in each groups

Table-2 showed that LH (mIU/ml) levels were increasing significantly (P<0.05) in non-pregnant PCOS group when compare with non-pregnant control group. The testosterone (ng/ml) levels were increasing significantly (P<0.05) in all four PCOS groups when compared with two control groups (pregnant and non-pregnant). The testosterone (ng/ml) levels in spontaneous abortion PCOS groups were increasing insignificantly when compare with successful pregnant PCOS group. The testosterone (ng/ml) levels in successful pregnant control group were increasing insignificantly when compare with non-pregnant control.

Groups \ Parameters	Non - pregnant control (n=12)	Non-pregnant PCOS (n=18)	successful pregnant control (n=27)	Successful Pregnant PCOS (n=20)	Missed Abortion PCOS (n=6)	Blighted ovum (Anembryonic pregnancy) PCOS (n=7)
LH mIU/ml (mean±SE)	A 1.726±0.240	B 4.447±1.210	-	-	-	-
Testosterone ng/ml (mean±SE)	B 0.237±0.002	A 0.748±0.0636	B 0.389±0.1966	A 0.588±0.1581	A 0.75±0.0360	A 0.632±0.1755

Table-2: Serum Luteinizing Hormone (LH) and testosterone levels in non-pregnant PCOS, successful pregnant PCOS, blighted Ovum PCOS, missed abortion PCOS, non-pregnant control and pregnant control groups.
Non-identical subscripts (A,B) among different groups considered significant difference (P<0.05) .
n = number of subjects in each groups

Table-3 showed IL-12 pg/ml levels were elevated in all four PCOS groups when compared with two control groups (pregnant and non-pregnant). In the four PCOS groups, the levels of IL-12 of non-pregnant PCOS group were increasing significantly (P<0.05) when compared with successful pregnant PCOS group, blighted ovum PCOS group and missed abortion PCOS group. Also in the four PCOS groups, the levels of IL-12 in missed abortion PCOS group were increasing significantly (P<0.05) when compare with successful pregnant PCOS group but insignificantly when compare with blighted ovum PCOS group. The sIL-2R ng/ml levels were increasing significantly (P<0.05) in spontaneous abortion PCOS groups and in non-pregnant PCOS group when compared with successful pregnant control group. Whereas the sIL-2R levels in successful Pregnant PCOS group and non-pregnant control group were increasing insignificantly when compared with successful pregnant control group.

Groups / Parameters	Non-pregnant control (n=12)	Non-pregnant PCOS (n=18)	pregnant control (n=27)	Successful Pregnant PCOS (n=20)	Missed Abortion PCOS (n=6)	Blighted ovum (Anembryonic pregnancy) PCOS (n=7)
IL-12 pg/ml (mean$\pm$SE)	AB 5.45$\pm$0.636	C 52.666$\pm$6.4291	B 5.00$\pm$0.818	A 17.514$\pm$13.357	D 38.00$\pm$2.549	AD 28.00$\pm$1.581
sIL-2R ng/ml (mean$\pm$SE)	AB 2.54$\pm$0.62	B 3.75$\pm$1.51	A 2.002$\pm$0.87	AB 2.81$\pm$0.09	B 4.75$\pm$0.05	B 4.27$\pm$1.14

Table-3: **Serum interleukin -12 (IL-12) and soluble Interleukin -2 Receptor (sIL-2R) levels in non-pregnant PCOS, successful pregnant PCOS, blighted ovum PCOS, missed abortion PCOS, non-pregnant control and pregnant control groups.**
Non-identical subscripts (A, B, C, D) among different groups considered significant difference ($P<0.05$) .
n = number of subjects in each groups.

Discussion:

The present study revealed that mean values of age (year) and BMI (Kg/m^2) were not changed significantly between all six groups enrolled in this study to eliminate any variations that may affect the results table (1). There is other study which claim that genetic problems are more likely to occur with older parents; this may account for the higher miscarriage rates observed in older women[24]. This was in line partly with other studies which demonstrated that PCOS is associated with a higher miscarriage risk in spontaneous pregnancies as well as in pregnancies after surgical treatment or induced ovulation with or without ovarian suppression, this is primarily related to obesity[25].

The present study revealed that weeks of gestation have not changed significantly between all pregnant and spontaneous abortion groups enrolled in this study to eliminate any variations that may affect the results table (1). There are specific fluctuations in the Th1:Th2 balance towards the Th2-type cytokines at implantation and during the initiation of parturition[26].

This study demonstrated that there were 9 of 20 successful pregnant PCOS (45%), 4 of 6 missed abortion PCOS (66.7%) and 5 of 7 blighted ovum PCOS (71.4%) have had previous abortion and the total of previous abortion were 18 of 33 pregnant women with PCOS (54.5%) . These results were in agreement with other studies which demonstrated that PCOS was diagnosed in about 40–80% of women with recurrent miscarriages[27,28].

In present study, according to ultrasound examination, 13 of 33 (39.4%) pregnant women with PCOS have had spontaneous abortion. This percentage was 3.9 fold higher compared with non-PCOS pregnant women .These results in consistent with most previous studies suggesting an increased risk of miscarriage in PCOS patients after spontaneous or assisted conception was reported up to a maximum of 30–50%[29] and the miscarriage rate seems to be 3-fold higher in PCOS subjects than in healthy women[30].

The present study table-2 revealed that the mean LH levels in non-pregnant PCOS group (4.447 mIU/ml) was increasing significantly when compare with non-pregnant control group (1.726 mIU/ml). This is due to an increased amplitude and frequency of LH pulses[31].

This study illustrated that mean levels of testosterone (ng/ml) were increasing significantly in all four PCOS groups when compared with two control groups (non-pregnant and successful pregnant), also spontaneous abortion PCOS groups (missed and blighted ovum) were increasing insignificantly when compare with successful pregnant PCOS group as demonstrated in table (2). These results were in agreement with other studies which reported that hyperandrogenemia is a common disorder in PCOS; it is mul tifactorial in origin, typically attributed to the ovary with substantial contributions from an adrenal source, and to a lesser extent adipose tissues[9,32]. Furthermore an association between hyperandrogenism and increased incidence of miscarriage in PCOS patients[11,9]. Also high levels of serum androgens have been associated with recurrent miscarriages in women with or without PCOS[33]. The levels of IL-12 of non-pregnant control group (5.45 pg/ml) which were slight increasing insignificantly when compared with successful pregnant control group (5 pg/ml) table-3. This result in consistent with other study which demonstrated that non-significant changes in serum levels of IL-12 were observed in pregnant compared with the normal control women[34].

Grasso (1998) suggest that hypothalamic peptides [luteinizing hormone-releasing hormone (LHRH) and thyrotrophin-releasing hormone (TRH)] directly, and/or indirectly pituitary hormones [prolactin (PRL), thyroid-stimulating hormone (TSH), follicle stimulating hormone (FSH), and LH] or IL-2, have stimulatory effect on IFN-gamma producing cells[35]. Furthermore, IFN-γ is a powerful potentiator of IL-12 induction and is thought to provide a basis for a positive feedback regulation of the cytokine[36].

Luteinizing hormone-releasing hormone has been reported that up-regulates IL-2 receptor expression in lymphocytes[37]. This may explain the high levels of IL-12 (pg/ml) and SIL-2R (ng/ml) which associated with high levels of LH (mIU/ml) in non-pregnant PCOS group when compared with non-pregnant control group as demonstrated in tables (2) and (3) respectively.

Significant positive correlation between the decreased CD8+ T cells in peripheral blood and the increased testosterone serum concentrations was noted in women with PCOS[38] and These CD8+ T cells are circulate in blood rather

than localize in decidua, and produce IL-10 and a progesterone-inducible NK cell blocking factor that reduces the expression of interleukin 12 via the inhibition of arachidonic acid metabolism[39]. This may explain the significance high levels of IL-12 (pg/ml) which are in parallel with the significance high levels of testosterone (ng/ml) in the spontaneous abortion PCOS groups (missed and blighted ovum) and successful pregnant PCOS group when compared with pregnant control group as demonstrated in tables (2) and (3) respectively.

Measurable amount (2.54 ng/ml) of sIL-2R levels in non-pregnant control group of this study table-3 which is in agreement with other study that demonstrated that little IL2Rα is expressed on unstimulated T cells or is found as s-Tac in the serum of healthy people[40].

The data presented in table-3 demonstrated that the levels of sIL-2R in successful pregnant PCOS (2.81 ng/ml) and spontaneous abortion PCOS groups (4.75, 4.27 ng/ml of missed abortion and blighted ovum PCOS respectively) which possessing previous abortion were increasing when compare with successful pregnant control group (2.002 ng/ml), these results is in consistent with other study reported that IL-2R were significantly elevated in patients with a poor obstetric history possessing recurrent aborters[41]. Also table-3 demonstrated that the sIL-2R levels in successful pregnant PCOS group was decreasing insignificantly when compare with spontaneous abortion PCOS groups, this was in line with other study which revealed that IL-2R values obtained during early pregnancy were lower in patients who subsequently had successful pregnancies than in those who aborted again[42].Paradisi 2003 found sIL-2R levels significantly higher in missed abortion than normal pregnant[43]. This may explain the significant increasing of sIL-2R levels in missed abortion and blighted ovum PCOS group when compare with pregnant control group as demonstrated in table-3.

High androgen levels have been negatively correlated with the concentration of PP14[33]. Recent experimental findings showed that PCOS patients have serum glycodelin concentrations significantly lower during the first trimester of pregnancy[27,28]. However, PP14 inhibits the production of IL-2 from mitogenically stimulated lymphocytes, and leads to a reduced IL-2R release[44]. This may explain the high levels of sIL-2R (ng/ml) which are in parallel with the high levels of testosterone (ng/ml) in the spontaneous abortion PCOS groups (missed and blighted ovum) and successful pregnant PCOS group when compare with pregnant control group as demonstrated in tables (2) and (3) respectively.

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