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RESEARCH ARTICLE

Study of IL-15, IL-11, and Some Physiological Parameters in Aborted Women

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ABSTRACT

Objective: The objective of current investigation is to know the roles of IL-15 and IL-11 with some physiological indicators in pathophysiology of aborted women. **Methods:** This investigation was conducted in the Medical City Hospital's gynecology consultant for period of March–May 2023. Thirty blood samples were taken from aborted women who visit hospitals and clinics. In addition to thirty blood samples were taken from healthy women who represented as a control group. The levels of IL-11 and IL-15 were detected by enzyme immunoassay (ELISA) (Immunotech, France), and random blood sugar observed by Biorex machine (UK). Levels of hematological indicators observed by complete blood count (CBC) machine (Sysmex, Japan company). Statistical Analysis System (SAS) program was used to analyze the current data. **Results:** Our findings showed no differences between patients than controls according to age. Significantly increases ($p < 0.05$) in the levels of IL-15 and IL-11 as well as in the RBS in patients in comparison with the healthy women. In contrast, our outcomes revealed no differences ($p > 0.05$) between study groups according to hematological markers. Finally, Present outcomes mentioned increases in the levels of IL-15 in patients ≥30 years than patients <30 years (53.62 , and decreases in the levels of WBCs in patients ≥30 years than patients <30 years with significant differences ($p < 0.05$). In contrast, another markers (IL-11, Hb, Glucose, Platelet, PCV, and RBC) didn't showed significant differences ($p > 0.05$) with patients age. **Conclusions:** Our study showed increases in the levels of interleukins (IL-15 and IL-11) in aborted women due to inflammation during abortion process. There are no significant differences between hematological indicators in aborted women than healthy women. Furthermore, diabetes observed in most women with abortion. Finally, increases the levels of IL-15 and decreases of WBCs indicators with age progression.

Keywords: Abortion women, IL-15, IL-11, Hematological indicators

1. Introduction

About 1–3 percent of women who want their own kids produce recurrent miscarriage (RM), an early pregnancy failure [30]. Early pregnancy is a frequent and complex condition

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that can have etiological causes that are genetic, anatomical, hormonal, or infectious, or they might have no known cause. A maternal immune component that interferes with the maternofetal tolerance might be among the root causes of unexpected recurrent abortions (RA) [24].

An essential part of being pregnant, through the implantation of embryos to baby birth, is the control of pro- and anti-inflammatory cytokines. Immunological homeostasis needs to be preserved at the mother-fetal interface, just like it is in a myriad of other situations, to protect both the mother and the developing fetus. Unwanted pregnancy results are linked to both improper immune activity and quiescence [2].

There is a pleiotropic cytokine called interleukin (IL)-11. Although IL-11 causes fibrosis in a variety of tissues, the exact process by which IL-11 causes fibrosis is unknown. Mother serum, deciduous tissue, and placenta from pregnancies with early-onset preeclampsia had higher levels of IL11 [12]. We have demonstrated that IL-11 suppresses human 1st trimester primary trophoblast cell expansion and an invading indicating a causative role for IL-11 in the development of early-onset preeclampsia [14]. Furthermore, the mid-gestational treatment of exogenous IL11 to pregnant mice mimics the characteristics of preeclampsia, including proteinuria, high blood pressure, fetal growth limitation, and preterm delivery [34]. Though IL-11 stimulates a number of pathways recognized to be changed in preeclampsia, the exact mechanism by which it triggers placental injury and preeclampsia remains unclear [25].

At the maternal–fetal interface, a variety of cytokines and chemokines control the distinct makeup and functionality of immune cells. Killer cell formation, upkeep, and activity have historically been supported by the pleotropic cytokine interleukin-15 (IL-15) [5]. In mice lacking IL-15, frequencies of remember CD8+ T cells, natural killer (NK) cells, and NKT cells are significantly reduced. In the uterus, NK cells are seen in startlingly high quantities compared to both lymphoid and non-lymphoid organs before pregnancy and during the early stages of gestation. It is now evident that NK cells are important for both healthy and difficult gestations, even if their exact roles in pregnancy are unknown [36]. A thorough investigation of IL-15 is necessary due to the significance and multiplicity of NK cells during gestation.

Among pregnant women, gestational diabetes mellitus (GDM) is a prevalent metabolic illness. Abortion history was linked to a higher incidence of GDM in expectant mothers, suggesting that it might be a risk factor for GDM prediction [33].

According to Biyik et al. [4], the complete blood count (CBC) is a frequently performed, affordable, and easily accessible test that is advised during the early stages of pregnancy to rule out pathological issues such anemia, thrombocytopenia, bleeding disorders, thrombosis, and thrombophilia.

The objective of current investigation is acknowledgment roles of IL-15 and IL-11 with some physiological indicators in pathophysiology of aborted women.

2. Materials and methods

2.1. Blood collection

This investigation was conducted in the Medical City Hospital's gynecology consultant for the period of March–May 2023. Thirty blood samples were collected from aborted women and thirty blood samples were collected too from healthy women that represented them as a control group. Study ages were ranged from 17–40 years.

2.2. Methods

The collected blood in gel tube was separated by centrifuge at (4000 rpm for 6 minutes) to has serum for detecting levels of IL-11 and IL-15 by enzyme immunoassay (ELISA) (Immunotech, France), and blood sugar by Biorex kit (UK). EDTA tube used to quantify levels of hematological indicators by complete blood count (CBC) machine (Sysmex, Japan company).

2.3. Statistical analysis

Statistical Analysis System (SAS) (2018) software was used, the impact of the patient and control groups' differences in the research variables was determined. The t-test was employed to contrast means statistically. In the present investigation, the chi-square test was utilized to compare percentages (0.05 and 0.01 likelihood) statistically significant.

3. Results

3.1. Average of age within study groups

Present research showed that no differences between patients than controls according to age as illustrated in Table 1.

Table 1. The average ages of the aborted women and the healthy group.

Group	Mean ± SE of age (year)
Patients	27.80 ± 1.07
Control	26.25 ± 1.08
T-test	3.046 NS
P-value	0.315

NS: Non-Significant.

3.2. Mean levels of IL-15 and IL-11 within study groups

Our study revealed a significant ($p < 0.05$) increases in the levels of IL-15 and IL-11 in patients (54.99 ± 1.59 and 18.41 ± 1.29) than controls (42.11 ± 1.70 and 14.03 ± 1.12) (Table 2).

Table 2. Comparison between the aborted women and the healthy group in IL-15 and IL-11.

	Mean ± SE	
Group	IL15	IL11
Patients	54.99 ± 1.59	18.41 ± 1.29
Control	42.11 ± 1.708	14.03 ± 1.12
T-test	4.667**	3.426**
P-value	0.0001	0.0013

**($P \leq 0.01$).

3.3. Mean levels of WBCs, Hb and Glucose within study groups

Present investigation showed a high means of Glucose in patients (82.77 ± 2.90) versus controls (73.17 ± 3.84) with significant differences ($p < 0.05$). In contrast, our outcomes

revealed no differences ($p > 0.05$) between study groups according to WBCs and Hb markers (Table 3).

Table 3. The levels of WBC, HB, and Glucose for aborted women and the healthy group.

	Mean ± SD		
Group	WBC (10^9/L)	Hb (g/dl)	Glucose (mmol/L)
Patients	8.97 ± 0.43	8.61 ± 0.30	82.77 ± 2.90
Control	7.92 ± 0.33	9.49 ± 0.51	73.17 ± 3.84
T-test	1.022 NS	1.191 NS	8.679*
P-value	0.141	0.145	0.049

*($P \leq 0.05$).

3.4. Mean levels of platelets, PCV and RBC within study groups

Current research presented no significant differences ($p > 0.05$) between study groups for platelets, PCV and RBC parameters as presented in Table 4.

Table 4. Comparison between the aborted women and the healthy group in PLT, PCV and RBC.

	Mean ± SD		
Group	Platelet (10^9/L)	PCV (%)	RBC (10^12/L)
Patients	194.76 ± 13.30	32.82 ± 0.79	4.21 ± 0.13
Control	186.29 ± 13.88	31.98 ± 0.69	5.34 ± 0.29
T-test	38.521 NS	2.098 NS	0.645 NS
P-value	0.661	0.418	0.201

NS: Non-Significant.

3.5. Relation of immunological and hematological markers with age of patients

Present outcomes mentioned increased levels of IL-15 in patients ≥30 years (57.73 ± 1.74) than patients <30 years (53.62 ± 1.93), and decrease levels of WBCs in patients ≥30 years (8.00 ± 0.68) than patients <30 years (9.45 ± 0.53) with significant differences ($p < 0.05$). In contrast, another markers (IL-11, Hb, RBS, Platelet, PCV, an8d RBC) don't showed significant differences ($p > 0.05$) with age patients (Table 5).

Table 5. Effect of age groups in parameters studied of the aborted women.

	Mean ± SE		
Parameters	<30 yr.	≥30 yr.	P-value
IL-15 (pg/ml)	53.62 ± 1.93	57.73 ± 1.74	0.0498*
IL-11 (pg/ml)	18.06 ± 1.54	19.11 ± 2.47	0.569 NS
WBC (10^9/L)	9.45 ± 0.53	8.00 ± 0.68	0.0387*
Hb (g/dl)	8.96 ± 0.32	7.92 ± 0.59	0.085 NS
Glucose (mmol/L)	84.74 ± 3.42	78.82 ± 5.39	0.147 NS
Platelet (10^9/L)	195.96 ± 15.31	192.40 ± 26.84	0.896 NS
PCV (%)	33.12 ± 0.81	32.24 ± 1.79	0.472 NS
RBC (10^12/L)	4.26 ± 0.16	4.09 ± 0.24	0.238 NS

4. Discussion

Abortion is a complex phenomenon that has a major impact on economic output and production since it can result in large financial losses, particularly during the latter stages of pregnancy. Numerous elements influence it, comprising non-infectious elements like medications, nutritive and chemical substances, plant poisons, hormones, and unidentified causes, as well as infectious elements like bacteria, viruses, fungi, and protozoan pathogens [8]. The etiology of abortion is heavily influenced by both infectious and non-infectious factors. Selection faults, dietary and chemical variables, poisons, poisonous plants, genetic factors, heat stress, hormonal changes, and fluctuations in blood metabolite concentration are examples of non-infectious causes [26]. Present investigation showed no differences between age of aborted women and controls due to samples size of participants. Moradinazar et al. [13] showed the age period 18–30 years scored highest percentage of abortion than >30 years. A prior study discovered a statistically significant correlation between age and ending a pregnancy, with women 45–49 years old having greater probabilities than younger women [23]. This might be partially caused by the reality that elderly women are more likely to experience medical conditions and pregnancy-related issues, such as diabetes, chromosomal abnormalities, and heart disease, which could make the pregnancy more difficult and have a worse prognosis [17]. In a similar vein, the size of their family might have reached its ideal level [18].

Outcomes of conducted study mentioned significant raised levels of IL-15 in aborted women than controls, and these outcomes associated with outcomes of Saldanha et al. [19]. The primary source of IL-15 was found to be trophoblast cells, and the authors revealed that IL-15 secretion is elevated in placental tissue of disrupted the initial trimester of pregnancy. Unrestrained production of IL-15 is linked to unexpected and repeated miscarriages, even though it is extensively produced in the uterus throughout pregnancy and in the uteroplacental unit when not pregnant [5]. Patients who experience repeated 8miscarriages may have disrupted implantation and vascularization with subsequent placental and fetal rejection, which might explain the increased production of IL-15 in their decidua [28].

Throughout pregnancy, the amount of IL-15 in the uterus is copious and closely controlled. According to multiple sources of evidence, maintaining IL-15 homeostasis is essential for the mother's and the fetus's health. Many biological substances have been created to imitate or suppress the action of IL-15 on target cells because to the extensive interest in IL-15 as a modulator of anti-tumor immunity in preclinical investigations [31]. When used alone, IL-15 agonists are effective in growing killer cells but not in rejecting human malignancies. These findings, which are believed to stem from IL-15's compensating activation of anti-inflammatory communication, might be very significant for procreation, as it requires healthy inflammation to preserve fetal tolerance [5].

Furthermore, the amount of uNK cells is correlated with the production of interleukin-15 (IL-15) and leukaemia inhibitory factor in the endometrium of women who have repeated unsuccessful implantation following in vitro fertilization (IVF), indicating a possible function for uNK cells in recurrent miscarriages [11].

Serum levels of interleukin (IL)-11 are higher in pregnancy that lead to the occurrence of early-onset preeclampsia. In pregnant mice, pharmaceutical rise of IL-11 leads to the expansion a number of symptoms similar to early-onset preeclampsia, such as proteinuria, hypertension, and fetal growth restriction [12].

Al-Kinani et al.'s [1] findings, which correlated with our analysis, revealed that aborted women had higher mean levels of IL-11 than controls. One important cytokine linked to implantation and decidualization is IL-11. Recurrent pregnancy losses (RPL) have endometrial tissues with lower expression of IL-11, indicating that RPL significantly prevents

abortion [35]. Therefore, addressing IL-11 signaling deficits in the endometrium may be a possible treatment for RPL. In IL-11R animals, there was impaired decidualization and a reduced number of uterine stromal cells. However, it is not possible for these in vivo intervention studies carried out in mice to accurately represent alterations in people [15]. Because an unplanned abortion happens in 30% of all female pregnancies, most of which occur prior to a clinical pregnancy test, defective implantation and placentation are serious issues in human pregnancy. Additionally, the human endometrium expresses IL-11. Therefore, in order to determine if the alterations in IL-11 and its receptors are connected to RPL, a pertinent research must be carried out.

The researchers show that in an animal model of preeclampsia, IL-11 triggered the maternal inflammasome, resulting in pyroptosis in a human maternal villus. According to Menkhorst et al. [12], this is the first proof that IL11 triggers the inflammasome in any kind of tissue. In women with increased blood IL11 in the early stages of pregnancy, therapeutic suppression of the NLRP3 inflammasome may be able to avoid IL-11-induced activation of the umbilical cord and eventual preeclampsia. Current research in numerous illnesses is focused on developing medications to block IL11-induced inflammation and fibrosis. One such medicinal properties. might target the inflammasome to stop IL11-induced fibrosis and inflammation in the placenta among other tissues. Nevertheless, this research also shows that reducing IL-11 action is necessary to enhance pregnancy outcomes and that merely blocking placental inflammasome activation to avoid preeclampsia-associated hypertensive is insufficient protection against insufficient placental supply.

Our research showed no differences between WBCs, PLT, PCV, RBCs and Hb parameters with study groups, and these outcomes were matcher with findings by Hajiabadi et al. [6]. Evidence from the past points to a possible link between inflammatory and spontaneous abortion. In particular, pathogens have been linked to 66% of late miscarriages and 15% of the earliest abortions [3]. Preterm birth, premature membrane split, spontaneous miscarriage, fetal infections, and congenital deformities are only a few of the unfavorable obstetrical consequences that can arise from pathogens during gestation [32]. Although inflammation plays a crucial and essential function in healthy pregnancies, a number of pregnancy diseases can result from aberrant and prolonged inflammation and the failure of anti-inflammatory cytokine-producing cells to resolve it [27].

The authors demonstrated that spontaneous abortion was at risk due to low hemoglobin levels. Additionally, they noted that in order to reduce the risk of anemia throughout pregnancy, women of reproductive age should take iron pills both before and during their pregnancies [10].

Because PLR has a high sensitivity and specificity in the pathological processes of abortion, a new study proposed utilizing it as a predictive indication to identify women who experience recurrent miscarriages [7]. Pregnancy may cause a greater incidence of platelet destruction. Pregnancy causes a rise in the amount of blood, which causes the spleen to enlarge and may kill additional platelets during the procedure of filtering [20]. In comparison with controls, those suffering from earlier loss of fetal tissue had platelets in an increasingly developed phase of stimulation, as evidenced by decreased platelet heights and membranes the degree of roughness values, a significant shift in the plasma membrane's modulus of flexibility, raised platelet microparticle manufacturing, and a higher level of procoagulant surface markers. These alterations were demonstrated to be correlated with platelet impulsivity, which was linked to the gestation stage at which the abortion transpired and a greater incidence of harboring polymorphisms in thrombophilic factor genes in patients relative to controls [9].

Similar to the current study, Wang et al. [33] found that aborted mothers had higher glucose levels versus controls. The exact cause of gestational diabetes in some women and

not in others is still unknown to researchers. Overweight before to conception frequently contributes. Normally, a number of hormones regulate blood sugar levels. However, the body finds it more difficult to handle blood sugar effectively during pregnancy because to changes in hormone levels [21]. Pregnant women with an abortion background had a higher chance of developing diabetes; this finding suggests that abortion history may be a risk factor for diabetes prediction. According to a recent investigation, women who have previously experienced abortions that were induced or abortions are more likely to develop diabetes during their first pregnancy after giving birth. Understanding this link will assist with diabetes screening and prevention [29]. According to earlier research, training during pregnancy that is aerobic, aerobic and strength mixed, or mind-body exercise is just as secure as it is beneficial for preventing diabetes [16].

Finally, present outcomes showed significant increased of IL-15 in patients >30 years due to increase inflammation in pregnant women with age progression than young age. In contrast, current findings showed decrease WBCs in patients >30 due to impaired immune status with age progression than young age.

5. Conclusions

Our study showed increases in the levels of interleukins (IL-15 and IL-11) in aborted women due to increase inflammation during abortion process.. There are no significant differences between hematological indicators in aborted women in comparison with the controls. Occurrence diabetes in most women with abortion. Finally, increases in the levels of IL-15 and decreases of WBCs indicators with age progression.

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