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Uric Acid Level and Correlation with Missed Abortion Biochemical Changes



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ABSTRACT

Background: Missed abortion is a dead embryo that kept within the uterus without unprompted abortion. The hormonal and biochemical defect in pregnant women has their association with an increasing rate of the missed abortion process in the first trimester. Elevated uric acid in the first trimester was correlated with rising risk of pre-eclampsia, insulin resistance inflammation, and fetal growth restriction. **The aim of the study:** we aim to find out the possible role of uric acid in missed abortion. **Methods:** This prospective study was done by collecting serum samples from the two groups (missed aborted=25, pregnant=25) with a limiting range of gestational age (6-11 weeks). All patients were tested for fasting serum glucose, insulin, uric acid, estrogen, progesterone, prolactin, testosterone, thyroid stimulating hormone, free T3 and T4. **Results:** A significant increase in uric acid level was shown in aborted women compared to control groups in addition to a significant reduction in progesterone, estrogen, and prolactin and testosterone level in aborted women. **Conclusion:** The data revealed that a high level of uric acid and a low level of progesterone, estradiol, and testosterone could be possible related causes of an increasing incidence of missed abortion.

1. INTRODUCTION

The most prevalent complication of early gestation is missed abortion (MA)(1). Which is a sort of abortion in which the dead embryo is conserved within the uterus (2).the overwhelmingly causes of missed abortion are maternal endocrine, immune disorganizations, metritis and chromosomal anomalies (3), however, in 26-66% of cases no apparent cause is detected for missed abortion(4).

Uric acid is the product of purine oxidation that at most excreted in urine (5). In beginning of conception the level of serum uric acid declines predominantly $\leq 3\text{mg/dL}$ that is related to the uricosuric impacts of the estrogen level(E2) in addition to renal blood flow augmentation (6).likewise elevated uric acid concentrations in the first trimester was correlated with rising risk of preeclampsia evolution (7), also related to insulin resistance by giving rise to endothelial function impedance and nitric oxide production reduction that is influential to glucose uptake and progression to insulin resistance (8, 9).

Uric acid may cause inflammation and oxidative effort in adipocytes that is a participant in the development of metabolic syndrome (10). The rising index indicates that a high serum uric acid in gestation could be a valuable biomarker of preeclampsia in addition to the contribution in the pathogenesis of the manifestations of maternal and fetal problems (6, 11).

The serum uric acid is robust negative feedback of the action of endothelium and glomerular function that prompts the increment of systemic blood pressure and can cross passively to the fetal vessels(6).

2. PATIENTS AND METHODS:

This study was conducted at the Obstetric and Gynecological Teaching Hospital. The study carried on 50 patients with gestational age (6-11w) allocated into two groups, the control group consisted in 25 women with normal pregnancy, while the second group consisted in 25 missed aborted women diagnosed by an ultrasound, which shows an empty gestational sac or embryo without cardiac activity (12). The picked out women were free from any diseases. All the participants signed the agreements and the committee of medical ethics approved the protocol of the study.

All patients in both groups were tested for a fasting serum glucose and fasting insulin level based on these tests, the HOMA-IR “a homeostasis model assessment of insulin resistance”, an index was calculated in addition to uric acid, estradiol (E2), progesterone, prolactin, testosterone, thyroid stimulating hormone (TSH), free T3 and T4 measured by using a ready-made kits for this purpose on cobas e immunoassay analyzers.

The Data analysis was performed by commercially available software (IBMSPSS version 22). Values were expressed as mean \pm SEM. Performed for comparison, Pearson’s correlation coefficients (r) were calculated to quantify the correlation between serum uric acid and other biochemical parameters, and statistical significance was defined as $P \leq 0.05$.

3. RESULTS:

A significant increase in uric acid level was shown in aborted women compared to control groups in addition to a significant reduction in progesterone, estrogen, and prolactin and testosterone level in aborted women

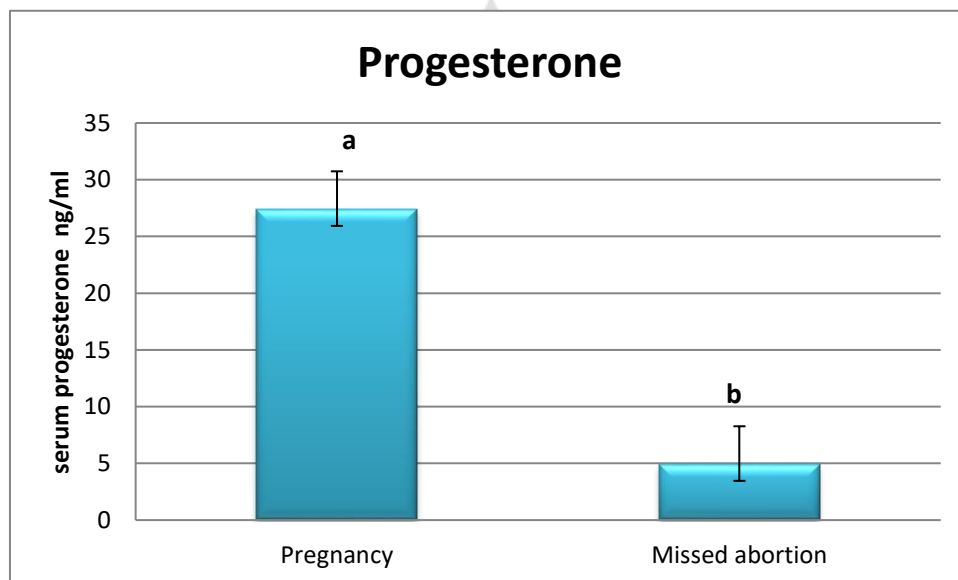


Figure (1): Progesterone level of pregnant & missed aborted women. Results with non-identical superscripts (a, b) between study groups were considered significantly different. ($P < 0.05$)

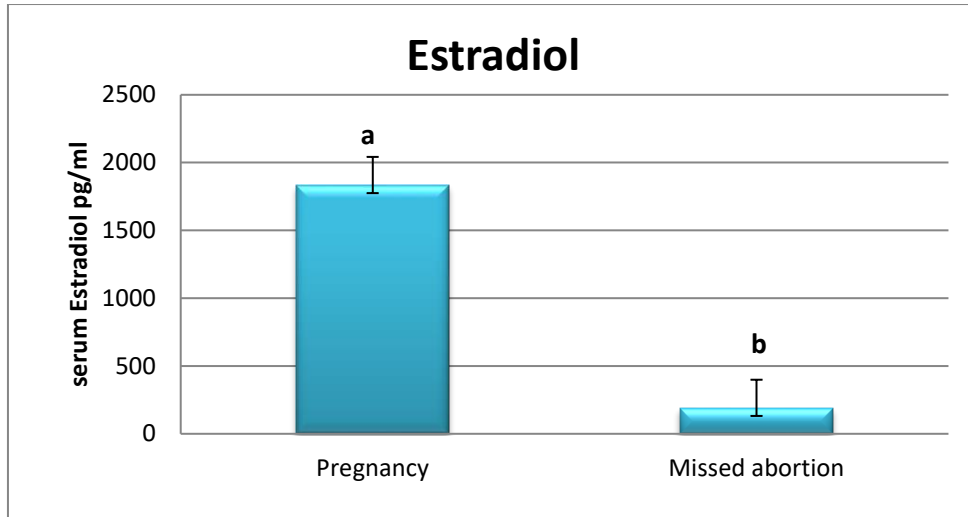


Figure (2): Estradiol level of pregnant & missed aborted women. Results with non-identical superscripts (a, b) between study groups were considered significantly different. ($P < 0.05$)

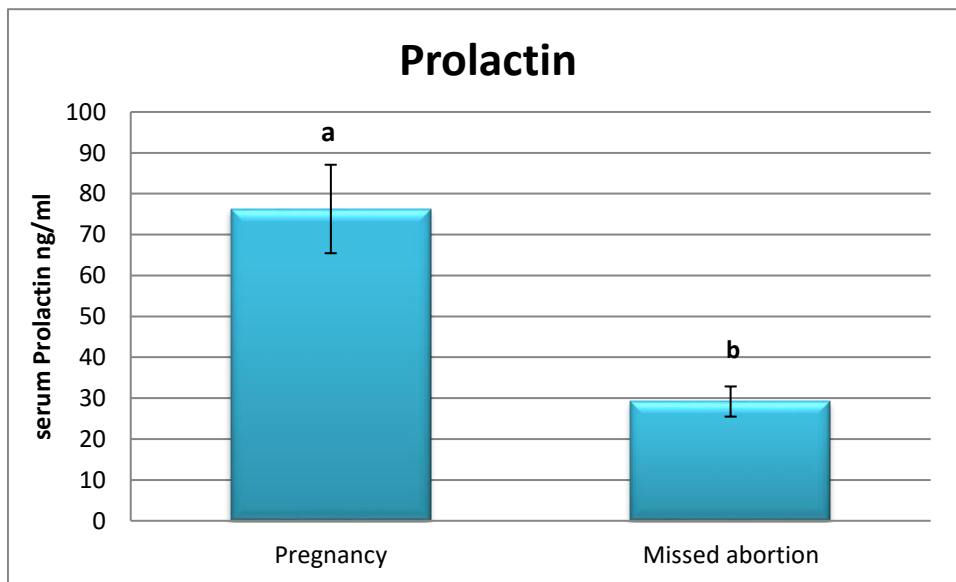


Figure (3-3): Prolactin level of pregnant & missed aborted women. Results with non-identical superscripts (a, b) between study groups were considered significantly different. ($P < 0.05$)

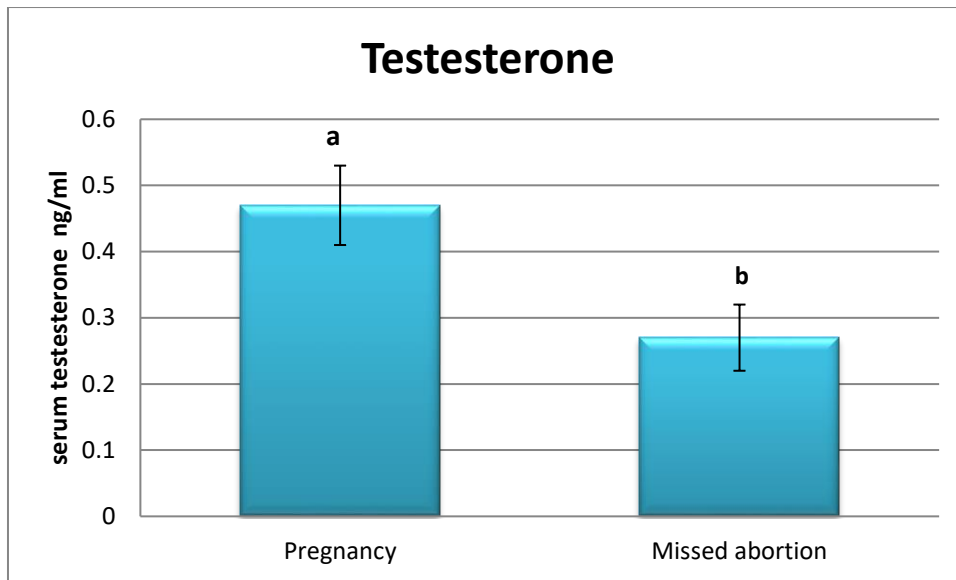


Figure (3-4): Testosterone level of pregnant & missed aborted women. Results with non-identical superscripts (a, b) between study group were considered significantly different. ($P < 0.05$)

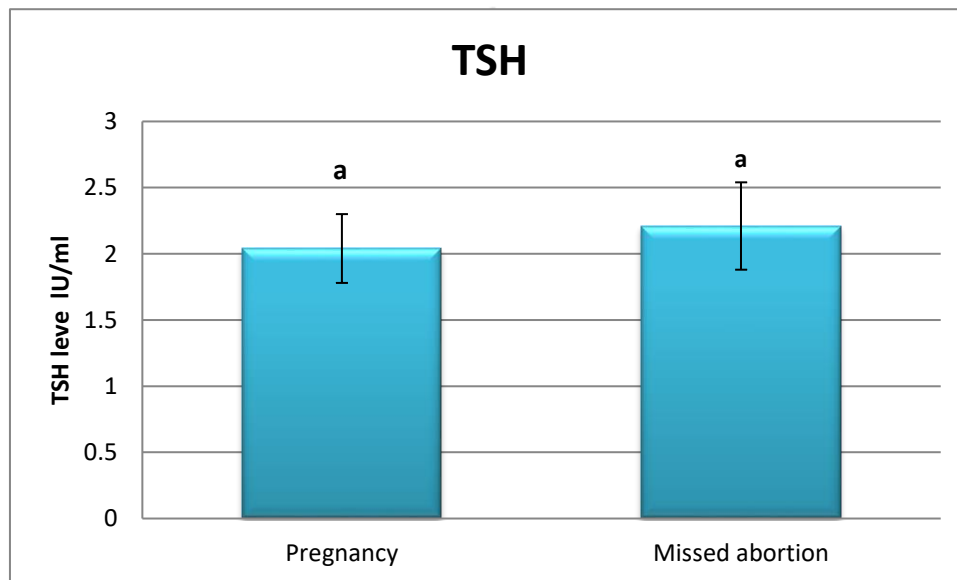


Figure (3-5): TSH level of pregnant & missed aborted women. Results with identical superscripts (a) between study groups were considered non-significantly different.

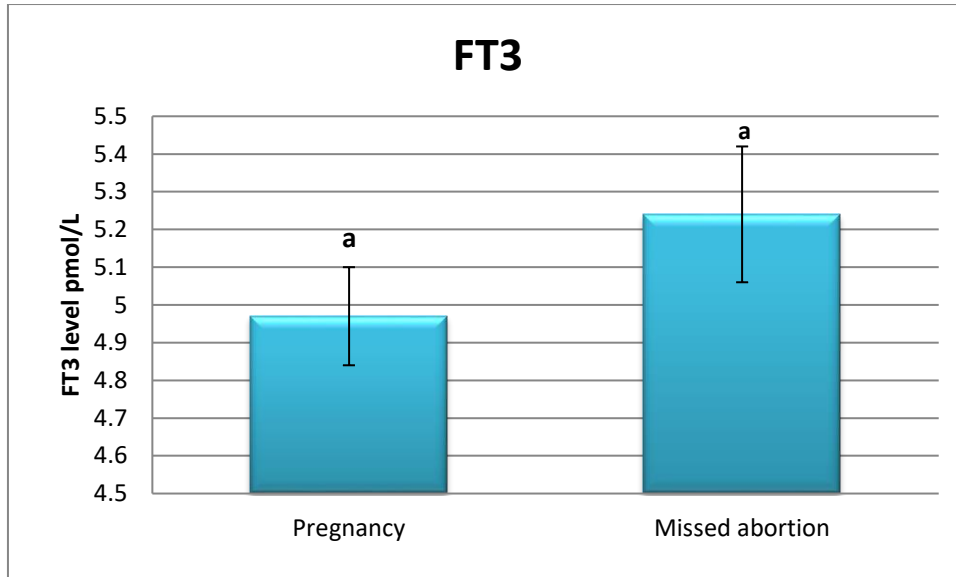


Figure (3-6): FT3 level of pregnant & missed aborted women. Results with identical superscripts (a) between study groups were considered non-significantly different

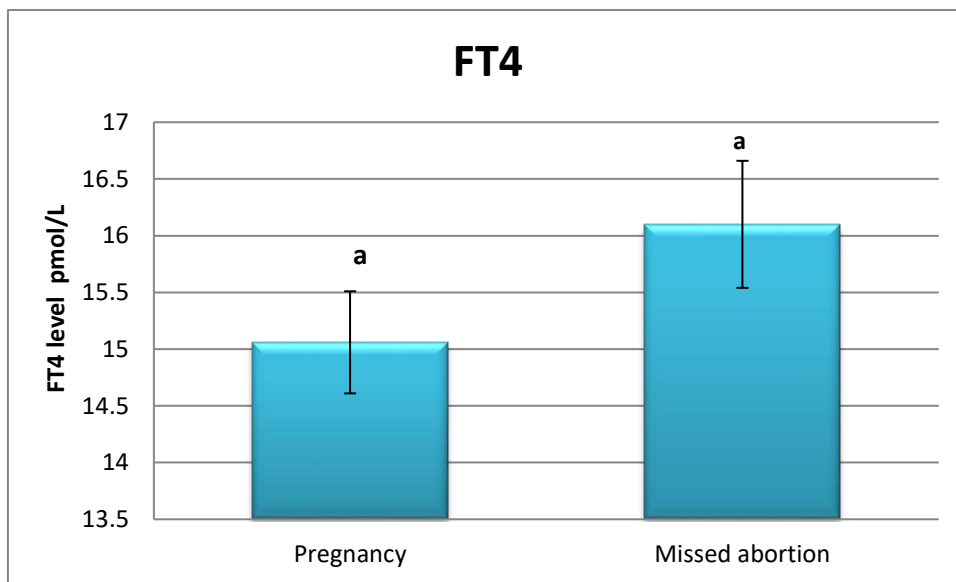


Figure (3-7): FT4 level of pregnant & missed aborted women. Results with identical superscripts (a) between study groups were considered non-significantly different.

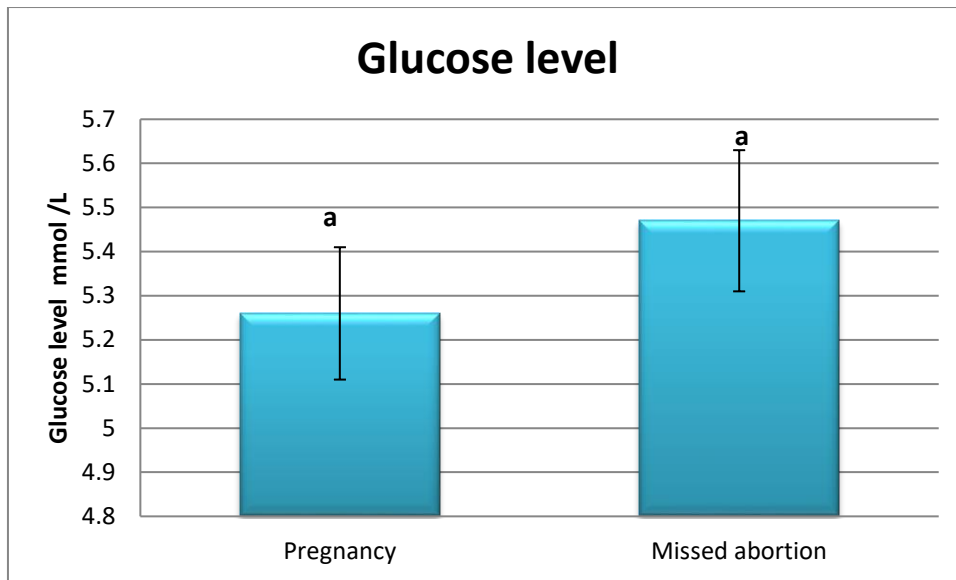


Figure (3-8): Glucose level of pregnant & missed aborted women. Results with identical superscripts (a) between study groups were considered non-significantly different.

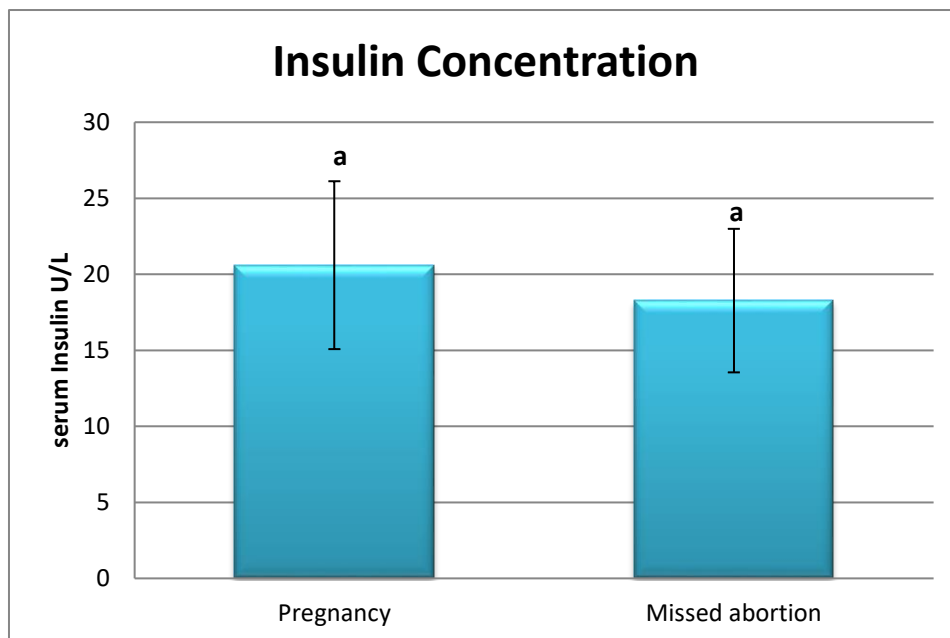


Figure (3-9): Insulin level of pregnant & missed aborted women. Results with identical superscripts (a) between study groups were considered non-significantly different.

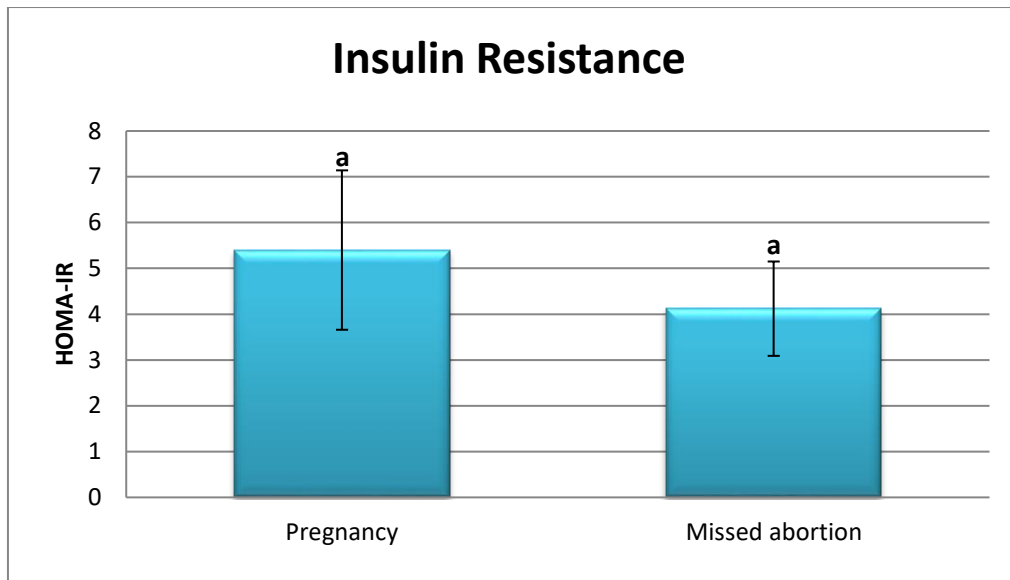


Figure (3-10): Insulin-Resistance of pregnant & missed aborted women. Results with identical superscripts (a) between study groups were considered non- significantly different.

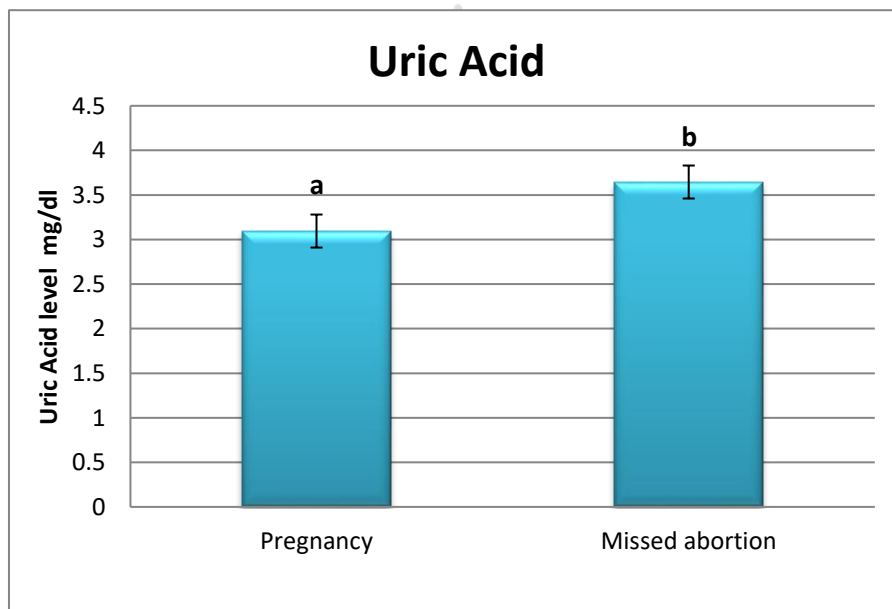


Figure (3-11): Uric acid level of pregnant & missed aborted women. Results with non- identical superscripts (a, b) between study groups were considered significantly different. (P < 0.05)

Table (1): The correlation between the hormones and other biochemical parameters in missed aborted women.

	Progesterone ng/mL	Estradiol pg/mL	Prolactin ng/mL	Testosterone ng/mL	FT3 pmol/L	FT4 pmol/L	TSH IU/mL
Uric acid mg/dL	r =-0.531* P<0.041	r =- 0.439* P<0.032	r =0.320 P<0.111	r =0.458* P<0.049	r =-0.129 P<0.530	r =-0.219 P<0.283	r =0.043 P<0.836

4. DISCUSSION

Missed abortion is depicted as an arrest of embryonic or fetal development (13). We intended to reveal the potential role of “uric acid” in the process of missed aborted women.

Progesterone has an important role in pregnancy, and the defect in progesterone level mentioned to be one of the main causes in abortion for its physiological function in maintaining early pregnancy. (14) Our obtained data revealed a significant decrease in the level of progesterone in missed aborted group and this may be due in part to a luteal phase defect which happened when the ovaries failed to produce a sufficient quantity of progesterone, or if the endometrium covering the lumen of the uterus when it failed to react to the effects of hormone which subsequently inducing termination of pregnancy. (15, 16, 17).

Since progesterone is considered the precursor of E2 and testosterone, the decrease in its level can express influencing of and subsequently decreasing in their levels as we had in our obtained data, which is revealed that progesterone has a positive correlation with E2. In addition, the low level of estradiol may cause disturbances in the process of implantation and primary growth of the fetus. (18)

“Hyperprolactinemia”, rather than “hyperprolactinemia”, considered also one of the contributing risks to cause abortion, as in Li et al. study, which is compatible with our obtained data, lower basal serum prolactin that is proportionally correlated with TSH; is associated with an increased risk of miscarriage. (19).

Although there is no significant difference in thyroid hormones between the two studied groups in our data, but it showed an increase in the level of FT4 in missed aborted women which is considered an indication for possible gestational hyperthyroidism state or pre- and possibly inducing of abortion due to placental abruption, pre-eclampsia, fetal growth restriction and

perinatal morbidity and mortality as sequelae, and this result is compatible with Davis et al and Maruo et al who also proposed that maternal thyroid hormone levels are one of the endocrine factors responsible for the abortion threat.(20,21) . The risk of hyperuricemia was significantly elevated in subjects with higher FT4 level (22), hyperuricemia in patients with over hyperthyroidism may be caused by the action of FT4 in the kidney (23).

An elevated level of serum uric acid has been substantially related with several pathologies particular to pregnancy such as pre-eclampsia, but also more recently related to fetal growth restriction (FGR) (24,25,26). according to our study, a significantly high level of uric acid was found in missed aborted women compared to normal pregnant women (control group) and this may be considered to a low level of serum estrogen “ As shown in Figure 2” In our study uric acid level is correlated negatively with estradiol and progesterone.

Biologically, uric acid level is found to be affected by uricosuric effects of estradiol action which inhibits renal tubular reabsorption of uric acid, rather than progesterone.(27,28,29) However, this inverse correlation between uric acid, and estradiol, progesterone is proved in our data where uric acid has observed in a negative correlation with both hormones.

Uric acid has been established to prohibit the “endothelial growth factor” of the vascular endothelium and impeding the generation of endothelium and consequently it may have a forthright part in prohibiting embryonic angiogenesis producing a small for date estimated gestation age of an infant (30), also elevation of serum uric acid can furthermore impede trophoblastic overrun “in vitro”(31) .

Also, studies in animals have revealed that insulin resistance is arranged by uric acid levels, also serum uric acid level was correlated with the evolution of resistance of insulin during gestation(32), that is concordant to our results where there is a respectable increase in glucose level exceeding 5.1 mmol/L limits of gestational diabetes which is positively related to uric acid level elevation (33, 34).

A study showed that uric acid was elevated in pregnancy with a reduced fetal movement as an aspect of fetal distress(25) without any hypertension or abnormal renal function. Marie et al study showed that uric acid crystal MSU (monosodium urate)has a causative factor in placental inflammation and dysfunction producing to increased trophoblastic death and impaired syncytialization in primary cytotrophoblasts and in placental explants that indicated a

paramount part of MSU Crystals and IL-1 in triggering placental inflammation with potential involvement in placental dysfunction leading to FGR (35).

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