Article

Estimation and study of some Elements and Hormones in Women with Recurrent Miscarriage

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ABSTRACT

Introduction : Recurrent miscarriage is defined as the loss of pregnancy due to more than one successive pregnancy, one after the other, before the twentieth week of pregnancy. Miscarriage is considered one of the complications of pregnancy. The reasons for miscarriage are wide-ranging, and among these reasons that are the focus of this study are (hormonal disturbances, nutritional factors, pollution, and the environment).

Methods: The case-control study included 50 sick women suffering from primary and recurrent miscarriage and 40 healthy women with no history of miscarriage in Basra Governorate. Some trace elements (iron, zinc, and magnesium) were measured from blood serum, and a colorimetric technique was used using a spectrophotometer to study the extent to which a decrease in these elements affects the success of pregnancy. The level of some hormones, including thyroid hormones (TSh, progesterone, and testosterone), were also measured using the fluorescent immunoassay technique.

Results: In this study, there was a decrease in the levels of trace elements (Fe, Mg, Zn) that were measured for women with first and recurrent miscarriages compared to the control group. The results for aborted women who lived in the district areas were found to be lower than in the city center areas, and they obtained Statistically significant P values = 0.000. As for hormones, progesterone levels were at low levels for the aborted women

compared to the control group, while TSH and testosterone levels were high among the aborted women for both the city center and the district compared to the control groups. P values were = 0.000.

Conclusions: A deficiency in the elements iron, zinc and magnesium has a negative effect on the success of pregnancy, and it also has an effect on the hormones TSH, progesterone and testosterone, so the nutrients must be preserved to have a successful pregnancy and the birth of a healthy child.

Keywords**:**
Recurrent Miscarrriage, Trace elements, TSH, Progesterone, Testosterone hormones

1.Introduction

Trace elements are linked to biochemical processes and thus play an important role in the formation and growth of the fetus inside the mother's womb (1). Also, the process of fetal growth requires certain concentrations of these essential elements for its growth during pregnancy. Therefore, the proportion of these elements is linked to the mother's physiology. Therefore, they will be involved in the process of miscarriage, fetal deformity, and hormonal disorders resulting from their deficiency, and thus the loss of the fetus (2).

The main element, iron, which participates in the formation of the protein hemoglobin and myoglobin, does not perform this role, but rather has several tasks, including the formation of mono-hormones, peroxidase enzymes, and cytochrome, as well as its transfer of auxin (3). Studies have shown that hemoglobin deficiency, which is caused by iron deficiency, leads to a lack of oxygen for the fetus and thus leads to premature birth and miscarriage (4).

Magnesium plays an important role in the health of a pregnant woman and her fetus. Some studies indicate that one of the factors that causes miscarriage is a lack of magnesium in the blood of the pregnant mother (5). The decrease in hydration levels during tight-lace pregnancy depends on many hormonal factors, including

epinephrine, norepinephrine, angiotensin II, serotonin, and bradykinin, which lead to increased blood pressure. Zinc is also one of the trace elements that is directly involved in stress and oxidative stress, which reaches its peak (6). In the blood vessels and leads to dysfunction in the fetus in the first month of pregnancy. In addition to engineering defects, it may cause hypertension by carbon reabsorption (7).

Progesterone is an endogenous steroid hormone that participates in the formation of the fetus. It also preserves the fetus and prevents miscarriage. Therefore, when there is a decrease in this hormone during pregnancy, it leads to premature birth. Also, the decrease in essential nutrients such as vitamins and trace elements such as zinc is necessary in maintaining the hormone level during pregnancy (**8**)

There is an increase in the level of testosterone in the blood circulation, and there is a relationship between this hormone and miscarriage (9) The dangers of testosterone are unknown, but its direct position is through its direct action on eggs The difference is that the focus is on the analysis of testosterone, which may have a simple effect on the uterus(10).

Pregnancy is associated with huge changes that can be linked to thyroid function. The functioning of the maternal thyroid gland is important during pregnancy for both the mother and the fetus (11). High maternal thyroid hormone (TSH) is associated with an increased risk of premature birth, fetal death, placental abruption, and decreased neurological development in the child (12).

2. 2. Material and Methods

2.1: Study Subject

Ninety participants were included in this study, divided into two groups: the case group, consisting of 50 patients, and the control group, comprising 40 women with no history of miscarriage. Samples were collected from Basra Women's and Children's Hospital in Basra and the Department of Chemistry, College of Science, University of Basra. Patients with recurrent miscarriages were further divided based on residence between the city center and the village. The age range of the study participants was between 18 and 40 years, encompassing reproductive age.

Sample Collection:

Blood samples of 8 ml were collected in gelatinous tubes and allowed to clot at 37°C for 30 minutes. Subsequently, they were centrifuged at 3000 rpm for 5 minutes to obtain serum samples for biochemical analysis. The serums were stored at freezing temperature (-20°C) for later use in measuring elements and biochemical factors. Additionally, 2 ml of blood was stored in tubes containing the anticoagulant EDTA for the measurement of blood levels and blood groups for the entire sample.

2.2: Biochemical Assessments:

The trace elements iron (Fe), zinc (Zn), and magnesium (Mg) were measured in the blood of the women who experienced miscarriages and the control group using a UV-vis Spectrophotometer device manufactured in England. Additionally, certain hormones were measured in both the patients and the control group, including thyroid hormone (TSH), progesterone, and testosterone, using the Fluorescent immunoassay technique with the Finecar plus device from China.

2.3: Statistical Analysis:

SPSS for Windows (version 26, USA) was employed to analyze the relationships between trace elements, thyroid hormone TSH, testosterone, and progesterone in both control groups and patients.

3-Results

The results of measuring trace and essential elements among the female participants in the study are presented in Table (1). Differences in the levels of iron, zinc, and magnesium were observed in women with recurrent miscarriage and those experiencing their first miscarriage, residing in both rural and urban areas, when compared to the control group. Notably, there were significant differences in the levels of iron, magnesium, and zinc between women experiencing their first miscarriage and those with recurrent miscarriages, across both geographical locations of urban and rural areas, when compared to the control group.

Table (1): Levels of Fe, Mg, and Zn in a group of women experiencing first and recurrent miscarriages and a healthy control group.

elements	Residency	Type of miscarriage	Groups		P-value
			Case	Control	
			Mean ± S.D	Mean ± S.D	
Fe (µmol/L)	Center	Primary	16.000 ± 4.320	17.055 ± 5.647	.000
		Recurrent	8.000 ± .647	17.055 ± 5.647	.000
	District	Primary	7.083 ± 1.240	18.705 ± 5.893	.000
		Recurrent	4.357 ± 1.716	18.705 ± 5.893	.000
Mg (mg/dl)	Center	Primary	1.492 ± .259	2.745 ± 3.827	.000
		Recurrent	1.350 ± .092	2.745 ± 3.827	.000
	District	Primary	1.333 ± .150	2.045 ± .157	.000
		Recurrent	1.104 ± .238	2.045 ± .157	.000
Zn (µg/dl)	Center	Primary	82.923 ± 10.41	111.25 ± 23.89	.000
		Recurrent	67.38 ± 2.722	111.25 ± 23.89	.000
	District	Primary	66.500 ± 7.503	101.25 ± 20.66	.000
		Recurrent	56.57 ± 20.665	101.25 ± 20.66	.000

The results of this study revealed that iron levels were significantly lower in the groups of patients residing in the city center, experiencing primary miscarriage, and recurrent miscarriage (16.000±3204, −8.000±647µmol/l) compared to the healthy control groups in the same area (17.055±5.647µmol/l), respectively. These differences were statistically significant (P value = 0.000, 0.000).

Iron levels in the district areas were lower than those in the city center for both first and repeated miscarriages, respectively (7.083±1.240, 4.357±1.716 µmol/l), and lower than the iron levels in the control group in the district, which were (18.705±5.893 µmol/l).

Additionally, there was statistical significance observed in iron values, indicating that iron levels during repeated miscarriages were lower than those during first miscarriages, and iron levels were lower in the district areas compared to the city center.

Furthermore, magnesium and zinc levels were notably low during repeated miscarriages in the district (1.104 ± .238 mg/dl, 56.57 ± 20.665 µg/dl) compared to first miscarriages (56.57 ± 20.665 mg/dl, 66.500 ± 7.503 µg/dl), and compared to the city center, where magnesium and zinc levels were higher than those in the district (1.350 ± .092mg/dl, 67.38 ± 2.722 µg/dl) and first miscarriages in the city center, respectively (2.045 ± .157, 2.745 ± 3.827mg/dl) (101.25 ± 20.66, 111.25 ± 23.89 µg/dl).

In comparison, the control group showed higher levels in both the city center and the district compared to abortion cases, indicating statistical significance for both elements (p-value=0.00).

Table (2): Levels of TSH, testosterone, and progesterone hormones in the group of women experiencing first and repeated miscarriages and the control group.

Hormones	Residency	Type of miscarriage	Groups		P-value
			Case	Control	
			Mean ± S.D	Mean ± S.D	
TSH (mlu/L)	Center	Primary	1.339 ± 2.037	3.280 ± .815	.000
		Recurrent	4.549 ± .318	3.280 ± .815	.000
	District	Primary	5.167 ± .615	3.599 ± .733	.000
		Recurrent	6.257 ± 1.734	3.599 ± .733	.000
Testosteron (ng/ml)	Center	Primary	.582 ± .350	.473 ± .207	.000
		Recurrent	1.137 ± .675	.473 ± .207	.000
	District	Primary	1.000 ± .111	.621 ± .214	.000
		Recurrent	1.400 ± .526	.621 ± .214	.000
Progestron (ng/ml)	Center	Primary	16.623 ± 7.222	81.500 ± 9.0201	.000
		Recurrent	8.438 ± .738	81.500 ± 9.0201	.000
	District	Primary	7.420 ± .991	68.654 ± 22.702	.000
		Recurrent	3.510 ± 4.508	68.654 ± 22.702	.000

Table (2) presents the study results, indicating a significant increase in TSH levels among women with recurrent miscarriages in the district (6.257 ± 1.734 miu/l) compared to those experiencing their first miscarriage (5.167 ± 0.615 miu/l) in the same geographical area. Similarly, TSH levels were higher among patients with recurrent and first miscarriages in the city center (4.549 ± 0.318, 1.339 ± 2.037 miu/l, respectively), suggesting hypothyroidism. When compared to the control group in both geographical locations (3.599 ± 0.733, 3.280 ± 0.815 miu/l), the differences were apparent.

There was also an increase in testosterone levels among women experiencing repeated miscarriages compared to those with their first miscarriage in the city center (1.137 ± 0.675, 0.582 ± 0.350 ng/ml, respectively), as well as when compared to the control group in the same area (0.473 ± 0.207 ng/ml). Table 2 demonstrates a concentration increase in testosterone during repeated miscarriages compared to first miscarriages in the district (1.400 ± 0.526, 1.000 ± 0.111 ng/ml), with a more pronounced increase observed in the city center compared to the control group in the same district (0.621 ± 0.214 ng/ml).

Regarding progesterone, the results showed a gradual decline in its levels. The values were lower during repeated miscarriages, followed by the first miscarriage in the district, and then repeated miscarriages and the first miscarriage in the city center (3.510 ± 4.508, 7.420 ± 0.991, 8.438 ± 0.738, 16.623 ± 7.222 ng/ml, respectively) compared to the control group for both the city center and the district (81.500 ± 9.0201, 68.654 ± 22.702 ng/ml), respectively. These differences were statistically significant, with p-values of (.000) for all hormones.

Table (3): The correlation between the hormones TSH, testosterone, and progesterone, and the elements Fe, Mg, and Zn.

		Fe (µmol/L)	Mg (mg/L)	Zn(µg/L)
TSH (MIU/L)	Pearson Correlation	-0.690**	-0.509**	-0.671**
	P-value	.000	.000	.000
	N	50	50	50
Testosteron (ng/ml)	Pearson Correlation	-0.551**	-0.255	-0.482**
	P-value	.000	.004	.000
	N	50	50	50
Progestron (ng/ml)	Pearson Correlation	0.679**	.574**	.775**
	P-value	.000	.000	.000
	N	50	50	50
***. Correlation is significant at the 0.05 level (2-tailed).**				
****. Correlation is significant at the 0.01 level (2-tailed).**				

From Table 3, it is evident that there is an inverse relationship between iron (Fe), magnesium (Mg), zinc (Zn), and thyroid-stimulating hormone (TSH) (r = -0.690**, -0.509**, -0.671**), respectively. Additionally, there is a negative correlation between iron (Fe), magnesium (Mg), zinc (Zn), and testosterone (r = -0.551**, -0.255, -0.482**), respectively. Conversely, there is a positive correlation between iron (Fe), magnesium (Mg), zinc (Zn), and progesterone (r = 0.679, 0.574**, 0.775**), respectively.

Discussion

This study was carried out to estimate the levels of some hormones (progesterone, testosterone, and TSH) and some essential and trace minerals in women with a history of recurrent miscarriage. This study may contribute to adding information about recurrent miscarriage. During pregnancy, several changes occur that may be complex between the genetic, anatomical, endocrine, nervous, and immune systems. When a defect occurs in these systems, pregnancy loss may occur(13).

The environment, lifestyle, and maternal nutrition play a fundamental role in the causes of spontaneous miscarriage of unknown cause. Trace elements such as Zn also play a role in steroid formation. As for iron and magnesium, their effectiveness in steroid formation has not been clearly determined. However, it is possible that magnesium is involved in the formation of progesterone in particular, but it may not be the reason for the repeated miscarriage(14). Progesterone is considered essential in maintaining pregnancy, as a deficiency in its production may lead to pregnancy loss, as proven by some reports.

In this study, there was a clear decrease in the level of the hormone progesterone in cases of recurrent and first miscarriage for women living in the district, and a lower decrease for women who had abortions in the city center compared to the control group. This reason is due to the variation in the decrease depending on the lifestyle, economic and job conditions, and this decrease is a cause of pregnancy loss in these cases (15).

A change in lifestyle, poverty, and malnutrition may also lead to a deficiency of vitamins and essential and trace elements. This deficiency can affect the production of the thyroid hormone TSH(16). Therefore, this deficiency in thyroid hormone affects the delay of the metabolic processes that the fetus and mother need(17).

In this study, hypothyroidism was found as a result of a decrease in the level of trace and essential elements, including zinc, iron, and magnesium. A significant decrease in the level of zinc was found. This is because zinc deficiency will lead to a decrease in the activity of 1,5-deiodinase in the liver and thus will reduce the conversion of T4 to active T3, and therefore the concentration of both T3 and T4

will decrease, so the concentration of TSH will increase(18). These results agree with 19).

Free testosterone is a free androgen (FAI) that can be elevated in the initial follicular stage(20). The most recent large-scale study with testosterone measurement found that FAI was detected in the first follicular period with a significantly increased risk of miscarriage with an increase in testosterone. High testosterone was found in the group of patients suffering from miscarriage. This is indicative of hyperandrogenemia(21).

Essential minerals such as magnesium play a crucial role in the success of pregnancy. Studies have shown that magnesium contributes to the pathophysiology of preeclampsia. Other studies have also highlighted the important role of magnesium in the success of pregnancy(22). This study also demonstrated a decrease in magnesium levels in women with recurrent miscarriages, indicating that the decrease in cases of recurrent miscarriage was higher than in the first miscarriage, and that the decrease in magnesium in rural areas was higher than in urban centers. Therefore, maintaining magnesium levels is necessary to ensure the outcomes of a healthy pregnancy(23). Studies have also recommended monitoring fetal and maternal health both before and after birth.

Furthermore, this study indicated that zinc deficiency was associated with an increase in miscarriages in women. Previous research has suggested that a deficiency in essential elements primarily leads to miscarriage(24). which in turn can cause endocrine disorders such as insulin resistance, decreased vitamin D levels, and imbalances in thyroid and sex hormones. This disruption can further lead to the impairment of sex hormone production, resulting in recurrent pregnancy loss (PRL)(25). Zinc deficiency may also affect sexual function(26). This study worked to understand the relationship between essential and trace elements and some hormones and their impact on recurrent and primary pregnancy loss. Diagnosing and treating patients with a history of recurrent pregnancy loss remains challenging

CONCLUSIONS

The present investigation is a pioneering endeavor to explore the relationship Between the levels of zinc, iron, magnesium and some hormones such as TSH, progesterone and testosterone and their effect on miscarriage. The research endeavor was to study miscarriages. From this study, it was found that the decrease in trace and essential elements, which play an important role in the

process of maintaining pregnancy and giving birth to a child with a healthy structure, the decrease in these elements also affects the hormones that have an essential role in the formation of the fetus. Therefore, pregnant women must avoid this decrease during pregnancy in order to maintain a healthy pregnancy and avoid the risk of miscarriage.Vital elements play a crucial role not only in the success of pregnancy but also in preventing endocrine disorders in the early stages of pregnancy. This study serves as a complement to previous research efforts, aiming to alleviate the burden of this challenging condition that has long troubled affected women, and potentially contribute to effective treatment strategies.

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