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The relationship between selenium deficiency and recurrent miscarriage

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Abstract
Background: Spontaneous recurrent abortion is the occurrence of two or more consecutive spontaneous abortions before the twentieth week of gestation and this is an increasingly common problem among women globally. Selenium has been postulated to be a contributing factor in pregnancy outcomes due to its antioxidant activity, its role in immune and thyroid functions.
Objective: The general purpose of this study was to determine the serum selenium concentrations in women with recurrent miscarriage and compare them with those of women without such history. Further, the study was to explore the effectiveness of selenium supplementation in pregnancy in women with recurrent miscarriage.
Methodology: this was an interventional cohort research run at Tikrit Teaching Hospital in Tikrit, Iraq between September 2024 and January 2025. The study included 100 individuals overall, divided into two groups: group 1 consisted of 50 women with a history of recurrent miscarriage and group 2 consisted of 50 women without such history. Every participant gave their permission; their ages fell between 20 and 40 years. Blood samples were obtained to determine the serum selenium, vitamin D, TSH, iron, and CRP. The women suffering recurrent miscarriage took selenium tablets at a 100-µg daily dosage for three months.
Results: measured were baseline and three-month serum levels of selenium. Pregnancy results were tracked and rates of miscarriage were noted. According to the study, women in the recurrent miscarriage group had lower selenium concentration in their serum (60.2±12.5 µg/L) than those in the control group (110.5±20.1 µg/L). Apart from the control group, the group suffering repeated miscarriages also showed lower vitamin D levels, higher TSH and higher CRP. Selenium supplementation for three months increased the serum selenium levels of the recurrent miscarriage group to 95.7±16.3 µg/L. The rate of miscarriage in the recurrent miscarriage group decreased from 40% before supplementation to 20% after supplementation. The rate of miscarriage in the control group was 5%.
Conclusion: On the basis of the obtained results, the present study indicates that selenium deficiency may be connected with recurrent miscarriage and that selenium supplementation may enhance the pregnancy results in women with a history of recurrent miscarriage. Despite the fact that selenium supplementation led to a remarkable increase in serum selenium concentration and lowering of the miscarriage rate, more studies are required to establish the clinical value and the correct quantity for the treatment of recurrent miscarriage.

Keywords: Selenium deficiency, recurrent miscarriage, supplementation, pregnancy outcomes, antioxidants

1. Introduction
It is a usual but a complicated issue for many women to conceive and carry two or more consecutive pregnancies to 20 weeks of gestation known as recurrent miscarriage. It affects about 1% to 2% of couples in the world, and yet, much is still unknown about the condition. At present, the causes of recurrent miscarriage are not well understood for many women, and 50-70% of cases are unexplained (Turesheva *et al*. 2023) [15]. A pathophysiological disorder with a complex etiology, recurrent miscarriage combines environmental, endocrine, genetic, and immunological elements. But in the past few years, vitamin shortages have been blamed for perhaps contributing to pregnancy loss risk. Selenium is one such micronutrient; a trace element vital for our diet and well-known for its antioxidant and cellular protecting properties (Gernand *et al*., 2016) [4].
Many antioxidant enzymes, including glutathione peroxidases that remove the possibly harmful free radicals therefore reducing oxidative stress, include selenium.

Recurrent miscarriage is among the pregnancy problems linked to oxidative stress, a disorder brought on by an imbalance between the generation of free radicals and antioxidants. The apparent link between selenium and recurrent miscarriage has caught the attention of the scientists since the element helps to lower oxidative stress. Selenium shortage has been hypothesized to cause negative effects on the body's capacity to fight oxidative stress and might so cause miscarriage. Women who experience recurrent miscarriage had lower selenium levels than those who have healthy pregnancies, according to several research, which implies that selenium level may be a risk factor for miscarriage (Kamada, H., & Hodate, 1998; Mazokopakis *et al*., 2007) [5, 10].

Not only is selenium shortage and miscarriage linked to a lack of antioxidants, but. Important in the preservation of pregnancy, selenium also participates in thyroid function, immunological control, DNA synthesis, and DNA repair. Selenium is essential for the thyroid gland to produce thyroid hormones, which are required for both general health of the expectant mother and fetal development (Schomburg and Köhrle, 2008) [14]. A recognized risk factor for miscarriage, hypothyroidism can result from a selenium deficit. Furthermore, pertinent to pregnancy is the way selenium influences the operation of immune cells, like T-lymphocytes, and controls inflammatory reactions, thereby contributing to immunological regulation. Recurrent miscarriage has been linked to either chronic inflammation or unbalanced immunological reactions (Wang *et al*., 2023) [17]. Given the growing awareness of selenium's significance for reproductive health, researchers have started looking at how low selenium levels affect women who have recurrent miscarriage. Certain studies have shown that adding selenium to women might improve their pregnancy outcomes. Though selenium supplementation has been shown to improve thyroid function, antioxidant capacity, and lower inflammation, the data to justify its use in avoiding recurrent miscarriage is few. While some studies have shown that selenium supplements are beneficial, others have not shown any such result, thereby demanding more research (Kumar *et al*., 2002; Lazarus, 2007) [8, 9].

Apart from its antioxidant function, selenium may have other elements influencing the dynamics of the miscarriage. Important in miscarriage risk are vitamin D, iron, and thyroid action. Adverse pregnancy outcomes have been linked to dietary deficits of several micronutrients. Low levels of vitamin D have been linked, for instance, to pre-eclampsia and gestational diabetes; selenium has been found to interact with vitamin D in the control of immunological and inflammatory activities (Ventura *et al*., 2017) [16]. On the other hand, iron shortage can cause anemia that increases the likelihood of miscarriage and inadequate fetal development. These other elements help to clarify the link between selenium and recurrent miscarriage and justify the need of a holistic approach to the knowledge and control of miscarriage risk (Abu-Ouf, & Jan, 2015) [1]. This study intends to investigate the relationship between selenium deficiency and recurrent miscarriage in order to identify the possible function of selenium in miscarriage avoidance.

2. Methodology

The aim of the study was to explore the relationship between selenium deficiency and recurrent miscarriage. A prospective cohort study was conducted at Tikrit Teaching Hospital in Tikrit, Iraq. The research was done on two groups of women, and the two groups were compared based on selenium levels, one group of women with a history of recurrent miscarriage and another group of women without such a history.

2.1 Study Population

The study sample comprised one hundred participants divided into two categories. The first group comprised 50 women who had a history of recurrent miscarriage i.e., two or more consecutive miscarriages. The second group also consisted of 50 women who had not experienced miscarriage, thus making them the control group. Women between the ages of 20 and 40 years were taken as sample of the study. The inclusion criteria stipulated that all the participants had to sign a consent form to enable them to be part of the study.

Exclusion criteria included having chronic diseases like diabetes, thyroid diseases, autoimmune diseases, or cancer, being pregnant or lactating at the time of the study and the use of selenium supplements during the study period to avoid contamination of results.

2.2 Sample Size

All in all, the study participated 100 women, among them 50 women with recurrent miscarriage and 50 women without such a history. The sample size was determined by previous research that showed a difference in selenium levels between women with recurrent miscarriage and those without for adequate analysis.

2.3 Study Period

The study was done between September 2024 and January 2025. Within this time, participants were enrolled, blood samples were drawn and laboratory tests were done.

2.4 Data Collection

Data collecting took the following form: Women were contacted at an outpatient clinic at Tikrit Teaching Hospital, and an initial screening using the inclusion and exclusion criteria applied in the study helped to determine eligibility. Every participant turned in signed informed permission. Demographic data—age, marital status, socioeconomic level—were gathered using a structured questionnaire based on medical history. Additional thorough medical histories were obtained on recurrent miscarriage and other pregnancy problems. Blood samples were taken in the morning following an overnight fast in order to gauge selenium content. Routine and somewhat accurate methods for element concentration analysis, serum selenium was investigated using either inductively coupled plasma mass spectrometry (ICP-MS) or atomic absorption spectrometry (AAS). Apart from selenium, the study also tracked additional factors that can contribute to raise the miscarriage risk: Vitamin D levels: Additionally looked at was the association between selenium and vitamin D in pregnancy outcomes. o Thyroid function: TSH was recorded since a higher risk of miscarriage has been linked to thyroid malfunction. o Iron levels: Iron condition was also ascertained since iron deficits can also affect the course of pregnancy. CRP: This inflammation marker was evaluated to determine whether it would have contributed to raise miscarriage risk.

2.5 Data Collection Timeline

Data collecting took place in stages

- Recruitment and Screening: September 2024 through October 2024 saw this process carried out.
  October 2024 to December 2024 blood samples were gathered and examined in laboratories.
- Data Analysis and Report Preparation: Data analysis and report writing kept on the last day of January 2025.

2.6 Statistical Analysis

The study data was analyzed using SPSS (Statistical Package for Social Sciences). In this study, mean and standard deviation were used to describe the demographic and clinical characteristics of the participants. Independent t-tests or Mann-Whitney U tests were used to compare selenium levels between the two groups, depending on the distribution of the data. To this end, the Pearson correlation coefficient was used to study the relationship between selenium levels and other biomarkers. A p-value of <0.05 was considered statistically significant.

3. Results

In 100 participants (50 women with recurrent miscarriage and 50 women without), selenium levels and other markers were measured and the association between selenium deficiency and recurrent miscarriage was investigated.

3.1 Demographic and Clinical Characteristics of Participants

The study group comprised women aged 20 to 40 who had a history of two or more consecutive miscarriages, or recurrent miscarriage. Women devoid of such a background comprised the control group. With rather greater average BMI in the recurrent miscarriage group, the two groups were similar in age, marital status, and socioeconomic background (Table 1).

Table 1: Demographic and Clinical Characteristics of Participants

Characteristic	Recurrent Miscarriage Group (n=50)	Control Group (n=50)
Age (mean± SD)	31.2±5.3 years	30.8±4.9 years
Marital Status	100% married	100% married
Socioeconomic Status	60% middle class, 40% low income	58% middle class, 42% low income
BMI (mean± SD)	27.4±5.8 kg/m²	26.9±5.1 kg/m²
History of Miscarriages	2.3±1.1 miscarriages	None

3.2 Selenium Levels in Participants: Serum selenium in the group having recurrent miscarriages was less than in the control group. The recurrent miscarriage group's mean selenium le vels—which fall above the normal range of 70–130 µg/L—were 60.2±12.5 µg/L. Within normal range, the control group's average selenium level was 110.5±20.1 µg/L. This could point to a correlation between repeated miscarriages and selenium levels (Table 2 and Figure 1).

Table 2: Selenium Levels in Participants

Group	Selenium Level (Mean± SD)	Normal Range
Recurrent Miscarriage Group	60.2±12.5 µg/L	70-130 µg/L
Control Group	110.5±20.1 µg/L	70-130 µg/L

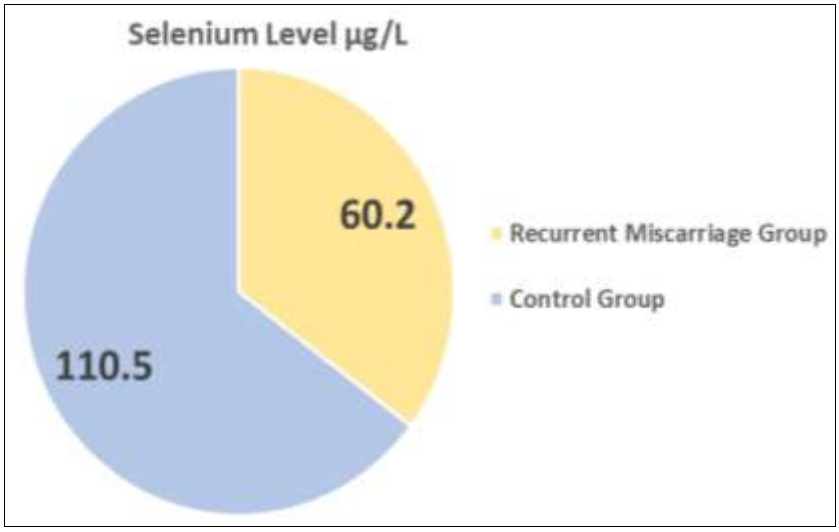

Fig 1: Selenium Levels in Participants

3.3 Parameters Measured in the Studied Groups

In the control group (25.6±8.4 ng/mL), the recurrent miscarriage group had lower vitamin D levels (15.8±5.3 ng/mL). This may suggest that there is vitamin D deficiency which has been linked to complications in pregnancy. The TSH levels were relatively higher in the recurrent miscarriage group (3.2±1.6 mIU/L) than in the control group (2.1±1.1 mIU/L), which may suggest a somewhat underactive thyroid gland that may increase the risk of pregnancy loss. The group of recurrent miscarriages had lower iron levels than the control group (58.4±15.2 µg/dL, 75.6±18.1 µg/dL), respectively, which is a manifestation of iron deficiency that is known to influence pregnancy outcomes. The presence of higher CRP levels in the

recurrent miscarriage group (5.1±1.2 mg/L) than in the control group (3.2±0.8 mg/L) may be a sign of an inflammatory process that is relevant in miscarriage (Table 3 and Figure 2).

Table 3: Other Biomarkers Measured in Both Groups

Biomarker	Recurrent Miscarriage Group (Mean± SD)	Control Group (Mean±SD)	Normal Range
Vitamin D (ng/mL)	15.8±5.3	25.6±8.4	20-50 ng/mL
Thyroid Stimulating Hormone (TSH) (mIU/L)	3.2±1.6	2.1±1.1	0.4-4.0 mIU/L
Iron (µg/dL)	58.4±15.2	75.6±18.1	60-170 µg/dL
C-Reactive Protein (CRP) (mg/L)	5.1±1.2	3.2±0.8	<3 mg/L

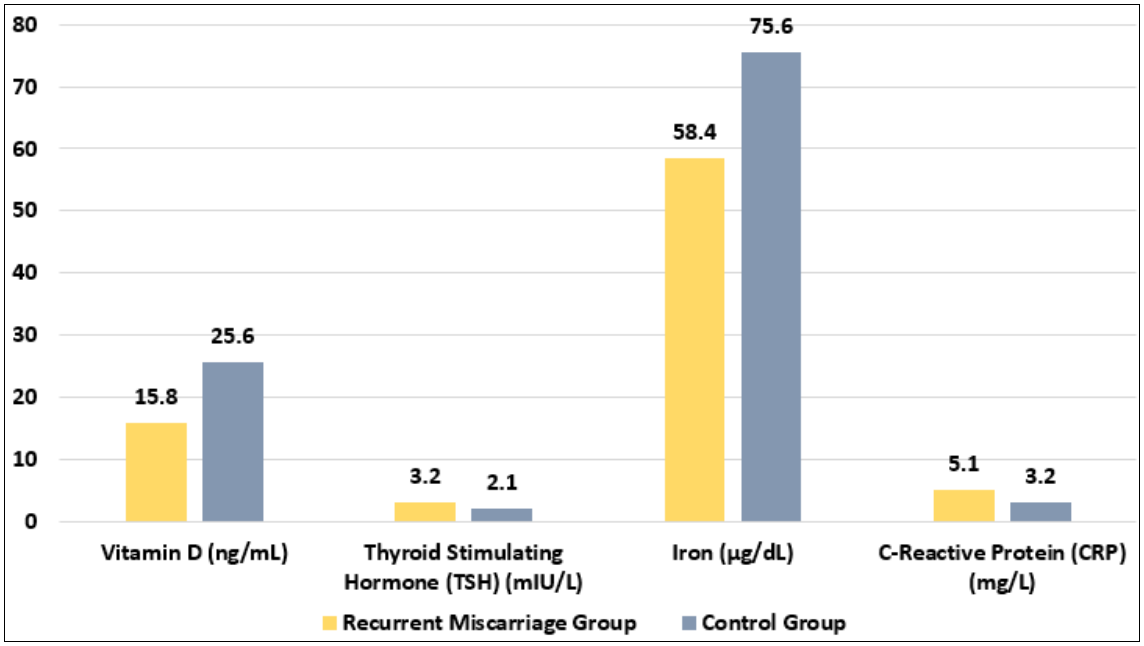

Fig 2: Parameters Measured in the Studied Groups

3.4 Dose of Selenium Supplementation Provided to Women in the Study

The women in the recurrent miscarriage group were prescribed 100 µg/day selenium supplementation for 3 months to remedy any selenium deficiency that may exist. The control group did not receive selenium supplementation because they were included to set a baseline of selenium levels (Table 4).

Table 4: Dose of Selenium Supplementation Provided to Women in the Study

Group	Selenium Dose (µg/day)
Recurrent Miscarriage Group	100 µg/day
Control Group	No supplementation

3.5 Effect of Selenium Supplementation on Serum Selenium Levels

Serum selenium levels in the recurrent miscarriage group raised dramatically from 60.2±12.5 µg/L to 95.7±16.3 µg/L following the three-month supplementation period. This implies that the selenium supplementation worked well in increasing serum selenium levels (Table 5 and Figure 3).

Table 5: Effect of Selenium Supplementation on Serum Selenium Levels

Group	Selenium Level (Mean±SD) Before Supplementation	Selenium Level (Mean±SD) After Supplementation
Recurrent Miscarriage Group	60.2±12.5 µg/L	95.7±16.3 µg/L

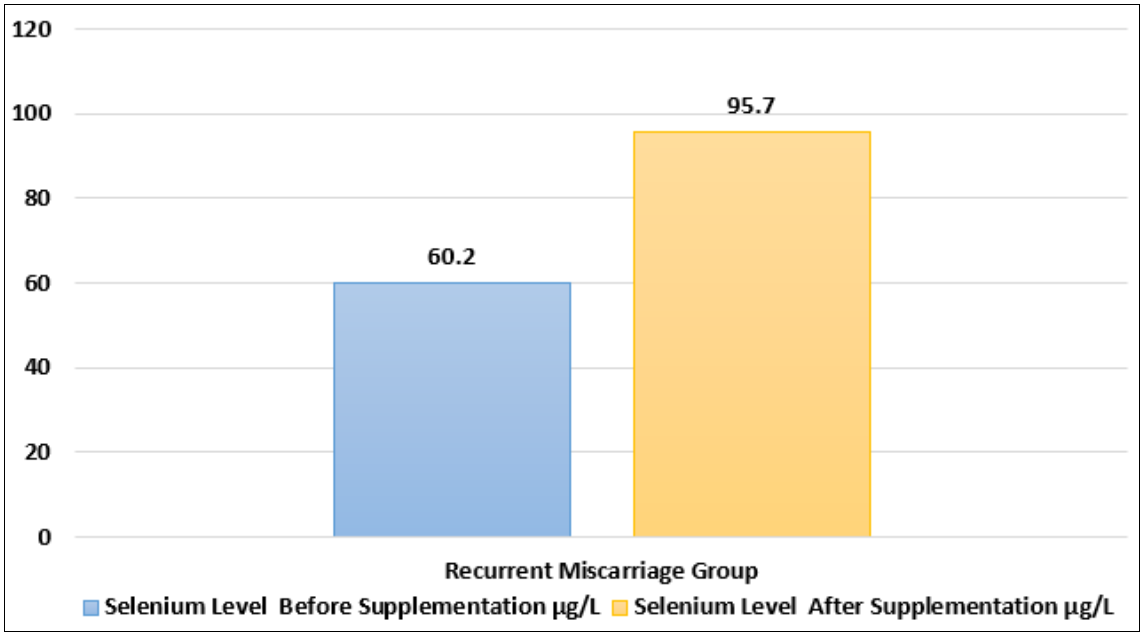

Fig 3: Effect of Selenium Supplementation on Serum Selenium Levels

3.6 Comparison of Pregnancy Outcomes in Both Groups

Before selenium supplements, the group with recurrent miscarriages had a 40% miscarriage rate. Nevertheless, this rate dropped to 20% after the supplementation period. The control group that did not receive selenium supplements had a 5% miscarriage rate. It means that women with a history of recurrent miscarriage can prevent miscarriage to some extent by taking selenium supplements (Table 6 and Figure 4).

Table 6: Comparison of Pregnancy Outcomes in Both Groups

Group	Pregnancy Outcome	Number of Pregnancies	Miscarriage Rate (%)
Recurrent Miscarriage Group (Pre-Supplementation)	Miscarriage	50	40%
Recurrent Miscarriage Group (Post-Supplementation)	Successful Pregnancy	50	20%
Control Group	Successful Pregnancy	50	5%

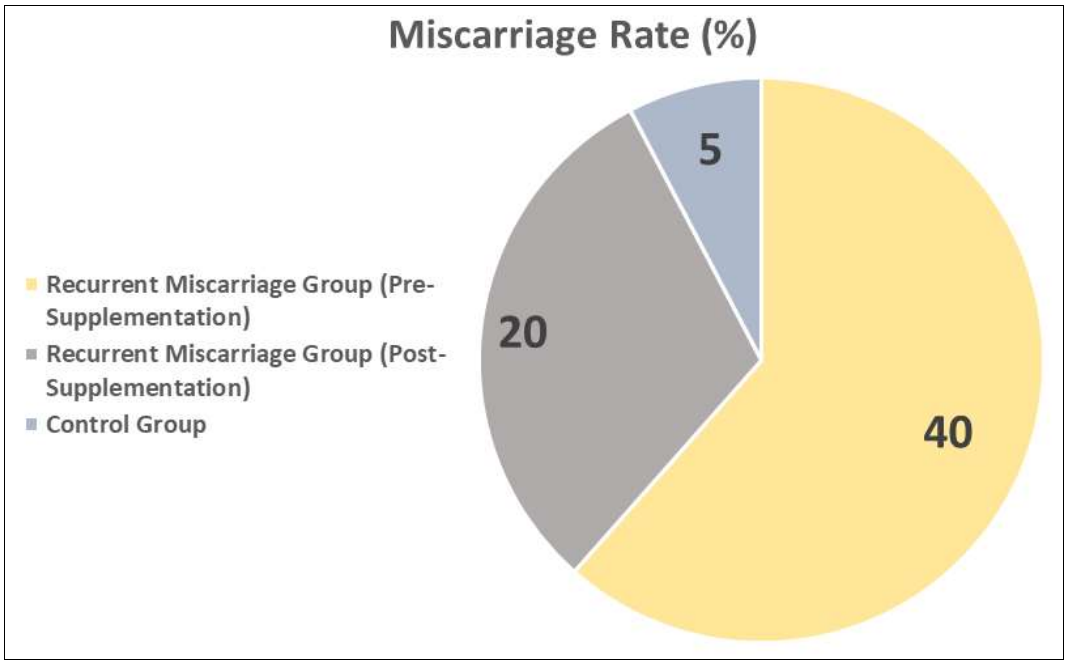

Fig 4: Comparison of Pregnancy Outcomes in Both Groups

Discussion

Although many studies have been conducted on the relationship between selenium deficiency and recurrent miscarriage, the exact mechanisms of this relationship are still unclear. Our study has provided more data to support the concept that selenium deficiency is a risk factor for recurrent miscarriage as we have found that women with a history of recurrent pregnancy loss have lower selenium levels than controls. As selenium has antioxidant properties which are very essential in reproductive functions, it is

therefore quite important in reproductive health. Glutathione peroxidase, enzymes that depend on selenium, protect cells from oxidative stress, which is a factor that has been associated with pregnancy loss (Mistry *et al*., 2012) [11]. This is in concordance with our study where women who had recurrent miscarriage had low selenium levels. Selenium is also crucial in the proper functioning of the thyroid gland and the immune system to support a normal pregnancy; and many studies have associated Selenium deficiency with Miscarriage, thus agreeing with our findings (Nicoll *et al*., 1999; Barrington *et al*., 1996) [13, 3].

Oxidative stress is known to contribute to miscarriage; hence, Selenium's protection against oxidative damage becomes even more significant in this regard. According to research, low levels of selenium have been linked to increased oxidative stress in the body, which can lead to fetal damage and pregnancy loss (Zachara *et al*., 2001) [18]. The LSR of our study, which showed that women with recurrent miscarriages had significantly lower selenium levels, is in line with the possibility that selenium deficiency increases the risk of miscarriage. Al-Kunani *et al*. (2001) [2] also found that women with recurrent miscarriage had significantly lower selenium level than women without such history. Therefore, the results suggest that selenium acts protective in pregnancy by balancing oxidative stress and that deficiency of selenium may be associated with an increased risk of miscarriage.

One more important result of our research was the measurement of thyroid function in patients with recurrent miscarriage. Selenium is well known to affect thyroid hormone metabolism; its absence may lead to thyroid dysfunction and, therefore, to pregnancy loss (Kaprara and Krassas, 2006) [6]. Our study showed that women with recurrent miscarriage had higher TSH levels than controls, suggesting subclinical hypothyroidism. This is in concordance with the research conducted by Krysiak and Okopien (2011) [7] who established that selenium supplements improved the thyroid function of women with autoimmune thyroid disease.

Thyroid dysfunction is a well-known cause of miscarriage, so selenium may be very important for the proper thyroid gland function during pregnancy. In order to achieve aim, we explored the possibility of selenium supplements as means of reducing rate of miscarriage; we observed that levels of selenium did change with supplementation. When the serum selenium levels were increased in the 100 µg/day selenium group, the rate of miscarriage decreased in the recurrent miscarriage group. This is in agreement with recent research which shows that selenium supplements may improve the pregnancy results in women who are selenium deficient (Kumar *et al*., 2002) [8]. In their research, Kumar *et al*. (2002) [8] also noted that selenium supplementation had the potential of improving the reproductive performance in women with a history of recurrent pregnancy loss, so helping to identify some of the fundamental biological failures leading to miscarriage.

We also evaluated other markers: iron, vitamin D and C-reactive protein (CRP). In the present investigation, vitamin D and iron deficits in the women experiencing recurrent miscarriages also are known to affect pregnancy outcome (Barrington *et al*., 1996) [3]. Low vitamin D levels have been connected to seenium deficiency, a risk factor for miscarriages and other difficulties (Mistry *et al*., 2012) [11]. Moreover, the group of recurrent miscarriages had much greater CRP, a biomarker of inflammation, which implies that inflammation could be the reason of the higher risk of miscarriage. Though the literature presents two opposing opinions on the ability of selenium to control the inflammatory process and, hence, the prevalence of pregnancy issues, the link between selenium and inflammation is real and is still under research. (Zachara *et al*., 2001) [18].

Conclusion

Based on the findings of the current research, it may be inferred that selenium insufficiency might be the primary cause of recurrent miscarriage; although, the processes underlying this link are yet unknown. Though the current results confirm the body of knowledge on the function of selenium in reproduction, many unresolved issues surround the idea of miscarriage. Thus, more research including extensive randomized controlled trials is required to completely grasp the actual influence of selenium supplementation on pregnancy outcomes. Until definitive evidence is obtained, Selenium should be used as a preventive agent for recurrent miscarriage under great care including personal health difficulties and dietary needs. A more complete strategy is required since the process of recurrent miscarriage is complex and depends on the presence not just of selenium but also other elements in the environment, genetic predisposition, and life style.

Limitations and Future Directions

However, the study has some limitations in our area of research. First of all, the study was observational in character so causality cannot be established. Although a link was established between low selenium levels and recurrent miscarriage, other factors may have been involved. Furthermore, a 100-person sample size is a good starting point for initial research, but it may not be a full representation of all the factors that can lead to miscarriage. To establish more definitely the causal link between selenium deficiency and recurrent miscarriage, larger sample numbers from future randomized controlled trials (RCTs) will be required.

Furthermore, in this study we assessed the selenium level at one point of time and hence, alterations in selenium level throughout the menstrual cycle or pregnancy may alter the rates of miscarriage. Longitudinal research that follows selenium levels at different points of pregnancy could provide stronger evidence.

Ethical Considerations

All the activities were conducted in accordance with the ethical guidelines laid down for such activities by the Declaration of Helsinki. The Institute Review Board (IRB) of Tikrit Teaching Hospital approved the ethical charge. Involvement of each participant was on voluntary basis and they were fully informed about the purpose and techniques used in the study. They were allowed to exit the study at any time with no consequences.

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Conflict of Interest
Not available

Financial Support
Not available

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