International Journal of Advanced Research in Medicine

E-ISSN: 2706-9575
P-ISSN: 2706-9567
IJARM 2022; 4(2): 104-108
Received: 05-07-2022
Accepted: 07-08-2022

Zubaida Falih Alzubaidi
Department of Clinical Laboratory Sciences, Faculty of Pharmacy, University of Kufa, Kufa, Iraq

Corresponding Author:
Zubaida Falih Alzubaidi
Department of Clinical Laboratory Sciences, Faculty of Pharmacy, University of Kufa, Kufa, Iraq

Evaluation of some trace elements in infertile women in Najaf city, Iraq

Zubaida Falih Alzubaidi

DOI: https://doi.org/10.22271/27069567.2022.v4.i2b.417

Abstract
A disorder of reproductive system called infertility is specified via the inability to get pregnant after a year of unprotected, normal sexual activity. The goal of the presented work is to evaluate Cu, Zn, Se, and Fe levels in female infertility in Najaf city, Iraq. Trace elements could induce infertility through altering several biological pathways within the body. A total of 200 people participated in the case-control study, with 100 fertile women acting as the control group and 100 women experiencing infertility acting as the case group. By using atomic absorption, the amounts of Cu, Zn, Se, and Fe in blood samples have been determined. When put to comparison with the control group, the patient group's serum Cu, Zn, and Se concentrations significantly decreased (p less than 0.05), whereas the patient group's serum Fe concentrations significantly increased (p less than 0.05). BMI and age variables, however, did not significantly differ between the two study groups. Between secondary and primary infertile women, there are no significant variations in mean serum Cu, Zn, Se, and Fe concentrations. The research found that levels of Cu, Zn, and Se concentrations in women with infertility have been significantly lower, whereas the results regarding Fe concentrations have been significantly higher in such women. Therefore, the research recommends that infertile women be treated by using supplements that contain such trace elements to make up for deficiencies.

Keywords: Psychiatric disorders, suicide, suicide attempt, first admission, recurrent admission; schizophrenia, bipolar disorder, depression, substance abuse disorder

Introduction

Infertility affects 48.5 million couples worldwide, or 15% of all married couples. From less than 5% to over 30%, different countries have different rates of infertility [1-3]. In addition, infertility is a reproductive system illness that, after a year of unprotected, normal sexual pregnancy, is defined by the WHO as the inability to conceive [4].

Two types of infertility exist: the term "inability to conceive within 2 years of exposure to pregnancy" is used to describe primary infertility, while "inability of conceiving within two years of the exposure to the pregnancy after a previous pregnancy" is used to describe secondary infertility. Primary infertility affects almost all infertile couples worldwide. Depending on the age of the partners and the age of the marriage, several causes of infertility apply [5].

Lifestyle, age, medicines, obesity, physiological issues, transmitted diseases, psychological stress, environmental variables, and biochemical components including trace elements, hormones, enzymes, and others could all contribute to infertility issues [6].

Many diverse biological functions depend on trace elements in one way or another. It has long been understood how distinct disease states and trace elements interact. Trace elements could disrupt a variety of biological processes within the body, which could lead to infertility [7-8].

Because Zn regulates reproductive hormones, egg maturation is hampered when there is insufficient Zn in the body. Zn is also required by follicle fluid levels to move the egg via the fallopian tubes. A Zn deficiency is linked to infertility and hypogonadism because it directly affects how proteins are made in cells [9-13].

One of the most frequent mineral imbalances causing infertility is copper [14]. By reducing progesterone levels and causing anovulation, implantation failure, or luteal phase abnormalities, this might have a direct impact on infertility rates. Numerous necessary elements, particularly Zn, that are directly connected to reproductive pathways have also been demonstrated to be blocked by copper [15-17]. Selenium has a crucial role in growth. Selenium deficiency could cause miscarriages, gestational complications and harm to the developing fetus' neurological and immunological systems.

Additionally, it was demonstrated that a low concentration of Se in blood serum early in pregnancy predicts a newborn's low birth weight [18-19]. Se inclusion in the selenoproteins, which have selenocysteine at their active center, allows us to understand Se involvement in nutrition [20]. Selenoproteins play a role in a variety of biological functions, which include but are not restricted to fertility and reproduction [21].

Being closely associated to brain development through neuronal and glial energy metabolism, myelination, neurotransmitter metabolism, and oxygen transport, adequate iron availability is also essential for fetal development [22]. Thus, intrauterine development retardation and adverse pregnancy outcomes are caused by Fe deficiency anemia. The results of meta-analysis showed a connection between increased birth weight and prenatal Fe intake [23]. Due to the strict regulation of Fe metabolism during pregnancy, there is an increase in Fe absorption and mobilization for meeting the body's needs. Impaired Fe metabolism could also lead to unfavorable pregnancy outcomes [24]. A greater birth of spontaneous abortions and preterm births is specifically linked to Fe deficiency [25]. Decreased Fe status in cases of ovulatory infertility is another indication of Fe's significant function in female reproduction [26].

The high iron body burden caused by insufficient iron supplementation or by a disordered Fe metabolism, on the other hand, could potentially have negative effects on pregnancy [27-33].

We thus sought to evaluate Cu, Zn, Se, and Fe levels in female infertility in the Iraqi city of Najaf in the current work.

Subject and Methods

1. Subjects

The case–control design study was performed on 200 persons. This study has been conducted at Biochemistry Laboratory in the College of Pharmacy, University of Kufa, Najaf city, Iraq at the period from March until September 2022.

According to a clinical examination and symptoms, the women are already classified as infertile or fertile by the consultant medical team at Fertility Center at the AL-Sadder Teaching Hospital in Najaf, Iraq.

The two groups of the study are classified as the following:

1. Fertility women: This group included 100 healthy women as the control group, age was 31.5±9.2 years (Range, 20 – 43 years).
2. Infertility women: This group included 100 infertile women as the case group, age was 32.5±11.8 years (range, 21 -44 years).

Based on the primary form of infertility, infertile women were split into two subgroups.

A. Primary (1˚) infertility, which includes 55 women.

B. Secondary (2˚) infertility which includes 45 women.

The research excluded women who had diabetes mellitus, chronic hypertension, chronic renal disease, multiple pregnancies, or chronic liver disease.

The estimation of BMI was done by dividing the weight by squared height (kg/ meter2), 23.88±7.19 kg/m2 for the case group and 23.43±5.45 kg/ m2 for the control group.

Sample

After an overnight fast, five milliliters of blood were drawn from each participant using a peripheral vein puncture. The blood was put into a plain tube and allowed to coagulate for around 15 minutes at 37 degrees before being centrifuged for 10 to 15 minutes at 3000 RPM to separate the sera, which were after that stored at -20 degrees.

2. Methods

The atomic absorption spectrophotometer (Shimadzu, Japan; AA-6300) was used for measuring the serum levels of Cu, Zn, Se, and Fe. The underlying idea was to separate the element from its chemical bond and after that place it in a neutral atom state, which could absorb light of its own wavelength. The concentration of radiant energy determines how much is absorbed [34].

Reagents: Prior to use, a standard solution of each element was made by serially diluting a 1000 mg/L stock solution with deionized water.

Table 1: Wave length of trace elements

Element	Wave Length (nm)
Zn	213.8
Cu	324.8
Fe	248.3
Se	196

The serum of the patients and control group was diluted with deionized water and homogenized prior to analysis [35].

Biostatistical analysis:

SPSS statistical program for social science, version 25.0, was used to analyze the data. Results were presented as SD, mean, range (minimum-maximum), and student-test was performed to show the difference in group variation, which is regarded significant when P values are ≤ 0.050.

Results

Table 2 summarizes characteristic features of all the individuals, the mean of Zn, Cu, Fe and Se concentrations of the infertility women was 713 ug/L, 987.4 ug/L, 127.9 mg/dl and 87.77 ng/ml respectively as compared to 1095.3 ug/L, 1524.6 ug/L, 83.1 mg/dl and 125.24 ng/ml in fertility women respectively.

When put to comparison with control group, the patient group's serum Zn, Cu, and Se concentrations significantly decreased (p less than 0.05), whereas the patient group's serum Fe concentrations significantly increased (p less than 0.05). In contrast, no significant difference in age and BMI variables between the two studied groups.

Association between trace elements of Primary (1˚) infertility women and secondary (2˚) infertility women of the mean value of serum Zn, Cu, Fe and Se concentration doesn't show any significant differences between the two groups as shown in Table 3.

Table (4) show a comparison between trace elements concentrations for fertile women, infertile primary women and secondary infertile women. The results exhibited a significant ($p<0.050$) decrease in the serum Zn, Cu, Se in women who have primary infertility women in comparison to fertile women, while the results of Fe concentration were significantly higher in women with primary infertility in comparison to fertile women, ($p<0.05$). Also, results had shown a significant ($p<0.05$) decrease in serum Zn, Cu, Se in women who have secondary infertility as compared with fertile women, while the results of Fe concentration were considerably higher in the women who have secondary infertility in comparison to fertile women, (p<0.05).

Table 2: Biochemical Parameters in infertile women and fertile women

Parameters	Fertile women N=100 Mean±SD	Infertile women N=100 Mean±SD	P value
Age (years)	31.5±9.2	32.5±11.8	N.S
BMI (kg/m2)	23.43±5.45	23.88±7.19	N.S
Zn (ug/L)	1095.3±31.2	713±20.9	<0.05
Cu (ug/L)	1524.6±22.4	987.4±28.5	<0.05
Fe (mg/dl)	83.1±35.8	127.9±22.8	<0.05
Se (ng/ml)	125.24±15.8	87.77±18	<0.05

NS= Not Significant, Significant at p p<0.05

Table 3: Association between infertile women (secondary and primary) and the mean concentrations of trace elements.

Parameter	Primary Infertility N=55 Mean±SD	Secondary Infertility N=45 Mean±SD	P- value
Zn (ug/L)	699.3±20.2	720.6±19.8	N.S
Cu (ug/L)	1014.9±28.3	989.1±27.9	N.S
Fe (mg/dl)	125.1±22.1	129.9±20.4	N.S
Se (ng/ml)	89.45±17.9	86.98±18.1	N.S

NS= Not Significant, Significant at p p<0.05

Table 4: Comparison between trace elements concentrations for fertile women, infertile primary women and secondary infertile women

Parameters	Fertile women	Primary Infertility	P-value	Secondary Infertility	P-value
Zn (ug/L)	1095.3±31.2	699.3±20.2	<0.05	720.6±19.8	<0.05
Cu (ug/L)	1524.6±22.4	1014.9±28.3	<0.05	989.1±27.9	<0.05
Fe (mg/dl)	83.1±35.8	125.1±22.1	<0.05	129.9±20.4	<0.05
Se (ng/ml)	125.24±15.8	89.45±17.9	<0.05	86.98±18.1	<0.05

Significant at p p<0.05

Discussion

Infertility, or inability to conceive or carry a pregnancy effectively to term, has grown to be a major public health issue on a global scale. While there are many known reasons of infertility including auto-immunity, genetic predispositions and endocrine disorders [36].

Researchers recently discovered that exposure to hazardous substance such as lead and mercury can have substantial adverse effects on human reproductive health and fertility. Likewise, shortages in trace elements like zinc, copper and selenium can have just as harmful a role [37].

Estimating Cu, Zn, Se, and Fe levels in the female subjects with infertility diagnoses (secondary as well as primary infertility) in comparison to controls (fertility females) was the aim of the current investigation.

When put to comparison with controls, participants who had been diagnosed with infertility had significantly lower serum Zn levels. Which is in line with the findings of Jameson, who found that a Zn deficit can impair maturation by multiplying the number of oocytes that are degenerating and increasing infertility problems [38]. There is a Zn shortage in infertility in spite of whether it is secondary or primary since there was no significant difference in Zn level between secondary and primary infertile subjects [39].

Another trace element which was valued in this work is copper, which supports good female fertility. We discovered that serum Zn level has been significantly lower in persons with infertility than in controls. Low levels of magnesium and copper have been linked in studies to decreased fertility. By disrupting normal metabolic processes, low Cu levels could lower female fertility. The low amounts of Cu and Zn found in the majority of infertile women are consistent with other researchers' findings. Unexplained infertility may be primarily caused by an imbalance in serum Cu levels [40-41].

In both the secondary and primary groups of the women with infertility group, in comparison with the controls, the results of this work showed a significant rise in the concentration of serum Fe. Some works have looked at the connection between iron toxicity and fertility, and even fewer have looked at female fertility. Yet, there is a connection between excessive Fe intake and female infertility [42-43]. The anterior pituitary produces less FSH and LH when there is an excess of Fe, which suggests that oocyte maturation is impeded and the ovarian reserve is inadequate. This finding conflicts with that of the 2016 study by Al Wais *et al*. [44].

In this investigation, secondary and primary infertile participants' serum Se levels were found to be significantly lower than those of control subjects. This is related to a discovery that Se levels were significantly lower in cases of primary infertility. A crucial trace element for human health and biology is selenium. Also, Se is thought to be significant for both animal and human reproduction and appropriate growth, according to researches [45-47]. Many reproductive and obstetric issues, such as female and male infertility, preeclampsia, miscarriage, preterm labor, fetal growth restriction, obstetric cholestasis, and gestational diabetes, are frequently linked to selenium insufficiency according to numerous reports [48].

Researchers found that sub-fertile women had Se levels that were significantly low. Se-binding protein-1, an ovarian autoantibody protein causing early ovarian failure (which is an infertility cause), might be the cause of this. Furthermore, it was demonstrated that deficiencies in Se levels can harm several fetal systems, including the neurological and immunological systems, and complicate pregnancy [49].

Conclusion

Infertility-related women had significantly lower levels of Cu, Zn, and Se concentrations, according to the research, but the Fe concentrations have been significantly greater. The research suggests that supplements containing such trace elements can treat infertility in women and address the deficiency. As a result, individualized trace element status evaluation and improvement could be thought of as a potential tool for improving the female reproductive system.

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How to Cite This Article
FA Zubaida. Evaluation of some trace elements in infertile women in Najaf city, Iraq. International Journal of Advanced Research in Medicine. 2022;4(2):104-108.