



## Zinc Deficiency and Risks of Toxoplasmosis-Related Miscarriage: Impacts of Socioeconomic Factors

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### ABSTRACT

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Toxoplasmosis is a parasite element mostly brought on by *Toxoplasma gondii*, which is found in cat feces and spreads through the consumption of raw meat and vegetables. Because this parasite may infect mammals. This parasite can cause a variety of health issues for mothers and fetuses, when it is transferred to a pregnant woman especially, with whom suffering from immunity deficiency, so the current study attempts to clarify the role of zinc metal with toxoplasmosis pathogenesis in infected women with *Toxoplasma gondii* and compare zinc levels in healthy women. Where, zinc metal is still unclear how toxoplasmosis affects the risk of miscarriage but Zinc is an element of widespread occurrence. And it is essential role for protein synthesis for immune function, that plays a role immune response against parasites. In this observational study, 60 samples of female participants were collected were gathered to assess the serum zinc level using a spectrophotometer. Based on the results of the Igg titer detector, participants were separated into two groups: 24 healthy controls and 36 women with toxoplasmosis. The current study shows significantly decreasing of serum zinc concentration in Women with a positive IGG compare to the control group, with corresponding means and standard errors of (60.909111.06) and (98.6612.37). This study's findings suggest that lowering zinc levels may have a significant impact in increasing the risk that women may be exposed to toxoplasmosis. Additionally, we advised taking zinc supplements to strengthen immunity and lower the risk of contracting toxoplasmosis, especially for pregnant women.

## 1. INTRODUCTION

*Toxoplasma gondii*, an obligate intracellular protozoan parasite linked to the phylum apicomplexan and the cause of toxoplasmosis, is an infection [1]. It is a zoonotic disease that can infect both humans and animals and cause a variety of health issues, including pneumonia, ocular encephalitis, and uveitis. Nearly a third of the world's population is exposed to this parasite, especially immunocompetent people [2]. *Toxoplasma gondii* threat serious repercussions, particularly when this illness is spread to a pregnant woman through infection, pregnancy is one of the most critical steps in women's lives, particularly those who want to become a mother for the first time. Where, the organism can result in multiple fetal malformations and miscarriages with additional birth difficulties. Regardless, if the woman was already infected before to conception, the illness becomes minimal; however, infections that occur during the first trimester of pregnancy tend to be more hazardous and effective. These are the three main routes of toxoplasmosis infection in humans:

**Foodborne transmission:** This is where you consume contaminated, undercooked meat (such as lamb, pork, and venison) or shellfish that contain cysts of the parasite. **Cat-associated transmission:** involves contact with the feces of infected cats. The parasite forms abscesses inside the cat's

intestines and is excreted in its feces. It is important to remember that feces need some time in the environment (a few days) to become infectious.

**Congenital transmission:** A pregnant woman recently infected with toxoplasmosis can transmit the parasite to her fetus, which may lead to health complications for the child. While healthy adults often have little or no symptoms from toxoplasmosis, it can be more serious for pregnant women and those with weakened immune systems [3]. *T. gondii* only reproduces within the parasitophorous vacuole (PV) that it inhabits [4]. By acting as a stimulant, inhibitor, or co-enzyme for enzymatic process and having an impact on cell membrane permeability [5], essential vitamins heavy metal like (Chromium, Cadmium) and trace elements such (zinc, copper, iron metals) play a crucial part in important processes. Further, several mechanisms that are integrated throughout maternal, placental, and fetal delivery support maternal and fetal health and safety development during pregnancy [6]. Deficiency or overabundance in these trace elements have clinical significance with connected various disorder [7]. Zinc is a metal whose presence is crucial for all human tissues and major organs. It also plays an essential role in the immune system by fostering an immunological response against this parasite [8]. The role of certain inflammatory products in regulating zinc levels has been well documented.

Consequently, leukocyte intrinsic mediators (interleukins) are released from activation macrophages cause decreased zinc levels resulting from increased zinc synthesis Metallothionein in the liver and other tissues. Additionally, it regulates around 300 mineral enzymes that are essential for various anabolic processes. Numerous studies have linked the possibility of developing severe insulin resistance issues, such as hyperlipidemia and raised blood glucose, to the presence of higher zinc levels in the body. The increased zinc levels could be the result of several factors. Increased oxidative stress, which can release zinc from its binding sites when it fulfills the coordinating role like a number of proteins, is one potential explanation for the elevated zinc levels. Zinc ions released by proteins can be in an oxidative state within the cell, function as signal transducers, and regulate mitochondrial metabolism. Zinc can increase a cell's capacity to neutralize free radicals or, in varying proportions, cause it to release more dangerous reactive oxygen species [9, 10].

During pregnancy: Zinc is crucial for a proper embryonic development. The amount of zinc that is passed to the fetus depends on the maternal zinc status throughout pregnancy [11]. As a result, when there is a zinc deficiency or restriction, the maturation of the fetus is put in risk. According to the World Health Organization (WHO), In the first trimester of pregnancy, a mother should consume between 1.1 and 2 mg of zinc per day [12]. During the latter stages of pregnancy, the dose should be increased to 3 mg per day. The current paper tries to elucidate the role of Zinc element, which is a play an independent role for support immunity to reduce the incidence of toxoplasmosis and decreasing the risk of miscarriage for infected women, in addition, a study was expanded to include whether the circumstances surrounding each case, such as residence and educational attainment, played a role in promoting or reducing the incidence of toxoplasmosis.

## 2. MATERIAL AND METHOD

Following a specialist doctor's diagnosis in the Central Analysis Center at Baquba Teaching Hospital, the blood samples were taken from 60 venipuncture victims. All specimens were to be collected between the beginning of December 2022 and the end of February 2023. All subjects were separated into two groups: a group of 24 individuals who were healthy as a control (They were selected on the basis that negatively with Igg antibody titer, they were free of any chronic diseases and that their data did not contain any family medical history furthermore did not use drugs or smoke) and a group of 36 individuals who had toxoplasma and the patients' ages ranged from (22 to 39) year. In addition, a complete history of their condition, including their length of sickness, family history of illness, blood pressure, and marital status, was taken from them. Twenty-four healthy individuals between the ages of 20 and 40, were used as a control group. For the purpose of performing the necessary analyses, all blood samples were obtained from the muscular vein in the humeral region. Three milliliters of blood were drawn from the syringe into an EDTA tube, centrifuged to obtain the serum, and then transferred to other tubes labeled with the same sequences for patient and secure storage at (-20)°C [13]. Using a mercury pressure monitor, which is the most accurate technique used in hospitals and medical facilities, is the recommended way to check blood pressure. The WHO advised that the normal value of blood pressure is (12/8) for

healthy adults. Blood pressure is expressed as two numbers, the first number (top no.) indicating blood flow when the heart muscle contracts and the second number (lowering no.) representing artery pressure during heart beats. All serum specimens have been screened for T. gondii IgG and IgM antibodies using a rapid diagnostic immunochromatographic test (Tox IgG, IgM Rapid Test Cassette), according to the manufacturer's instructions (Egyptian company for Biotechnology, Egypt). Toxoplasmosis is an immune infection that can be predicted by the diagnosis of toxoplasma antibodies. The spectrophotometer was used in this investigation to estimate the concentrations of zinc and fasting blood sugar in serum samples. After setting up the spectrophotometer and calibrating it. The absorbance of zinc and random blood sugar were measured at (546) and (5600) nm, respectively.

## 3. STATISTICAL ANALYSIS

Statistical Packages for Social Sciences (SPSS) version 26 was used to analyze the data. The result was expressed as mean  $\pm$  SE. ANOVA was used to determine the difference between three independent variables, post hoc, correlation coefficient (r) between parameters, and T-test. The statistical significance is determined by the probability value, which showed a significant difference at  $p \leq 0.05$  and no significant difference at  $p > 0.05$ .

## 4. RESULTS AND DISCUSSION

One of the most frequent causes of increased abortion risk is maternal toxoplasmosis [14]. In this study, 60 women were enrolled. They were divided into two groups: 36 toxoplasmosis patients matched with 24 naturally healthy controls. The current findings of toxoplasmosis infection are shown in Table 1 by toxoplasma antibody detection. Table 1 shows general characteristics for all specimens expressed by (mean  $\pm$  SE), including BMI, age, SBP, and DBP, to compare physical characteristics for both groups (patients and controls). For both groups, there were no differences that were statistically significant.

Despite the fact that both groups may be experiencing abortions for any reason, all cases have been identified based on testing for IGG and IGM toxoplasma. Gindii antibodies, their characteristics were shown in Table 2 which revealed seroprevalence of T.gondii Igg result positively for only 36 women (68.57%) (toxoplasmosis women) who were suffering from miscarriage. Conversely, Table 2 shows negatively results for Igg were correlative with control (31.43%). While the current results not appear any subjects for acute infection of toxoplasmosis, IGM were negatively seroprevalence in this study. Only globulin immunity (IGg) has been a serum positively with the women who are experiencing miscarriage (31.43%) deals with (12) and without response for IGM for both women (miscarriage and control). Gondii (IGm, and IGg) for 60 women, using LAT as a screening test [15]. When there is no indication of an acute infection in the current study, which is associated to no positive cases for (IGm) [16]. The seroprevalence (IGg) in all miscarriages is caused by the general sluggish maturation of response antibodies for T.gondi (IGg) infection. Rahman et al. [17], who conducted a survey on 240 women, discovered that IGg antibodies were present in

both the case group (47.4%) and the control group (46.3%), however our survey indicated that IgG antibodies were only

seroprevalent in miscarriage victims. Utilizing the ALT fast immunochromatographic test, all data were obtained.

**Table 1.** The mean ( $\pm$ SE) values for BMI, SBP, DBP, and age, of the studied groups with their significance

Variable	Groups	N	Mean	Std. Error	P
BMI (Kg/m <sup>2</sup> )	Healthy pregnant	24	25.53	2.22632	0.54
	Toxoplasm	36	27.5	4.74019	
Age (year)	Healthy pregnant	24	21.0000	2.50940	0.32
	Toxoplasm	36	24.0909	2.29408	
SBP (mm Hg)	Healthy pregnant	24	8.5833	0.50331	0.63
	Toxoplasm	36	9.3636	0.47238	
DBP (mm Hg)	Healthy pregnant	24	6.0000	0.36614	0.43
	Toxoplasm	36	5.8182	0.44350	

**Table 2.** Distribution of anti-T gondii IgG and IgM antibodies for all subjects using rapid immunochromatographic method

Anti-Toxoplasma Antibodies	Examine NO	Positive NO		Negative NO	
		N	%	N	%
IgG	60	36	68.57	24	31.43
IgM	60	0	0	0	0
IgM +IgG	60	0	0	0	0

Note: NO means: the number of blood tests performed by the volunteer.

**Table 3.** The mean ( $\pm$ SE) values for (Zinc and sugar) serum concentration of the studied groups with their significance

Variable	Groups	N	Mean	Std. Error Mean	P
Serum zinc ( $\mu$ g/dl)	Healthy pregnant	24	98.6667	12.37351	0.036
	Toxoplasm	36	60.9091	11.06711	
RBS ( $\mu$ g/dl)	Healthy pregnant	24	91.2500	4.06347	0.21
	Toxoplasm	36	100.6	8.87824	

According to the findings presented in Table 3, the zinc levels for the patient groups and control groups are shown to be [(60.909  $\pm$  111.06) and (98.66  $\pm$  12.37)], respectively. Additionally, Table 3 revealed that there were no statistically significant variations in serum random blood sugar levels between the control and toxoplasmosis groups ( $p > 0.05$ ) (mean  $\pm$  SE (91,2500  $\pm$  4,036) (100.6  $\pm$  8.87824)). The relationship between serum zinc levels and infection has been established in Table 3. This study demonstrates a significant decline in serum zinc in toxoplasmosis-infected women compared to healthy controls. The current findings are consistent with those reported by Al-Bakry and Al-Khshab [18], who observed a decrease in serum zinc in toxoplasmosis-infected humans and animals. The human body needs zinc to sustain the immune system's security [19], and as a result, zinc plays a crucial part in the immune system's defence against parasites [20]. Toxoplasmosis infection in white blood cells (leukocytes), platelets, and reticulocytes caused a considerable drop in the serum zinc level in mammals, which was significantly correlated with repeated abortion in cows. Additionally, compared to pre-infection levels, the relative proportion of lymphocytes and granulocytes varies. a rise in the functional activity of granulocytes [21], as well. These alterations are the result of localized trace element concentrations, including zinc, in the extracellular and intracellular fluids. Numerous studies using rodents infected with *T. gondii*, a particular diet that was approved [22], and zinc supplements [23] were done. since it has been discovered that this mechanism boosts CD8 total lymphocytes and encourages cellular immunity. Due to zinc's redistribution in the hepatic circulation during recurrent spontaneous abortion (RSA), toxoplasmosis results in a drop in zinc levels. It is

connected to albumin [24], which is related to *t. gondii*, in addition to the absence of albumin, where the majority of the zinc content exceeds 70%. Immunity and zinc have a strong relationship, and any zinc deficiency results in reduced responder immunity. The current findings supported Indian research [25], it was discovered that the mean serum levels of Zn were greater in the SAb subjects.

Figure 1(a) and Figure 1(b) show the percentage of abortions between two groups (women with toxoplasmosis and those with no infection), showing that there were no statistically significant variations in the percentage of abortions among all patients ( $p$  value  $> 0.005$ ). Figure 1(a) depicts the distribution of abortions for the control group graphically, showing that 50% (12 women) had one abortion whereas the remaining 50% (12 women) had two. In contrast to the toxoplasmosis women, whose distribution was depicted graphically in Figure 1(b) as random and not equal to the control group, the current findings revealed that 16 (45.5%) patients had one abortion, 12 (36.4%) patients had two miscarriages, and 8 (18.2%) patients had three abortions.

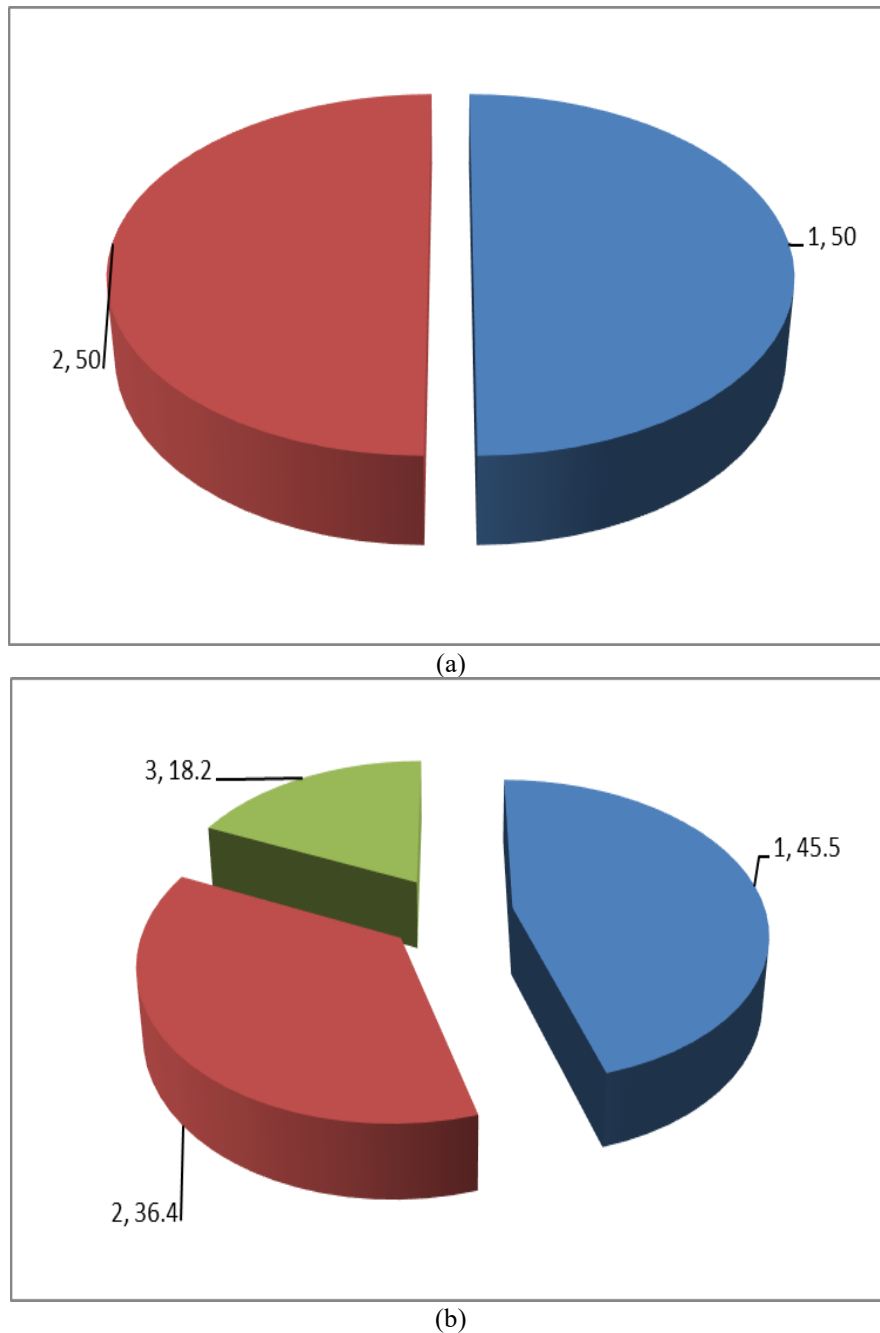
Figure 2 illustrates how academic achievement affects the prevalence of toxoplasmosis by comparing the proportion of toxoplasmosis cases among women with different levels of education. Figure 2 shows that more than half (54%) of the samples of toxoplasmosis-infected women were educated beyond the most basic levels. This conclusion differs from that of Ebrahimi et al. [26], who discovered that knowledge about the parasite's specifics and its causes is crucial for preventing infection and preventing the spread of the parasite. Likewise, the current findings show a rise in the number of infected women with higher levels of education. Whereas another study found no relationship between education level and

toxoplasmosis in women [27]. It is likely that the infection rate will rise among educated women because they have a greater chance to enter the career path, which gives them more opportunities to come into contact with others and spread infection, whether viral or bacterial.

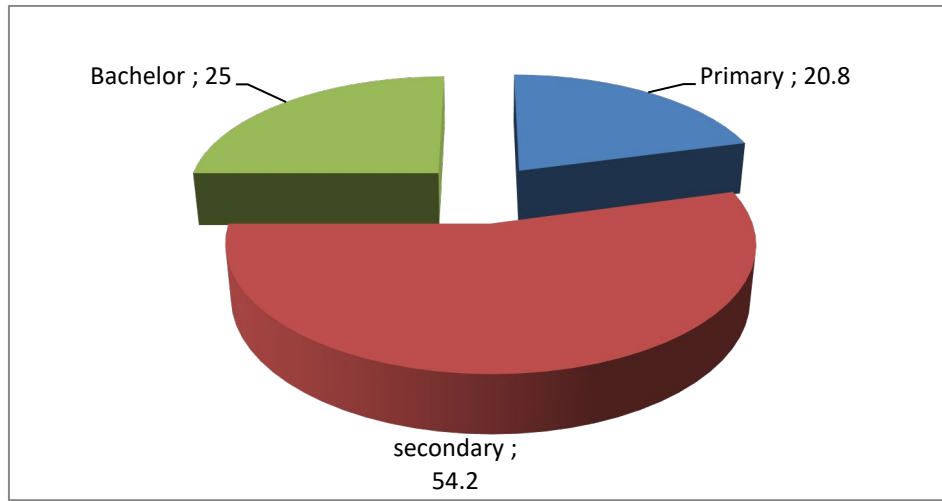
Regarding accommodations, Figure 2 depicts the connection between toxoplasmosis and infection in women according to their place of residence. Figure 3(a) makes it clear that a large percentage of toxoplasma-infected women (54.4%) lived in urban areas. In contrast, in the control group, the majority of affected women (62%) resided in rural areas.

Regarding the elements in our environment that could pose a danger for abortion. Figure 3 depicts a notable distinction between toxoplasmosis-infected women who lived in urban or rural areas in terms of where they resided. A higher percentage of toxoplasma women (54.4%) resided in cities, which is

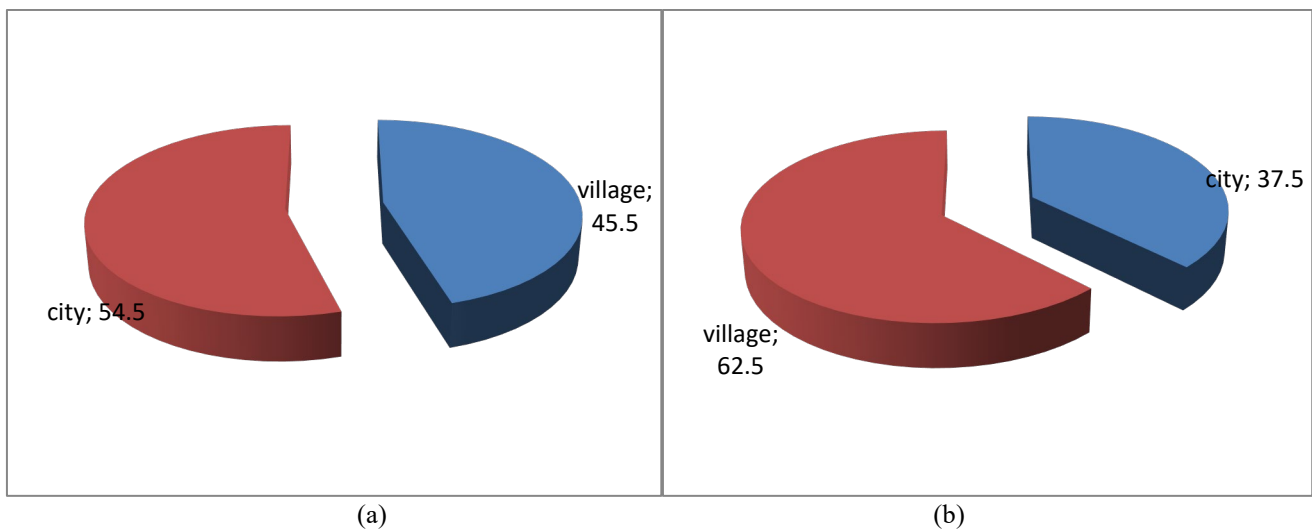
related to the nature of urban development and the leaking of gases containing heavy metals and is sufficient to be a significant contributor to air pollution in the neighborhood. In addition, many abortions rise among urban-dwelling women due to stress, lifestyle choices, and smoking exposure. In contrast to Maywald and Rink [20], our study shows no statistically significant variations between the infection rate in the city and the countryside. According to this, there were fewer cases of toxoplasmosis in the rural area as a result of increased awareness and participation in training sessions emphasizing the importance of maintaining good personal and general hygiene. The current findings are consistent with research conducted in India, where it was found that serum zinc levels in RSA women between the ages of 21 and 42 were on average 74.98 11.88 g/dl, compared to 82.90 12.36 g/dl in healthy individuals [28].



**Figure 1.** (a) Pie charts for the distribution of abortion number among healthy women, (b) Pie charts for the distribution of abortion number among women with toxoplasma infection



**Figure 2.** Pie charts for the distribution of academic achievement among toxoplasma infection women groups



**Figure 3.** (a) Pie charts for the distribution of residence among women with toxoplasma infection groups, (b) Pie charts for the distribution of residence among women without toxoplasma infection groups

The limitation of the current study that should be avoided in future studies is that the average lifespan of women increases > (42) year, and adopting more vital variables, such as another trace elements and hormones, especially thyroid hormone, according to the many studies that have proven the effect of gland disorder and its association with high levels of miscarriage.

## 5. CONCLUSION

Toxoplasmosis is an infection caused by *Toxoplasma gondii*, *T. gondii* related to phylum apicomplexan, has the ability to infect humans and animals which displays a series health problem. Especially for immunocompetent individuals. Zinc plays an important role in supporting immunity. According to the current results, the relationship between maternal zinc status was studied, as the blood serum containing a normal level of zinc supplements leads to a statistically significant decrease in the loss of the child due to miscarriage or premature birth. However, the relationship between maternal zinc status during pregnancy and premature birth needs to be determined through a large longitudinal investigation. The current study has been found that low zinc levels in infected women with toxoplasma compare with control ( $p \leq 0.05$ ) at

variance blood pressure, (SBP, DBP) no significant differences appeared ( $p \geq 0.05$ ) between toxoplasmosis women and control. Likewise, the surrounding conditions, such as education and residence have a fundamental role in determining the severity of toxoplasmosis infection, (who live in urban) have more tendency to infected with toxoplasma. One of the recommendations of this stud. The current study recommends that the levels of other minerals be taken into consideration in future research to determine their effect on the incidence of toxoplasmosis.

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