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ROLE OF COPPER METAL AND BIOLOGICAL MARKERS IN PATIENTS WITH ENTEROBIASIS

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KEYWORDS

Enterobiasis

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ABSTRACT

The primary goal of this study was to determine the effect of copper in patients with *Enterobius vermicularis* infection, as well as its association with IgE and TRFC. The study was carried out with 583 suspected and thirty healthy respondents of the same age who visited the AL-Zahra maternity and pediatrics laboratory, AL-Hakeem hospital, in AL-Najaf province(Iraq) from July 2020 to June 2021. This study aimed to estimate the level of copper, IgE, and TRFC in patients suffering from enterobiasis. The concentration of three biomarkers (copper, IgE, and TRFC) in serum was determined using the ELISA technique as per the manufacturer's instructions while the concentration of copper was assessed by using the colourimetric method. Results of the study revealed that the concentrations of IgE and TRFC significantly increased ($P \leq 0.05$) in the blood sample of *E. vermicularis* infected patients, while the serum concentrations of copper decreased significantly ($P \leq 0.05$) compared to the control group. The results of the current study suggested that the *E. vermicularis* infection alters serum IgE and TRFC concentrations, which significantly impacts copper levels in the blood.

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1 Introduction

Enterobiasis, also known as oxyuriasis, is a common infection caused by the helminthic parasite *Enterobius vermicularis*, which has a global distribution but is most prevalent in temperate areas (Mohammad & Koshak, 2011; Meletis et al., 2019). *E. vermicularis* is a parasitic helminth that infects about 300 million people globally, that making it the most common human parasitic helminth infestation (Dezsényi et al., 2018). *E. vermicularis* spreads via the fecal-oral route when a patient ingests eggs previously present in the perianal area of infected individuals (Meletis et al., 2019).

Many disorders such as malnutrition, intestinal disorders, and intestinal malabsorption are associated with copper metal deficiency (Stephenson et al., 2000). To achieve optimal growth, better immune response, and intellectual aptitude, intestinal parasite infections must be diagnosed and treated at the early stage (Pegelow et al., 1997; Stephenson et al., 2000). Furthermore, Koltas et al. (1997) suggested a significant effect of parasite infection on the mean copper concentration, which explained that the mean level of serum copper was considerably lower in the *E. vermicularis* infected group than the control group children. T-helper (Th) cells differentiate into Th1, Th2, Th17, and T-regulatory (Treg) subpopulations due to innate immunological identification, immune stimulation, activation, and their subsequent functional contact with B lymphocytes (Abd-Aljabar & Aljanaby, 2021). The presence of intestinal helminths stimulates the immune system, it responds with a type-2 directed response that attempts to expel the worms (Patsantara et al., 2016). T-helper (Th2) cytokines such as interleukin 4, 5, and 13 are commonly used in the immune response against pinworms (Sulk & Ehrchen, 2019; Rashad & Aljanaby, 2021). During pinworm infection, eosinophils and immunoglobulin E (IgE) levels notably rise in the youngsters (Dawood et al., 2016; Kara & Volkan, 2018). Intestinal parasites use host carbohydrates, lipids, minerals, vitamins, and other food sources to get essential energy for the life cycle. These minerals have an important role in the human body's metabolism and physiology, especially in growing children. Several studies have been reported that mineral elements such as copper and zinc have a vital role in children's regular growth and development (Hesham et al., 2004). The significant reduction in serum copper level in parasite-infected children is probably due to malabsorption and anorexia (Uwah et al., 2012). To understand the relationship between the parasite and human immune response especially on the level of copper, IgE, and TRFC, this study was carried out in patients with enterobiasis.

2 Materials and Methods

In the current study, identification of *E. vermicularis* infections was based on the various visible clinical symptoms such as severe anal

itching (especially at night - the most common), irritability, lack of appetite, abdominal pain, urinary tract infections, yellowing of the face, and weight loss. The samples were collected from the 583 possible respondents from July 2020 to June 2021 and identified using a light microscope and wet mount preparation for adult pinworms or eggs detection at the microbiological laboratory, department of biology, college of science, Al-Kufa University's. To detect the presence of *E. vermicularis* eggs, all faeces samples were examined using the saline wet mount technique, which involved placing a drop of saline (0.9 percent) on a glass slide. For this, a small amount of faeces samples were spread over the glass slide, mixed with a saline drop, covered with a coverslip, and observed at 100 X and 400 X, magnifications under a light microscope. Positive samples were defined as those that contained one or more eggs; all positive samples were frozen at -20 °C to preserve them for further analysis (Garcia et al., 2018; Al-labban et al., 2021).

2.1 Serum biomarker detection

From the selected 583 respondents, 60 were found positive for the *E. vermicularis* infection, blood samples of these 60 patients and 30 healthy youngsters who served as controls were collected for the serum collection and further analysis. The ELISA technique (Human reader, Germany) was used to determine the concentration of three biomarkers in serum (copper mg/dl, IgEng/ml, and TRFC ng/ml), as suggested by the manufacturer Company. The presence of the copper is assessed using the colourimetric method (Al-Hadraawy et al., 2016; Azeez el al., 2021) and BTLAB provided these biomarkers units with Cat.No. E0188Hu, and Cat.No.E0259Hu respectively.

2.2 Statistical analysis

The healthy and control groups were compared using Graph-pad prism version 10-computer software (T-test). Statistical significance was defined as a P-value of less than 0.05 (Al-Hadraawy et al., 2016; Al-Hadraawy et al., 2019; Mohy et al., 2019).

3 Results and Discussion

Results of this study are presented in table 1 and suggested a significant increase ($P = 0.05$) in the concentrations of IgE (ng/ml), and TRFC (ng/ml) in the *E. vermicularis* infected patients as compared to the healthy control while a significant reduction was reported in the concentration of copper (mcg/dl). Further, no significant gender effect was reported in the current study, and both males and females are showing similar values of IgE, TRFC, and copper. Overall, the concentration of IgE, TRFC, and copper was reported 373.39 (ng/ml), 972.93 (ng/ml) and 90.08 (mcg/dl) in the total patients infected by *E. vermicularis* while this value was reported 299.09 (ng/ml), 739.09 (ng/ml) and 128.17 (mcg/dl) respectively in the healthy control.

Table 1 Effect of *E. vermicularis* infection on the selected biological markers

Respondents	Biological Markers		
	Copper (mcg/dL)	IgE (ng/ml)	TRFC (ng/ml)
Male (Patients)	89.75±0.92	372.46±4.68	961.96±12.10
Male (Control)	130.20±2.23	321.24±16.42	749.31±9.50
Female (Patients)	90.42±0.89	374.33±4.42	983.91±10.53
Female (Control)	126.13±1.26	276.95±7.33	728.75±22.09
Total Patients	90.08±0.64	373.39±3.19	972.93±8.09
Total Control	128.17±1.31	299.09±9.75	739.03±11.97

As compared to the control group, the concentration of copper in males and females infected with *E. vermicularis* infection was significantly lower. This could be attributed to intestinal parasites that convert the host's carbohydrates, lipids, minerals, vitamins, and other dietary sources into necessary energy for the life cycle (Hesham et al., 2004). Minerals (copper, zinc, and magnesium) are essential for growth and development in developing children and play an essential role in the human body's metabolism and physiology (Hesham et al., 2004; Ramana, 2012). These findings are consistent with the findings of Culha & Sangün (2007) and Arbabi et al. (2015), those who found a significant reduction in the serum copper levels in children infected with enterobiasis. Similarly, Uwah et al. (2012) reported lower serum zinc, copper, and magnesium level in patients with parasite infection as compared to the control group. While the results of the current study are contradictory to the finding of Sadraei et al. (2007), those who reported significantly higher serum copper levels in patients infected with *E. vermicularis* intestinal infection as compared to the healthy control in Hatay Province.

The results of the study showed that IgE concentration in males and females infected with *E. vermicularis* was significantly higher than the control group; this could be due to allergic and pruritus action caused by enterobiasis infection (Arruda & Santos, 2005; Schroeder et al., 2018). Chronic infection with geohelminths causes polyclonal activation which resulted in high serum IgE levels (Scrivner et al., 2001; Sales et al., 2002). The helminths boost antiparasite IgE production and accelerate polyclonal IgE synthesis, which results in extremely high levels of total IgE in the bloodstream (Cooper et al., 1998). Although the link between helminthic infections and IgE antibody levels is controversial, IgE antibody is an essential component of the immune response against parasites (Allen & Maizels, 1996). IgE appears to play a role in the host's defenses against toxins, as tissue injury appears to be the primary trigger of immune responses in Th2 cells (Kelly & Grayson, 2016; Mukai et al., 2016). Similarly, various previous studies also suggested that patients infected with *E. vermicularis* had higher levels of IgE than those in the control group (Ganguly et al., 1988; Zarebavani et al., 2012; Al-kabee et al., 2014; Solmaz

et al., 2018). Khazaal et al. (2020a) explained that immunoglobulin levels increased dramatically, with a mean of 227.07 IU/ml compared to 48.66 IU/ml in the control group. While the results of the current study are contradictory to the findings of Essawy et al. (1989), Delialiglu & Nutman (2004), and Al-Daoudy & Al-Bazzaz (2020), those who reported no significant effect of the *E. vermicularis* on the levels of serum total IgE.

Th2 cell' response determines the acquired immunity of the host against the worms, other infections, poisons, and hazardous chemicals (Al-Hasheme et al., 2020). The results demonstrate that the concentration of TRFC in males and females infected with *E. vermicularis* was significantly higher than in the control group. This could be because infection hinders iron absorption from the gastrointestinal tract (Stoltzfus et al., 1997; Olsen et al., 1998; Tomanakan et al., 2020; Khazaal et al., 2020b).

These findings are differing from the results of Kuvibidila et al. (1995), those who found that TRFC levels are unaffected in *Plasmodium falciparum* infection. At the same time, the findings of the current study were consistent with those of Kuvibidila et al. (1995) those who reported lower TRFC levels in patients with acute malaria. Also, the study by Mockenhaupt et al. (1999) found that mean TRFC values were higher in *P. falciparum* infected children as compared to the non-infected children. Similarly, Stoltzfus et al. (1997) and Verhoef et al. (2001) found an increase in sTfR concentrations with parasite density in children with malaria infection. These researchers reported that sTfR concentrations increased with parasite density in children with asymptomatic malaria infection. According to Hung et al. (2007), parasites do not influence the level of the transferrin receptor in parasite-infected individuals.

Conclusions

Results of the current study can be concluded that *E. vermicularis* infection has a significant effect on the various biomarkers and the children infected with *E. vermicularis* had lower copper levels and higher IgE and TRFC levels in the blood serum.

Conflict of Interest: Nil

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