

# Changes in the Levels of Some Biochemical Parameters in the Serum of Children in Response to the Giardiasis Infection

Sarmad N. Mageed

Department of Medical Microbiology, Faculty of Science and Health, Koya University, Daniel Mitterrand Boulevard, Koya KOY45, Kurdistan Region – F.R. Iraq

**Abstract**—*Giardiasis* is one of the most common intestinal protozoan infections worldwide. The study aimed to determine the levels of a number of biochemical parameters in the sera of children with giardiasis without receiving any medication for the treatment of giardiasis or intestinal helminthic infections in the previous 7 days. The study conducted 34 (19 females and 15 males) children and 34 (18 females and 16 males) healthy children as a control group. The mean ages of infected children and control groups were  $8 \pm 2$  and  $7 \pm 2$  years, respectively. Serum levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatinine, urea, sodium, potassium, uric acid, and albumin were determined. AST level in males was significantly higher than healthy children control ( $14.20 \pm 1.896$  and  $10.06 \pm 0.699$ ), respectively ( $P < 0.05$ ), and no significant difference in females was noticed whereas the significant increases in ALT level were found when compared to control ( $12.43 \pm 0.806$  and  $8.666 \pm 0.449$ ), for female, respectively, whereas no significant change in males was observed. Creatinine levels showed significant decrease in females when compared to control ( $57.72 \pm 1.170$  and  $73.37 \pm 1.635$ ) ( $P \leq 0.001$ ), respectively.

**Index Terms**—Biochemical parameters, Children, Giardiasis, Males and females.

## I. INTRODUCTION

*Giardia intestinalis* (*G. intestinalis*) is a worldwide cause of gastrointestinal infection known as giardiasis, which infects the small intestine of human at different ages, particularly children (Magdieva et al., 1984; Mel'nik, 1985) (Khudair, 2010). It is a flagellated enteric protozoon that infects humans and other mammals and is a major cause of morbidity and mortality in tropical and subtropical countries (Bansal et al., 2005). Infants and young children have more susceptibility to giardiasis due to behavioral and immunological factors (Sotto and Gra, 1986). The infection is transmitted easily by direct fecal-oral contact,

by contaminated drinking water (waterborne diseases) (Craun, 1984; Osterholm et al., 1981), food (Osterholm et al., 1981), or by abnormal sexual practices (Mildvan et al., 1977)(Miller and Hendrie 2000).

It exists in trophozoite and cyst forms, and the infective form is the cyst. Trophozoites of *G. intestinalis* are found in the upper part of the small intestine, where they live closely attached to the mucosa. They are found at times in the gallbladder and in biliary drainage. *G. intestinalis* infection causes severe intestinal disorder, most commonly, diarrhea and related symptoms due to malabsorption of fat; fat-soluble vitamins, and disaccharides (Bogitsh et al., 2013; Burke, 1975).

During infection, *Giardia* trophozoites colonize the proximal small intestine and adhere to the apical surface of the enterocyte. This close association between the parasite and the small intestinal epithelium initiates a succession of pathophysiological processes, leading to a diffuse shortening of the epithelial microvilli. The reduction of small intestinal absorptive surface area causes disaccharides deficiencies and malabsorption of nutrients, water, and electrolytes (Rosenberg et al., 1977).

There is a close relationship between intestinal parasitic infections such as giardiasis in particular, and malnutrition in children, especially those at school age that has direct effect on their growth and educational outcome (Nematian et al., 2008). Giardiasis infection has the ability to impede child growth even when asymptomatic, which can be through malabsorption and block the absorption of many essential biochemical elements for the child's growth (Simsek et al., 2004). The deficiency of these elements can adverse effect on the production of many other essential elements for the biochemical pathways to be performed and main the homeostasis of the body (Al-Mekhlafi et al., 2005; Botero-Garcés et al., 2009; Nematian et al., 2008; Prado et al., 2005; Simsek et al., 2004). Giardiasis was also found to have a close relationship with the development of malnutrition in infants as a result of absorption obstruction that reflected in more severely diarrhea in those children with prolonged nutrition deficiency (Mondal et al., 2012). *Giardia* infection may results in severe acute diarrhea in children at the age of less than 5 years old. Relatively, chronic infection may

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Corresponding author's e-mail: sarmad.mageed@koyauniversity.org

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consequently lead to weight loss and retardation of growth (Teixeira et al., 2007) (Júlio et al., 2012).

Liver and kidney function tests are known as a group of blood tests, which also referred to as a hepatic and renal panel that reveal and provide information regarding the general status of a patient's liver and kidney in relation to a specific disorder or abnormal health condition (Lee, 2009). These tests are performed on serum samples taken from patients of different ages. These tests comprise an assessment of a number of biochemical parameters such as serum levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatinine, urea, uric acid, and albumin.

Clinically, the most significant alterations in the activities of liver enzyme are found in the form of elevated aminotransaminase activities in case of hepatocellular damage, and elevated alkaline phosphatase, 5'-nucleotidase, and  $\gamma$ -glutamyltransferase activities in case of cholestasis (Burtis and Bruns 2015). As an effective way to detect hepatic dysfunction or abnormality, liver function tests are very helpful and practical screening tool. No single test is sufficient to provide a complete estimate of liver function due to that the liver carries out a number of various functions at the same time. Physicians are often faced reports that do not consist or comply with the clinical state of the patient and they face difficulty in interpreting the results (Thapa and Walia, 2007).

Creatinine, urea, and uric acid are considered as nonprotein nitrogenous metabolites that are excreted by the kidney out of the body following glomerular filtration. Measuring the concentrations of these metabolites in the plasma or serum (Concentrations of creatine, urea, and uric acid in serum, and plasma are equivalent) are commonly used as indicators of normal or abnormal kidney function and other conditions (Burtis and Bruns, 2015).

Albumin is the most commonly measured serum protein and is synthesized exclusively by the liver. With liver disease, hypoalbuminemia is noted primarily in cirrhosis, autoimmune hepatitis, and alcoholic hepatitis (Burtis and Bruns, 2015).

In general, infected individuals are not showing any symptoms; however, clinical appearances may involve simple flatulence, acute, or chronic diarrheal infection accompanied by abdominal pain and nausea, to severe malnutrition (Jasinska and Granicki, 1982; Misra et al., 1995; Prado et al., 2005; Sotto et al., 1990; Telichko et al., 1973). In severe cases, the malnutrition as a consequence of malabsorption can lead to a noticeable weight loss. The rate of infection is determine the severity of the malabsorption (Kremery et al., 1989).

There is still lack of understanding of the mechanisms of pathogenicity and malabsorption in giardiasis (Kremery et al., 1989; Roxström-Lindquist et al., 2006). Some patients exhibit a reduction in length of their small intestinal villi (Heyworth, 1996; Koot et al., 2009) or even obstruct the microvilli of the small intestine (Kremery et al., 1989).

To date, no research has been published that investigate the changes in biochemical parameters that accompany giardiasis infection in male and female children. This study has been undertaken to elucidate the effect of giardiasis on the levels

of some biochemical parameters in the serum of infected children comparing with their non-infected counterparts. The study aimed to highlight the malnutrition and homeostasis complication consequences under conditions of natural human infection as a result of changes in the level of a number of essential biochemical parameters in the serum of studied children.

## II. MATERIALS AND METHODS

In this study, blood samples were taken from 34 children (19 females and 15 males) with chronic giardiasis and 34 healthy children (18 females and 16 males) as a control group was included. The study was conducted over a period of 8 months from April 2017 to November 2017.

The children with chronic giardiasis consisted of cases that were referred to the Azadi Hospital in Kirkuk city for diarrheal symptoms. Children at the age 2–12 years with giardia infection, as demonstrated by the identification of trophozoites and/or cysts of *Giardia lamblia* in stool specimens were entered in this study.

Those suffering from acute febrile conditions, chronic diarrhea, and severe malnutrition or receiving long-term therapy were excluded from the study. None of the children entered in this study had received any medication for the treatment of giardia or intestinal helminthic infection in the previous 7 days. The control group consisted of children who were referred to the same hospital outpatient clinic for a routine checkup and had normal physical examination and laboratory results.

The serum is the liquid portion of blood that remains after coagulation has occurred; it is the specimen of choice for many analyses, including but not limited to aminotransferases enzymes, creatinine, urea, sodium, potassium, uric acid, and albumin. Samples were collected into test tubes without any additives or clot activators and allowed to complete the coagulation process before further processing. Aspartate AST (glutamic-oxaloacetic transaminase [GOT]), ALT (glutamate pyruvate transaminase [GPT]), urea, uric acid, sodium, and potassium levels were measured (by colorimetric method), creatinine level (by kinetic method) and albumin (Bromcresol Green method) by specific kits of BIOLABO Company (France) through using spectrophotometric technique according to the manufacturer procedure, whereas levels of sodium and potassium were measured (colorimetric method) by linear company kit using spectrophotometric technique according to the manufacturer procedure.

### A. Parasitological Examination

Stool samples were examined for cysts and/or trophozoites of *G. intestinalis* by a wet mount of the fresh specimen by direct saline and Lugol preparation. Stools were concentrated for examination using the formalin-ethyl acetate sedimentation technique and were also stained by acid-fast staining for cryptosporidiosis and cyclosporiasis. Slides were prepared from fresh and concentrated specimens.

III. RESULTS AND DISCUSSION

The mean ages of children of both genders with chronic giardiasis and the control group were  $8 \pm 2$  and  $7 \pm 2$  years, respectively.

Table I shows serum levels of AST, ALT, creatinine, urea, sodium, potassium, uric acid, and albumin. The results showed that AST level significantly increased in males as a consequence of the infection in comparison to those from the healthy children controls ( $14.20 \pm 1.896$  and  $10.06 \pm 0.699$ ), respectively ( $P < 0.05$ ), and no significant difference was noticed in females, Table I, whereas the significant increase was found in females' ALT levels when compared with healthy control ( $12.43 \pm 0.806$  and  $8.666 \pm 0.449$ ) ( $P \leq 0.001$ ), respectively, whereas no significant increase was observed in males (Table I). Creatinine levels showed significant decrease in females comparing to controls ( $57.72 \pm 1.170$  and  $73.37 \pm 1.635$ ), respectively ( $P \leq 0.001$ ), which is consistent with the data that have been published by Charalabopoulos et al., 2004; Rosa et al., 2007, (Miller, L. and Hendrie, N. 2000) (Nash et al., 1987) (Table I).

As related with other parameters, the results showed significant decreases in the levels of urea, sodium, potassium, uric acid, and albumin in both males and females as compared with control (Table I). Decreases level of serum albumin was previously reported in giardiasis patients (Abdumadjidova and Inoyatova, 1998; Cusack et al., 2001), and with a history of infectious enterocolitis determined by *Escherichia coli* enteropathogenic (Melit et al., 2017). Diet with adequate calories but low protein intake has been known to lead to malnutrition due to protein deficiency, with decreased serum albumin (Burtis and Bruns, 2015).

The activity variation of liver enzymes (AST and ALT) in serum is commonly considered as an indicator of a number of pathological changes of tissue and liver. Improper regulation of ALT synthesis would have great effect on the liver's ability to metabolize amino acids for energy production within the cell (Ragbetli et al., 2014).

Table II revealed more interesting results when the comparison made between infected males and females with chronic giardiasis. Creatinine and urea levels were significantly increased in males comparing to females  $73.73 \pm 1.911$  and  $57.72 \pm 1.170$  and  $4.013 \pm 0.197$  and  $3.949 \pm 0.114$  ( $P < 0.05$ ), respectively, providing further support to the previous results when compared between infected and healthy controls, whereas no significant changes were observed in the level of the remaining parameters ( $P > 0.05$ ) as a comparison between the infected males and females.

Sandstead et al., 1965, have confirmed marked intermittent increases in serum liver transaminases aspartate transaminase (AST or serum GOT) and alanine transaminase (ALT or serum GPT) in children.

The results were inconsistent with previous studies by that have shown higher rates of infection among males (48%) than females (28%). Epidemiological studies have reported that giardiasis infection rates to be higher in

TABLE I  
SERUM LEVELS OF DIFFERENT BIOCHEMICAL PARAMETERS IN AFFECTED MALE AND FEMALE CHILDREN WITH GIARDIASIS COMPARING TO NON-INFECTED CONTROLS

Parameters	Gender	Control	Patient	P value
AST (U/L)	Male	10.06±0.699	14.20±1.896	0.023
	Female	10.28±0.989	11.30±0.883	0.455
ALT (U/L)	Male	9.048±1.041	11.43±1.459	0.181
	Female	8.666±0.449	12.43±0.806	0.001
Creatinine (mg/dl)	Male	73.04±1.645	73.73±1.911	0.790
	Female	73.37±1.635	57.72±1.170	0.0001
Urea (mg/dl)	Male	5.077±0.208	4.013±0.197	0.032
	Female	5.027±0.126	3.949±0.114	0.0001
Sodium (mmol/L)	Male	140.2±0.713	138.0±0.317	0.01
	Female	141.2±0.772	138.7±0.387	0.002
Potassium (mmol/L)	Male	4.273±0.116	3.677±0.080	0.001
	Female	4.270±0.091	3.758±0.050	0.0001
Uric acid (mg/dl)	Male	300.9±9.620	264.0±11.90	0.020
	Female	294.6±6.369	275.6±6.837	0.04
Albumin (g/L)	Male	53.64±1.768	46.53±0.999	0.001
	Female	50.29±2.098	44.13±0.810	0.002

TABLE II  
COMPARISON OF SERUM LEVELS OF BIOCHEMICAL PARAMETERS BETWEEN INFECTED MALES AND FEMALES WITH CHRONIC GIARDIASIS

Parameters	Male	Female	P value
AST (U/L)	14.20±1.896	11.30±0.883	0.125
ALT (U/L)	11.43±1.459	12.43±0.806	0.518
Creatinine mg/dl)	73.73±1.911	57.72±1.170	0.0001
Urea (mg/dl)	4.013±0.197	3.949±0.114	0.007
Sodium (mmol/L)	138.0±0.317	138.7±0.387	0.971
Potassium (mmol/L)	3.677±0.080	3.758±0.050	0.397
Uric acid (mg/dl)	264.0±11.90	275.6±6.837	0.373
Albumin (g/L)	46.53±0.999	44.13±0.810	0.082

males than in females. However, the reasons behind these observed differences still need to be explained. However, increased exposure to contaminated environments can illustrate the higher rates of infection in males, due to the nature of their normal daily tasks as being spend most of their times outdoors and mostly in low-level sanitation environments (Kasim and Elhelu, 1983). In contrast, females play and spend most of their time at or close to their homes in relatively more clean (In term of Giardia infections) environments (Cheesbrough, 1987).

Giardiasis as one of the parasitic diseases is characterized by undernutrition and deficiency of essential micronutrient, problems with digestion, reduction in nutrients absorption and chronic inflammation (Hesham et al., 2004).

In giardiasis patients, the levels of electrolytes are expected to decrease as a consequence of lack of absorption. Gastrointestinal parasitism can lead to similar electrolyte deficiency as it happens classically in hyperkalemia and hyponatremia (DiBartola et al., 1985; Willard et al., 1991).

For the purpose of acid-base balance as well as osmotic pressure, sodium (Na) and potassium (K) as electrolytes, play an important role in this regard. A decrease in the levels of these ions can result in severe complications and uncontrollable events in body functions. The lack of these

macro elements can consequently lead to clinical disorder, weight loss and may end in death, especially with an increased load of parasites if untreated (Krajničáková et al., 2003; Kulcu and Yur, 2003; Tanyuksel et al., 1995).

Hypokalemia was noticed more than hyponatremia, and significant decrease in the level of serum urea and creatinine was also observed in patients as a consequence of the infection. Therefore, electrolytes deficiency should be closely monitored in patients with acute gastroenteritis (Baghaei, 2015; Korman et al., 1990; Özçay et al., 2013).

In immunocompetent and immunocompromised patients, giardiasis has been reported to induce many cases of myopathy following hypokalemia (Cervello et al., 1993; Geovese et al., 1996). This leads to conclude that *Giardia* can work out of the control of the host's immune status by showing the ability to trigger muscular manifestations independently. Relatively, potassium loss during giardia infection is directly affected by the number of bouts of diarrhea per day (Geovese et al., 1996).

Severe and transient myopathy can be triggered by hypokalemia due to loss of potassium (Geovese et al., 1996). Evidently, muscular manifestation can improve dramatically alongside with recovery from diarrhea and increased levels of potassium (Cervello et al., 1993). Although it is very uncommon that hypokalemia results in myopathy due to diarrhea by *Giardia*, it looks like that the symptoms' period is critical for hypokalemic myopathy development (Geovese et al., 1996).

For the diagnosis purposes and to find the organism as a confirmation of the infection, stool samples or duodenal secretions were required, before taking blood samples. *Giardia* parasite can be readily found in the stool in acute infections, whereas repeated stool samples were essential in chronic cases, as excretion is irregular (Goka et al., 1990).

Studies of intestinal mucosa through using light microscope revealed that *G. intestinalis* attach to epithelial layer and mucosal filaments that are located at the intervillous space, where the active absorption occurs. This attachment results in a mechanical block and mucosal layer inflammation, which is consequently cause malabsorption and loss of many nutrients, such as proteins (Farthing et al., 1986).

Although that up to recent date, only few scientific researchers have revealed extra-intestinal manifestations due to giardiasis. However, approximately third of infected patients with giardia parasite have been estimated to exhibit long-term extra-intestinal complications according to a recent study, proposing that this phenomenon is less surprising and is not unexpected as considered in the past (Cantey et al., 2011).

The facts that have been revealed by recent studies in which *Giardia* may results in chronic post-infectious gastrointestinal complications have highlighted the topic as a very interesting for intense research. Post-infectious clinical aspects caused by *Giardia*, although that complete elimination of the parasite has been confirmed remains a mystery (Halliez and Buret, 2013).

#### IV. CONCLUSION

The study was able to demonstrate, by examining the blood serum of infected children, that there are significant changes in the level of a number of biochemical parameters among infected children with giardiasis that may be specifically recognized as a consequence of malabsorption during infection and may lead to transient or chronic malnutrition status.

Therefore, these transmitted infections among young generations, through contaminated water and food sources, require close attention, in term of prevention and control before treatment. The prevention strategies will avoid, to a great extent the consequence outcomes of having such long-term children patients with chronic malabsorption. Further studies on a large scale of cases are needed to investigate and confirm the health impact and consequences on infected individuals as a result of this infection.

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