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Effects of Pretreatment with Lead on Susceptibility and Resistance of Mice to Schistosomiasis

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ABSTRACT

Despite control efforts over the infected areas with schistosomiasis in the world, about 200 million people are still infected, of which 120 million suffer severe morbidity and complications. The clinical symptoms of Schistsomiasis include hepatosplenomegaly, liver fibrosis, portal hypertension, and liver cirrhosis. The aim of the present study was to show the effects of pretreatment with lead on the course of schistosomiasis and to investigate the possible role of it on susceptibility and resistance of mice to infection. Mice were used in this study as experimental animals, these were randomly divided into two main groups as follows: Group I, which was divided into: Ia: Control group and Ib: Infected group with *S. mansoni* and were sacrificed at the end of the 8th week after infection. Group II, which was divided into: IIa: Control group and IIb: pretreated group with Pb for 4 weeks and and infected with *S. mansoni* and were sacrificed after another 8 weeks. This study concluded that pretreatment with lead acetate to *S. mansoni* infected mice resulted in significant reduction in the harmful effects on the liver, hematological data, and body and organ weight, as compared with *Schistosoma mansoni* infected groups.

KEY WORDS: Schistosomiasis, Lead, Liver, Hematological data

1. INTRODUCTION

Morbidity and mortality due to schistosomiasis are very high among developing countries in Africa, South America and Asia. Despite control efforts over the infected areas with schistosomiasis in the world, about 200 million people are still infected, of which 120 million suffer severe morbidity and complications (Jenkins-Holick and Kaul, 2013). The main agent of human schistosomiasis is *Schistosoma mansoni* (dos Santos, 2007). Predominantly, eggs of *Schistosoma mansoni* are deposited in the liver and intestines which resulting in parasitic disease (Allam, 2007). The clinical symptoms of Scistsomiasis include hepatosplenomegaly, liver fibrosis, portal hypertension, and liver cirrhosis. Acute symptoms of schistosomiasis include fever, diarrhea, abdominal pain, weight loss, and eosinophilia (David, 1980 and Mahmoud, 2002).

Eggs of *Schistosoma mansoni* are transported to the liver by portal circulation and acute schistosomiasis is associated with heavy primary infections and with the initiation of egg production (Chang, 2006). The eggs are deposited in the portal venous system while eggs are trapped in the peri-sinusoidal spaces of the liver, thus leads to periportal granulomatous inflammation and the deposition of scar tissue around the eggs trapped inside the liver (Andrade, 2009). Granulomas are formed of inflammatory cells as macrophages, eosinophils and lymphocytes.

Lead is considered one of the main environmental pollutants in Egypt as a result of industrialization of society, which is a prime factor of increased incidence of lead intoxication. Lead based paints, pesticides, storage batteries, ceramic glazes and other industrialized byproducts contribute to everyday lead exposure. Much of this environmental lead can end up in the form of minute particulate airborne lead or in soils, leading to its accumulation in plants and animals. Adults consume approximately 300 μg of lead each day of which only 10% is absorbed. Unlike adults, children absorb about 50% of ingested lead. A single chip of paint the size of a thumbnail can contain 50 - 200 mg of lead; the consumption of a few such chips a day equals 1000 times the allowable intake for an adult. So, children are more susceptible to develop lead toxicity than adults (El-Gohary, 2003).

The aim of the present study was to show the effects of pretreatment with lead on the course of schistosomiasis and to investigate the possible role of it on susceptibility and resistance of mice to infection.

2. MATERIALS AND METHODS

Experimental animals: Male albino mice *(Mus musculus)*, Weighing about 18g (16 - 20g), obtained from Schistosoma Biological Supply Program (SBSP), Theodor Bilharz Research Institute, Egypt, were used as experimental animals throughout the present research work. Animals were housed in groups in plastic cages and were maintained under standard controlled condition. Cercariae of *schistosoma mansoni* were obtained from the Schistosome Biological Supply Program (SBSP), Theodor Bilharz Research Institute and used within ½ hr of being shed.

Chemicals: Lead acetate was used as the source of lead in this study. Lead acetate is a substance with small white transparent crystals with an acetous odour and a sweet taste. This substance becomes anhydrous at 40°C and rendered basic when heated. Lead acetate has been used at a dose 250 ppm in drinking water.

Experimental design: Animals were randomly divided into two main groups, each one were divided into two subgroups 10 animals in each as follow:

Group I, which was divided into:

Ia: Control group: These mice were fed on a balanced diet and received water *ad libitum.* Animals were sacrificed at the end of 8th weeks of the experiment.

Ib: Infected group with *S. mansoni*: A group of this animals were fed with the same diet as a control group and infected by subcutaneous injection with 100 cercariae of *S. mansoni* for each mouse. Cercariae of *S. mansoni* were obtained from Theodor Bilharz Research Institute, Egypt. Animals were sacrificed at the end of the 8th week after infection.

Group II, which was divided into:

IIa: Control group: These mice were fed on a balanced diet and received water *ad libitum.* Animals were sacrificed after 12 weeks from beginning of the experiment.

IIb: Pretreated group with Pb and infected with *S. mansoni*: These animals was fed with balanced diets and were treated with 250 ppm of lead acetate in drinking water for 4 weeks and infected subcutaneously with 100 cercariae of S. *mansoni* by the former method. After another 8 weeks of post-infection, the animals were sacrificed.

Collection of blood samples: Blood samples were received in clean and dry glass tubes contained EDTA as anticoagulant for the hematological examinations and the Hematological parameters were determined using an automated hematology analyzer sysmex (K-1000). Leucocyte differential counted was preceded according to Turgeon (2005) by using Giemsa stain (Atlas Medical Company, UK).

Collection of serum samples: Blood Samples were received in conical glass centrifuge tubes and put for 1 hr in the refrigerator for clotting after which sera were separated using cooling centrifuge at 1000 g for 5 min. and Kept at -20°C till analysis within one week.

Biochemical analyses: Serum aminotransferases (ALT and AST), total proteins, albumin and globulins were determined using an automatic multiparameter apparatus, ASTRA 8-Synchron.

Histological Preparation and measurement of granuloma diameter: Experimental animals were sacrificed by cervical decapitation. They were immediately dissected, and small pieces of the liver were quickly removed and fixed in Bouin's fluid. After fixation specimens were dehydrated in an ascending series of alcohol, then kept in terpineol for three days to ensure complete dehydration and clearing purposes. Cleared specimens were rinsed in three changes of xylol before embedding in paraffin wax (m.p.56-58°C). Three sections of 5 microns thick were taken from each liver sample, each being at a distance of at least 500 microns from the proceeding one and mounted on clean slides without adhesive medium. For histological examination, sections were stained with Ehrlich's haematoxyline and eosin.

Individual granulomas were measured, only granulomas containing single egg were selected for measurement. Each section was examined for schistosome eggs, and the diameter of each egg, including the reaction around it, was determined by measuring two diameter at right angles to each other with a calibrated ocular micrometer *(Boros & Warren, 1970)*. The mean of periovular granuloma diameter of each group was calculated for about 40 lesions.The percent change between any two groups was calculated a ccording to the formula: percentage of change = (A-B) /A × 100, where, A: Mean granuloma diameter of infected group, B: Mean granuloma diameter of treated-infected group.

Statistical Analysis: Data are expressed as mean±SD. The level of statistical significance was taken at $P < 0.05$, using one way analysis of variance (ANOVA) test followed by Dunnett test to detect the significance of differences between each group and control. All analysis were performed by using, GraphPad Prism software version 5.

3. RESULTS

The tabulated data in table (1) illustrate the effects of infection with *S. mansoni* with or without pretreatment with lead acetate. These results showed highly significant increase in both serum AST and ALT in infected group by 63% and 67% respectively, on the other hand these differences in enzymes activities were reduced in the pretreated group with lead acetate for 4 weeks and infected with *S. mansoni* to 19% and 35% for AST and ALT respectively. The effect of infection with *S. mansoni* and pretreatment with lead acetate, also showed significant changes in plasma proteins. Total proteins were increased in infected group and pretreated and infected group by 9% and 14% respectively, but albumin concentrations, were reduced by -7% and -21% in the same time plasma globulins were elevate significantly by 27% and 55% and A/G ratio were reduced by -28% and -49% in both infected and pretreated and infected groups respectively.

Table.1. Liver function tests in mice as affected by Schistosomiasis and pretreatment with Lead

Animal groups	**Group I Control**	**Group I Infected with S. *mansoni***		**Group II Control**	**Group II Pretreated with Pb and infected with *S. mansoni***	
Parameters	M±SD	M±SD	%diff	M±SD	M±SD	%diff
sAST IU/L	143.6±10.3	234±11.1**	63	150.4±8.4	177±4.9**	19
sALT IU/L	53.8±4.8	90±2.9**	67	56.4±4.5	76±3.9**	35
Total Proteins gm/dl	5.47±0.07	5.98±0.1**	9	5.51±0.04	6.26±0.12**	14
Albumin gm/dl	3.04±0.05	2.82±0.1**	-7	3.01±0.03	2.38±0.08**	-21
Globulins gm/dl	2.48±0.03	3.16±0.1**	27	2.5±0.03	3.88±0.05**	55
A/G ratio	1.23±0.04	0.89±0.1**	-28	1.2±0.05	0.61±0.07**	-49

*: Significant (P < 0.05); **: Highly significant (P< 0.01).

Table.2. Hematological parameters in mice as affected by Schistosomiasis and pretreatment with Lead

Animal groups	**Group I Control**	**Group I Infected with S. *mansoni***		**Group II Control**	**Group II Pretreated with Pb and infected with *S. mansoni***	
Parameters	M±SE	M±SE	%diff	M±SE	M±SE	%diff
RBCs Count($x10^6$)	8.4±0.18	6.94±0.2**	-17	8.05±0.19	7.06±0.6**	-12
Hb (g/dL)	15.34±0.23	12.9±0.6**	-16	14.9±0.52	12.92±0.9**	-13
Ht (%)	43.22±1.4	36.7±1.4**	-15	40.76±1	35±3.4**	-14
MCV	45±1.2	52.98±0.5	-2	53.6±0.6	50.7±1.2**	-5
MCH (Pg)	19.86±0.31	18.3±0.3**	-8	19.5±0.76	17.9±0.4**	-8
MCHC	36.69±0.35	35±0.21**	-5	36.6±0.37	35.38±1.1*	-3
WBCs(10^3/μL)	8±0.6	7.5±0.8	-6	7.9±0.5	12±1**	52
Lymphocytes %	65±2	67±2	3	64±2.9	49±2.6**	-23
Neutrophils %	27±1.9	23±2.5*	-15	27±2.5	31±1.6*	15
Monocytes %	6.3±1.2	3.4±1.5**	-46	6.3±1.4	10±2.6**	59
Eosinophils %	1.2±0.8	6±0.5**	400	2.4±1	7±0.5**	192
Basophils %	0.5±0.40	0.5±0.40	20	0.3±0.30	3.00±1.60**	900

*: Significant (P < 0.05); **: Highly significant (P< 0.01)

The data of table (2) illustrate the hematological changes in mice as a result of bilharzial infection alone or pretreatment with lead acetate for 4 weeks before bilharzial infection. These data showed that, red blood cells count, hemoglobin concentration, and hematocrit, were reduced in infected group by -17%, -16, and -15% respectively, but this reductions of these data were slightly relieved in the pretreated and infected group to reach -12%, -13, and -14%. The data of table (2) also showed the changes in blood indices as MCV, MCH, and MCHC, the effects of infection with *S. mansoni* alone on these indices were, -2%, -8% and -5%, these also was changed in the pretreated and infected group by, -5%, -8% and -3%. The changes in total leucocytes and differential count were illustrated in table (2), these data were showed different variations in both groups, total leucocyte count did not show significant change in infected group, on the other hand, this parameter was increase in pretreated and infected group by 52%. The different types of white blood cells were showed dramatic changes and variations in both groups, neutrophils were reduced in infected group but increased in pretreated and infected group by -15% and 15% respectively, also monocytes were reduced in infected group by -46% and increased in pretreated and infected group by 59%. The changes of eosinophil percentages were high significant in both group, they were increased in infected group by 400% and in pretreated and infected group by 192%, this increase was also occurred among basophils, which increased by 20% and 900% in both infected group and pretreated and infected group respectively. Lymphocytes did not show any significant change in infected group, but this percentage of these cells were reduced by -23% in pretreated and infected group. The data in table (3) showed the variations in body weights, liver, and spleen weights. These weights were changed significantly compared to their corresponding control by -7%, 51% and 137% in infected group respectively, on the other hand, these changes were -8%, 25% and 136% among the pretreated and infected group.

Table.3. Body and organ weights in mice as affected by Schistosomiasis and pretreatment with Lead

Animal groups	Group I Control	Group I Infected with *S. mansoni*		Group II Control	Group II Pretreated with Pb and infected with *S. mansoni*	
Parameters	M±SE	M±SE	%diff	M±SE	M±SE	%diff
Body weight (gm)	35.8±0.77	33.2±0.67**	-7	38.4±1.7	35.3±1.3**	-8
Liver weight (gm)	4.54±0.22	6.84±0.26**	51	4.75±0.36	5.95±0.29**	25
Spleen weight (gm)	0.40±0.04	0.95±0.03**	137	0.38±0.03	0.90±0.04**	136

*: Significant (P < 0.05); **: Highly significant (P< 0.01).

Liver histology of control animals showed as in other mammalian animals, the structural unit of the mouse liver is the hepatic lobule which is made up of radiating plates of cells forming a network around a central vein (Fig.1). The hepatic cells are polyhedral in shape with large, centrally located nuclei and granular cytoplasm. The sinusoids are narrow blood spaces with irregular boundaries composed of endothelial cells in addition to large kupffer cells which are known to be actively phagocyte cells. The bile ductile appears rounded and is bounded by a layer of cuboidal cells encircled by a thin sheath of connective tissue. The portal veins are comparatively large in size being either empty or containing a few blood cells.

Animals examined at 8 weeks post-infection with *S.mansoni* showed granulomas with different sizes and the hepatic tissue around the granulomas showed some pathological changes such as congestion of central vein, dilation of sinusoid spaces and leucocytic infiltration (Fig.2). These granulomas were characterized by epithelioid macrophages and huge population of fibroblasts. The periphery of the granuloma showed numerous lymphocytes and plasma cells while the center, in which the damaged egg is present, there is clusters of eosinophils (Fig. 2, 3 and 4). The mean diameter of these granulomas was 397±59.9 µm (Table.4).

Table.4. Granuloma diameter in the liver of mice as affected by schistosomiasis and pretreatment with lead

Parameter	Group I Infected with *S. mansoni*	Group II Pretreated with Pb and infected with *S. mansoni*	%diff
Granuloma diameter	397±59.9	286 ±17.8**	-28

*: Significant (P < 0.05); **: Highly significant (P< 0.01).

Examination of liver sections obtained from mice treated with lead acetate for 4 weeks and then infected with *schistosoma mansoni* for 8 weeks showed small periovular granulomas (Fig. 5). The main cellular constituents in granuloma were eosinophils, neutrophils, lymphocytes and macrophages (Fig. 6). Concerning the hepatic tissue around the granulomas, the hepatocytes appeared normal while the central vein showed congestion (Fig. 5). In another liver section of the same group, there was a congested portal vein surrounded with huge leucocytic infiltration were observed (Fig. 7). The mean diameter of these granulomas appeared significantly reduced (286±17.8µm) when compared to the mean granuloma diameter of untreated group (397±59.9µm), (Table 4). The percentage of suppression in the mean granuloma diameter as a result of lead acetate administration was 28%.

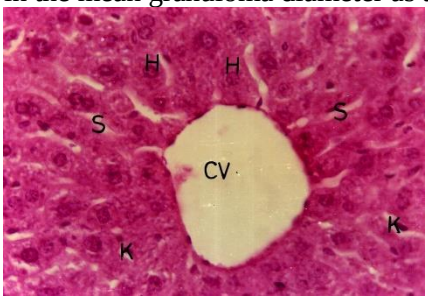

Figure.1. Section of the liver a Control mouse (x450), H: Hepatocyte, S: Sinusoid space, K: Kupffer cell, CV: Central vein

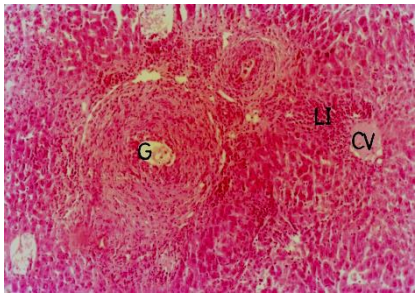

Figure.2. Section of the liver in infected mouse with S. mansoni (x110) G: Periovular granuloma, CV: Congested central vein, LI: Inflammatory leucocytes infiltration

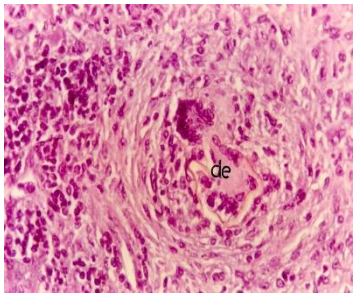

Figure.3. Section of the liver in infected mouse with S. mansoni (x450), de: Dead egg invaded by macrophage

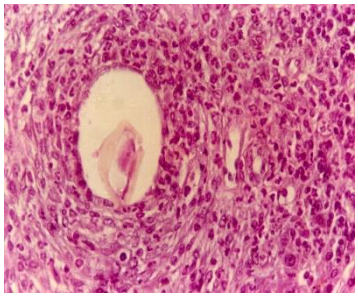

Figure.4. Section of the liver in infected mouse with *S. mansoni* (x450)

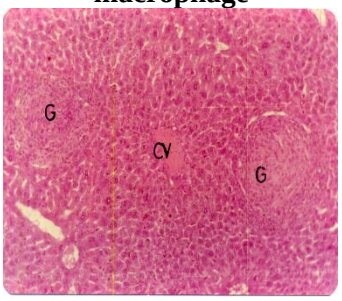

Figure.5. Section of the liver in Pretreated mouse with Lead and infected with *S. mansoni*

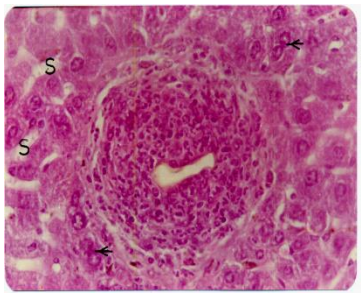

Figure.6. Section of the liver in Pretreated mouse with Lead and infected with *S. mansoni*

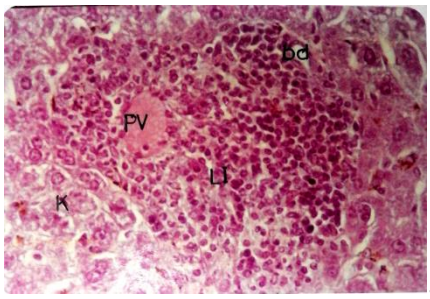

Figure.7. Section of the liver in Pretreated mouse with Lead and infected with *S. mansoni*

DISCUSSION

Chang *(*2006), reported that eggs are transported to the liver by portal circulation. Acute schistosomiasis is associated with heavy primary infections and with the initiation of egg production. In the portal venous system eggs are deposited while eggs are trapped in the peri-sinusoidal spaces of the liver, thus causing periportal granulomatous inflammation and the deposition of scar tissue around the eggs trapped inside the liver (Andrade, 2009). Granulomas are formed of inflammatory cells "eosinophils, macrophages, and lymphocytes" (Brito and Borojevic, 1997).

Granulomas were remarkable by concentric fibrosis and many fibroblasts encircled the trapped eggs (Amer, 2013; Kadry, 2013). Moreover, Dkhil (2014), reported that infection with *S. mansoni* caused a severe hepatic granulomatous inflammatory response which appears in form of inflammatory cellular infiltration, cytoplasmic vacuolation and degeneration of hepatocytes. The presence of huge number of granulomas resulted in disorganization of the hepatic strands and lobular structure where granulomas are surrounded by a cuff of aggregated lymphocytes, epitheloid cells, eosinophils and collagenous fibres. Also, the hepatic sinusoids were dilated and apparently contained more Kupffer cells. From the previous studies; parasite induced a marked hepatic oxidative stress in schistoseme-infected mice. (Amer, 2013; Dkhil, 2014) deduced that *S. mansoni* altered the levels of free radicals and enzymatic/non-enzymatic antioxidants significantly. In the same manner, Fahmy (2014), reported that schistosome infected mice elevated the level of MDA, while decreased the GSH level and catalase activity significantly in hepatic tissue. A significant elevation was noticed in MDA and nitrite/nitrate levels, meanwhile; a significant reduction was tabulated in an antioxidant markers (GSH, glutathione reductase, catalase, thioredoxine reductase) of infected liver. *S. mansoni* infection induced formation of periovular granulomas at the 8th week of infection which, at the cellular level, composed of eosinophils, macrophages, lympbocytes and fibyoblasts and the mean diameter of these granulomas was 397 ± 59.9 µm. These results were in agreement with those of (Bolch, 1972; Akl, 1992) who reported that *S.mansoni* infection induced formation of periovular hepatic granulomas which were composed of prominent eosinnophils, macrophages, lymphocytes, epitheloid cells, plasma cells, mast cells and fibroblasts at the 8th week of infection. Likewise, Knauft and Warren (1969), found that the maximum diameter of heptic granuloma was observed

at the 8th week of infection and decreased markedly at the 16th weeks of infection. Also, Bolch (1972), found that the hepatic tissue intimately adjacent to granulomas was abnormal. The abnormality was exhibited by distortion of liver cells and sinusoids. It is to be mentioned in this respect that Byram (1977), recoded that the schistosome eggs produced various materials including soluble lipids, enzymes and antigens, some of which diffuse into host tissues through minute pores in the egg shell. These substances in addition to spines of eggs were responsible for granuloma formation. The small sizes of granulomas were noticed in mice firstly treated with lead acetate and then infected with *S. mansoin*. Although granulomas had small size they showd the same cellular structure as those appeared after infection with *S. mansoni* only. The decrease in granuloma's diameter might be due to the toxicity of lead which increased the serum globlins (and hence immunoglobulins) and white blood cells which are considered as lines of defence in the body.

The study of El-Gohare (2003), has shown that pretreatment with lead acetate to *S. mansoni* infected hamsters resulted in significant reduction in the number of adult worms as well as in the number of ova per gram stool, liver and intestine as compared with *Schistosoma* infected groups. These findings might be attributed to the toxic effects of lead on *Schistosoma* worms as evidenced by EL-Khafif (2001), who have shown that chronic lead exposure of *Schistosoma* infected albino mice has resulted in pathological degenerative changes in *S. mansoni* worms. Additionally, Wanas (1998), have shown that lead has a toxic effect on miracidia and cercaria; it decreases longevity of cercariae, thus reducing their ability to survive following penetration. The percentage reduction found in the study El-Gohary (2003), in the number of adult worms was 43.69% for *S. mansoni* and 50.58% for *S. haematobium.* Meanwhile, the percentage reductions in the number of ova per gram stool, liver and intestine were 47.86%, 43.22% and 35.23%, respectively, for *S. mansoni*. Further reduction was recorded, 54.54%, 46.37% and 48.21%, respectively, for *S. haematobium.* This means that lead has exhibited more toxic effects on *S. haematobium* worms. *S. mansoni* infection induced neutropenia, eosinophilia and decrease in monocyte percentage. These results are in agreement with those of El-Rafie (1988) who found that eosinphilia was characteristic of *S.mansoni* infection in early and late stages of infection. Likewise, El-Rafie (1988) and Omran (1992) found that neutropenia, lymphopenia and reduction in concentration of peripheral blood monocytes were detected in late stages of hepatosplenic schistosomiasis. Excessive recuitment of monocytes due to bilharzial granulomata around eggs might led to a depletion of circulating monocytes. Exposure of mice infected with *S.mansoni* to lead acetate and infection of mice pre-treated with lead acetate induced also, lymphopenia, neutrophilia, monocytosis and eosinophilia which might be due to removal of cell damage by break down of *S. mansoni* eggs and phagocytosis.

The present work showed that *S. mansoni* infection induced highly significant reductions in body weight of infected animals. These results run in agreement with those of Warren, 1966 and Knauft and Warren (1969), who recorded moderate decreases of body weight (9-11%) at the 8th week post-infection in mice infected with 35 and 40 cercariae of *S. mansoni*. Also, these results run parallel to those of (De Witt and Warren, 1959; Cheever, 1965) who recorded decreases of body weight (9-15%) at the 8th week post-infection of mice infected with 125-140 cercariae of *S .mansoni*. These reduction of body weight might be due mainly, to anaemia. Similarly, Salah and Hamza (1984), found increase of the size of the liver of *Tilapia zillii* inhabiting the polluted water which might be due to the high accumulation of lead and cadmium in the liver. Similar increases in relative liver weights were also recorded as a result of *S. mansoni* infection. These changes were correlated with the advancement of the disease. These results run in agreement with the results recorded by (Warren, 1966; Knauft & Warren, 1969) in female Swiss albino mice infected with 34-35 cercariae of *S. mansoni* and also, run in parallel with those of De Witt and Warren (1959), obtained by using mice infected with 125 cercariae. Hepatomegaly in mice infected with *S. mansoni* might cause by host's granulomatous and fibrotic reaction to the eggs (De Witt and Warren, 1959; Bloch, 1972). Hypersplenism is associated with increased destructive changes in the peripheral blood. The enlarged spleen probably acts by sequestering large numbers of red cells, granulocytes, and platelets, which may then be damaged or destroyed there (Walter, 1987; Terayama, 1993) recorded a shortening of erythrocyte survival time in anemia caused by lead (Pb) in rats. It is speculated that decreases in membrane sialic acid content and deformability of RBCs induce shortening of erythrocyte survival time. Splenomegaly in chronic lead poisoning might be due to over activity of spleen mononuclear phagocytic cell system for removing damaged red cells.

S. mansoni infection also induced a marked and gradual enlargement of spleen (i.e depended on the stage of infection) which runs in agreement with Knauft and Warren (1969*)* who found an increase in spleen weight as percent of body weight reached 117% in mice infected with 34 cercariae at the 8th week of infection. Similar increases in spleen weight as percent of body weight were recorded by Warren (1966). Also, in heavier infections, the spleen weight as percent of body weight increased to 156% in mice infected with 135 cercariae at the 8th week of infection (Cheever, 1965; Woodruff, 1966) mentioned that pathological processes accompanied with anaemia in schistosomiasis were associated with gross splenomegaly. Also, splenomegaly might be caused by over activity of spleen for sequestering large numbers of red cells, granulocytes, and platelets, which damaged or destroyed there.

The present study showed that S.*mansoni* infection induced elevations in serum enzyme activities, however, sALT activity was highly affected in response to infection than sAST, which also reflects the effect of *S. mansoni* on the liver. Here again, it is relevant to emphasize that the elevations were correlated with the progress of the disease (i.e. depended on the stage of infection). These results run in agreement with findings of Saif, (1964) who recorded elevations in both enzymes activities in hepatic bilharziasis. Similar elevated values in aminotransferase activities both in early as well as in late stages were also recorded by other investigators (Sadun and Williams, 1966 and Abdel Ghaffar, 1987) in albino mice infected with *S. mansoni*. They also attributed this change to persistent active hepatic cell damage and/or increased permeability of the cells due to toxic or anoxic effects. Infection of mice pretreated with lead acetat induced also highly significant influence but, less than the former cases. This may refer to the death of some cercariae of *S. mansoni* due to lead toxic effects or may be due to decrease of ovulation of *S. mansoni* worms under these conditions.

S. mansoni infection did markedly elevate serum total proteins; such manifestations were correlated with the progress of the disease. Additive elevation in serum total proteins were produced when the bilharzial animals were exposed to lead when animals were pretreated with Pb before infection with *S. mansoni*, compared to infected and control groups. These results are in agreement with those of El-Husseini, (1986) who reported that *S. mansoni* infection induced a gradual increase in serum total proteins with increasing the infection period in mice exposed to 100 cercariae. Also, (Metwally, 1990; El-Fandy, 1992) were recorded an elevation in serum total proteins. Serum globulins showed increase in all experimental animal groups. These results are in agreement with those of Eissa, (1993) who recorded elevation of serum globulins in workers exposed to lead in battery industry. Similarly, serum globulins were found to be gradually elevated in mice infected with *S. mansoni* (Bloch, 1972 and El- Husseini, 1986).

4. CONCLUSION

This study concluded that pretreatment with lead acetate to *S. mansoni* infected mice resulted in significant reduction in the harmful effects on liver, hematological data, and body and organ weight, as compared with *Schistosoma* infected groups.

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