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Study of Physiological and Histological Changes in Rabbits induced with Hepatic Coccidiosis

دراسة التغيرات الفسلجية والنسجية في الأرانب المصابة تجريبيا بالكوكسيديا ألكبدية

Muna H. AL-Saeed* Arwa H. AL-Saeed** Muna M. Jori***

*Department of Physiology, Pharmacology and Chemistry, College of Veterinary Medicine, University of Basrah.
**Department of Chemistry, College of Science, University of Basrah. Basrah, Iraq.
***Department of Veterinary Public health, College of Vet. Med., University of Basrah. Basrah, Iraq.

Abstract

In this study, 20 rabbits belonging to different ages, sexes but all these rabbit in same breed (local breed) during 1/6/2012- 31/12/2012. The rabbits were divided into two groups (10 rabbits each group). The first group was designated as healthy control group. Second group rabbits were infected Hepatic coccidiosis induction in 10 rabbits with 8.000 sporulated oocysts of E. stiedae. Clinically, the severely affected rabbits showed decreased growth rate, anorexia, debilitation, listlessness, diarrhea, and rough hair coat.

Haematological analysis showed RBC, Hb, PCV, MCV value as well as percentage of lymphocyte decreased in infected group compared with control whereas WBC and percentage of neutrophiles, eosinophiles and basophiles increased.

Serum bilirubin, creatinin, uric acid, ALT and AST activities increased but albumin value decreased. Plasma MDA concentrations increased. Mean oocyst numbers in per gram faeces increased in infected group during the study. Postmortem examinations revealed hepatomegly, with presence of discrete yellowish-white nodules 1mm to 1cm size on the surface and throughout the parenchyma, was seen. Bile ducts were dilated. The livers of these animals were enlarged and typical macroscopic and microscopic findings of coccidiosis were present. Necropsy of these animals showed no visible lesions related to hepatic coccidiosis although a few oocysts were detected in the bile duct epithelial cells.

المستخلص

للفترة من 2012/6/1 إلى 2012/12/31 ، تم فحص20 من الأرنب يتراوح أعمارهم مابين (7-9 شهور) من النسل المحلي ولكلا الجنسين. قسمت الأرانب إلى مجموعتين (10 لكل مجموعة). وعينت المجموعة الأولى كمجموعة مراقبة في حين استحدثت الإصابة بالكوكسيديا الكبدية بالمجموعة الثانية وبواقع 8.000 بيضة من الايمرية الستيداوية *Eimeria stiedae*عن طريق العلف الملوث.

سريريا، أظهرت الأرانب المصابة انخفاض في معدل النمو، وفقدان الشهية، الوهن والخمول، والإسهال وخشونة الشعر. كما شمل فحص الدم اذ تم سحب الدم عن طريق القلب وتم تقسيم عينات الدم إلى جزئين احدهما يضع في أنبوب اختبار حاوي على مانع تخثر لدراسة التغيرات الفسلجية التي تحدث خلال الإصابة إذ تم حساب المعايير الدمية مثل عد كريات الدم الحمراء(RBC)، الهيموكلوبين (خضاب الدم Hb)،مكداس الدم (PCV)،حجم الكرية الحمراء(MCV)، وكمية الهيموكلوبين (MCH)، وتركيز الهيموكلوبين(MCHC) في الكريه الحمراء، وعد خلايا الدم البيضاء(WBC) ، والعد التفريقي لخلايا لدم البيضاء(DWBC).

واظهرت التحاليل الدمية انخفاض معنوي في كل من MCHC,,PCV,Hb,RBC,وكذلك النسبة المئوية للخلايا اللمفاوية في المجموعة المصابة مقارنة بمجموعة السيطرة في حين لوحظ زيادة معنوية للعد الكلي لكريات الدم البيضاء وارتفاع النسبة المئوية للخلايا المتعادلة والقاعدية والحامضية .

والجزء الأخر من الدم تم وضعه في أنبوب اختبار غير حاوية على مانع للتخثر لغرض فصل المصل وقياس بعض المعايير الكيموحيوية مصل الدم خلال الإصابة مثل (البروتين الكلي، الالبومين، الكلوبيلين ، السكر، البليروبين الكلي، الكرياتنين ، حامض اليوريك) و AST وALTوMDA.

أظهرت النتائج زيادة في السكر ،البيليروبين المصلي والكيراتينين ، وحمض اليوريك وAST وALT وتركيز MDA بينما انخفضت قيمة الزلال. كما ارتفع المعدل الإجمالي لعدد البيوض في كل غرام من البراز في المجموعة المصابة خلال فترة الدراسة.

كشفت الفحوص بعد الترشيح وجود الكبد، مع وجود عقيدات وندب بيضاء مصفرة منتشرة بحجم 1mm إلى 1cm على سطح وضمن النسيج الحشوي، كما لوحظ توسع القنوات الصفراوية مع توسع اكباد الحيوانات المصابة وتواجد الكوكسيديا عيانيا ومجهريا. كما اضهر تشريح هذه الحيوانات عدم وجود أفات مرئية للكوكسيديا الكبدية على الرغم من ان تم الكشف عن عدد قليل من المكيسات في الخلايا الظهارية من القناة الصفراوي

Introduction

Coccidiosis, caused by species of intracellular protozoan parasites belonging to the genus *Eimeria* (Phylum: Apicomplexa), remains one of the economically most important diseases in modern poultry production [1]. Rabbit coccidiosis is considered to be the most threatening factor affecting rabbit production [2,3] as it causes severe pathological changes to infected animals leading finally to huge economic losses in industrial rabbit farms [4,5]

Coccidiosis is a highly contagious sporozoal infection in rabbits, with low prognosis of healing Healthy rabbits can be asymptomatic "carriers" of the protozoa, and the oocysts (eggs), shed with the feces, will contaminate the environment, food and water [1]. While the rabbits that recover frequently become carriers Transmission of both the hepatic and intestinal forms is by ingestion of the sporulated oocysts, usually in contaminated feed or water [6].Therefore, clinical coccidiosis is most prevalent under conditions of poor nutrition, poor sanitation, or overcrowding, or after the stresses of weaning, shipping, sudden changes of feed, or severe weather[7].

The rabbits ingest sporulated oocysts. Sporulated oocysts contain four sporozoites that hatch and travel via the hepatic portal vein to the liver, and eventually penetrate the bile duct epithelium, where they undergo asexual reproduction known schizogony. Rupture of the schizont consequently causes epithelial cell rupture and death. Merozoites will penetrate other cells and create more merozoites for one to several rounds. Eventually, a merozoite becomes a male microgamecyte and asexually reproduces in epithelial cells. A ruptured microgamecyte infects a cell with the female macrogamecyte and through sexual reproduction create a zygote. The zygote develops a protective shell before expulsion in the bile excreation and then the feces as an oocyst.

Haematological changes recorded with coccidiosis included a decrease in erythrocytic count (RBCs) and hemoglobin concentration (Hb). In addition, the disease is associated with leucocytosis, eosinophilia and neutrophilia.

The serum biochemical changes associated with rabbits coccidiosis included an increase in glucose. In addition, analysis of liver function in rabbit coccidiosis produced an increase in the levels of serum alanine aminotransferase (ALT), aspartate aminotransferase (AST) and bilirubin.

Therefore, the aim of the study is to accomplish this task and study the physiological and histological changes in affected livers with coccidosis in rabbits.

Materials and Methods

In our study we used (20) rabbits were divided into two groups, every group included(10) belonging to different ages, sexes but all these rabbit in same breed (local breed. First group acted as control non-infected group while the second group was inducted with *E.stiedae* sporulated oocysts. *E. stiedae* used in this study is a pathogenic species of the liver (hepatic coccidiosis).

The parasite has a life-cycle, which lasts 4 to 14 days. It starts after oral ingestion of food and water contaminated by oocysts. The oocyst wall will be broken down in the stomach and spores will be released[1].

Oocysts were collected from faeces of rabbits naturally infected with *E. stiedae* and then surface sterilized with sodium hypochlorite and washed at least four times in a sterile saline solution prior to oral inoculation as described by[8]. These oocysts were used to inoculate rabbits by oral gavaging each rabbit with 50,000 sporulated oocysts of *E. stiedae* suspended in 1 ml sterile saline. Once every 24 h, fresh faecal pellets were collected and weighed for each rabbit and the bedding was changed to eliminate reinfection. Oocyst output was measured as previously described [8].

Faecal pellets were suspended in 2.5% (wt/vol) potassium dichromate and diluted in saturated sodium chloride for oocyst flotation. Oocysts were counted in a McMaster chamber and expressed as number of oocysts per gram of wet faeces

Blood was collected through the heart from each rabbits; 5ml divided into parts. First part was dispensed into clean container containing anticoagulant EDTA. The anticoagulant blood was used to determine haematological examination. Second part was dispensed into clean container without anticoagulant. The rest was allowed to clot for the obtained serum. Haematological examination was done according to [9] including red blood cells count (RBC) and white blood cells count (WBC) with haemocytometer, hemoglobin concentration (Hb) was determined by Sahel method, packed cell volume (PCV) was determined using microhaematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC). Blood smears were stained with Giemsa stain for differential white blood cells count (DWBC) [10].

Biochemical serum analysis include Serum total protein, Albumin,Globulin, Bilirubin, Aspartate aminotransferase (AST), Alanine aminotransferase(ALT) and plasma Malondialdehyde (MDA)were estimated spectrophotometry by using commercial chemical kits supplied by (SPECTRUM).

The sample obtained from the (liver). This tissue fixed with formalin then dehydrated by graded alcohol, this is followed by dealcoholization with xylol and embedding with paraffin wax and blocking. Histological sections of 5-6 µ thickness were obtained by a microtom. Dewaxed , dehydrated, and staining by hematoxlin and eosin stain, from all rabbits [11].

In order to determine the statistical significances among different variables SPSS program (Statistical program for social sciences) version 16.Students *t-test* was used for comparison between two groupes (control and diseased rabbits). All hematological and biochemical test values were expressed as mean and stander error of mean and $P<0.05$ was considered as statistically significant[12].

Results

The results of some hematological parameters have been presented in the Table (1). The results indicated that the RBC, Hb, PCV, MCHC, WBC, Lmphocyte, Monnocyte values were highly significant ($P\leq0.05$) decreased in infected rabbits with hepatic coccidosis compared with control group while MCV, Neutrophils, Eosinophils and Basophils values were highly significant ($P\leq0.05$) increased in infected rabbits with hepatic coccidosis compared with control group but MCH value was non significant changes in infected rabbits with hepatic coccidosis.

Table (1): Effect of Hepatic Coccidosis on Some Hematological Parameters in Rabbits.

(Mean±SD) N=10

Hematological parameters	Control animals	Infected animals
RBC $\times10^6$ /µl	6.13 $\times10^6\pm$ 1.2	3.1$\times10^6\pm$0.9**
Hb (g/dl)	12.00±1.03	8.4±0.59**
PCV (%)	37.81±1.40	26.55±4.56**
MCV (fl)	50.09±4.08	61.09±7.55**
MCH (pg)	15.85±0.26	15.27±0.255NS
MCHC (%)	32.32±2.67	24.71±4.55**
WBC $\times10^3$/µl	7.53$\times10^3\pm$ 1.91	5.013$\times10^3$ ± 1.11**
Lymphocytes(%)	48.5±4.58	21.74±2.9**
Neutrophils (%)	44.2±3.76	71.89±3.7**
Monocytes (%)	4.5±0.11	2.76±2.65**
Eosinophils (%)	0000	4.0±0.13**
Basophils (%)	0000	0.22± 0.01**

N= Number of animals, NS=non significant,**=$P\leq0.01$

The results of some biochemical parameters have been presented in the Table (2). The results indicated that the total protein, albumin, globulin values were significant (P≤0.05) decreased in infected rabbits with hepatic coccidosis compared with control group while glucose, bilirubin, creatinin, uric acid, urea, ALT,AST and MDA values were highly significant (P≤0.05) increased in infected rabbits with hepatic coccidosis compared with control group.

Table (2): Effect of Hepatic Coccidosis on Some Biochemical Parameters in Rabbits.
(Mean±SD) N=10

Biochemical Parameters	Control Animals	Infected Animals
Total protein(g/dl)	7.5±1.49	4.78±1.96*
Albumin (g/dl)	4.6±1.35	2.99±1.70*
Globulin(g/dl)	2.9±0.15	1.59±0.26*
Glucose(mg/dl)	95.62±3.74	158.91±20.36**
Bilirubin (mg/dl)	0.27±0.011	5.78±1.79**
Creatinin (mg/dl)	1.77±0.021	7.64±1.53**
Uric acid(mg/dl)	2.45±0.14	15.89±6.51**
Urea(mg/dl)	39.66±9.58	75.46±18.69**
ALT (U/L)	12.46±3.83	78.41±8.67**
AST(U/L)	10.48±2.45	80.58±11.86**
MDA	0.25± 0.03	0.49 ± 0.07**

N= Number of animals, NS=non significant, *=P≤0.05,**=P≤0.01

The main clinical signs showed by the infected rabbits were depression, anorexia, brown watery diarrhea, emaciation, rough hair coat, pendulous and distended abdomen and hepatomegaly noted on abdominal palpation, progression weakness. Ictrus was also reported in all infected rabbits.

Fig.(1): Rabbits normal (control group).

Fig.(2): Rabbit infected with *Emeria stiedae.*

After sacrificed infected rabbits were showed that the size and weight of livers of infected rabbits significant (P≤0.05) increased. The liver was pale. The nodular exudes expressed on pressing were either milky or thick cheesy. The gall bladders were distended with thick green bile. Postmortem examination of ascites cases revealed dirty straw colored peritoneal fluid.

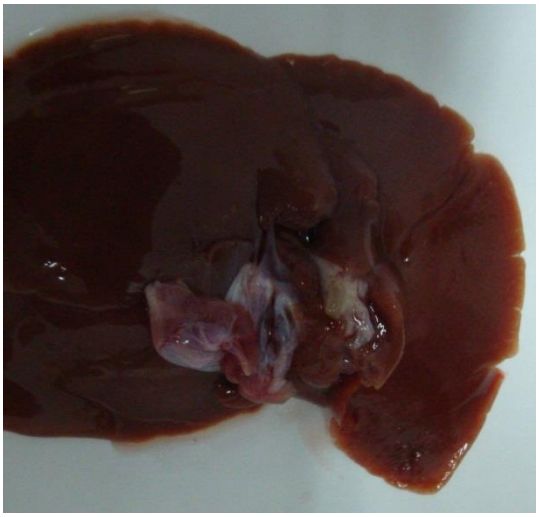

Fig.(3): The liver of rabbit normal (control group).

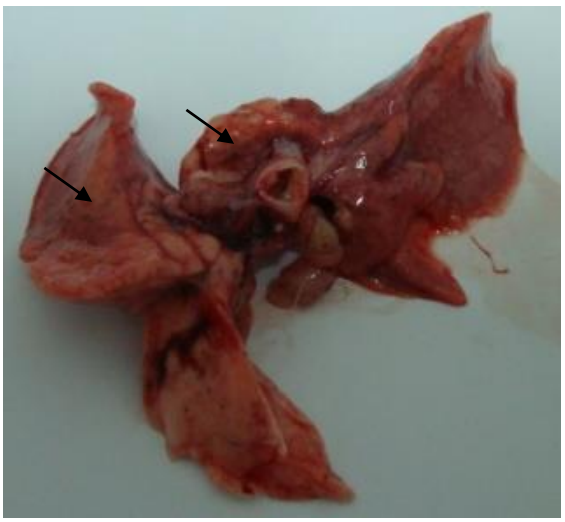

Fig.(4): Gross lesion in the liver of rabbit infected with *E. stiedae* showing.

The lesions of the liver tissue sections of infected rabbits mainly confined to the liver and bile ducts consisted primarily of extensive hyperplasia of bile ducts. The bile ducts were markedly enlarged and lined by hyperplastic columnar epithelial cells.

In one animal, the epithelium of a dilated bile duct appeared focally hyperplastic with a few mitoses, and contained spherical structures identifiable as the oocysts of the coccidian parasite *Eimeria stiedae* measuring approximately 36 µm in length (Fig.5). Oocysts of *E. stiedae* were also evident within the lumen of the bile ducts, admixed with eggs and inflammatory cell debris.

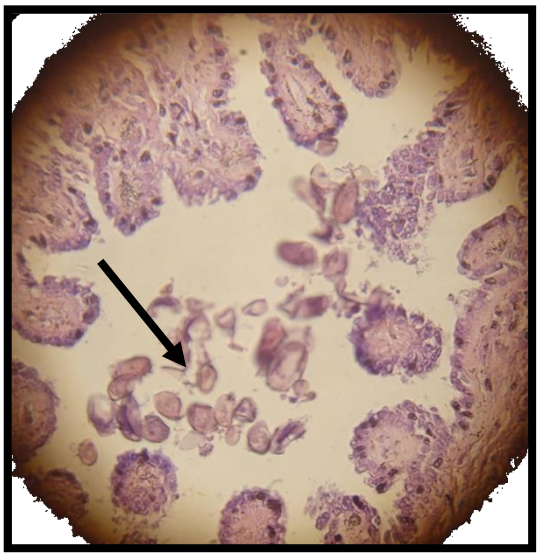

Fig.(5):section of liver in rabbit infected with E. stiedea showing multiple papillary fronds in the bile ducts due to extensive hyperplasia of biliary columnar epithelial cells (➡) (H&Ex100).

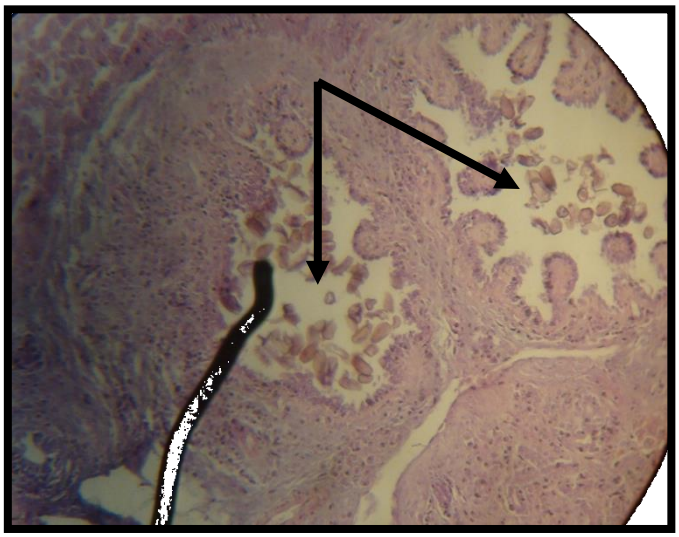

Fig.(6): section of liver in rabbit infected with E. stiedea showing multiple papillary fronds in the bile ducts due to extensive hyperplasia of biliary columnar epithelial cells (➡) (H&Ex100).

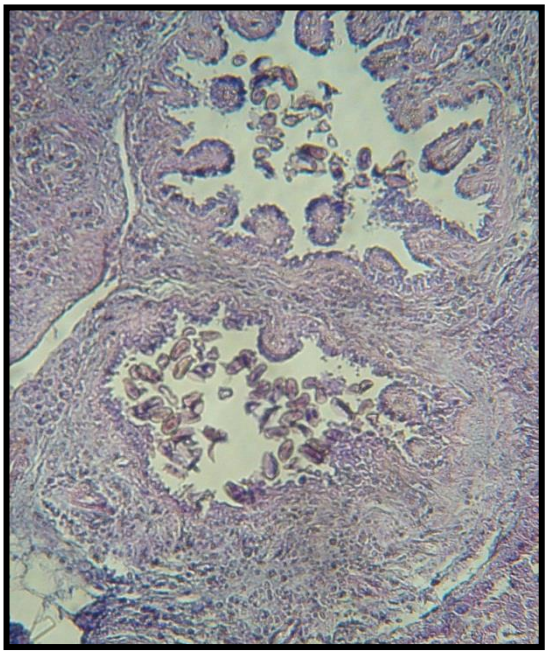

Fig.(7): section of liver in rabbit infected with coccidiosis showing the replacement of parenchyma with fibrous connective tissue infiltrated with mononuclear cells with atendency to formation of newly formed bile ductules. Oocyst granuloma in which coccidial oocyst were observed in the central region.(H&Ex400).

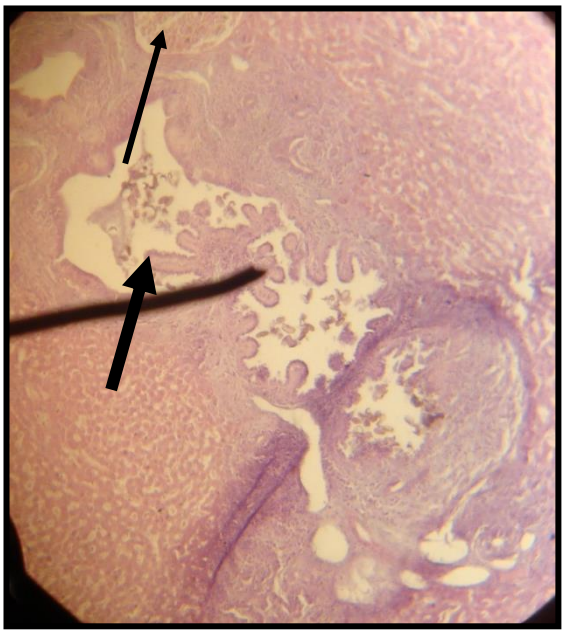

Fig.(8 section of liver in rabbit infected with coccidiosis showing peribiliary fibrosis with infiltration of mononuclear cells (→) and papillary projections of epithelium (➡) with precence *E.stiedae* oocytes in the lumen of these bile ducts.(H&Ex100).

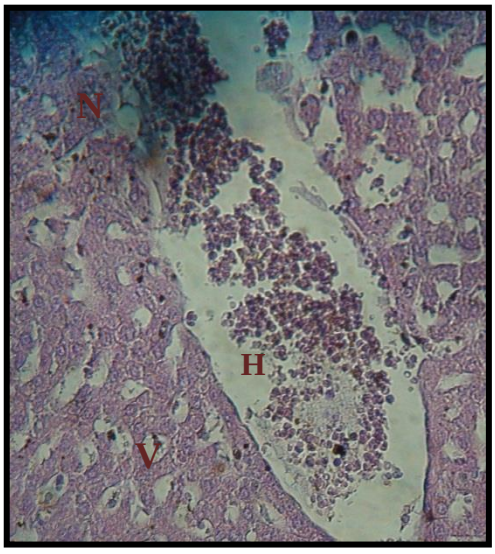

Fig.(9): Section of liver of infected rabbits showing the hepatic parenchyma showed dilation and congestion of portal veins and sinusoids with rupture of lining endothelial layer; in addition to vacuolar(V) degeneration and necrosis(N) of hepatocytes. The portal areas and liver parenchyma were infiltrated with mononuclear cells, severe hemorrhage (H) in the necrotic area.
(H&Ex400).

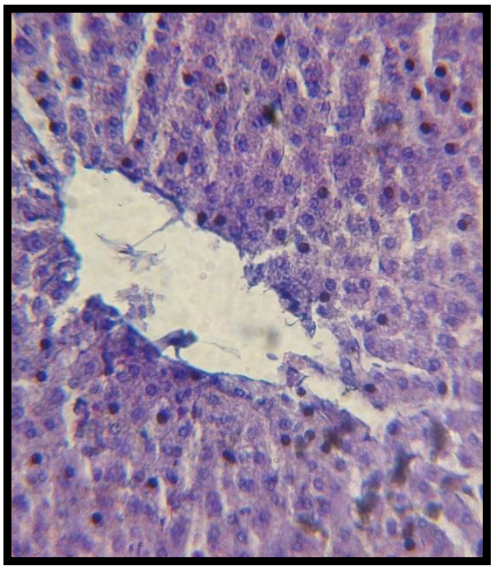

Fig.(10): section of liver of rabbit in control group showing normal hepatocytes and portal vein. (H&Ex400).

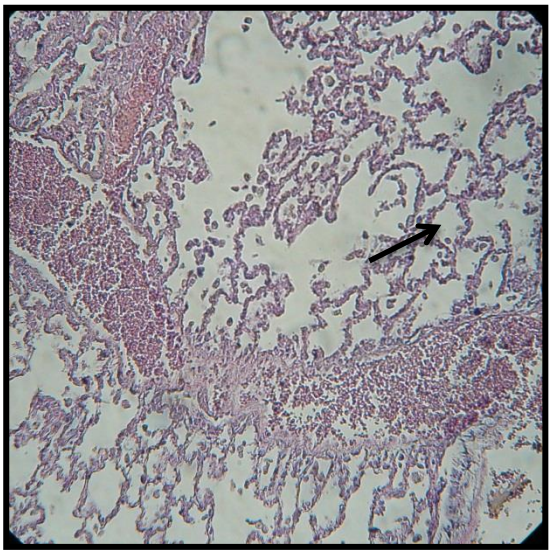

Fig.(11): Section of Lungs of infected rabbits with coccidosis appearing congested and oedematous. Alveoli (arrow)with inflammatory cells. (H&Ex400).

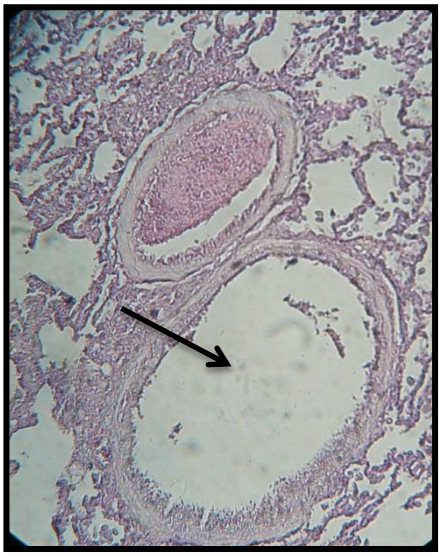

Fig.(12):Section of Lungs of infected rabbits with coccidosis appearing dilated bronchi(arrow), with foreign particles, it could be during dosing inflammatory cells. (H&Ex400).

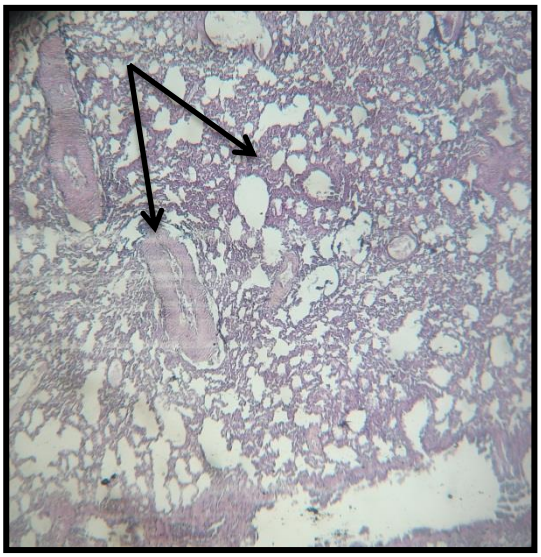

Fig.(13): Section of Lungs of infected rabbits with coccidosis appearing bronchioles & alveoli with inflammatory cells, also area of emphysema (H&Ex400).

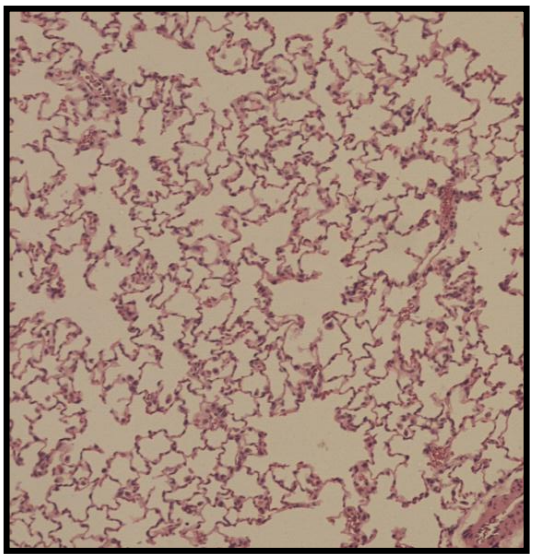

Fig.(14): Section of Lung of rabbits control. Showing normal appearing bronchioles & alveoli, stain (H&E) 100X .

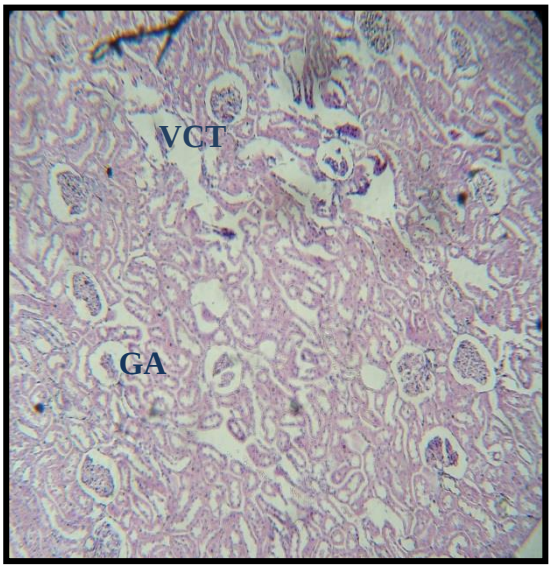

Fig.(15): Section of kidney of rabbits infected with coccidosis appearing vacuolation of cortical tubules(VCT), atrophy glomeruli (GA), stain (H&Ex100).

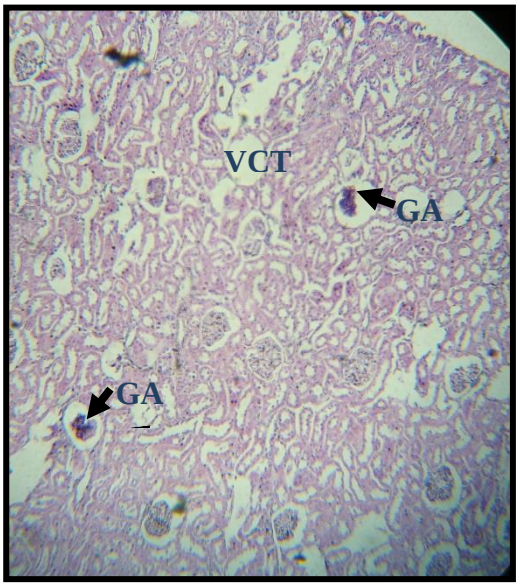

Fig.(16): Section of kidney of rabbits infected with coccidosis. Showing minimal vacuolation & dilated of renal cortical tubules(VCT), atrophy glomeruli(GA), Inflammatory cellular infiltrations appeared in some areas, stain (H&E) 100X.

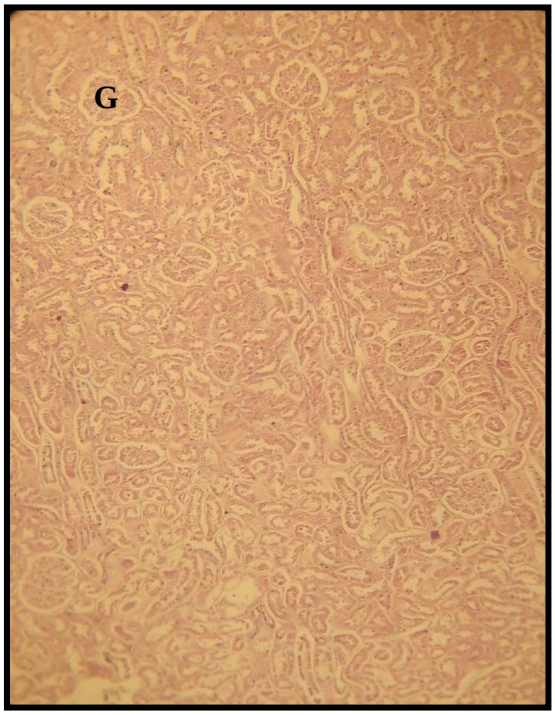

Fig.(16): Section of kidney of rabbits control. Showing normal glomeruli (G) and normal renal cortical tubules stain (H&E) 100X .

Discussion

Hepatic coccidiosis in rabbits caused by *Eimeria stiedae* [13]. Hepatic coccidiosis in rabbits occurs due to ingestion of sporulated oocysts having four ovoid sporocysts containing 2 sporozoites each. The sporozoites penetrate the mucosa of small intestine and pass via the mesenteric lymph nodes and hepatic portal system to the liver where they enter the epithelial cells of the bile duct becoming trophozoites and then schizonts. These results were agreed with [14,15]stated that diarrhea, emaciation, and rough hair was due to infection of the intestine before the penetration of the sporozoites to the mucosa of small intestine and passing via the hepatic portal system to the liver to start the hepatic form. The increased size and weight of livers of infected rabbits due to excessive proliferation of bile duct epithelium resulting in hepatomegaly which is characteristic of this disease leading to pendulous and distended abdomen. Oocysts pass out in the bile and appear in the faeces 18 days after infection, sporulation occurs in three days [16,17,18,19].

The present result showed that all animals were affected with the *E. stiedae* and that may be due to their younger age since it is almost known that hepatic coccidiosis which caused by *E. stiedae* is a primary disease of young rabbits [20]. Coccidial infection is affected by the host age; The highest incidence was in 2-months rabbits and then the infection rate decreased as the age increased. The high level of susceptibility of infection in young rabbits may be due to their immune, feeding and reproductive status. This observation is consistent with the results previously reported [21,22].

Haematological changes of infected rabbits (Table, 1) included a significant decrease of total erythrocytic count and hemoglobin concentration. This result was in accordance with those recorded previously by several investigations. The significant reduction of RBCs, Hb content and PCV% might be attributed to the haemorrhagic hepatitis associated with coccidiosis. In this study, infected rabbits had leucocytosis with significant eosinophilia. This result was in agreement with a previous study that referred these changes to inflammation of liver. The lymphocytopenia appeared in this study might be attributed to lymphocyte depletion and atrophy of the

Biochemical serum analysis for lambs with coccidiosis (Table2) demonstrated a significant reduction in the level of sodium (hyponatremia) and slight increase of the level of potassium. Changes of these electrolytes are usually related to diarrhea with loss of sodium ions.

These results were comparable to those previously recorded. Serum calcium, copper and glucose levels were slightly (non-significantly) decreased with coccidiosis, a result that was observed in other studies. The decrease in these parameters might be attributed to suppression of appetite associated with coccidiosis. On the other hand, serum iron level was significantly decreased, which could be attributed to the bloody diarrhea and the inappetance occurring concurrently with eimeriosis. Moreover, there was a significant decrease in serum zinc level that could be attributed to the secondary bacterial infection following coccidian infestation and the malabsorption syndrome occurring subsequently to damage of intestinal mucosa and loss of surface epithelial cells and villous atrophy associated with first-generation meronts, crypt destruction and crypt hyperplasia. The significant decrease of serum total protein might

be attributable to decreased absorption of nutrients from infection sites at intestinal mucosa due to damage and cell sloughing caused by coccidia.

The decrease in lymphocyte could be attributed to its supply of globins,which is under the control of adrenocortical hormones upon lymphoid tissues and lymphocytes, resulting in increase rate of cytoplasmic budding and dissolution of cells during the infection.

Regarding liver function parameters, there was a significant increase in serum ALT, AST, ALP, GGT and total bilirubin in lamb with coccidiosis compared to control (Table 2). This result was nearly similar to those previously observed1**.** Comparable results were demonstrated in calves during experimental and natural infections with *Eimeria.* The alterations of liver enzymes, total protein and bilirubin levels suggested that the liver adversely affected by coccidiosis.

The elevated serum glucose level observed may have resulted from increased mobilization of glucose for metabolism or may be due to reduced glucose uptake into cells [23] caused by infection. Infection caused a marked liver injury as indicated by histopathological alterations as well as the significant increase in liver aspartate aminotransferase (AST), alanine aminotransferase, alkaline phosphatase (ALP) and bilurubin. Also, infection induced a significant increase in malondialdehyde (MAD**)**. This is also suggestive of a possible modulation of the capacity of the renal tubule by the infection to reabsorb glucose actively from the blood [23]. *E. stiedae* infection induced higher serum urea concentration may impair the secretory function of the kidney [24]. Malfunction in the glomerular filtration results in the retention of substances including urea, and this may be responsible for their high serum levels in the infected group.

The recorded renal tissue damage due to infection with *E. stiedae* in the present investigation. The kidney is the main excretory organ of the body, so the elevation of the parasite residues concentration in the blood must be faced by capillary constriction to decrease the glomerular filtrate containing the parasite to minimize its effect and protect the tubular cells. At the same time, the mesangial cell processes may be retracted due to the contraction of their filaments (myosin-like filaments) which may be stimulated by angiotensin II present in these cells[25]. The altered mesangial cellularity may increase its phagocytic function to clear some of the parasite residues from the circulating blood, and also secrete more angiotensin II to constrict the glomerular capillaries, slowing the blood flow to decrease the glomerular filtrate, so a minimum amount of parasites residues reaches the tubular lumen with the glomerular filtrate and in the blood capillaries surrounding these tubules[26]. The tubular lesions observed in the present study were accompanied by invasion of inflammatory cells to the intertubular tissues in a trial to minimize the injury. Some of these external stressors apparently caused the tubular lesions. Renal tubules appeared with cytoplasmic vacuolation which is mainly a consequence of considerable distur-bances in lipid inclusions and fat metabolism occurring under pathological cases[27,28].

Hepatomegaly with irregular yellowish white nodules on the surface. (Fig.4). Thick creamy white exudates from their cut surface, hepatic parenchyma was firm and gall bladder was distended. The peritoneal cavity showed increased dirty dull straw colored peritoneal fluid. The hepatomegaly was due to marked proliferation and distention of bile ducts forming nodules raised above the surface causing increase in secretion of mucous appeared as a creamy, white fluid on cut surface. The proliferated bile ducts cause damage to the liver parenchyma leading to post-necrotic scarring this explain, the firm consistency of hepatic parenchyma. These results agreed with [14, 15] that these lesions lead to disturbance of liver functions leading to decrease in α- lipoprotein, glucose and proteins; in addition to increase in bilirubin in blood serum [29].

The lesions of the liver tissue sections of infected rabbits mainly confined to the liver and bile ducts consisted primarily of extensive hyperplasia of bile ducts. The bile ducts were markedly enlarged and lined by hyperplastic columnar epithelial cells thrown into multiple arborizing papillary fronds extending into the ductal lumina, resembling adenomatous hyperplasia with presence of developmental stages of the parasite (Fig.5). Numerous protozoal stages including microgametocytes, macrogameteocytes and oocysts were also seen (Fig.6) Other sections showed that the bile ducts were highly dilated with flattened epithelium having no or minimum projection to the lumen which are filled with numerous thin walled, ovoid oocysts (Fig.7) The hyperplastic bile ducts were surrounded by large amount of fibrous connective tissue infiltrated with mononuclear cells(Fig.8) Furthermore, the ducts were filled with sloughed biliary epithelial cells. In animals with jaundice their liver sections showed deposition of bile pigment in hepatic parenchyma (fig.9). This hepatic coccidiosis caused severe damage to the liver and it is more pathogenic in young rabbits among these animals [10]. The proliferation of the bile duct epithelium might be due to the predilection and proliferation of the *E. stiedae* within the epithelium, whereas extensive dilation with little or no proliferation of bile duct epithelium might indicate the cell turn over which was also proved by the fact that these ducts contained more numbers of oocysts as compared to ones that had conspicuous proliferation. The wide spread sinus dilation, associated with fibrosis in and

around the cords might be attributed to the obstructed hepatic blood flow especially in the portal veins by immensely proliferating and dilating bile ducts. The stagnation of the blood flow would also result in hepatocyte cellular degeneration and atrophy of the cords. These histopathological observations are in agreement with those described by others [21, 14, and 22]. If the hepatic continuity of epithelium of bile ductules is broken the coccidian organism or oocyst would act as foreign bodies it might involve typical foreign body granuloma. [29] reported granulomatous hepatitis in coccidial infection in which coccidial oocysts were observed in central region of granuloma which later results in destruction and fibrosis of large area of hepatic lobules. The hepatic parenchyma showed areas of fibrosis with obstructive jaundice and that occurred due to massive necrosis of parenchyma leading to post-necrotic scarring. The bile pigment deposition was due to obstruction of the main ductal system from local swelling and jaundice is almost always present and that in agreed with previous studies [30, 14].

As the coccidial oocysts are shed with the faeces contaminating the environment, food and water the rabbit's cages, food dishes and water containers need to be routinely disinfected. Avoidance of stress and strict sanitary measures are thought to reduce or prevent clinical disease[31]

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