Toxic Effect of Babesiosis in Cattle and Chemotherapiotic Treatment in Egypt

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Abstract Babesia bigemina plays an important role in causing liver and kidney dysfunction in affected animals. The aim of this study evaluating the toxic effect of babesiosis on liver and kidney by measuring biochemical parameters and pathological tissue changes in infected animals with B. Bigemina and chose the best method of treatment. A total of 40 cattle age 1-3 years 30 were suffered from increase in temperatures, off food, Hemoglobin urea, red water from endemic area with babesia. Take sample from infected animals & examine it with microscopic examination found babesia bigemina and confirm by inoculation of heparinized blood from this animals in rats and found rats death at fifth day from infection and histopathological exam found babesia in piroplasma form in pathological tissue of rat’s liver & kidney. The infected animals were divided into three groups each group 10 animals untreated group use as control positive and treated groups divided into two groups first group treated with imidocarb only and the second group use imidocarb and lincomcyn as antibiotic drug and compare between two groups by measuring liver& kidney function improvement and compare two groups with negative and positive group which method of treatment more effective in treatment of babesia & decrease toxic effect of babesia.

Keywords: cattle, babeseosis, histopathological changes in experimintal infected rat

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1. Introduction

This review deals primarily with the treatment of babesiosis in cattle. It is thought that these animals are the most severely affected by Babesia infection from an economy point of view, [1]. Present anemia may attributed to, Immunomediated phenomena by which autoantibodies directed against component of membrane of infected and uninfected erythrocytes, production of toxic hemolytic factors of the parasite, mechanical damage by trophozoite intra erythrocytes binary fission. erythrophagocytosis and through of release vasoactive molecules such as kallikrein [2,3,4], and [5]. On the other hand, according to the role of liver in lipidbiosynthesis, it can be argued that liver may play an important compensatory role in balancing lipid components in blood flow to prevent anemia during bovine tropical theileriosis [6]. Babesiosis is disease world-wide distribution affecting many species of mammals principally cattle and man. major impact occurs in the cattle industry where bovine babesiosis has had huge economic effect due to loss of meat and beef production of infected animals and death [7] and [8]. Now days to those costs must be added the costs of tick control. There are limited chemotherapeutic choices reliable and fast detection methods. Detection and treatment are important tools to control babesiosis. Microscopic examination still cheapest and fastest methods used to identify babesia parasites [9] and [10].

2. Material and Methods

A total of 40 cattle age 1-3 years. 30 were suffered from increase in temperature, off food, hemoglobin urea, red water from endemic area with babesia. Take two samples from infected animals first with anticoagulant for blood smear and experimental infection by inoculation in rats and second sample to separate serum to determined biochemical changes associated with babesia Bigemina infection in cattle as (Fe, NO, SOD, Cholesterol, Triglyceride, BUN, Creatinine, GOT, GPT and TAC) according to [11]. By microscopic examination found positive to babesia Bigemina, babesia Bigemina is large in size and can extend in the full diameter of an erythrocytes, diagnosis of babesiosis are made by examination of three blood film with Giemsa for the best results. Blood films should be prepared from capillary blood collected for instance, after pricking the margin of an ear and confirm microscopic examination with inoculation of heparinized blood in experimental animals as rats transemation test
was performed in Rats groups by challenging them with 1 ml of infected haparenized blood (5x106 babesia Bigemina) infected parasitic erythrocytes were maximum at 5 days post experimental infection so all rats died, when compare with control group clinical signs appear at fourth day of infection, histopathological sections of inflammation of rats were done and indicated that the liver and kidney were severely affected, according to this test the infected cattle were divided into three groups each group consists of 10 animals, treated groups divided into two groups first group treated with imizol only at dose (Imizol 12 % - 1 ml /100 kg by s/c injection) and the second group use imizol and lincomycin as antibiotic at dose (1.2 g paranterally, twice daily for seven or ten days and third untreated group use as control positive.

3. Results

![Figure 1. Blood smear show different shapes of babesia bigemina shizonts, aclassic tetrad in anRBCs of expermintal infected rat arranged in the form of maltase cross and pyriform shapes (wright-Giemsa,x100)](image)

Liver of rats experimentally infected with babesia showing (A), severe congestion of hepatic blood vessels with the presence of eosinophils, lymphocytes and macrophages (arrow, x200), (B) hemorrhagic area scattered in the hepatic parenchyma accompanied by destruction of some hepatic cells (arrow, x200), (C) periportal leukocytic cellular infiltrations with mild hyperplasia of the bile duct (arrow, x200), (D) babesia parasitized RBCs inside the hepatic blood vessels (arrow, x1000). H&E stain

![Figure 2.](image)

Kidney of rats experimentally infected with babesia showing (A), severe congestion of inter-tubular blood capillaries in the renal medulla (arrow, x200), (B) perivascular mononuclear leukocytic cellular infiltrations (white arrow) with degenerative changes in the cytoplasm of the lining epithelium of the renal tubules (black arrow, x200), (C) hypersegmentation of the glomerular tuft (white arrow). Note also vacuolization of the lining epithelium of the renal tubules (black arrow, x200), (D) vesiculation of the endothelial lining of the capillary tuft of the glomeruli with periglomerular edema (black arrow) and leukocytic cellular infiltration (white arrow, x200), (E) shrinkage of the glomerular tuft (white arrow) or even complete destruction of the glomerular tuft (black arrow, x200), (F) babesia parasitized RBCs inside the glomerular capillaries (arrow, x1000). H&E stain.

| Groups | Parameter | Control Negative | Control Positive | Treat 1 Imizol | Treat 2 Imizol and clidamycin |
|--------|-----------|------------------|------------------|---------------|------------------------------|
| Fe     | 1.650±0.24588 | 0.5733±.64888 | 0.660±0.064.88 | 29.84±3.286 | 25.69±2.55 |
| NO     | 11.08±0.3551a | 44.44±3.355 | 9.70±0.24678 | 14.53±1.677 | 1.22±0.1080 |
| SOD    | 25±0.579 | 9.34±4.41268 | 12.6±10.01 | 12.3±3.48 | 13.7±3.027 |
| Cholesterol | 110, ±10.11 | 183.3±5.696 | 94.00±7.00 | 39.7±3.027 | 32.80±2.782 |
| Triglyceride | 57.67±1.202 | 94.00±7.00 | 46.2±12.08 | 39.7±3.027 | 32.80±2.782 |
| Urea (BUN) | 30.40±3.881 | 51.80±0.028 | 42.60±5.437 | 39.7±3.027 | 32.80±2.782 |
| Creatinine | 0.8800±0.07767 | 2.197±0.2867 | 1.11±0.06445 | 1.157±0.02899 | 1.157±0.02899 |
| GOT    | 53.40±6.562a | 154.7±8.090 | 101.2±7.049 | 82.67±9.7801 | 37.00±6.11 |
| GPT    | 25.8±2.131 | 59.67±4.417 | 54.67±3.160 | 37.00±6.11 | 2.143±6.3123 |
| TAC    | 2.823±0.6041t | 1.410±0.2631t | 1.987±1.062 | 2.143±6.3123 | 2.143±6.3123 |
Figure 1 showed that different forms of shizonts of babesia bigemina in RBCs of infected rat which challenge with infected blood from cattle naturally infected with babesia Bigemina this test confirm diagnosis babesia Bigemina in these animals to help treatment and control, The microscopically examination of various organs of rats experimentally infected with babesia bigemina revealed various histopathological changes in different organs such as liver, kidneys. The examined livers showed severe congestion of hepatic blood vessels and blood sinusoids. The blood vessels were enriched with high number of eosinophils, lymphocytes and macrophages (Figure 1A). Focal areas of hemorrhages in between degenerated hepatocytes and accompanied by destruction of few hepatic cells were also observed (Figure 1B). The Von-kupffer cells are enlarged. Furthermore, peri-portal as well as peri-vascular mononuclear leukocytic cellular infiltrations mainly lymphocytes and macrophages was demonstrated, in association with mild hyperplasia of the bile duct (Figure 1C). Additionally, babesia was found parasitized the erythrocytes (Figure 1D). Histological abnormalities were detected in the kidneys of rats experimentally infected with babesia. Severe congestion of the inter-tubular blood capillaries in the renal medulla was demonstrated (Figure 2A). Furthermore, most of the investigated kidneys were destructed, as the renal tubules showed degenerative changes in the cytoplasm of the lining epithelial cells in association with perivascular mononuclear leukocytic cellular infiltrations mainly lymphocytes and macrophages (Figure 2B). Additionally, hyaline casts were observed in the lumen of renal tubules together with accumulation of edematous fluid was also noted in the renal tissue with destruction of the basement membrane of some renal tubules. Furthermore, vacuolation of the lining endothelial cells of the glomerular capillaries and Peri-glomerular edema and leukocytic cellular infiltrations were demonstrated (Figure 2C). Occasionally, hypersegmentation of the glomerular tuft was also noticed (Figure 2D). However, edema and thickening in the wall of the capillary of glomerular tuft were also detected. Occasionally, fusion of the glomerular tuft with the parietal layer of Bowman's capsule was seen. Sometimes, various pathological changes were observed in the glomeruli such as shrinkage of the glomerular tuft or even complete destruction of the glomerular tuft (Figure 2E). Interestingly, babesia was found parasitized RBCs inside the renal blood vessels as well as inside the glomerular capillaries (Figure 2F).

Table 1 showed that significant different Values are expressed as mean and mean of standard error, values with different superscriptions (a,b and ab) in rows differ significantly (P<0.05). In general infected animals had lower values of antioxidant parameters as(TAC, SOD and Fe) when compared with healthy animals. On other side value of oxidant markers (NO) significant increase in blood of infected group and significant different in Cholesterol, Triglyceride, Urea (BUN), GOT and TAC when compare healthy group. When compare between control groups (negative and infected) and treated groups (treated with Imizol only GI and Imizol associated with clindamycine antibiotic GII) found significant changes among four groups in antioxidant and oxidant parameters. When compare groups with healthy group found significant different increase oxidants and significant different decrease antioxidants enzymes activity among infected group, treated group with Imizol only and non significant different between healthy group and treated group with imizol

3.1. Statistical Analysis

The results were analyzed by a one-way analysis of variance (ANOVA) followed by the Duncan test for multiple comparisons using computer software, Duncan’s Multiple Range Test.

4. Discussion

Tick fever or cattle fever (babesiosis) is economically the most important arthropod-borne disease of cattle worldwide Our study revealed that kaliobia governorate endemic with Babesia Bigemina and when examine animals aged from 1-3 years suffered from increase temperature emaciated, off food, bloody urine and by blood smear found babesia Bigemina after an infectious tick bite [12] The parasites invade red blood cells and first type of trophozoite differentiates, replicating asexually by budding with the formation of two to four merozoites tetrad formation. A second type of undifferentiated trophozoite is also formed that does not replicate but enlarges and differentiates into gametocyte-like forms similar to that seen in Plasmodium species. Merozoites eventually disrupt infected erythrocytes and reinvade other red blood cells the presence of tetrad formation often is mentioned as a diagnostic aid, trophozoites may be seen outside erythrocytes extracellular forms, which suggests the possibility of transmission by plasma and platelet products with Babesia infection this came agree with [13,14,15,16] and [17] who concluded that three distinguishing features differentiate the Babesial organisms usually form tetrads (“Maltese cross”), do not have hemozoin pigments within the affected red blood cells and have extracellular merozoites,. Our investigation confirm infection with babesia by intraperitoneal inoculation of 1.0 mL of heparinized-anticoagulated whole blood of diseased animals into the peritoneum of rats followed by smear positively and rats death at fifth days from infection after clinical signs appear, this results came agree with [18] and [19] who reveal that when confirm babesia infection by inculcation of heparinized blood from infected animals in rats found that rats death in 5 days post infection with clinical signs appear on it from fever parasitemia shivering, bloody urine progressive rise in rectal temperature to 40c & death to animals. when compare with control, in histopathological showed that different forms of shizonts of babesia Bigemina in RBCs of infected rat which challenge with infected blood from cattle naturally infected with babesia Bigemina this test confirm diagnosis babesia Bigemina in these animals to help treatment and control, The microscopical examination of various organs of rats experimentally infected with babesia bigemina revealed various histopathological changes in different organs such as liver, kidneys, testes, intestine and brain. The examined livers showed severe congestion of hepatic blood vessels and blood sinusoids. The blood vessels were enriched with high number of eosinophils, lymphocytes and macrophages, Focal areas of hemorrhages in between
degenerated hepatocytes and accompanied by destruction of few hepatic cells were also observed, The Von-kupffer cells are enlarged. Furthermore, peri-portal as well as perivascular mononuclear leucocytic cellular infiltrations mainly lymphocytes and macrophages was demonstrated, in association with mild hyperplasia of the bile duct. Additionally, babesia was found parasitized the erythrocytes, Histological abnormalities were detected in the kidneys of rats experimentally infected with babesia. Severe congestion of the inter-tubular blood capillaries in the renal medulla was demonstrated, Furthermore, most of the investigated kidneys were destructed, as the renal tubules showed degenerative changes in the cytoplasm of the lining epithelial cells in association with perivascular mononuclear leukocytic cellular infiltrations mainly lymphocytes and macrophages. Additionally, hyaline casts were observed in the lumen of renal tubules together with accumulation of edematous fluid was also noted in the renal tissue with destruction of the basement membrane of some renal tubules. Furthermore, vacuolation of the lining endothelial cells of the glomerular capillaries and Peri-glomerular edema and leukocytic cellular infiltrations were demonstrated, Occasionally hyper segmentation of the glomerular tuft was also noticed. However edema and thickening in the wall of the capillary of glomerular tuft were also detected Occasionally fusion of the glomerular tuft with the parietal layer of Bowman's capsule was seen. Sometimes, various pathological changes were observed in the glomeruli such as shrinkage of the glomerular tuft or even complete destruction of the glomerular tuft. Interestingly, babesia was found parasitized RBCs inside the renal blood vessels as well as inside the glomerular capillaries. This results agree with [20] who found that rats death at fifth day from infection and histopathological exam found babesia in piroplasma form of babesia in pathological tissue of rat's liver & kidney. Hyperplasia of Kupffer cells were detected in liver sections of infected gerbils, this is due to the need of phagocytosis as a protective mechanism during the course of infection and babesia parasite, like theleria and malaria parasites, invade erythrocytes of infected animals resulting in destruction of parasitized erythrocytes. Immune response of gerbils due to Babesia rodhaini infection,. hepatic tissue showed cytoplasmic vacuolation which is mainly a consequence of considerable disturbances in lipid inclusions and fat metabolism occurring under pathological cases [21]. Our study investigated significant changed in lipid profil synthesize in liver as cholesterol and triglyceride due to toxic effect of babesia on liver when compare control positive with control negative and treated groups. these results were agree with [22] who reported a marked increase in cholestrolemia in experimentally T. annulata-infected cattle and stated that this increase was probably due to liver damage and this investigation agree with [23] who concluded that insulin concentration in dog with babesiosis is important than hemoglobinuria in damaging kidney of ovine Babesia infections. Main observed histopathological changes in kidneys in naturally acquired B. canis infected were vacuolar infiltration, including the lipid transport proteins, but differ with [24] who concluded that cholesterol is a major component of the erythrocyte membrane and triglycerides concentration and the lipids are the major part of red blood cells membrane, the unchanged serum lipid composition and cholesterol in the infected animals could imply that the plasma lipid concentration probably have not a marked responsibility for the increased fluidity and permeability of Theileria annulata in infected erythrocytes.

Our study investigated increased in GPT and GOT enzymes when compare control positive with control negative and treated groups and when evaluate TAC, SOD, Gsh, and Fe as antioxidants found significant decrease when compare control positive with control negative and treated groups and significantly higher alkaline phosphate (ALP) alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activity, phosphorus, sodium, potassium, bilirubin (direct and indirect) and (Otsuk, et. al 2002 [21] who concluded that the activeties of SOD and TAC and the concentration of GSH were low Hypoglycaemia such as increased glucose consumption, depletion of hepatic glycogen stores, and hepatic dysfunction with impaired gluconeogenesis [27]. Acute hepatopathy was detected in all dogs with elevated ALT activity in animals infected with babesia while [23] observed that Babesia species produce haemolysis of erythrocytes so lead to production of erythrocytes from bone marrow to compensate decrease in erythrocytes level, this lead to decrease serum level of iron which is necessary for erythrocyte production. Our study found significant changes in kidney functions tests as (BUN & creatine) which increase in infected animals when compare with healthy and treated animals this agree with [21] significantly higher blood urea Nitrogen (BUN) concentrations than the healthy cattle. [28,29] and [30] Renal function also is affected occasionally and Interleukin-1 release. [23] Observed elevation in BUN and creatinine level might have resulted from kidney dysfunction, muscle catabolism, and colonization of B. ovis in the renal blood circulation. It is suggested that in ovine babesiosis many potential factors leading to impairment renal function. In our study most of the investigated kidneys were destructed, as the renal tubules showed degenerative changes in the cytoplasm of the lining epithelial cells in association with perivascular mononuclear leukocytic cellular infiltrations mainly lymphocytes and macrophages, acute diffuse proliferative glomerulitis, acute glomerular hemorrhage, presence of thrombi, congestion and stasis in glomerular capillaries, acute glomerular hemorrhage and acute tubular necrosis. Main observed histopathological changes in kidneys in naturally acquired B. canis infected were vacuolar-hydropic degeneration, necrosis, detachment of renal tubular epithelial cells in proximal convoluted and hemoglobin casts. Moreover; hypoxia appears to be more important than hemoglobinuria in damaging kidney of experimentally and naturally Babesia infected dog Mathe et. al. 2007 [31] it seems that elevation in BUN and creatinine level ascribes to kidney malfunctions in
infected small ruminants with babesia.. when compare control groups with treated groups found group treated with antiparasitic imizol and clindamycin is the best group than other groups in results & propagation since return to normal faster. When compare among treated groups which return to normal faster and all functions test return to normal when compare with control groups. This study agrees with [32] and [33], Imizol has been successfully used as a chemo prophylactic, Exchange transfusion, together with antibabesial chemotherapy, may be necessary in critically ill patients. This treatment is usually reserved for patients who are extremely ill with blood parasitemia of more than 10 percent, massive haemolysis and asplenia and [34] and [35] babesiasis may continue for more than 2 months after treatment and when left untreated, silent babesial infection may persist for months or even years when compared the duration of parasitemia in persons who had not been treated. Babesial DNA persisted for 16 days in 22 actually ill subjects who received clindamycin and quinine therapy but among the subjects who did not receive specific therapy symptoms of babesiosis persisted up to 114 days, clindamycin is promising and may become prominent in the future Antibabesial chemotherapy & Antibiotic necessary in critically, ill patients. This treatment is usually reserved for patients who are extremely ill- with blood parasitemia. Clindamycin, the treatment of choice for Babesia microti, the chief Babesia species that infects humans, can be used against Babesia in dogs, since this is a readily available antibiotic and the drugs specific for Babesia, clindamycin represents an excellent starting point for therapy In clinical cases, a combination of clindamycin and quinine is administered as the standard treatment [18] and [36]. Lincomycin and clindamycin are the only members of the relatively small lincosamide antimicrobial class marketed for use in humans clindycin gradually reduced parasitemia levels and induced morphological changes in parasites that indicate degeneration of parasites as segmentation size reduction, localization in the cell limbic, tornstate of nucleus and disappear of cytoplasm, clindamycin treatment reduce clinical signs of babesia infection, it still enjoys use in the therapy and prophylaxis of a large number, protozoa [1] and [37].

5. Conclusion

To our knowledge, The observed increase BUN and creatinine indicate renal failure and increase in GPT, GOT and decrease lipids profile (triglycerids and cholesterol) indicate disturbance in liver function and oxidative stresses associated with infection as SOD TAC and Fe came in agreement with those reported earlier. Anorexia in relation to high rise of body temperature.

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References

[1] Henri J, Vial *. A. Gorenflof Chemotherapy against babesiosis Veterinary Parasitology 138 (2006) 147-160.
[2] Trotta M, Carli E,Novari G, clinicopathological findings, molecular detection and characterization of babesia gibsoni infection in a suck dog from italy vet-parasitol 2009, 165-318-322.
[3] Rubino G,Cito Am, Laciniot, Hematology and some blood chemical parameters as function of tick-borne disease signs in hars. J Equine Vet Sci 2006: 26: 475-480.
[4] Rafag RB, Mrljk V, KucerN et.al. Protein C activity in babesiosis of dogs, Vet. Arhir, 2007, 77, 1-8.
[5] ZobbAR Adru M, Niccolini S, et. al. Clinical laboratory finding in equine piroplasmosis, J equine Vet. Sci. 2008, 28, 301-308.
[6] Kamile BicRK, yeten Deger, Sedar Deger, some biochemical and haematological parameters in dogs infected with babesia species YYU vet Fak Derg 2005,16 (1): 33-35.
[7] Omer O.H., EL-MAILIK K.H, MAGZOUB M. MAHMOUD O.M., HAROUN E.M., HAWAS A., OMAR H.M.: Biochemical profiles in Friesian cattle naturally infected with Theileria annulata in Saudi Arabia vet. Res. Comm., 2003, 271-25.
[8] YA DA C.K. Sharma N.N. changes in blood chemical components during experimentally in duced Theileria annulata infections in cattle Vet. Parasitol 1986; 21, 91-98.
[9] Mosqueda J,Olevera-Rainerez A, Aguilar-Tipacamu GJ Current advances in detection and treatment of babesiosis. Curr Med Chem.2012; 19 (10), 1504-18.
[10] Bock R. L.Deucke, A.DE vos and W.Jorgensen. Babesiosis of cattle parasitology (2004), 5247-5269.
[11] Koracevic, D, Koracevic, G. et al, Total Antioxidant Capacity. J Clin Pathol. 54, 356-361 (2001)El-Aaser, A.A. (unpublished).
[12] Spach DH,Liles WC, Campbell GL, quick RE, Anderson DE, fritsche TR. Tick-borne diseases in the united states. N Engl J Med. 1993; 30: 936-47.
[13] El Sawaily, A. A. (1999): "Veterinary Infectious Diseases" 2nd Edit. Ahram Distribution Agency, Egypt.
[14] Sumanssetty, MD, PhD, Zena Khalil MD,Pamela, Schori,MT (ASCP), Migul Azar, MD, Babesiosis two atypical cases from minnesota and reosta, Am. J. Clin. Pathol. 2003: 120,554-559.
[15] Gelfand JA, Babesia, In: Mandell GL, Douglas RS, Bennett JE, DolinR, eds. Mandell, Douglas and Bennett’s, principles and practice of infectious diseases. 5th ed. New York: Churchill Livingstone, 2000; 2899-902.
[16] Pruthi RK, Marshall WF, Wiltse JC, Persing DH. Human babesiosis. Mayo Clin Proc. 1995; 70: 853-62.
[17] Boustani MR, Gelfand JA. Babesiosis. Clin infec Dis. 1996; 22: 611-5. Cats. Afr.vet.ver. (2000) 71 (1): 53-5.
[18] Bonoan JT, Johnson DH, Cunha BA. Life-threatening babesiosis in an asplenic patient treated with exchange transfusion, azithromycin, and atovaquone. Heart Lung. 1992; 27: 424-8.
[19] Loutan L, Rossier J, Zufferey G, Cuendol D, Hatz C, Marti HP, Genn L. Imported babesiosis diagnosed as malaria [Letter]. Lancet. 1993; 342: 749.
[20] DKhI, M.A. S.A.L. Quraisyh, A.S. Abdel Baki. Hepatic tissue damage induced in meriones ungliculatus due to infection with Babesia divergens-infected erythrocytes Saudi journal of Biological sciences (2010) 17, 129-132.
[21] Otsuka, Y.,Anasaki, M.,Yamoto, O.,Maede,Y., Theeffect macrophages on the erythrocytes oxidative damage and pathogenesis of anemia in babesia gibsoni infected dogs with low parasitism J. Vet. Med. 2002. D Sci. 64: 221-223.
[22] Mathe A, Voros K,Nemeth T,Biksi IHetyey C,Manczur F,Tekes L, Dackson, A.DE vos and W.Jorgensen. Babesiosis of cattle parasitology (2004), 5247-5269.
[23] Rees p, schoman JP plasma insulin concentrations in hypoglycemic dogs with Babesia canis rossi infection Vet Parasitol 2008; 152: 60-66.
[24] Angel Tomas CAMACHOA, Francisco Javier GUITIANB, Estrella PALLASC, Juan Jesus GESTALd, Sonia OLMEDAd, Heidi GOETHERTHi, g, Sam TELFORD IIIg, Andrew SPIELMANFa. Serum protein response and renal failure in canine Babesia annae infection Vet. Res. 36 (2005) 713-722 713.
[25] Okubo K, Yokoyama N, Takabatake N, Okamura M, Igarashi 12007, Amount of cholesterol in host membrane affects erythrocyte invasion and replication by Babesia bovis, Parasitology. 2007 May; 134 (Pt 5): 625-30. Epub 2006 Dec 6.
[26] Bijan Esmaeilnejad, Mousa Tavassoli, Siamak Asri-Rezaei, Investigation of hematological and biochemical parameters in small ruminants naturally infected with Babesia ovis Veterinary Research Forum. 2012; 3 (1) 31-36.

[27] El Moghazy F.M, Impact of parasitic infection on Ovariaan Activity in Buffaloes-Heifers with Emphasis on Ascariasis, World journal of Zoology 6 (2): 196-203,2011.

[28] Sumamsetty, MD, PhD, Zena Khalil MD, Pamela Schori, MT (ASCP), Migul Azar, MD. Babiosis two Atypical cases from Minnesota and review, Am. J. clin. pathol. 2003: 120: 554-559.

[29] White DJ, Talarico J, Chang HG, Birkhead GS, Heimberger TM, Morse DL. Human babiosis in New York state: Review of 139 hospitalized cases and analysis of prognostic factors. Arch intern Med. 1998; 158: 2149-54.

[30] Camacho At, Gutian FJ, Pallas E, et. al. Serum protein response and renal failure in canine babesia annae infection Vet. Res. 2005, 36, 713-722.

[31] Mathe A, Dobos, Kovacs M, Voros K, Histological and ultrastructure studies of renal lesions in Babesia canis infected dogs treated with imidocarb, Acta Vet Hung 2007 Dec; 55 (4): 511-23.

[32] Wittner M, Rowin KS, Tanowitz HB, Hobbs JF, Saltzman S, Wenz B. Successful chemotherapy of transfusion babiosis. Ann Intern Med. 1982, 96, 601-4.

[33] Rowin KS, Tanowitz HB, Wittner M. therapy of experimental babiosis. Ann Intern Med. 1982, 97, 556-8.

[34] Krause PJ, Spielman, Am Telford SR 3rd, Sikand VK, McKay K, Christianson D, et al. Persistent parasitemia after acute babiosis. N Engl J Med. 1998; 339: 160-5.

[35] Pezhorn BI, Lewis BD, Lopez-Rebolla LM and Swan GE, Tydskr S, nscreening of five drugs for efficacy against babesia felis in experimentally infected, South Africa Vet. Ass. 2000, 71: 1: 53-57.

[36] Marcia LBuck., pharm.D., FcCP. Use of clindamycin in pediatric infection volume 14 number 2 february 2008.

[37] Dorota M. Radomska-Leśniewska, Ewa Skopińska-Różewska, Jacek Małeżyk, Lincocin Experimental immunology. The effect of clindamycin and lincomycin on angiogenic activity of human blood mononuclear cells Centre Eur J Immunol 2010, 35 (4) 217-222.