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Highlighting on Bovine Tuberculosis infection in cattle

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ABSTRACT

This work was directed to isolate the mycobacterium tuberculosis complex from the infected samples (positive or suspicious reactor to tuberculin test) and evaluate the ELISA and PCR assays for the diagnosis of bovine tuberculosis as well as to ascertain the changes in hematological and biochemical constituents of blood as a result of mycobacterium tuberculosis infection in cattle.

A total of 500 animals from private cattle farm and abattoir aged between 2-5 years were tested by tuberculin test during the period from April 2019 to October 2021 at Sharkia Governorate (360 positive tuberculin test and 140 negative tuberculin test). Blood and lymph nodes were collected for bacteriological examination, Elisa assay and molecular identification of mycobacterium tuberculosis complex.

For hematological and biochemical investigation. A total of 60 blood samples were collected with and without heparin from animals showing negative tuberculin test (group l). Moreover, 120 blood samples were collected with and without heparin from animals showed positive tuberculin test without lesions (group 2) and with lesions (group 3) 60 for each.

The obtained results showed that 210 samples were found positive for bovine tuberculosis by traditional culture method with a percentage of isolation reached 58.3% while the presence of acid fast bacilli of the same tested samples reached 219 samples with a percentage of 60.8% The results of ELISA assay for detection of mycobacterium antibodies in sera of tuberculin positive animals were reported and the results showed that , 313 out of 360 samples harbored mycobacterium antibodies with a percentage of 87% while the results of tuberculin negative animals showed the presence of mycobacterium antibodies in sera of 16 tuberculin negative animals out of 140 animals with a percentage of (l I .4%). The results of RT PCR were recorded, which showed that 184 out of 210 isolates of mycobacterium spp. proved to be mycobacterium bovis with a percentage of (87.6%).

Concerning hematological examination there is a significant decrease in

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total red blood cells count. and hemoglobin concentration ($P < 0.05$) accompanied by higher values of Total leukocyte count (TLC) lymphocyte, eosinophil. monocytes and lowered neutrophil count recorded in infected and contact cows compared to control group. The obtained results indicated that there was a significant increases ($P < 0.05$) in the levels of malondialdehyde (MDA) in T.B infected cattle, and contact group compared with negative group, In contrast, there was a significant reduction ($P < 0.05$) in the level of R.GSH ,catalase, vit A and vit C. Biochemical analysis of positive cases and their contact revealed significant increase in globulin content and decrease in albumin content, resulting in altered A/G ratio Serum enzymes analysis revealed significant ($P<0.05$) increase in alkaline phosphatase activities (ALP) aminotransferases (AST, ALT activities) creatinine phosphokinase (CPK), gamma. glutamyl transferase (GGT), and lactate dehydrogenase (LDH) in infected and contact cattle in comparison with negative group.

INTRODUCTION

Bovine tuberculosis (BTB), chronic granulomatous disease of cattle, is caused mainly by *Mycobacterium bovis (M. bovis),* a member of Mycobacterium tuberculosis complex (MTBC) **(Romha et al. 2018).**

Bovine tuberculosis is a chronic infectious disease of animals characterized by the formation of granulomas in tissues and organs ,more significantly in the lungs, lymph nodes, intestine and kidney, Bovine tuberculosis is caused by slow growing non photochromogenic bacilli members of mycobacterium tuberculosis complex, however, M.bovis is the most universal pathogen among mycobacteria and affects many animals species of all age group as well as human, **(Thoen et al. 2006).**

Mycobacterium tuberculosis is an intracellular pathogen, which grow and replicate in the host macrophages, It is well known that macrophages undergo respiratory burst after contact with this microorganism. The mechanism of the phagocytic process is the killing of microbes by bombarding them with oxidants without adequate antioxidant nutrient reserves. cellular machinery will be damaged by the free radicals, thereby reducing the effectiveness of the immune cell **(Mohankumar et al. 2011).**

When antioxidant capacity is limited, the lifespan of immune cells is reduced and an infection can become established or severity of an infection can increase **(Kanchan et al. 2008).** The infection due to M. bovis which is the most principal agent of zoonotic tuberculosis in cattle, is a human health issue , the role of the different commodity claim (milk and meat) has to be evaluated , farm animals , pets, food and milk all pose a potential threat to our health **(AnaeJon et al. 2010).** However, many diagnostic tools was carried out and evaluated either conventional traditional methods or/and recent methods, the bacteriological isolation procedures are tedious and time consuming as it require 6-8 weeks or longer **(Thoen et al. 1981).**

Tuberculosis, is **accompanied** by a complex variety of nutritional and metabolic responses within the body. The response to infection is associated with an increase in the energy expenditure of the animals and various degrees of tissue breakdown (**Coskun et al. 2012**).
The standard field diagnostic test of tuberculosis is the single intradermal tuberculin test **(Wood and Rothel, 1994)**. Most of the tests still suffer from lack of sufficient sensitivity and specificity, this lead to inability to detect the infected cases early enough which play an important role in the failure of the tuberculosis control programs **(Stylo, 1989)**

For all these factors, it becomes necessary to overcome these **limitations** in diagnosis by DNA amplification of specific sequence of DNA by polymerase chain reaction (PCR) for detection of bovine tuberculosis in infected herd **(Gaborick et al. 1996) (Ibrahim et al. 2020).**

So, the aim **of** this work was directed to isolate the *M. tuberculosis* complex from the infected samples (positive or suspicious reactor to tuberculin test) and evaluate the ELISA and PCR assays for the diagnosis of bovine tuberculosis as well as to ascertain the changes in hematological and biochemical constituents of blood especially some antioxidants as a result

of mycobacterium tuberculosis infection in cows.

MATERIALS and METHODS

A total of 500 animals from private cattle farm (suspect to be infected by TB.) and its neighboring abattoir aged between 2-5 years were tested by tuberculin test according to **(OiE 2009)** during the period from April 2019 to October 2021 at Sharkia governorate (360 positive tuberculin test and 140 negative tuberculin test and their contacts). Blood and LNs were collected for bacteriological examination, ELISA assay and molecular identification of mycobacterium tuberculosis complex. For hematological and biochemical investigation ,a total of 60 blood samples were collected with and without heparin from animals showed negative tuberculin test (groupl), moreover, 120 blood samples were collected with and without heparin from animals showed positive tuberculin test without lesions (group 2) and with lesions (group 3) 60 for each.

Bacteriological Examination.

All collected samples (LNs) were treated according to petroffs method, **(Chadwide, 1981) and (Collee, 1996).** Ziehl Nealsen's stain (Oxoid ,England) was carried out for all prepared smears from the sediment and examined microscopically, the inoculum from the sediment was streaked onto the surface of L.J media ,inoculated at 37°C for 6-8 weeks and examined at intervals. The suspected growing colonies were examined microscopically, culturally according to **(Boron and Finegold 1990),(Collee 1996) and (Virella 1997)**.

The assay of Enzyme linked immunosorbent was carried out according to **(Hall and Thoen, 1985)** using bovine PPD antigen and standard product of ELISA produced by (KPL), (USA).

A serum dilution was considered positive if it yielded a mean O.D of each group equal to or greater than the cut off value. The cut —off value was calculated according to (**Dimitri et al. 1996).** which is equal to the mean O.D of negative serum plus 2 standard deviations.

Suspected M. bovis colonies were identified by performing a real time PCR using MTplex dtecRT-qPCR Test (Edifici -Qu6rum3, Spain) that comprises a series of species-specific targeted reagents designed for detection of all species contained in the Mycobacterium tuberculosis complex, according to **(Ben Kahla et al. 2011).**

Primer Sequence :

INS1: CGTGAGGGCATCGAGGTGGC

INS2:GCGTAGGCGTCGGTGACAAA

The reaction of 20 µl final volume consisted of 10 µl Hot Start-Mix qPCR 2x, 1 µl MTplex dtec-qPCR-mix, 4 µl DNase/RNase free water and 5 µl DNA sample., the reaction conditions consisted of one cycle of 95˚c for 5 min followed by 45 cycles of 95˚c for 30 sec and 60˚c for 60 sec for hybridization, extension and data collection. The reaction was run in Applied Biosystem Step One TM Real Time PCR System and FAM fluorogenic signal was collected and the cycle threshold of the reactions was detected by StepOne™ software version 2.2.2 (Life Technology)..

Hematological and biochemical investigation. The blood collected on heparin for both groups were used for the determination of the following parameters represented in (tablel). Blood film from each blood sample was stained with Leishman stain and observed microscopically to study WBCs differential count according to **(Schalm, 1986).**

Table 1. Methods adopted for hematological and some antioxidant analysis of blood in cattle.

Parameter	Reference
Malondialdehyde (nmol/L)	Placer et al. (1966)
Reduced glutathione (mmoVL)	Beutler et al. (1963)
T.RBCs, WBCs count and	Schalm (1986).

The collected serum samples were used for the determination of the following parameters represented in table (2).

Table 2. Methods adopted for biochemical analysis of serum in cattle.

Parameter	Reference
Serum catalase (U/ml)	Aebi (1984)
Serum Total protein (g/dl)	HQffamann and Richterrich(1970)
Serum Albumin (g/dl)	Dumas et al (1971)
Serum Aminotranseferases (activity level)	Reitnlan and Frankel (1957)
Serum LDH(IU/L)	Cabaud and Worblewski (1958)
Serum CPK (IU/L)	Horder and Rej (1983)
Serum GGT (IU/ml)	Geriich (1983))
Serum Alkaline phosphtase (activity level)	Kilchling and Freiburg (1951
Serum vita (gg/dl)	Suzuki and Kaloh (1990)
Serum vitC (gg/dl)	Omaye et al (1979)

Statistical analysis.

The mean values obtained from hemograms and biochemical assays of positive samples were compared with data of negative samples using the SPSS14 software. Differences were considered to be statistically significant with values of $P<0.05$ according to (Petrie and Watson, 1999).

Results

The bacteriological examination of the collected samples from reactor animal (tuberculin positive animals) was carried out for detection of the mycobacterium tuberculosis complex by microscopical examination, traditional cultural method, ELISA assay and PCR.

Table 3. Bacteriological findings of examined tuberculin positive animals.

No / Type of samples	Bacteriological finding		PCR
	Culture	Microscopical	
360 (LA^T)	210 (583%)	219 (60.8%)	184/210 (88%)

The obtained results showed that 210 out of 360 samples were positive for bovine tuberculosis by traditional culture method with a percentage of isolation reached 58.3% while the presence of acid fast bacilli of the same tested samples reached 219 samples with a percentage of 60.8% as shown in table (3)

Table 4. Bacteriological findings of examined Tuberculin negative animals

Bacteriological findings				ELISA		PCR	
culture		Microscopical		No.	%	No.	%
No.	%	No.	%				
8/16	50%	10/16	62.5	16/140	7.9	8/8	100

The obtained results showed that 8 out of 16 samples (from tuberculin negative animals) were positive for bovine tuberculosis by traditional culture method with a percentage of isolation reached 50% while the presence of acid fast bacilli in the same tested samples reached 10 out of 16 samples with a percentage of 62.5% as shown in table (4).

The results of ELISA for detection of mycobacterium antibodies in sera of tuberculin positive animals were reported and the results showed that, 313 out of 360 samples were harbored mycobacterium antibodies with a percentage of 87% while the results of tuberculin negative animals showed the presence of mycobacterium antibodies in sera of 16 tuberculin negative animals out of 140 animals with a percentage of (1 1.4%).

The results of RT PCR were recorded, which showed that 184 out of 210 isolates (from tuberculin positive animals) proved to be mycobacterium bovis with a percentage of (88%), while 8 out of 8 isolates (from tuberculin negative animals) with a percentage of 100% proved to be mycobacterium bovis. The amplification plot of positive culture was presented in fig (l).

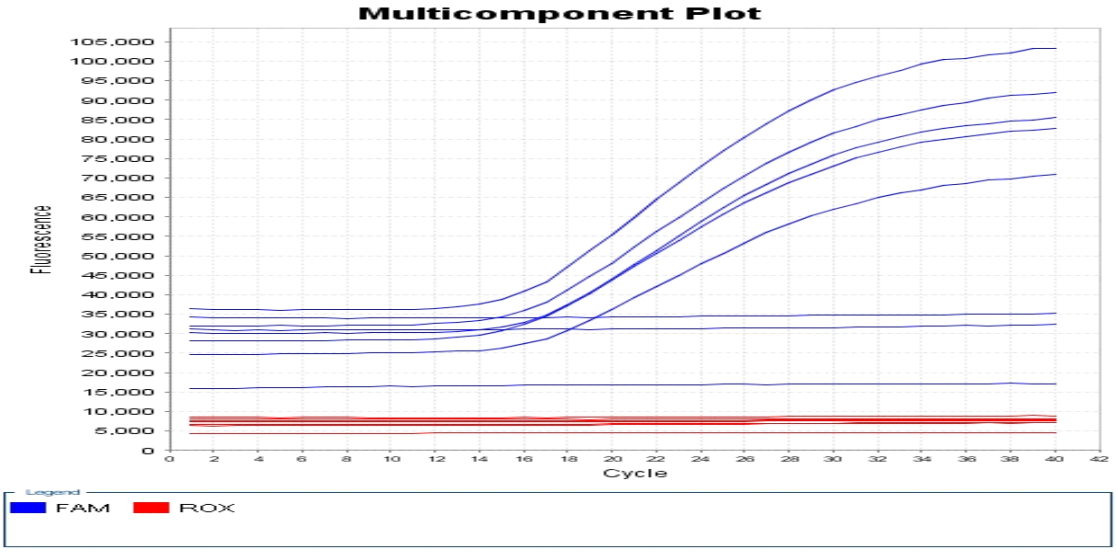

Fig.(1) : The amplification blot of tuberculous samples.

Table 5. Effect of *mycobacterium tuberculosis* infection on blood hematology in cattle .

Parameters	Group I	Group2	Group3
RBCs / 10^6 gl	4.93±0.035	4.35±0.047 [a]	3.37±0.006 [a]
1--1b (Wdl)	10.8±0.16	8.95±0.14 [a]	8.49±0.10 [a]
TLC/10^3 pi	5899±1.66A	6854±1.23 [a]	8012±1.42 [a]
Lymphocyte%	36.1±0.55 [A]	42.0±0.69 a	46.0±0.62 [a]
Neutrophils%	55.70±0.39A	48.30±0.78 [a]	42.4±0.89 [a]
Eosinophil%	3.3±0.26 [A]	3.5±0.34 [a]	3.8±0.29
Monocytes%	4.5±0.27 [A]	5.9±0.31 [a]	7.1±0.41 [a]
Basophil%	0.4±0.16	0.3±0.15	0.2±0.13

Values are expressed as mean ±S.E. A,a. small letters significant difference against capital letters at (P<0.05) using LSD

Table 6. Effect of mycobacterium tuberculosis infection on oxidative stress indicators in cows.

Parameters	Group I	Group2	Group3
Glutathione(mmoll)	14.65±0.12 A	9.28±0.22' 47.9±122'	7.16±0.15' 62.2±1.51 '
	24.6±0-87		
Catalæse (UJtnI)	4.77±0.047	3.13±0.052	2.90±0.081
VitA (gg 'dl)		25.2±0.99'	9.8±0.95 [a]
VitC (gg'dl)		23.5±0.77'	17.0±1.01

Values are expressed as mean± S.E A,a- small letters significant difference against capital letters at . p<0.05

Table 7. Some biochemical changes in cattle infected with *mycobacterium tuberculosis.*

Parameters	Group I	Group2	Group3
Total protein(g/dl)	7.11±0.11	7.03±0.05	6.96±0.07
Albumin(g/dl)	3.40±0.88A	2.98±0.038	2.82±0.059
Globulin(g/dl)	3.71±0.06A	4.05±0.04	4.14±0.06a
A/G ratio	0.92±0.0322 [A]	0.74±0.0122	0.68±0.018'
ALT(IUI'L)	18.9±0.6 [A]	35.6±0.77	47.30±0.7
AST (IU[L)	34.8±1.00A	53.20±1.42 •	60.4±0.99 [a]
AIP (IU/L)	104.12±1.22A	149.55±1.1?	152.90±2.4 [a]
LDH(IU/L)	699.5±1.04 [A]	780±1.ssa	857±1.55[a]
CPK(IU/L)	14.11±2.01A	21.67±2.43'	29.65±1.80 [a]
GGT(1U/m1)	7.15±022A	12.76±1.21 [a]	17.07±1.8a

Values are expressed as mean ±S.E
A, a small letters Significant difference against capital letters at (P<0.05) using LSD

DISCUSSION

Bovine tuberculosis caused by mycobacterium bovis as a chronic infectious disease of life stock. the global active TB cases in humans were estimated to be ten million incident cases, among them, 140,000 (range 69,800–235,000) were estimated to be new zoonotic TB cases (1.4%) of which approximately death was reported in 11,400 (8.1%, range 4470–21,600) (WHO 2020). In developing countries, about 10-15% of human TB cases are caused by M.bovis **(Algammal et al. 2019).** Conventional bacteriological procedures are tedious and time consuming after requiring 6-8 weeks or longer **(Thoen et al. 1981)** the standard field diagnostic test for tuberculosis in the single intradermal tuberculin test which is one of the immunological test of the wide use **(Wood and Rothel, 1994) and (Ibrahim et al. 2020)** however most of them are still suffer from lack of sufficient sensitivity, specificity and uniform applicability to all clinical samples, which load to inability to detect infected cases early enough that may play an important role in the failure of tuberculosis control programs **(Stylo, 1989)** so, many recent techniques are carried out to overcome these problem including ELISA and PCR techniques. In this study, a total of 360 tuberculin positive animals were examined by different procedures for detection of mycobacterium , 210 out of 360 cases were positive for tuberculosis by cultural method with percentage of isolation reached 58.3%, and 219 out of them were harbored acid fast bacilli by microscopical examination with a percentage of 60.8% while 8 out of 16 tuberculin negative tested animals were positive for bovine tuberculosis by traditional culture method with a percentage of isolation reached 50%. These results are in agreement with **(Duffield et al. 1989)** who recorded that sensitivity of cultural method was not 100% due to the harsh decontamination technique which was done **(Victor et al. 1992), (Quinn ct al. 1994) and (Sohair and Riad 2002).** Concerning the ELISA results, 313 out of 360 tuberculin positive tested animals were proved to harbored mycobacterium antibodies with a percentage of 87%, while 16 out of 140 tuberculin negative tested animals were proved to harbored mycobacterium antibodies with a percentage of I I .4%. these results were in consistence with that reported by **(Riad, 2004), (Mikhail et al. 1997) and (Gad El said et al. 2001)** who reported that ELISA is a rapid, sensitive assay for detection of bovine tuberculosis. As regards to PCR assay, the results showed that 184 out of 210 isolates (from tuberculin positive animals) proved to be mycobacterium bovis with a percentage of (88%), while 8 out of 8isolates(from tuberculin negative animals) with a percentage of 100% proved to be mycobacterium bovis. These results agreed with those obtained by **(Savic et al. 1992) (Dimitri et al. 1996) and (Sayed M. et al. 2022)** who found that sensitivity of PCR assay was high due to the ability of PCR to detect a very little amount of mycobacterium DNA **(Kolk et al. 1992)** and also can detect the viable as well as non-viable mycobacterium **(Li'ebana et al. 1995).** Hematologic values are a representation of the health status of the animal.

In the present investigation, total red blood cells count, and hemoglobin concentration were significantly lowered ($p < 0.05$). However, higher values of total leukocyte count (TLC) lymphocyte, eosinophil, monocytes and lowered neutrophil count recorded in infected and contact cows compared to control and contact group (Table 5). These results are in agreement with **(Muhammad et al. 2006) (Javid et al. 2006) (Latif 2010) (Javid et al. 2010) (Praveena et al. 2010) and (Quevillon et al. 2013).**

Weiss (2002) Karyadi et al. (2007) and Praveena et al. (2010) had explained the mechanism of anemia in pulmonary tuberculosis disease. They concluded that the invasion of bacteria leads to activation of Tlymphocytes and macrophages, which induce the production of the cytokines like interferon gamma (INF-gamma), tumor necrosis factoralpha (INF-alpha), interleukin-I (IL-I) and interleukin-6 (IL-6)which with their products will cause diversion of iron into iron stores in the reticuloendothelial system resulting in decreased iron concentration in the plasma thus limiting it's availability to red cells for hemoglobin synthesis, In addition, TNF-alpha directly damages erythrocytes and decreases red cell life span.

So the anemia of infection is therefore basically due to iron restriction, combined with inability of erythropoiesis to compensate adequately for the anemia.

Data obtained from table (5) showed a significant leukocytosis due to the significant increase of lymphocytes, eosinophil and monocytes.ln infectious diseases, lymphocytosis typically reflects a generalized state of lymphoid hyperplasia as a result of persistence of infectious process, and immune stimulation (**Praveena et al. 2010) and (Hossain et al. 2018).**

Kumar et al. (1994) reported that monocytes have an important role in the cellular response to the tubercle bacillus and it is responsible for degradation of the phospholipids of the bacterial cell wall, monocytes later transform into epithelioid cell which is a characteristic feature in tubercular granulomas, so, monocytosis can be regarded as an evidence of active extension of tuberculosis process.

The Oxidative stress of Tuberculosis occurs when production of free radicals exceeds the capacity of the antioxidant system of body cells, cells are protected from free radicals by specific endogenous antioxidants system to ensure the removal of such free radicals **(Gaal, et al 2006) and (Hossain et al. 2018).**

The present study is a comprehensive evaluation of concentrations of circulating antioxidants and markers of oxidative stress in pulmonary tuberculosis, the obtained results presented in table (6) indicated that there was a significant increases ($p < 0.05$) in the levels of MDA in T.B infected, and contact cattle compared with negative group, in contrast, there was a significant reduction ($p < 0.05$) in the level of R.GSH, catalase, vit A and vit C. These results come in accordance with **(Madebo et al. 2003) (Ylldrz et al. 2004) (Narsimha et al. 2009) (Kanchan et al. 2008) (Shubhangi and Dalvi 2012) and (Shiloh et al. 2010).**

Our finding of a significant correlation between high MDA concentrations and low concentrations of some antioxidants suggests increased utilization by ROSs as an important contributing factor to the lower concentrations of antioxidants in tuberculous animals. Glutathione, ascorbic acid, are integral components of a regenerating redox cycle **(Reddy et al. 2004).** Thus, a combined decrease in this antioxidant may markedly decrease antioxidant capacity in these animals. Moreover glutathione and vitamin C may act synergistically to protect cells from oxidative-stress-induced damage. the combined deficiency of these antioxidants may markedly increase oxidative stress. (**Ylldrz et al. 2004**). Oxidative stress in tuberculous animals, may lead to increased levels of reactive oxygen species, which may be adversely affecting the immune response, pulmonary damage and lung fibrosis, Vitamin A enhances white blood cell function, enhances resistance to infection and maintains membrane defenses to infection **(Narsimha et al. 2009).**

Significant decrease ($p<0.05$) in the level of serum vitamin A, could be explained by either direct effect of bacterial infection on the liver (site of storage) which increased vitamin A consumption to restores the tracheo-bronchial epithelium destroyed during infection process, as the interaction of epithelial cells with mycobacterium tuberculosis is an important step for bacteria to entry into the host body **(Li et al. 2012)**

Linden et al. (2008) found that epithelial mucosal cells play important roles in this process, a microbial attack may damage the mucosal layer, so the epithelium of respiratory tract becomes keratinized and cracks occur, giving easy access to bacteria, resulting in infectious diseases.

Furthermore, acute circulatory changes due to systemic stress cause an increase in vitamin A consumption and a reduction of liver mobilization rather than depletion of reserves, vitamin A-deficient cattle suffered from depressed activity of natural killer cells, decreased antibody production, decreased responsiveness of lymphocytes to mitogenic stimulation, and increased susceptibility to infection (**Abebe and Bjune, 2009) and (Hossain et al. 2018).**

Vitamin C functions as an "electron sink" as it donates its electron to the free radical species, there by converting it to less harmful forms and thus prevent the chain reaction of lipid peroxidation **(Dalvi et al. 2012).** Reduction in blood serum vit C can be attributed to imbalance between the synthesis of vit C and high consumption of this vitamin needed for protection of the lung during bacterial infections, as well as the free radicals generated in the lung resulting from inflammatory cell invasion, lead to lowering of the concentration of ascorbic acid when the capacity of ascorbic acid is exceeded free radicals can then diffuse to cell membranes and initiate lipid peroxidation the decrease in vit C is based on its role in the prevention of cellular damage. Moreover, vit C enters in the animal defense mechanism during disease condition by its detoxified action **(Vijayamalini and Manoharan 2004).**

Biochemical effects of Tuberculosis: The results indicated that there was no significant difference in the total protein contents between the infected and non-infected but there was significant difference in the levels of albumin, globulin and A/G ratio ($P<0.05$). Infected and contact cattle showed an increase in globulin content and decrease in albumin content and resulting in altered A/G ratio. These results come in accordance with **(Muhammad et al. 2006) (Latif, 2010) (Javid et al. 2010) (Coskun et al. 2012) and (Ramesh et al. 2012).**

Albumin is one of the most important serum proteins produced in the liver. It represents 50 to 60% by weight of all plasma proteins. Recent evidence indicates that albumin may provide antioxidant protection by functioning as a serum peroxidase in the presence of reduced olutathione, which is an intracellular antioxidant (**Kuppamuthu et al. 2008) and (Hossain et al. 2018).**

In the present study, serum albumin levels were significantly decreased as compared to healthy controls. This result come in accordance with **Muhammad et al. (2006), Latif (2010), Coskun et al. (2012) and Ramesh et al. (2012).** The possible cause for the low albumin in pulmonary tuberculous animals and contact groups were considered to be nutritional factor enteropathy and acute phase reactions, The hepatic synthesis of acute phase proteins is induced by cytokines such as, interleukin and tumor necrosis factor which inhibit the production of serum albumin and cause dramatic shifts in the plasma concentration of certain essential micronutrients and albumin **(Kuppamuthu et al. 2008).** The significant increase in serum globulins in the infected and contact groups may be due to the stimulation of the immune system (especially gamma globulins) or induction against infection (**Braun et al. 2010**).

Tuberculosis is the chronic infectious disease affecting many organs, plasma hepatic enzyme activities increased when enzymes were released to blood circulation in case of necrosis, cell damage, tissue regeneration **(Madebo et al. 2003).**

Serum enzymes analysis revealed significant ($P<0.05$) increase in activities of alkaline phosphatase AST, ALT, creatinine phosphokinase, gamma-glutamyl transferase (GGT), and lactate dehydrogenase in infected and contact cattle in comparison with negative group. Similar findings were recorded by **(Madebo et al. 2003), (Narsimha et al. 2009) and (Coskun et al. (2012). (Cobben et al. 1999)** recorded that, cellular enzymes such as gamma-glutamyl transferase (GGT), lactate dehydrogenase (LDH), creatinine phosphokinase (CPR) and alkaline phosphatase (ALP) can be used as sensitive markers of cellular damage in organisms with pulmonary diseases. Also, These enzymes are usually increased in serum when hepatocytes or muscle cells have suffered cellular damage, these increases are usually associated with leakage from the cytoplasm of injured cells. The significant increase in the levels of transaminases could be due to process of necrosis or degeneration taking place in the body due to infection with tuberculosis (**Turk and Casteel 1997).**

CONCLUSION

Bovine tuberculosis poses a significant risk to human and animal health. The only way to be protected from the disease is through prevention. It is important to limit the exposure of

the herd to other infected cattle. Routine tuberculin testing has to be carried out, also oxidative and hemato- biochemical changes, which may indicate of tissue damage and might form an indicative basis for subsequent studies, and it should be used as a useful tool for diagnosis, prognosis, and evaluation of the control programs.

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