Kocatepe Veterinary Journal

Kocatepe Vet J. (2024) 17(1):55-61
DOI: 10.30607/kvj.1375796

RESEARCH ARTICLE

Determination of Malondialdehyde, Nitric Oxide, Reduced Glutathione, Sialic Acid and Ceruloplasmin Levels in Sheep Liver Tissue With Hydatic Cyst

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ABSTRACT

Cystic echinococcosis is a prevalent helminth-zoonosis that poses a significant threat to human and animal health worldwide. Although it typically shows an asymptomatic clinical course, it has been reported to cause many damages and biochemical changes in tissues and organism. The aim of this study was to investigate the concentrations of nitric oxide (NO), reduced glutathione (GSH), malondialdehyde (MDA), ceruloplasmin (Cp), and total sialic acid (TSA) in sheep liver tissue affected by cystic echinococcosis. The study was carried out on sheep between 4-5 years of age brought to the slaughterhouse in the Igdir territory. The livers were examined post-mortem for cystic echinococcosis and cystic structures. Sheep liver tissues that tested positive for protoscolex were designated as the 'infected group', while healthy sheep liver tissues without lesions were assigned to the 'control group'. The results showed significantly higher levels of NO, MDA, Cp and TSA in the infected group compared to the control group ($p<0.05$), while GSH levels were significantly lower ($p<0.05$). These findings indicate that cystic echinococcosis in sheep is closely associated with mechanisms of inflammation, oxidative stress, and tissue damage. Moreover, our study provides insights into the oxidative response of cystic echinococcosis in liver tissue and enhances our understanding of the disease's pathogenesis.

Keywords: Cystic Echinococcosis, Inflammation, Oxidative Stress, Sheep

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Hidatik Kistli Koyun Karaciğer Dokusunda Malondialdehit, Nitrik Oksit, İndirgenmiş Glutatyon, Sialik Asit ve Seruloplazmin Düzeylerinin Belirlenmesi

ÖZ

Kistik ekinokokkoz, dünya çapında insan ve hayvan sağlığına ciddi bir tehdit oluşturan yaygın bir helmint-zoonozdur. Genellikle semptomsuz bir klinik seyir göstermesine rağmen, birçok doku ve organizmada hasara ve biyokimyasal değişikliklere neden olduğu bildirilmiştir. Bu çalışmanın amacı, kistik ekinokokkoz etkisi altındaki koyun karaciğer dokusunda nitrik oksit (NO), indirgenmiş glutatyon (GSH), malondialdehit (MDA), seruloplazmin (Cp) ve toplam sialik asit (TSA) konsantrasyonlarını araştırmaktı. Çalışma, Iğdır bölgesinde kesimhaneye getirilen 4-5 yaş arası koyunlar üzerinde gerçekleştirildi. Karaciğerler, ölümden sonra kistik ekinokokkoz ve kistik yapılar için incelendi. Protoskol eksisi pozitif çıkan koyun karaciğer dokuları "enfekte grubu" olarak adlandırıldı, lezyon olmayan sağlıklı koyun karaciğer dokuları ise "kontrol grubu" olarak atanmıştır. Sonuçlar, enfekte grubun NO, MDA, Cp ve TSA seviyelerinin kontrol grubuna göre önemli ölçüde yüksek olduğunu gösterdi ($p<0.05$), buna karşın GSH seviyelerinin önemli ölçüde düşük olduğunu ortaya koydu ($p<0.05$). Bu bulgular, kistik ekinokokkozun koyunlarda iltihaplanma, oksidatif stres ve doku hasarı mekanizmalarıyla yakından ilişkili olduğunu göstermektedir. Ayrıca, çalışmamız kistik ekinokokkozun karaciğer dokusundaki oksidatif yanıtını anlamamıza ve hastalığın patogenezi hakkındaki anlayışımızı artırmamıza yardımcı olmaktadır.

Anahtar kelimeler: İnflamasyon, Kistik Ekinokokkozis, Oksidatif Stres, Koyun

To cite this article: Kiziltepe S. Okulmuş Ç. Merhan O. Mor N. Uzlu E. Determination of Malondialdehyde, Nitric Oxide, Reduced Glutathione, Sialic Acid and Ceruloplasmin Levels in Sheep Liver Tissue With Hydatic Cyst. Kocatepe Vet J. (2024) 17(1):55-61

Submission: : 16.10.2023 **Accepted:** 01.03.2024 **Published Online**: 06.03.2024

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INTRODUCTION

Echinococcus granulosus (E. granulosus) is a cestode parasite that primarily resides in the intestines of wolves, jackals, foxes, dogs, and cats. The parasite's eggs are excreted into the environment through the feces of infected carnivores (Craig et al. 2007). The main mode of transmission is the consumption of food contaminated with feces containing parasite eggs. Additionally, uncontrolled contact with contaminated items or intermediate hosts can also contribute to transmission. Upon oral ingestion, the eggs form oncospheres due to the action of stomach acid. These oncospheres then travel from the small intestine to the liver through the portal vein, where they invade and develop. Oncospheres that enter the circulation can also settle in various organs such as the brain, eyes, lungs, heart, kidneys, spleen, pleura, and bones. The clinical manifestation that occurs in the intermediate host organism, resulting from the growth of larvae derived from settled oncospheres in the intermediate host organs, is known as cystic echinococcosis (Mc. Manus et al. 2003; Oku et al. 2004; Craig et al. 2007; Ersayit et al. 2009).

Diagnosis of cystic echinococcosis typically involves the use of radiology, ultrasonography (USG), and serological methods. However, it can often be misdiagnosed as a tumor, abscess, or other types of cysts (Nart 2004; Şener et al. 2004; Özcel et al. 2007). In animals, the definitive diagnosis of cystic echinococcosis is often not cost-effective or practical. Generally, cystic echinococcosis is an asymptomatic disease in animals and is frequently detected during postmortem examinations in slaughterhouses. Despite being asymptomatic, cystic echinococcosis poses significant economic losses and health risks, making it a highly important parasitic disease (Gıcık et al. 2004; Latif et al. 2010; Demir and Mor 2011; Saadi et al. 2020).

Cystic echinococcosis is a prevalent helminth-zoonosis that poses a significant threat to human and animal health worldwide. In Turkey, factors such as extensive sheep farming, inadequate wildlife control, and insufficient implementation of control measures (such as parasitic spraying and breeder education) contribute to the high prevalence of cystic echinococcosis (Yıldız and Gürcan 2003; Gıcık et al. 2004).

In parasitic infestations, the disruption of the antioxidant defense balance leads to an increased production of reactive oxygen species, which can cause damage to host cells. Various studies investigating different parasitic agents have reported changes in antioxidant levels and the occurrence of oxidative stress during infestations. Lipid peroxidation (MDA) and other oxidative stress mechanisms (Cp, NO, TSA, and GSH) have been implicated in the pathogenesis of several parasitic diseases affecting animals (Sanchez-Campos et al. 1999; Kilic et al. 2003; Derda et al. 2004; Kolodziejczyk et al. 2006; Şimşek et al. 2006; Kaya et al. 2007; Gabrashanska et al. 2008; Saleh 2008; Saleh et al. 2009; Dimri et al. 2010; Heidarpour et al. 2012).

Numerous studies have documented the occurrence of oxidative stress in parasitic diseases (Boczon et al. 1996; Shousha et al. 1999; Sanchez-Campos et al. 1999; Derda et al. 2004; Şimşek et al. 2006; Saleh, 2008; Saleh et al. 2009; Dimri et al. 2010). Moreover, oxidative stress plays a significant role in the general pathogenesis of various liver diseases. Assessing oxidative damage in live animal liver tissue is challenging, which is why oxidative stress markers are often measured in blood and blood products in such diseases.

Several studies have been conducted to determine the antioxidant and oxidative stress markers in the blood of humans, cattle, sheep, and camels with cystic echinococcosis (Kilic et al. 2010; Heidarpour et al. 2012, Heidarpour et al. 2013 a, b; Mahmood et al. 2020). In contrast, some studies suggest that direct detection methods are more reliable for evaluating antioxidant status and oxidative stress (Fang et al. 2002; Değer et al. 2008; Aslam et al. 2023). However, there is a lack of reports on direct tissue analysis of oxidative stress and antioxidant defense systems specifically related to cystic echinococcosis in sheep.

In recent years, the veterinary field has seen increased investigation into oxidative stress parameters such as MDA, NO, and GSH, as well as acute phase proteins like TSA and Cp. However, there is still limited research on how these parameters change in parasitic conditions such as cystic echinococcosis, which continues to pose a risk in industrial livestock farming and has zoonotic implications. Therefore, the current study aims to investigate the levels of liver MDA, Cp, NO, TSA, and GSH in infected sheep, with the goal of assessing the oxidative response and providing insights into the pathogenesis of the disease.

MATERIALS AND METHODS

The study utilized liver samples obtained from between sheep 4-5 years of age brought to the slaughterhouse from sheep farms in the Iğdır territory. Prior to inclusion in the study, a comprehensive health examination was conducted on all sheep brought for slaughter. After slaughtering the animals, all organs were examined to identify hydatid cysts, and only sheep with liver cysts were included in the study. During sample collection, particular attention was given to ensuring that each liver had at least three cyst foci. The cyst contents of these samples were examined under a microscope for parasitological analysis, and a total of 40 sheep livers with positive protoscoleces (fertile cysts) were assigned to the experimental group. The control group consisted of 10 sheep livers that did not show any pathological lesions during general organ examinations and appeared healthy in the physical examination.

Tissue samples from the study group were taken from the cyst site and cyst membrane, measuring approximately 1 cm^3 in size. Tissue samples from the control group were obtained from the middle lobe of the liver, also measuring approximately 1 cm^3. All samples from both groups were stored at -20 °C for further analysis.

Homogenization of Liver Tissue

Tissue sample taken from liver were immediately fixed with PBS (7.4 pH) at +4 °C and homogenized at 290 g for 3 minutes with the help of a cooling homogenizer (Wiggen-Hauser D-500, Germany). During homogenization, the samples were kept in ice for 15-20 seconds once a minute to prevent heating. The homogenates were centrifuged for 15 minutes at 4 °C at 2400 rpm (Hermle Z 326 K, Germany), and the supernatants obtained were stored at -80 °C until analyzed.

Biochemical Analyses

The concentrations of nitric oxide (NO), reduced glutathione (GSH), malondialdehyde (MDA), ceruloplasmin (Cp) and total sialic acid (TSA), respectively, Miranda et al. (2001), Beutler et al. (1963), Yoshioka et al. (1979), Colombo and Richterich (1964) and Sydow et al. (1988) spectrophotometrically measured (Epoch®, Biotek, USA) according to the method reported.

Statistical Analysis

The data of the study were statistically evaluated using the SPSS 20.0 (SPSS Inch. Chicago, IL, USA) package program. Kolmogorov-Smirnov test was performed and it was determined that the groups showed normal distribution. Student's t test was used to compare groups.

RESULTS

Table 1 displays the levels of MDA, NO, GSH, Cp, and TSA obtained from sheep livers with hydatid cysts (Figure 1) and healthy sheep livers. In comparison to the control group, the infected group exhibited significantly higher levels of MDA, TSA, Cp, and NO, along with lower levels of GSH ($p<0.05$). The disparity between the measurements was particularly significant in the MDA and TSA parameters ($p<0.001$).

Table 1. Malondialdehyde (MDA), reduced glutathione (GSH), nitric oxide (NO), ceruloplasmin (Cp) and total sialic acid (TSA) levels in liver tissue.

Parameters	Control group	Infected group	P value
MDA (µmol.g−1 wet tissue)	0.61±0.14 ^{x}	2.28±0.24^{y}	p<0.001
TSA (mg.g^{-}−1 wet tissue)	0.83±0.12 ^{x}	1.34±0.08 ^{y}	p<0.001
Cp (mg.g−1 wet tissue)	0.27±0.11 ^{a}	0.73±0.09 ^{b}	p<0.05
NO (µmol.g^{-}−1 wet tissue)	0.83±0.05 ^{a}	1.29±0.09 ^{b}	p<0.05
Reduced GSH (µmol.g−1 wet tissue)	5.84±0.36 ^{a}	4.66±0.19 ^{b}	p<0.05

***** The difference between groups with different (a, b) signs in the same lines is significant ($p<0.05$).
**The difference between groups with different (x, y) signs in the same lines is significant ($p<0.001$).

Figure 1: Sheep liver samples with hydatid cyst after slaughter at the abattoir.

DISCUSSION

Cystic echinococcosis is a parasitic and zoonotic disease that exhibits a higher incidence in regions where traditional sheep breeding is common and rural populations are concentrated. Typically, cystic echinococcosis has an asymptomatic clinical course. Various studies have demonstrated that parasites can induce biochemical changes by damaging the tissues and organs they inhabit (Mert et al. 2003; Ayaz et al. 2006; Şahin and Akgül 2006).

One of the reactions observed in cellular damage caused by free radicals is lipid peroxidation in cell membranes. Elevated levels of MDA, an end product of lipid peroxidation, are considered an indicator of oxidative damage in multiple tissues and organs. Aslam et al. (2023) found significantly higher concentrations of MDA ($p<0.05$) in cystic echinococcosis cysts and infected buffalo liver tissues compared to uninfected liver tissues in their study. Similarly, in the present study, it is hypothesized that cystic echinococcosis cysts cause significant cellular damage in liver tissue due to their space-occupying effect and mechanical pressure. This damage is believed to be the underlying cause of the elevated MDA levels, which serve as a strong indicator of oxidative stress due to increased lipid peroxidation. In our study, infected sheep exhibited higher MDA levels compared to the control group. Moreover, it is worth noting that several studies conducted with humans, camels, cattle, and sheep infected with Echinococcus granulosus have also reported significantly higher MDA levels compared to healthy individuals, which supports the findings of our study (Heidarpour et al. 2012, 2013a; Merhan et al. 2017; Aslam et al. 2023).

Acute-phase proteins serve as clinically useful and convenient biochemical markers for disease diagnosis, treatment, and prognosis monitoring (Nakajima 1993; Mc Pearson 1996; Gruys et al. 1994; Floris et al. 2000; Bozukluhan et al. 2020). Additionally, sialic acid undergoes significant changes in diseases associated with tissue damage or inflammation, where the acute-phase response is stimulated. The level of sialic acid is considered an indicator of the acute-phase reaction due to its structural characteristics (Erdogan et al. 2008; Yarım et al. 2010). Studies have shown that serum TSA levels increase in buffalo and cattle naturally infected with cystic echinococcosis (Yarım et al. 2010; Mohammadpour et al. 2021). In our current study, we observed statistically significant elevation ($p<0.001$) in TSA concentrations in the cystic echinococcosis-infected group compared to the control group. We attribute this increase to the induced acute-phase reaction triggered by parasitic infection.

Peptide-structured glutathione (GSH), which can be synthesized in the liver, plays a crucial role in the antioxidant defense system that combats oxidative damage caused by free radicals and peroxidases (Karaman et al. 2008; Koltas et al. 2008). During parasitic infections, the glutathione system demonstrates its protective effect against the detrimental effects of lipid peroxidation by interacting with free radicals and peroxides (Dede et al. 2000; Değer et al. 2008). Previous studies conducted on cattle infested with Dictyocaulus viviparus (Değer et al. 2008), goats naturally infected with Haemonchus contortus (Rashid and Irshadullah 2019), and buffaloes infested with Fasciola gigantica (Rehman et al. 2021), as well as cystic echinococcosis-infected buffaloes (Kolodziejczyk et al. 2006), have reported a decrease in GSH concentration in serum or liver tissue examinations, highlighting the history of liver tissue damage in the pathogenesis. In our study, we also found lower liver tissue GSH concentrations ($p<0.05$) in the infected group compared to the control group, aligning with the findings of the aforementioned research. We believe that this observation is a result of the reaction occurring with the protective effect of GSH as an antioxidant in response to the oxidative stress induced by the damage to cells, tissues, and organs infested with cystic echinococcosis.

Ceruloplasmin (Cp) is another important acute-phase protein for sheep (Bozukluhan et al. 2018; Ulutaş et al. 2008). In certain infections, it has been reported to increase up to half of the normal value (Nispet et al. 2008). In addition to its acute-phase protein properties, Cp is involved in the transport of antioxidants and copper in the bloodstream (Ulutaş et al. 2008; Gökce and Bozukluhan 2009; Tuna and Ulutaş 2015). This characteristic makes it a potential diagnostic marker for diseases (Erkılıç et al. 2019; Kırmızıgül et al. 2020). In a study conducted by Nisbet et al. (2008) in cattle with cystic echinococcosis, they found that serum Cp levels were higher in the patient group compared to the group of healthy animals. Similarly, in a study by Eser et al. (2013) in individuals with pulmonary echinococcus (PE), they reported higher Cp values in the PE group compared to the healthy group. They also observed a significant decrease in Cp values in the PE group after surgical removal of the cysts, compared to the initial values obtained from the patients. In our study, the concentration of Cp in the cystic echinococcosis-infected group was found to be higher than in the control group ($p<0.05$). This elevation is likely attributed to the inflammatory changes associated with cystic echinococcosis.

CONCLUSION

In conclusion, the significant differences observed in MDA, NO, GSH, TSA and Cp levels in cystic echinococcosis-infected sheep liver tissues compared

to healthy sheep indicate the presence of significant oxidative stress in the livers of infected sheep. In addition, it is thought that direct measurement of these parameters from liver tissue may be a more reliable diagnostic method.

Conflict of interest: The authors have no conflicts of interest to report.

Authors' Contributions: SK and CO performed the research, OM, NM and CO analysed the data, SK, EU and CO designed the research study and wrote the paper.

Ethical Approval: This research was approved by The Ethics Committee of the Faculty of Veterinary Medicine, Kafkas University (KAU-HADYEK, Ref No: 2021/81, Tarih: 4/2021)

Financial Disclosure: No financial support was received in the preparation of this article.

REFERENCES

Aslam, H., Bi, S., Irshadullah, M. (2023). Analysis of antioxidant enzymes and oxidative stress markers in the liver of naturally infected Indian water buffalo (Bubalus bubalis) with cystic echinococcosis. Journal of Parasitic Diseases, 1-9. 47(2):340–348. https://doi.org/10.1007/s12639-023-01578-7

Ayaz, E., Ertekin, A., Ozdal, N., Tas, Z. (2006). Some Biochemical Parameters in Sheep Infected with Endoparasites (Fasciola spp. Dicrocoelium dendriticum, Hydatid cysts, Trichostrongylidae and Protostrongylidae). Turkiye Parazitol Derg, 30(4), 57-61.

Beutler, E., Duron, O., Kelly, B.M. (1963). Improved method for determination of blood glutathione. Journal of Laboratory and Clinical Medicine. 61, 882-888.

Boczon, K., Hadas, E., Wandurska-Nowak, E., Derda, M. (1996). A stimulation of antioxidants in muscles of Trichinella spiralis infected rats. Acta Parasitologica, 3(41).

Bozukluhan, K., Merhan, O., Gökçe, H. İ., Metin, Ö., Atakişi, E., Kızıltepe, Ş., Gökçe, G. (2018). Determination of some acute phase proteins, biochemical parameters and oxidative stress in sheep with naturally infected sheeppox virus. Kafkas Üniversitesi Veteriner Fakültesi Dergisi, 24(3),437-441. DOI : 10.9775/kvfd.2017.19167

Bozukluhan, K., Merhan, O., Kızıltepe, Ş., Harmankaya, A., Gökçe, G. (2020). Determination of oxidative stress and ceruloplasmin levels in sheep with toxoplasmosis. Van Veterinary Journal, 31(2). https://doi.org/10.36483/vanvetj.646976

Colombo, J., Richterich R. (1964). Zur Bestimmung Des ceruloplasmin in plasma. Schweiz Med Wschr, 94, 715-720.

Craigi, P.S., Mc. Manus, D.P., Lightowlers, M.W. et al. (2007). Prevention and control of cystic echinococcosis. Lancet Infect Disease, 7, 385-394. doi: 10.1016/S1473-3099(07)70134-2.

Dede, S., Değer, Y., Değer, S., Alkan, M. (2000). Bazı endoparazitlerle (Fasciola sp. + Trichostrongylidae sp. + Eimeria sp.) enfekte koyunlarda lipit peroksidasyonu ve antioksidan durumunun saptanması. Türkiye Parazitol Dergisi, 24(1), 190-193.

Deger, Y., Ertekin, A., Deger, S., Mert, H. (2008). Lipid peroxidation and antioxidant potential of sheep liver infected naturally with distomatosis. Turkiye Parazitol Derg, 32, 23–26.

Değer, S., Değer, Y., Ertekin, A., Gül, A., Biçek, K., Özdal, N. (2008). Dictyocaulus viviparus ile enfekte sığırlarda lipit peroksidasyon ve antioksidan durumunun saptanması. Türkiye Parazitol Dergisi, 32(3), 234-237.

Demir, P., Mor, N. (2011). Kars Belediye Mezbahasında Kesilen Sığırlarda Kistik Echinococcosis' in Yaygınlığı, Mevsimsel Dağılımı ve Ekonomik Önemi. Turkiye Parazitol Dergisi, 35, 185-188.

Derda, M., Wandurska-Nowak, E., Hadas, E. (2004). Changes in the level of antioxidants in the blood from mice infected with Trichinella spiralis. Parasitol. Research, 93, 207–210. DOI 10.1007/s00436-004-1093-9

Dimri, U., Sharma, M.C. Yamdagni, A., Ranjan, R., Zama, M. M. S. (2010). Psoroptic mange infestation increases oxidative stress and decreases antioxidant status in sheep. Veterinary Parasitology, 168, 318–322. https://doi.org/10.1016/j.vetpar.2009.11.013

Erdogan, H. M., Karapehlivan, M., Citil, M., Atakisi, O., Uzlu, E., Unver, A. (2008). Serum sialic acid and oxidative stress parameters changes in cattle with leptospirosis. Veterinary Research Communications, 32, 333-339. DOI 10.1007/s11259-008-9036-z

Erkılıç, E., Merhan, O., Kirmizigul, A., Ogun, M., Akyuz, E., Citil, M. (2019). Salivary and serum levels of serum amyloid a, haptoglobin, ceruloplasmin and albumin in neonatal calves with diarrhoea. Kafkas Universitesi Veteriner Fakultesi Dergisi, 25(4). DOI: 10.9775/kvfd.2018.21424

Ersayit, D., Kilic, E., Yazar, S., Artis, T. (2009). Oxidative stress in patients with cystic echinococcosis: relationship between oxidant and antioxidant parameters. Saglık Bilimleri Dergisi, 18, 159-166.

Eser, İ., Ulaş, T., Kürkçüoğlu, İ. C., Aydoğan, H., Sak, Z. H. A., Aydın, M. S, Aksoy, N. at al. (2013). Evaluation of ceruloplasmin levels in patients with pulmonary cystic echinococcus. Clin Ter, 164(2), e89-92. doi: 10.7417/CT.2013.1537. doi: 10.7417/CT.2013.1537

Fang, Y.Z., Yang, S., Wu, G. (2002). Free radicals, antioxidants, and nutrition. Nutrition, 18, 872–879. https://doi.org/10.1016/s0899-9007(02)00916-4

Floris, G., Medda, R., Padiglia, A., Musci, G. (2000). The physiopathological significance of ceruloplasmin: a possible therapeutic approach. Biochem Pharmacol, 60(12), 1735-1741. https://doi.org/10.1016/S0006-2952(00)00399-3

Gabrashanska, M., Teodorova, S.E., Anisimova, M. (2008). Oxidative-antioxidant status of Fasciola hepatica-infected rats supplemented with zinc. A mathematical model for zinc bioaccumulation and host growth. Parasitol Research, 104, 69–78. DOI 10.1007/s00436-008-1160-8

Gıcık, Y., Arslan, M. Ö., Kara, M., Köse, M. (2004). Kars ilinde kesilen sığır ve koyunlarda kistik ekinokokkozisin yaygınlığı. Türkiye Parazitoloji Dergisi, 28(3), 136-139.

Gökce, H. İ., Bozukluhan, K., (2009). Çiftlik hayvanlarında önemli akut faz proteinleri ve bunların veteriner hekimlik alanındaki kullanımı. Dicle Üniversitesi Veteriner Fakültesi Dergisi, (1), 1-14.

Gruys, E., Oblowo, M.J., Toussaint, J. (1994). Diagnosis significance of major acute phase proteins in veterinary clinical chemistry: A review. Vet Bull, 11, 1009-1015.

Heidarpour, M., Mohri, M., Borji, H., Moghadas, E. (2013a). Oxidant/antioxidant balance and trace elements status in sheep with liver cystic echinococcosis. Comparative Clinical Pathology, 22, 1043–1049. DOI 10.1007/s00580-012-1523-5

Heidarpour, M., Mohri, M., Borji, H., Moghdass, E. (2012). Oxidative stress and trace elements in camel (Camelus dromedarius) with liver cystic echinococcosis. Veterinary Parasitology, 187, 459–463. doi: 10.1016/j.vetpar.2012.01.015

Heidarpour, M., Mohri, M., Borji, H., Moghdass, E. (2013b). Oxidant/antioxidant status in cattle with liver cystic echinococcosis. Vet Parasitol, 195, 131–135. doi: 10.1016/j.vetpar.2013.01.018.

Karaman, U., Celik, T., Kiran, T. R., Colak, C., Daldal, N. U., (2008). Malondialdehyde, glutathione, and nitric oxide levels in Toxoplasma gondii seropositive patients. The Korean Journal of Parasitology, 46(4), 293. DOI: 10.3347/kjp.2008.46.4.293

Kaya, S., Sutcu, R., Cetin, E.S., Arıdogan, B.C., Delibas, N., Demirci, M. (2007). Lipid peroxidation level and antioxidant enzyme activities in the blood of patients with acute and chronic fascioliasis. International Journal of Infectious Diseases: Home Page, 11, 251–255. DOI: 10.1016/j.ijid.2006.05.003

Kilic, E., Yazar, S., Baskol, G., Artis, T., Ersayit, D., (2010). Antioxidant and nitric oxide status in patients diagnosed with Echinococcus granulosus. African Journal of Microbiology Research, 4(22), 2439-2443.

Kilic, E., Yazar, S., Saraymen, R., Ozbilge, H. (2003). Serum malondialdehyde level in patients infected with Ascaris lumbricoides. World Journal of Gastroenterology, 9(10), 2332-2334. doi: 10.3748/wjg.v9.i10.2332

Kırmızıgül, A. H., Erkılıç, E. E., Merhan, O., Öğün, M., Ölmez, N., Taşçi, G. T., Vatansever, Z. (2020). The serum amyloid-a, haptoglobin, ceruloplasmin and albumin levels in dogs which are infected with Babesia canis. Kocatepe Veterinary Journal, 13(2), 219-223. DOI: 10.30607/kvj.670744

Kolodziejczyk, L., Siemieniuk, E., Skrzydlewska, E. (2006). Fasciola hepatica: effects on the antioxidative properties and lipid peroxidation of rat serum. Experimental Parasitology, 113, 43–48. https://doi.org/10.1016/j.exppara.2005.12.005

Koltas, I.S., Yucebilgic, G., Biligin, R., Parsak, C.K., Sakman, G. (2006). Serum malondialdehyde level in patients with cystic echinococcosis. Saudi Medical Journal, 27, 1703–1705. PMID: 17106545

Latif, A.A., Tanveer, A., Maqbool, A., Siddiqi, N., Kyaw-Tanner, M., Traub, R.J. (2010). Morphological and molecular characterisation of Echinococcus granulosus in livestock and humans in Punjab, Pakistan. Veterinary parasitology, 170(1-2), 44-49. DOI: 10.1016/j.vetpar.2010.02.003

Mahmood, E. A. K., Handan, M., Nihat, M. (2020). Determination of Oxidant/Antioxidant Levels in Sheep with Hydatite Cyst in Liver. Indian Journal of Forensic Medicine & Toxicology, 14(2), 1235-1238. https://doi.org/10.37506/ijfmt.v14i2.3075

McManus, D.P., Zhang, W., Li, J., Bartley, P.B. (2003). Echinococcosis. Lancet, 362, 1295–1304. DOI: 10.1016/S0140-6736(03)14573-4

McPearson, R. (1996). Clinical Diagnosis and Management by Laboratory Methods. In: Henry JB, W.B. Saunders Company Philadelphia, 237-257.

Merhan O., Bozukluhan K., Gokce H.I. (2017). Acute phase proteins and biochemical and oxidative stress parameters in Hypoderma spp. infested cattle. Journal of the Hellenic Veterinary Medical Society, 68(4), 535-540. https://doi.org/10.12681/jhvms.16049

Mert, N., Kozat, S., Ekin, S., Gunduz, H., Denizhan, V. (2003). Doğal kronik Fasciolasisli koyunlarda serum sialik asit ve serum lipid-bağlı sialik asit düzeyleri. 13. Ulusal Parazitoloji Kongresi, 8-12 Eylül 2003, Konya, Turkey.

Miranda, K.M. ,Espey, M.G., Wink, D.A. (2001). A rapid, simple spectrophotometric method for simultaneous detection of nitrate and nitrite. Nitric Oxide, 5(1), 62-71. DOI: 10.1006/niox.2000.0319

Mohammadpour, O., Rasouli, S., Azimzadeh, K., Salarpour, M., Narouie, A. (2021). Evaluation of plasma changes of hepcidin, total sialic acid and sphingosine 1 phosphate in buffaloes with hepatic hydatidosis. Journal of Basic and Clinical Veterinary Medicine, 2(1), 32-37.

Nakajima, Y., Momotani, E., Murakami, T., Ishikawa, Y., Morimatsu, M., Saito, M., Suzuki, H., Yasukawa, K. (1993). Induction of acute phase protein by recombinant human interleukin-6 (IL-6) in calves. Vet Immunol Immunopathol, 35, 385-391. https://doi.org/10.1016/0165-2427(93)90047-8

Nart, D. (2004). Cystic ve alveolar echinococcosis patogenezi. In: Altıntas N, Tınar R, Çoker A. (Eds.), Echinococcosis. Hidatitoloji Dern Yay 1, 149–158.

Nisbet, C., Çenesiz, S., Açıcı, M., Umur, Ş. (2008). Kistik ekinokokkozisli sığırlarda serum malondialdehit, seruloplazmin ve adenozin deaminaz düzeylerinin belirlenmesi. Erciyes Üniversitesi Veteriner Fakültesi Dergisi, 5(1), 1-5.

Oku, Y., Malgor, R., Benavidez, U., Carmona, C., Kamiya, H. (2004). Control program against hydatidosis and the decreased prevalence in Uruguay. International Congress Series, 1267, 98-104. https://doi.org/10.1016/j.ics.2004.01.087

Özcel, A., İnci, A., Turgay, N., Köroğlu, E. (2007). Tıbbi ve Veteriner İmmunoparazitolojisi. Kistik Ekinokokkozis ve İmmunolojisi. Altıntaş N, Yolasığmaz A, Türkiye Parazitoloji derneği yayınları, 259.

Rashid S, Irshadullah M (2019). Evaluation of antioxidant and oxidant status of goats (Capra aegagrus hircus) naturally infected with Haemonchus contortus. Journal Helminthology, 94, 36. DOI: https://doi.org/10.1017/S0022149X19000117

Rehman, A., Rehman, L., Ullah, R., Beg, M. A., Khan, M. H., Abidi, S. M. A. (2021). Oxidative status and changes in the adenosine deaminase activity in experimental host infected with tropical liver fluke, Fasciola gigantica. Acta Tropica, 213, 105753. https://doi.org/10.1016/j.actatropica.2020.105753

Saadi, A., Amarir, F., Filali, H., Thys, S., Rhalem, A., Kirschvink, N., Raes, M., Marcotty, T., Oukessou, M., Duchateau, L., Sahibi, H. (2020). The socio-economic burden of cystic echinococcosis in Morocco: a combination of estimation method. PLoS Negl Trop Dis, 14, e0008410. https://doi.org/10.1371/journal.pntd.0008410

Saleh MA. (2008). Circulating oxidative stress status in desert sheep naturally infected with Fasciola hepatica. Veterinary Parasitology, 154, 262–269. https://doi.org/10.1016/j.vetpar.2008.03.012

Saleh, M. A., Al-Salahy, M. B., Sanousi, S. A. (2009). Oxidative stress in blood of camels (Camelus dromedaries) naturally infected with Trypanosoma evansi. Veterinary Parasitology, 162, 192–199. https://doi.org/10.1016/j.vetpar.2009.03.035

Sanchez-Campos, S., Tunon, M. J., Gonzales, P., Gonzales-Gallego, J. (1999). Oxidative stress and changes in liver antioxidant enzymes induced by experimental dicrocoeliosis in hamsters. Parasitology Research, 85, 468–474.

Shousha, S. A., Khalil, S. S., Rashwan, E. A. (1999). Oxygen free radical and nitric oxide production in single or combined human schistosomiasis and fascioliasis. Journal of the Egyptian Society of Parasitology, 29(1).

Sydow, G., Wittmann, W., Bender, E., Starick, E. (1988). The sialic acid content of the serum of cattle infected with bovine leukosis virus. Arch Exp Veterinarmed journal articles from PubMed, 42, 194-197.

Şahin, T., Akgul, Y. (2006). Investigation of Some Trace Element Levels and Biochemical Parameters in Sheep with Endoparasite. YYÜ Sağlık Bilimleri Dergisi, 9(1), 100-106.

Şener, S., Yazar, S., Şahin, İ. (2004). Cystic Echinococcosis'in indirekt fluoresan antikor testi (IFAT) ile tanısında kullanılan antijenlerin tanı değerlerinin araştırılması. Erciyes Üniversitesi Sağlık Bilimleri Dergisi, 13(1), 1-6.

Şimşek, S., Yüce, A., Ütük, A. E. (2006). Determination of serum malondialdehyde levels in sheep naturally infected

with Dicrocoelium dendriticum. FU Saglık Bil Dergisi, 20(3), 217-220.

Tuna, G. E., Ulutaş, B. (2015). Hastalıkların biyobelirteçleri olarak akut faz proteinleri. Türkiye Klinikleri J Vet Sci Intern Med-Special Topics, 1(1), 8-19.

Ulutaş, P.A., Voyvoda, H., Ulutaş, B., Aypak S. (2008). Miks helmint infeksiyonlu keçilerde haptoglobin, serum amyloid A ve seruloplazmin konsantrasyonları. Türkiye Parazitololoji Dergisi, 32 (3), 229-233.

Ulutaş, B., Bayramlı, G., Ulutaş, P. A., Karagenc, T. (2005). Serum concentration of some acute phase proteins in naturally occurring canine babesiosis: preliminary studies. Veterinary Clinical Pathology, 34, 144-147. https://doi.org/10.1111/j.1939-165X.2005.tb00028.x

Yarım, G. F., Şinasi, U., Açıcı, M., Beyhan, Y. E. (2010). Kistik ekinokokozisli sığırlarda serum sialik asit düzeyleri. Ankara Üniversitesi Veteriner Fakültesi Dergisi, 57(1), 61-63. https://doi.org/10.1501/Vetfak_0000002311

Yıldız, K., Gürcan, S. (2003). Prevalence of Hydatidosis and fertility of Hydatid cysts in sheep in Kırıkkale, Turkey. Acta Veterinaria Hungarica, 51, 181-187. https://doi.org/10.1556/avet.51.2003.2.6

Yoshioka, T., Kawada, K., Shimada, T., Mori, M.(1979). Lipid peroxidation in maternal and cord blood and protective mechanism aganist activated-oxygen toxicity in the blood. American Journal of Obstetrics & Gynecology: Home Page, 135(3), 372-376. https://doi.org/10.1016/0002-9378(79)90708-7