

1-1-2003

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### Recommended Citation

SEVİNÇ, MUTLU; BAŞOĞLU, ABDULLAH; GÜZELBEKTAŞ, HASAN; and BOYDAK, MURAT (2003) "Lipid and Lipoprotein Levels in Dairy Cows with Fatty Liver," *Turkish Journal of Veterinary & Animal Sciences*: Vol. 27: No. 2, Article 2. Available at: <https://journals.tubitak.gov.tr/veterinary/vol27/iss2/2>

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## Lipid and Lipoprotein Levels in Dairy Cows with Fatty Liver

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Received: 30.11.2000

**Abstract:** The purpose of this investigation was to establish whether there were any differences in the lipid and lipoprotein levels of dairy cows with fatty liver. Fifty-four dairy cows with fatty liver and 12 healthy dairy cows were used in the study. The liver fat content was determined in all cows histologically. Cows with fatty liver (n = 54) were grouped according to liver fat content as cows with mild (n = 17), moderate (n = 17) or severe (n = 20) fatty liver. Fat infiltration in the liver was not observed in the healthy group of cows. Some serum chemical parameters including albumin, triglyceride, total cholesterol, high-density lipoprotein, and low-density lipoprotein levels were measured in all the cows. Very low-density lipoprotein levels were calculated by the following formula: triglyceride/5. There was a significant decrease (p = 0.000; p = 0.005; p = 0.011, respectively) in albumin, total cholesterol and low-density lipoprotein levels in cows with moderate and severe fatty liver, while triglyceride and very low-density lipoprotein levels were significantly lower (p = 0.000) in all the fatty liver groups. High-density lipoprotein levels were significantly lower (p = 0.028) in cows with moderate fatty liver. There was a significant negative correlation between the degree of fat infiltration and other parameters except for high-density lipoproteins. In conclusion, notable changes in lipid and lipoprotein levels were determined in cows with moderate and severe fatty liver.

**Key Word:** Lipid, lipoprotein, fatty liver, dairy cows

### Karaciğer Yağlanmalı Sütçü Sığırlarda Lipid ve Lipoprotein Düzeyleri

**Özet:** Bu çalışma, karaciğer yağlanmalı sütçü sığırlarda lipid ve lipoprotein düzeylerinde meydana gelen değişiklikleri belirlemek amacıyla yapıldı. Materyal olarak 54 baş karaciğer yağlanmalı sütçü sığır ve 12 baş sağlıklı sütçü sığır kullanıldı. Tüm sığırlarda, karaciğerdeki yağlanma yüzdeleri histolojik olarak belirlendi. Karaciğer yağlanması tespit edilen sığırlar, karaciğerlerindeki yağlanma yüzdelerine göre hafif (n = 17), orta (n = 17) ve şiddetli (n = 20) derecede karaciğer yağlanması olarak gruplandırıldı. Kontrol grubu olarak seçilen sığırların ise, karaciğerlerinde yağlanmaya rastlanılmadı. Araştırmadaki tüm sığırların serumlarında albumin, total kolesterol, trigliserid, yüksek dansiteli lipoprotein ve düşük dansiteli lipoprotein düzeyleri ölçüldü. Çok düşük dansiteli lipoprotein düzeyi ise, trigliserid/5 formülüne göre hesaplandı. Karaciğer yağlanması tespit edilen tüm gruplardaki trigliserid ve çok düşük dansiteli lipoprotein düzeyleri önemli derecede düşük bulunurken (p = 0.000), albumin, total kolesterol ve düşük dansiteli lipoprotein düzeyleri orta ve şiddetli derecede karaciğer yağlanması tespit edilen gruplarda önemli derecede düşük (sırasıyla p = 0.000, P = 0.005, p = 0.011) bulundu. Yüksek dansiteli lipoprotein düzeyi ise, sadece orta derece karaciğer yağlanması tespit edilen grupta düşük (p = 0.028) bulundu. Yüksek dansiteli lipoprotein fraksiyonu hariç, diğer tüm parametreler ile karaciğer yağlanma yüzdesi arasında negatif bir korelasyon belirlendi. Sonuç olarak orta ve şiddetli derecede karaciğer yağlanmalı sığırların lipid ve lipoprotein düzeylerinde önemli değişiklikler kaydedildi.

**Anahtar Sözcükler:** Lipid, lipoprotein, karaciğer yağlanması, sütçü sığır

### Introduction

Fatty liver is a frequent disorder in high-producing dairy cows during early lactation and is characterised by progressive depression and failure to respond to treatment. It is associated with excessive mobilisation of fat to the liver in obese/well conditioned cows. This mobilisation of fat is induced by the negative energy balance that occurs during the periparturient period (1-5).

Fat is stored as triglycerides and from deposits it is transported as free fatty acids bound to albumin. A considerable part of these acids is taken up by the liver. There they can be oxidised to CO<sub>2</sub> or to ketone bodies, or esterified and combined with phospholipids, cholesterol and apoproteins to form lipoproteins, especially very low density lipoproteins (VLDL) (6-9). This lipoprotein fraction transports triglycerides to different organs and tissues. After the loss of triglycerides, low density

lipoproteins (LDL) are formed and after further metabolism high density lipoproteins (HDL) are also formed (8-10).

The diagnosis of fatty infiltration of the liver in dairy cattle is presently based mostly on biochemical analysis, biopsy and histological analysis of hepatic tissue. Biochemical analysis had a relatively high negative predictive value but low positive predictive value with the increasing severity of fatty infiltration (11-15). Abnormal lipid and lipoprotein concentrations are often associated with liver disorders and the determinations of plasma or serum lipoproteins in dairy cows seem to be of interest both in understanding the pathogenesis of fatty liver syndrome and for diagnosis purposes (8,9,12,16).

The objective of the present study was to provide a unique insight into changes in lipid and lipoprotein levels in dairy cows with fatty liver.

## Materials and Methods

### Animals

Fifty-four Holstein dairy cows with fatty liver in early lactation (1-6 weeks postpartum; mean age  $6.1 \pm 1.2$  y) and 12 healthy Holstein dairy cows selected as a control group in the same period were used in this study. All the cows were multiparous and in early lactation. Cows with fatty liver and the controls were selected after clinical examination and liver biopsy. The cows were split into groups according to their percentage of fat in the liver.

### Blood Sampling and Serum Analysis

Blood samples were taken from the jugular vein just before the liver biopsies were obtained. Serum was analysed for triglyceride (TG), total cholesterol (T.Chol), HDL, LDL and albumin. The analyses were performed on an automated analyser (Olympus AU 5200) using commercial test kits (Olympus Diagnostica GmbH) and VLDL levels were calculated by the following formula:  $\text{triglyceride}/5$  (17).

### Liver Biopsy

Liver biopsies were performed in the right, 11<sup>th</sup> to 12<sup>th</sup> intercostal space (18). Liver samples were put in Baker's formol-Ca solution and fixed for 16 h (19). Thin sections (12  $\mu\text{m}$ ) were cut from each sample and stained with Oil Red O and Sudan Black B. The sections were examined under light microscopy. The percentage volume

of visible fat in hepatic parenchymal cells was estimated by the sterological point counting method (20). Five fields were examined at  $\times 1000$  from each animal using the oil immersion lens of a light microscope and a 100-point eyepiece granule. The average volume fraction of liver cell parenchymal occupied by an Oil-Red O positive droplet was recorded. The percent of fat infiltration with less than  $10 \mu\text{m}^2/100 \mu\text{m}^2$  was considered mild, and those with 10 to  $20 \mu\text{m}^2/100 \mu\text{m}^2$  moderate, while those with over  $20 \mu\text{m}^2/100 \mu\text{m}^2$  were designated as having severe fatty liver (21).

### Statistical Analysis

ANOVA test and Duncan's multiple range test were used to evaluate differences between the groups and levels of significance. (SPSS 8.0 for Windows).

## Results

Histological examination of liver biopsies in cows revealed in 17 cases mild, in 17 moderate and in 20 cows severe fatty liver. The mean percentage of fat in the liver was  $43.2 \pm 3.5\%$  (range from 28% to 67%), and  $15.2 \pm 0.6\%$  (range from 11% to 19%), and  $6.2 \pm 2\%$  (range from 3% to 9%) in cows with severe, moderate and mild fatty liver, respectively. Fat infiltration in the liver was not observed in the healthy group of cows. The cows with severe fatty liver showed typical signs of anorexia, depression, weakness, a marked decrease in milk production and progressive debilitation. The clinical signs in cows with mild and moderate fatty liver were non-specific, such as anorexia or a decrease in milk production.

There was a significant decrease ( $p = 0.000$ ) in the albumin levels of cows with moderate and severe fatty liver compared with those of the control and mild fatty liver groups. Albumin levels were also significantly different between the moderate and severe fatty liver groups. Total cholesterol levels were significantly lower ( $p = 0.005$ ) in cows with moderate and severe fatty liver than in the control group. Triglyceride and VLDL levels in all fatty liver groups were significantly lower ( $p = 0.000$ ) than in the controls. Also those with moderate and severe fatty liver were significantly lower than mild fatty liver group. The LDL level in moderate and severe fatty liver groups was significantly lower ( $p = 0.011$ ) than in the control and mild fatty liver groups. The level of the HDL in cows with moderate fatty liver was significantly lower

( $p = 0.028$ ) when compared with the control and mild fatty liver groups (Table 1).

There was a significant negative correlation between the degree of fat infiltration and the parameters, except for HDL (Table 2).

## Discussion

The present study describes the serum lipid and lipoprotein fraction changes which take place simultaneously in the liver during fatty liver and the correlation between them.

The clinical findings observed in cows with fatty liver agreed with those published previously on the illness (15,22-25).

In ruminants almost no plasma lipids arise from ingested fat. Most of them are the result of de novo synthesis. Fat is stored as triglycerides and from the deposits it is transported as free fatty acids bound to albumin (8). Albumin is indicative of the liver's synthetic function (15). Hepatic function can be severely impaired by fatty infiltration of the liver. One of the many results of this impairment of liver function is a drop in serum

albumin levels (26). Hypoalbuminaemia is a common terminal feature of chronic liver disease, occurring when the functional hepatic mass has been reduced to 20% or less (27). The same author reported that albumin level was lower in cows with liver failure than in cows with fatty liver. According to West (15) there is a negative correlation between the degree of fatty changes and albumin levels in dairy cows. In the present study, the albumin level was significantly decreased in cows with moderate and severe fatty liver than those cows in the control and mild fatty liver groups, and there was also a significant difference between the moderate and severe fatty liver groups. Thus albumin levels may be associated with hepatic function impairment.

High serum free fatty acid concentrations and low serum triglyceride and cholesterol concentrations have been observed in cattle with fatty liver (16,22-24). Başoğlu et al. (12) showed that triglyceride levels were decreased in normal cattle after calving. In the present study, triglyceride levels were significantly decreased in all fatty liver groups of cows and the cholesterol levels in cows with moderate and severe fatty liver were also lower. There was a significant negative correlation between the parameters above and fatty liver. Low

Table 1. Results of chemical parameters (mean  $\pm$  SEM) in dairy cows with mild, moderate and severe fatty liver.

Parameters	Control (n:12)	Fatty Liver			P
		Mild (n: 17)	Moderate (n:17)	Severe (n: 20)	
Albumin (g/dl)	3.40 $\pm$ 0.07 <sup>a</sup>	3.25 $\pm$ 0.05 <sup>a</sup>	2.68 $\pm$ 0.08	2.1 $\pm$ 0.09	0.000
T.hol (mg/dl)	150.08 $\pm$ 9.29 <sup>a</sup>	127.12 $\pm$ 8.20 <sup>ab</sup>	107.18 $\pm$ 9.249 <sup>b</sup>	110.15 $\pm$ 7.21 <sup>b</sup>	0.005
TG (mg/dl)	25.66 $\pm$ 1.01 <sup>a</sup>	20.11 $\pm$ 1.02 <sup>b</sup>	16.76 $\pm$ 1.51 <sup>c</sup>	13.80 $\pm$ 0.89 <sup>c</sup>	0.000
VLDL (mg/dl)	5.10 $\pm$ 0.20 <sup>a</sup>	4.02 $\pm$ 0.20 <sup>b</sup>	3.11 $\pm$ 0.28 <sup>c</sup>	2.76 $\pm$ 0.17 <sup>c</sup>	0.000
LDL (mg/dl)	39.32 $\pm$ 7.05 <sup>a</sup>	38.65 $\pm$ 6.65 <sup>a</sup>	27.12 $\pm$ 4.38 <sup>b</sup>	19.05 $\pm$ 2.15 <sup>b</sup>	0.011
HDL (mg/dl)	97.91 $\pm$ 4.26 <sup>a</sup>	87.52 $\pm$ 10.36 <sup>a</sup>	75.64 $\pm$ 5.42 <sup>b</sup>	84.35 $\pm$ 4.80 <sup>ab</sup>	0.028

<sup>abc</sup> means with different superscripts within one row differ significantly ( $p < 0.05$ )

Table 2. Pearson's correlation coefficient (r) and level of significance between liver fat and clinical parameters.

	Albumin		T.Chol		HDL		LDL		TG		VLDL	
	r	p	r	P	r	p	r	p	r	p	r	p
Liver Fat %	-0.80	0.000	-0.26	0.034	-0.20	0.107	-0.35	0.004	-0.51	0.000	-0.51	0.000

triglyceride and cholesterol levels can be thought to be caused by an influx of free fatty acids from adipose tissues near the time of parturition and a low output of lipoprotein by the liver.

Lipoproteins are complex molecules that are heterogeneous in composition, size and biological activity. In early lactation in cows with a severe negative energy balance, the capacity of the liver to maintain the export of triglyceride in the form VLDL in balance with hepatic triglyceride production is not always adequate (8,28,29). Rayssiguier et al. (9) found that the VLDL level was extremely low two weeks after calving in cows with fatty liver. Başoğlu et al. (12) showed that it was significantly decreased in postpartum cows. In the present study, there was a significant decrease in the VLDL level of all fatty liver group cows compared with those cows in the control group. There was also a negative correlation between the VLDL level and fatty liver. This may show that a major factor contributing to the development of fatty liver is the chronic slow output of hepatic triglyceride, which forms part of the VLDL. Other studies have already noted that the accumulation of fat in the liver cells and development of fatty liver is caused by a reduced synthesis of VLDL (8,9,12,16,29). Reduced VLDL synthesis is most probably associated with feeding factors (8). The decrease in LDL is especially pronounced in cows with severe fatty liver. During the same period, animals in the moderate fatty liver group were no

different from the controls regards LDL levels. In contrast, by the fourth week animals with moderate fatty liver have an LDL fraction that is significantly lower than controls (9,16). The present study showed that there was a significant decrease in the LDL level in cows with moderate and severe fatty liver. Decreased LDL concentrations in the serum of cows with moderate and severe fatty liver could result from several mechanisms including decreased VLDL secretion, and decreased conversion of VLDL to LDL. The fact that LDL originates from VLDL is well established. Another explanation for the LDL decrease would be that VLDL transformation into LDL was reduced or that the LDL catabolism was increased (9). According to Rayssiguier et al. (9), animals with moderate steatosis have significantly lower values of HDL than control animals. Severe steatosis was associated with smaller changes in HDL concentration. Sevinç et al. (16) reported that HDL levels were significantly reduced in ketotic cows with fatty liver. In the present study, the HDL level was significantly decreased in the moderate fatty liver group in accordance with Rayssiguier et al. (9). This decreased level of HDL may be related to the lower cholesterol level in cows with moderate fatty liver, because HDL consists of about 60% cholesterol.

In conclusion, the results indicate notable changes in lipid and lipoprotein fractions in cows with moderate and severe fatty liver which might be useful for diagnostic purposes.

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