Hyperlipemia in a Population of Aged Donkeys: Description, Prevalence, and Potential Risk Factors

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Background: Hyperlipemia is a common disorder of the donkey, with mortality rates of up to 80% reported. Such a poor prognosis makes prevention of this disorder or amelioration in the early stages crucial.

Objectives: The objective of this study was to describe and determine the prevalence of hyperlipemia in a population of donkeys and to determine risk factors for development of the disease.

Animals: A total of 449 cases were investigated from a population of 3829 donkeys; donkeys were resident at The Donkey Sanctuary, a charity providing refuge for unwanted donkeys in the UK. Animals were selected on the basis of presence of clinical disease.

Methods: A retrospective case—control study design was used, and all donkeys presenting with hyperlipemia over a 4-year period were included. Each case was matched with 2 controls that had not suffered from hyperlipemia in the previous month. Multivariable analysis was carried out to determine risk factors.

Results: A total of 449 clinical cases of hyperlipemia were reported with an associated mortality rate of 48.5%. Concurrent disease was present in 72% of donkeys and was the greatest risk factor (OR = 76.98); others included cardboard bedding (OR = 3.86), movement (OR = 3.94), weight loss (OR = 6.4), dental disease (OR = 1.73), and concentrate feeding (OR = 1.87).

Conclusions: This study shows that this population of donkeys in the UK often develops hyperlipemia, particularly in response to stress or primary illness, and provides useful insights in to health and management risk factors that may be addressed to decrease the risk of hyperlipemia both in the study population and in other similar donkey populations.

Key words: Equine; Hyperlipemic; Hypertriglyceridemia.

Hyperlipemia is a common disorder of the donkey and is characterized by increased plasma triglyceride concentrations (>4.4 mmol/L) and subsequent infiltration of organs by fat. This disorder arises from an imbalance in lipid metabolism resulting from mobilization of body fat in response to negative energy balance. During fasting or negative energy balance, the activity of hormone-sensitive lipase is increased (mobilizing fat), and insulin concentrations are decreased (decreasing esterification) resulting in very high concentrations of free fatty acids (FFAs) circulating in the bloodstream.² The liver subsequently re-esterifies the FFAs to triglycerides and very low density lipoproteins (VLDL) and releases them into the bloodstream leading to hyperlipidemia and potentially hyperlipemia. Increased production of VLDL rather than decreased clearance of VLDL from the serum results in hyperlipemia.² If this process continues, fatty infiltration of the liver results in eventual liver failure.^{3,4}

Donkeys and small ponies are at greatest risk of hyperlipemia, with a prevalence of 3–5% in the general population and 11–18% in inpatient populations in veterinary hospitals.⁵ Previous studies have determined risk factors for the disease in populations of equids

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Submitted February 9, 2011; Revised July 29, 2011; Accepted August 12, 2011.

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10.1111/j.1939-1676.2011.00798.x

Abbreviations:

FFA free fatty acids
OR odds ratio

VLDL very low density lipoproteins

and have shown obesity, pregnancy, stress, and concurrent diseases to be important predisposing or precipitating factors for the development of hyperlipemia in both donkeys and ponies. Hyperlipemia may be a primary disease or may be secondary to another disease. Such patients are invariably difficult to manage and mortality rates of 60–80% frequently are reported. This poor prognosis makes prevention of hyperlipemia or amelioration in the very early stages, crucial. The aim of this study was to determine risk factors for the development of hyperlipemia in a donkey population based at The Donkey Sanctuary, UK using a retrospective case—control approach.

Materials and Methods

Retrospective Case-Control Selection

A retrospective case-control study was carried out and it included all donkeys presenting with clinical hyperlipemia over a 4-year period between January 1, 2005 and December 31 2008. Each case was matched with 2 controls that were resident at The Donkey Sanctuary in the same month. Controls were donkeys resident at The Donkey Sanctuary during the study period that had not suffered an episode of hyperlipemia in the previous month. All controls were selected by ordering according to identification number and subsequent random number generation using Excel.^a

All records present in an Access database for donkeys' resident at any of The Donkey Sanctuary's UK residential farms during the study period were reviewed to identify all cases of hyperlipemia (defined by triglyceride concentrations \geq 4.4 mmol/L based on the Donkey Sanctuary laboratory normal reference range). Clinical notes also were examined to confirm the diagnosis of hyperlipemia. For inclusion as cases, donkeys had increased triglyceride concentrations in addition to clinical signs as assessed by a veterinarian. Cases without accompanying clinical histories were excluded. Control donkeys did not have blood samples available. Therefore, screening was undertaken by examination of detailed clinical notes to ensure that the donkey did not present with clinical signs of hyperlipemia within the month before selection. Peak serum triglyceride concentration was recorded for donkeys sampled multiple times; however, the episode was deemed to begin on the date of the first evidence of increased triglyceride concentration.

Blood Biochemistry

Serum triglyceride concentrations were determined from serum samples using an automated analyzer.^b

Data Collection

Potential risk factors that were examined for both cases and controls are shown in a Table 1. Donkey clinical and management records were maintained in database.^c

Statistical Analysis

Descriptive statistics were calculated for mortality, age, sex, and seasonal data. Confidence limits for proportional data were calculated using the Wilson Score Method. Data were analyzed using PASW Version 18.d Univariable logistic regression analysis was carried out as an initial screening step to determine the effect of predictor variables (Table 1) on the dependent variable (presence of hyperlipemia). Variables with P < .2 in the univariate analysis were selected for inclusion in the multivariable model. Multivariable logistic regression analysis then was performed to control for potentially confounding factors and subsequently to examine interactions. Interactions were examined by including interactions in the model one at a time to assess their effect. Any nonstatistically significant main effects or interactions were removed and the model was rerun. Variables with P < .2 in the univariate analysis were selected for inclusion in the multivariable model. The level of significance was set at P < .05.

Results

General

A total of 449 cases of hyperlipemia were diagnosed in 409 individual donkeys (10.7%) in the population of 3829 donkeys that were resident at The Donkey Sanctuary during the 4-year period studied. A total of 898 randomly assigned controls were assessed from the resident population. The incidence rate for new cases of hyperlipemia in this period was 12 new cases per 100 donkeys per year. The mortality rate for case donkeys associated with hyperlipemia with or without concurrent disease was 48.5%; the crude mortality rate in the control population was 28.9%.

Clinical Details

The mean age of donkeys with hyperlipemia was 28.6 years (SD = 7.9) with a range of 5–50 years. The

Table 1. Variables investigated for cases and controls at time of diagnosis with hyperlipemia or time when used as a control.

Variable	Description and Units			
Age	Years Farm location when at time of sampling, 8 sites			
Site				
Time owned by the Donkey	Time under Donkey Sanctuar			
Sanctuary	management relinquished			
Weight	Weight taken recorded preceding 4 weeks (kg)			
BCS	Body condition score (1–5 including ½ scores) Weight loss or gain of >10 kg in preceding month			
Weight change				
Extra Rations*: Fiber or cereal based	Concentrate feed			
Bedding*: Straw, cardboard, wood shavings	Bedding donkey kept on			
Changes*: New farm, new barn, transport, loss of	Change in preceding 2 or 4 weeks in normal routine			
bonded companion, change in extra ration				
Routine treatments*:	Routine treatment in			
Dental, vaccination, deworming, delousing, farriery	preceding 2 or 4 weeks			
Concurrent disease	Other disease process present			
Medical examination*: Digestive problems, colic, ophthalmology,	Veterinary examination in preceding 6 months			
kidney disease, liver disease, behavioral (other than dullness),				
dullness, inappetance, recumbency, weight loss, dermatology,				
cardiovascular disease, laminitis, lameness, respiratory, and				
accidental				
Surgery	Surgery in preceding 6 months			
Dental disease	Dental disease present			
Medications*: NSAIDs, antibiotics,	Medications given			
steroids, other oral treatment, or other external treatment	in preceding 4 weeks			

^{*}All categories were tested individually in the univariable and multivariable analyses.

mean age of the control population was 24.2 years (SD = 9.2) with a range of 1–52 years (Fig 1). Those donkeys that recovered from hyperlipemia had a mean age of 27.4 years (SD = 8.2); those that were euthanized entirely or partly because of hyperlipemia being diagnosed had a mean age of 29.6 years old (SD = 7.4). There were 226 females, 220 geldings, and 3 stallions in the case group with 401 females, and 494 geldings, and 3 stallions in the control group; none of the females were pregnant or lactating (The Donkey Sanctuary has a no breeding policy). Median body condition score (BCS) for the case population was BCS 3 (range, 1–5) and for the control population was BCS 3 (range, 1.5–5). Body condition score distribution is shown in Figure 2. Both populations showed a

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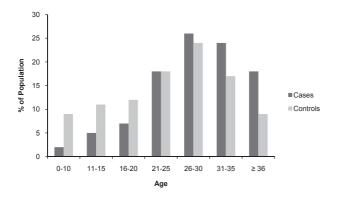


Fig 1. Age distribution of hyperlipemia case population and the control population.

skewed distribution toward ideal and obese animals as opposed to underweight animals. Concurrent disease was present in 324 donkeys (72%) with hyperlipemia and in 50 control donkeys (6%). The most common concurrent diseases in the case population were liver disease with 87 donkeys affected, colic (62 donkeys), kidney disease (16 donkeys), respiratory disease (24 donkeys), and laminitis (17 donkeys). The clinical outcome was dependent on the degree of hyperlipemia (P < .001); donkeys that survived had a mean triglyceride concentration of 9.3 mmol/L compared to 14.2 mmol/L in those that did not survive.

Triglyceride Concentrations

The mean peak triglyceride concentration was 11.8 mmol/L (SD = 10.2) with a range of 4.4–95.3 mmol/L. Triglyceride concentrations were separated into previously defined clinical categories³ and mortality rates were calculated as shown in Table 2. Mortality rates were significantly (P < .001) associated with peak serum triglyceride concentration.

Case-Control Study – Univariable and Multivariable Analysis

Initial univariable analysis identified several variables that were associated with development of hyperlipemia (P < .20) and warranted further analysis by multivariable analysis. The variables found to be associated with development of hyperlipemia at the univariable level were sex, site, age, BCS, weight change in the previous month, weight (kg), type of bedding, concentrate rations, changes in management within 2 weeks (site, residential group, feeding, transport), change of management within 4 weeks (site, residential group, feeding, transport), any illness within 6 months, examined by a veterinarian for particular illness within 6 months (digestive problems, decreased appetite, colic, weight loss, respiratory disease, skin problems, laminitis, other lameness, accidental injury, dullness, liver disease, kidney disease), concurrent disease, specified veterinary treatment within 4 weeks (dental examination, delousing treatment, vaccination, antibiotics,

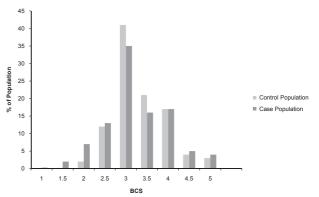


Fig 2. Distribution of body condition scores (scale 1–5) in hyperlipemic case population and control population.

analgesia, other orally administered treatments), and dental disease.

Final multivariable analysis showed that several variables were associated with development of hyperlipemia as shown in Table 3. Older donkeys were at an increased risk of developing hyperlipemia (P = .002). Site of donkeys was shown to be a risk factor for hyperlipemia, which apart from 1 particular site (Site 4 – isolation unit) could not be explained by the other variables investigated in this study. Management factors such as feeding of concentrate rations and keeping donkeys on cardboard bedding put donkeys at an increased risk of developing hyperlipemia OR 1.87 (1.18-2.96) and 3.86 (1.40-10.68). Weight loss of >10 kg within the previous month put donkeys at a significant risk with an OR of 6.40 (3.62–11.33). BCS was not associated with hyperlipemia (P = .11) and there was no predilection for donkeys with a high BCS. Health also had a significant effect on the development of hyperlipemia with any concurrent disease giving an OR of 76.98 (45.76–129.48). Finally, administration of antibiotics was protective with an OR of 0.3 (0.15-0.61).

Discussion

The results of this study show that the donkeys in this population commonly develops hyperlipemia, particularly in response to stress or other illness. The incidence of this disorder in the population of mainly aged donkeys studied is high at 11% when compared to previous studies which found incidence rates of 3⁷ and 5% in donkeys and ponies, respectively. These differences may be accounted for by the vigilance of

Table 2. Mortality rates associated with varied triglyceride values.

Plasma Triglyceride Concentration (mmol/L)	No. of Cases	Mortality Rate (%)	95% CI
4.4–8	214	41	35–48%
8-10	51	51	37-65%
10-15	69	49	37-61%
15-20	60	70	57-81%
Over 20	55	76	46-73%

Table 3. Final multivariable model of risk factors associated with hyperlipemia in donkeys at The Donkey Sanctuary during the period January 1, 2004–December 31, 2008.

Variable		Odds Ratio	Lower 95% CI	Upper 95% CI	<i>P</i> - Value
-					
Age		1.26	1.09	1.45	.000
Site	Site R	1.00			
	Site 1	2.60	1.08	6.24	.003
	Site 2	3.11	1.25	7.75	.001
	Site 4	14.19	4.78	42.14	<.000
	Site 6	3.75	1.52	9.24	.000
Concentrate feed	No	1.00			
	Yes	1.87	1.18	2.96	.000
Cardboard bedding	No	1.00			
	Yes	3.86	1.40	10.68	.000
Weight loss of	No	1.00			
>10 kg in month	Yes	6.40	3.62	11.33	<.000
New site in previous	No	1.00			
2 weeks	Yes	3.94	1.28	12.13	.001
Concurrent disease	No	1.00			
	Yes	76.98	45.76	129.48	<.000
History of	No	1.00			
inappetance in	Yes	3.23	1.33	7.85	.000
previous 6 months					
Weight loss in last	No	1.00			
6 months	Yes	2.03	1.05	3.94	.003
Dental disease	No	1.00	1.00	2.,	.002
D circui disetto	Yes	1.73	1.08	2.76	.002
Antibiotics	No	1.00	1.00	2.70	.002
1 milotottes	Yes	0.30	0.15	0.61	.000

veterinarians working at The Donkey Sanctuary. All donkeys presenting with an acute disease have blood samples collected if any suspicion of hyperlipemia exists to ensure that they do not have hypertriglyceridemia. Thus, animals with relatively minor increases in triglyceride concentrations are identified and treated. In the past, some of these cases may have been self limiting and not included in hyperlipemia studies. Sadly, the mortality rate in this study was high at 49%, but this figure is favorable when compared to earlier studies that have reported mortality rates in hyperlipemic ponies of 67² and 80%. ⁹ It is similar to a study in miniature horses which reported a mortality rate of 50%. ¹⁰

Older donkeys were at greater risk of developing hyperlipemia and also were more likely to be euthanized attributable to hyperlipemia, with or without concurrent illness. This is in contrast to a recent study in which there was no age predilection for development of hyperlipemia in 44 equids. The population studied herein was mainly geriatric, with the average age being 24 years old. Older donkeys are more prone to developing diseases such as colic and dental disease that may be associated with hyperlipemia. The decisions to euthanize these animals also are likely to be influenced by chronic disease processes occurring concurrently with hyperlipemia as well as acute disease. Older donkeys may be more prone to bullying

and find it difficult to compete for food in mixed age groups.

Interestingly, this study showed no increased risk for female donkeys when compared to geldings (stallions were not available for study in this population as the charity has a strict no breeding policy), although other studies have found that females are more susceptible to hyperlipemia. A previous study looking at this population of donkeys found a hazard ratio of 1.49 for females regardless of breeding status.⁷ Other studies also have found females to be more at risk, particularly those that are pregnant or lactating² which is potentially explained by the energy demands placed upon the mare by her foal. A possible explanation for the change in risk in this population since the earlier study is the greater segregation of mares and geldings in resident groups. Many gelding donkeys are highly sexually driven often years after castration and inseason mares may be repeatedly mounted and harassed by some geldings, possibly leading to stress, primary disease, or inability to access feed, which may precipitate the development of hyperlipemia.

In this population of donkeys, 72% of those presenting with hyperlipemia had concurrent disease. This is similar to the studies conducted by Rush et al. (1994)¹⁵ and Mogg et al (1995)¹⁰ which reported concurrent disease in 87 and 100% of miniature donkeys and horses, respectively. In ponies, concurrent disease was only noted in approximately 33% of cases.^{2,9} Concurrent disease may be a particularly important predisposing factor in this population attributable to the age distribution of the population. Donkeys that are in pain or stressed by a disease process are likely to become inappetent, leading to negative energy balance and thus are at an increased risk of developing hyperlipemia.

Concurrent disease was the factor that produced the highest risk of a donkey developing hyperlipemia (OR = 76.98; 45.76-129.48). The mere fact of the donkey being ill is more important than the specific disease process that put the donkey at risk. In some cases, the concurrent disease may be secondary to the hyperlipemia (eg, increases in liver enzyme activities caused by hepatic lipidosis). When analyzed, no specific disease, except dental disease, was a risk factor by itself and one must assume that it is more likely the inappetence often associated with illness in the donkey or the stress associated with veterinary treatments for the primary disease process that contributed to hyperlipemia. The level of risk associated with concurrent disease confirms the long held belief that every sick donkey must be considered either to have hyperlipemia or to be at great risk of developing hyperlipemia. Dental disease was the only disease that was a significant risk factor in itself with an OR of 1.76 (1.08-2.76) and was highly prevalent in this population of aged donkeys with 57% having recorded dental disease. The association of dental disease with hyperlipemia is unsurprising because impaired dental function or dental pain has been shown to be a risk factor for colic 12,16 and weight loss 13 and undoubtedly may lead 1424 Burden et al

to a donkey being unwilling or unable to obtain sufficient energy for its daily needs.

Donkeys that had been examined by a veterinarian in the preceding 6 months for either inappetence or weight loss were at increased risk of developing hyperlipemia in the following 6 months. Both weight loss and inappetence may be indicative of numerous health issues in donkeys and may suggest an underlying disease or changes in the ability to maintain a healthy balance between dietary intake and energy requirements. Aged donkeys are prone to weight loss, often exacerbated by failing dentition, lack of mobility, and a decreased appetite. Along with concurrent disease, perhaps one of the best predictors for donkeys at risk of developing hyperlipemia was donkeys losing more than 10 kg in the month before the onset of illness. Donkeys presenting with such weight loss had more than 6 times the risk compared with those that did not lose such a substantial amount of weight. All the Donkey Sanctuary's resident donkeys are weighed once per month using electronic scales as a management tool, and the importance of such monitoring to assess overall health is shown by this study. Regular weight monitoring by all donkey owners and keepers should be encouraged because such an early warning system could prove invaluable; even the use of less accurate measures such as heart girth measurements and nomograms will allow large weight losses to be detected. In contrast to previous studies, 1,7 this study showed no increased risk of developing hyperlipemia for overweight donkeys. Such increased risk has been attributed to increased insulin resistance and body fat reserves in these animals.^{2,3} The knowledge of clinicians and caregivers about the risk of hyperlipemia in obese donkeys may have led to improved observation and management of such donkeys to prevent hyperlipemia and particular care is taken to decrease stress.

Different sites (residential premises) had different levels of risk associated with them with 1 site (Site 4) having an OR of 14.19 (4.78–42.14); this site is the isolation unit for all new arrivals. All donkeys that enter this site are new to The Donkey Sanctuary and will spend 6–12 weeks in this facility before being integrated into the main residential herds. Most donkeys that are relinquished to the sanctuary are likely to have been in private homes with caring owners and are unlikely to have been kept with more than 1 or 2 other equids. The experience of entering such an alien environment is likely to be very stressful and although all attempts are made to make this transition as stress free as possible it is likely to be considerably unsettling for many donkeys, leading to the development of hyperlipemia. This finding is in agreement with an earlier study that looked at this population and also showed that donkeys new to the population were at increased risk of hyperlipemia. Other sites also were identified as putting donkeys at risk of developing hyperlipemia. These differences are likely to be attributable to differences in management practices or population structures or other factors that create bias that were not examined as part of this study. The change

of site also predisposed donkeys to developing hyperlipemia. Again, the stress of having to adapt to new surroundings, caregivers, and herd members may lead to decreased appetite or inability to consume sufficient energy.

The practice of giving concentrate meal feeds put donkeys at increased risk (OR = 1.87; 1.18-2.96), which also was found to be a risk factor for impaction colic in a previous study. ¹² Concentrate rations were given to donkeys that were underweight, sick, or had other clinical needs; traditionally feeds were given once or twice a day. The practice of feeding irregularly may produce peaks of insulin and may lead to the donkey being satiated for short periods of time. If dental issues preclude chewing of forage in between feeds, this practice may lead to the donkey developing health issues. Donkeys are trickle feeders and have evolved to eat for 14-18 hours per day, making such sporadic feeding practices less than satisfactory for this species. ¹⁷ A previous study looking at gastric ulcers in donkeys at necropsy showed that those donkeys fed concentrates were at greater risk of developing ulcers and were consequently at greater risk of having concurrent hyperlipemia.¹⁸ Recent changes to feeding practices have been made and more emphasis now is put on the use of hay replacement products to imitate natural feeding behavior. The results of these changes were not available for study.

Perhaps the most surprising risk factor for the development of hyperlipemia was the risk conveyed (OR = 3.86; 1.40-10.68) by the use of chopped cardboard and paper as bedding for donkeys. A previous study also showed an increased risk of donkeys developing impaction colic when bedded on cardboard. 19 Donkeys are browsers as well as grazers and have been observed to consume substantial amounts of cardboard when allowed access to clean bedding material. Donkeys have been noted to preferentially graze cardboard over freely available fresh haylage and straw. It is hypothesized that the donkey's natural preference for highly fibrous forages leads them to associate cardboard with food. Such a hypothesis is borne out by the fact that working equids in some parts of the world occasionally are fed on chopped cardboard and glucose syrup. Donkeys preferentially eating cardboard may use up valuable gastrointestinal tract capacity and time on a food source that is unlikely to offer any nutritional benefit, and this may be to the detriment of eating other forages that are energy sources. Since the publication of the previous study and this study, The Donkey Sanctuary has ceased to use cardboard or paper as bedding materials, and we would urge other donkey owners and keepers to consider discontinuing this practice. Of particular note is the trend of some veterinary hospitals to use such materials for inpatients.

Of all risk factors investigated, one was protective. If donkeys were being administered short-term antibiotics, they were at decreased risk of developing hyperlipemia (OR = 0.30; 0.15-10.61). The reasons for such decreased risks are unclear, but animals receiving these drugs may be closely monitored at least twice per day

by nursing staff and special attention may be given to the animal's demeanor and clinical signs.

Finally, the potential for bias in the study should be noted. A number of control donkeys may have been suffering from nonclinical hypertriglyceridemia not noted during the study. Because of lack of blood samples from healthy controls, such information was not available for a retrospective study. This is noted as a potential source of bias because some controls may have had subclinical increases in triglyceride concentrations. This study focused only on clinical cases of hyperlipemia and should not be extrapolated to animals with mild increases in serum triglyceride concentrations without accompanying clinical signs.

This study has demonstrated the propensity of the donkey for developing hyperlipemia, particularly when ill, which further confirms the requirement for all sick donkeys to be considered at high risk of becoming hyperlipemic. The study provides useful insights into health and management risk factors that may be focused on to further decrease the risk of hyperlipemia both in the population of donkeys studied and in the donkey population as a whole.

Footnotes

Acknowledgments

We acknowledge the veterinary surgeons at The Donkey Sanctuary for their assistance in collating clinical data.

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^a Microsoft Excel; Microsoft, Redmond, WA

^b Integra 400; Roche, NJ

^c Microsoft Access; Microsoft

^dPASW Version 18; SPSS Inc, Chicago, IL