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Clinico-Pathological Studies on Equine Metabolic Syndrome

A thesis
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LIST OF ABBREVIATIONS

ACVIM	American College Of Veterinary Internal Medicine
ANC	Average Neck Circumference
APP	Acute Phase Proteins
BC	Belly Circumference
BCS	Body Condition Score
BIA	Impedance Analysis
BFM	Body Fat Mass
BM	Body Mass
BMI	Body Mass Index
CGIT	Combined Intravenous Glucose – Insulin Test
CHO	Carbohydrates
CNS	Cresty Neck Score
CV	Coefficient Of Variation
D2O	Deuterium Oxide
DM	Diabetes Mellitus
DMI	Dry Matter Intake
EBW	Estimated Body Weight
ECD	Equine Cushing's Disease
ELISA	Enzyme – Linked Immunosorbent Assay
EMS	Equine Metabolic Syndrome
FAT	Fat Rich
FFA	Free Fatty Acids
FSH	Follicle Stimulating Hormone
GC	Girth Circumference
GLUT-4	Glucose Transporter 4
HbA1c	Glycosylated Hemoglobin
HG	Heart Girth
HMW	High Molecular Weight
HPG	Hypo-Physeal Gland
HW	HeightAt Withers
IGF-1	Insulin Like Growth Factor-I
IL	Interleukin
IR	Insulin Resistance
IRS-1	Insulin Receptoe Substrate-1
IS	Insulin Sensitive
LH	Lutinizing Hormone
MS	Metabolic Syndrome
NC	Neck Circumference
NCHR	Neck Circumference To Height Ratio
NO	Nitric Oxide
NOMs	Nitric Oxide Metabolities
NSC	Non Structural Carbohydrate
PPID	Pituitary Pars Intermedia Dysfunction
RTU	Real- Time Ultrasonography
RF	Rump Fat
SAA	Serum Amyloid A
SC	Subcutaneous
SEM	Standard Error Of Mean
SF-Skin	Subcutaneous Fat – Plus – Skin Thickness
SM	Skeletal Muscle
SOCS	Suppressors Of Cytokine Signaling
SOCS-3	Cytokine Signaling 3
TLR-4	Toll-Like Receptor 4
TNF-α	Tumor Necrosis Factor -Alpha
VIS	Visceral (VIS) Adipose Tissue
WLR	Weight Loss Resistance

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Introduction

Equine metabolic syndrome (EMS) is a recently described endocrine pathological condition of obese horses that is associated with insulin resistance (IR), laminitis, and fat redistribution. IR is the hallmark of EMS (**Frank, 2009**). The term equine metabolic syndrome (EMS) was first introduced by **Johnson (2002)** to better define a condition that was previously attributed to hypothyroidism.

Components of EMS include obesity, regional adiposity, insulin resistance (IR), hypertriglyceridemia, and hyperleptinemia, and this condition is associated with increased laminitis risk, altered reproductive function, and seasonal alterations in arterial blood pressure (**Frank et al., 2006; Treiber et al., 2006; Bailey et al., 2008)**. Hepatic insulin resistance could occur in obese and lean horses with EMS if lipid accumulates in the liver as a result of elevated free fatty acids (FFA) concentrations (**Wasada et al., 2008)**. Lipid accumulation also affects other liver functions, including bile excretion.

EMS was previously confused with equine Cushing's disease (**ECD**), which is also called pituitary pars intermedia dysfunction (**PPID**). Some of this confusion can be attributed to the use of the term peripheral Cushing's syndrome. This term was first introduced in the original description of EMS because it was hypothesized that affected horses synthesized more cortisol within their visceral adipose tissues (**Johnson, 2002)**.

Regional adiposity refers to the expansion of adipose tissues in certain regions of the body. Adipose deposits are detected in the prepuce or close to the mammary glands in obese horses and occasionally appear as randomly distributed subcutaneous masses along the sides of the abdomen. Expansion of adipose tissues within the neck region is proved to be the best indicator of EMS in horses and ponies, and a scoring system has been established to assess expansion of adipose tissues around the nuchal crest of the neck (**Carter et al., 2009a)**. This physical characteristic is commonly referred to as a ‘‘cresty neck’’ and increased neck circumference has been associated with IR in both horses and ponies (**Frank et al., 2006; Carter et al., 2009b).**

Equine metabolic syndrome is less commonly detected in leaner horses, and it is conceivable that affected animals suffer from a different manifestation of the condition. The key features of EMS in leaner horses are regional adiposity and increased laminitis risk. Leaner horses with EMS usually fall into two categories: (1) horses that were previously obese and are now being maintained in a leaner body condition through effective management and (2) leaner horses with regional adiposity, IR, and laminitis that do not test positive for PPID. Middle-aged (10-20 years) or older horses in this category are likely to suffer from PPID that has not progressed to the point of affecting diagnostic test results (**Wasada et al., 2008)**.

Equine metabolic syndrome can also develop in younger horses that remain lean overall. Regional adiposity, IR, and laminitis are detected; yet the animal is leaner across the ribs

and top line. Affected horses have adipose tissues in certain regions of the body that are more metabolically active which is characterized by increasing fatty acid uptake into the liver, resulting in hepatic IR (**Frank, 2009)**.

In Egypt, no records were published investigating EMS in horses but the disease was observed in some exercise horses given their nutritional requirements while being lamed or off training and the predisposition of EMS to laminitis, cardiovascular disturbance, fatal colic and infertility leading to great economic losses.

Aim of the work

To diagnose equine metabolic syndrome (EMS) through measuring some biochemical and hormonal parameters in blood samples of animals suspected to be diseased, by performing ultrasound examination of mares for measuring rump fat and estimating body fat mass and measuring body condition. As well as, this study aimed to monitor the responses of obese mares to supplementation with carbohydrate ration for 60 days.

Review of Literature

A disease with similarities to human metabolic syndrome is recognized in the horse and is termed equine metabolic syndrome (EMS, **Frank et al., 2010)**. Obesity and insulin resistance (IR) are factors shared by both syndromes (**Johnson et al., 2005**). The presence of, or history of laminitis is also characteristic of the EMS phenotype (**Treiber et al., 2006**). Hypertriglyceridaemia (**Frank et al., 2006**), hyperleptinaemia (**Cartmill et al., 2003**), arterial hypertension (**Bailey et al., 2008**), increased systemic markers associated with obesity (**Vick et al., 2007**), and altered reproductive cycling (**Vick et al., 2006**) are also associated with EMS.

Equine obesity has recently become an epidemic. A plenty of fat horses had been recently recorded and are noticeable (**Sillence et al., 2006**). In the UK, the fat horse or pony is now so commonplace that it has come to represent the norm in the eyes of many owners. Once the problem of human obesity reaches a certain scale it can seem unstoppable despite the attendant risks, costs and consequences (**Sillence et al., 2006**).

In livestock, body condition scoring (BCS) systems was previously accepted to measure and monitor of body 'fatness' (**Laflamme, 1997a,b**) by evaluating the superficial 'flesh' to facilitate nutritional management and improve economic efficiency (**Jeffries, 1961**).

Instead, measuring back fat became more reliable to evaluate body condition according to the fat deposition (**Abdelmageed and Abo El-Maaty, 2012**). Increased fat deposition was previously preferred for meat animals but risks of increased cardiovascular disease in obese human and laminitis in obese horses (**Frank, 2011**) became no longer preferred.

In horses, the association between BCS and body fat was non-linear (**Martin Rosset et al., 2008**). In stallions, back fat decreased with increasing age and also related to semen parameters (**Abo El-Maaty et al., 2014**). Females seem to deal more successfully with energy deficits because they defend their body weight in a more efficient manner than males (**Nance et al., 1977; Cortright et al., 1997; Gayle et al., 2006**).

1. Equine metabolic syndrome (EMS)

The American College of Veterinary Internal Medicine commissioned a panel of specialists interested in equine metabolic syndrome (EMS) to develop a consensus statement that has provided a syndrome definition based on current knowledge (**Frank et al., 2010)**. The recent American College of Veterinary Internal Medicine (ACVIM) consensus statement on EMS indicated that there is a scarcity of epidemiological data on the components of EMS, including obesity (**Frank et al., 2010)**. National Animal Health Monitoring System (**NAHMS, 1998**) estimated that approximately 1.5% of the US horse population was over conditioned or obese.

Insulin resistance (IR) and diabetes in obese horses is known as equine metabolic syndrome (**Durham et al., 2009**). Horses with equine metabolic syndrome are predisposed to develop laminitis (**Frank et al., 2010; Frank, 2011**).

Demonstration of insulin resistance (IR) in horses with aspects of obesity represents the cornerstone of the EMS definition, as it does in the human syndrome. Similar to human MS, there is now evidence that EMS-affected horses can be further characterized by demonstrating up-regulated markers of inflammation (**Vick et al., 2007, 2008**), and a propensity to develop arterial hypertension (**Rugh et al., 1987; Bailey et al., 2008**).

Obesity is considered to be a primary (although perhaps not essential) component of equine metabolic syndrome (EMS), a condition of horses and ponies that is characterized by insulin health care, with the aim of reducing the risk of conditions such as insulin dysregulation and laminitis (**Thatcher, 2012)**. Obesity is a condition in which excessive body fat accumulates to an extent that it may adversely affect the health of an individual. In horses, obesity has been defined as a body condition score (BCS) ≥ 7 (**Geor, 2008**) on the modified 9-point Henneke scale (**Henneke et al., 1983; Kohnke, 1992**). The prevalence of obesity among populations of pleasure ponies and horses appears to be as high as 45–50% in the UK and the USA (**Wyse et al., 2008; Harker et al., 2011; Stephenson et al., 2011; Thatcher, 2012**).

Clinical recognition of EMS portends increased risk for the development of several important equine diseases, including

laminitis (“founder”), hyperlipemia syndrome (hepatic lipidosis), osteochondrosis, and type 2 diabetes mellitus (**Johnson, 2002; Frank et al., 2010; Frank, 2011**). Laminitis is a common, painful equine condition in which lameness results from abnormalities of growth and degenerative changes in the hoof lamellar interface, the epidermo–dermal connection that attaches the hoof wall to the underlying connective tissue of the third phalanx (responsible for weight bearing in this species). Laminitis represents the most common clinically important chronic disease for which identification of EMS contributes increased risk (**Johnson, 2002; Frank et al., 2010; Frank, 2011**).

Equine metabolic syndrome (EMS) is characterized by the clustering of obesity, regional accumulations of fat, IR, hyperleptinaemia and hyperinsulinaemia predicts an increase in the risk of pasture-associated laminitis in ponies presenting this metabolic syndrome phenotype (**Geor, 2008**).

Johnson et al. (2012) described that equine metabolic syndrome (EMS) is similar to the human MS in that both insulin resistance (IR) and aspects of obesity represent cornerstones of its definition. Unlike its human counterpart, identification of the equine metabolic syndrome (EMS) portends greater risk for development of laminitis, a chronic, crippling affliction of the equine hoof. When severe, laminitis sometimes necessitates euthanasia.