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# **Diagnosis, Treatment and Prevention of Pregnancy Toxemia in Ewes**

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### ABSTRACT

Thin ewes or very over-conditioned ewes and ewes carrying multiple pregnancies are more likely to develop pregnancy toxemia (ketosis). Pregnancy toxemia is a metabolic disorder characterized by hypoglycemia and hyperketonemia resulting from incapacity of the ewes to maintain adequate energy balance (usually in the last 5-6 weeks). Available information about pregnancy toxemia focuses mainly on pathogenic mechanisms and clinical features, early diagnosis, and therapeutic options. However, the pathophysiology and metabolic changes of this disorder remain poorly understood. An immediate and accurate diagnosis usually increases the possibility for their successive treatment and prevention. The objective of this review was to increase awareness of the disease, its likely cause, and practical treatment and prevention measures.

Keywords: Diagnosis, Pregnancy toxemia, Prevention, Sheep, Treatment

# INTRODUCTION

Pregnancy toxemia is a metabolic disorder characterized by hypoglycemia and hyperketonemia resulting from incapacity of the animal to maintain adequate energy balance. Negative energy balance during late pregnancy in ewes is an important cause of pregnancy toxemia. It is characterized by negative energy balance (low blood glucose). Ewes are usually recumbent down and off feed. Clinically, the ewes have neurologic signs and are weak. Specifically, toxemia appears in the last 5-6 weeks of pregnancy when the fetuses have reached 2/3 of their prenatal development. Almost 80% of the fetal growth takes place in the final 6 weeks of pregnancy, with 30–40% of the maternal glucose supply being utilized by the fetal–placental unit (Rook, 2000). If ewes do not receive at least half of the required energy during this period, fat depots are mobilized in large quantities (Firat and O<sup>°</sup> zpinar, 2002). Ketones are toxic byproducts of excessive breakdown of body fat to compensate for the negative energy condition. The serum Beta Hydroxybutyric ( $\beta$ -HB) concentration is the final product of fat metabolism and is the predominant circulating ketone body (Moghaddam and Hassanpour, 2008). The elevated  $\beta$ -HB levels inhibit the hepatic gluconeogenesis, and

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thus further increase maternal hypoglycaemia (Schlumbohm and Harmeyer, 2004). Risk factors include multiple fetuses, poor quality of ingested energy, decreased dietary energy level, genetic factors, obesity, lack of good body condition or high parasite load, lack of exercise and ewes carrying multiple pregnancies (Rook, 2000). Olfati and Moghaddam (2013) reported that crossbred ewes carrying multiple pregnancies are much more likely to experience ketosis. Further, it can also be observed in poorly nourished sheep with only a large single fetus (Bani Isail et al., 2008). The aim of this restricted review is to summarize and discuss the principal advances in our understanding of diagnosis, treatment and prevention of pregnancy toxemia in ewes.

#### DIAGNOSIS

Ewes should be in normal health during and after pregnancy so as to produce viable lambs. Early and accurate diagnosis of subclinical metabolic disorders, like pregnancy toxemia and ketosis, is important for the dairy sheep industry. Pregnancy toxemia is a metabolic disease of pregnant ewes which causes significant economic losses to in the sheep industry due to maternal and fetal death. Prognosis of pregnancy toxemia is generally very poor. Symptoms of ketonemia include depression, anorexia, weakness, staggering gait, apparent blindness, recumbency, coma, and death (Al-Qudah, 2011). Due to non-specific clinical symptoms, the presence of pregnancy toxemia in ewes can only be determined by elevated plasma ketone body concentrations, i.e. of β-HB (Duehlmeier et al., 2011). To compensate for the lack of glucose, maternal triglycerides are mobilized, resulting in increased plasma levels of non-esterified fatty acids (NEFA). Due to the incomplete NEFA break down, the plasma  $\beta$ -HB concentrations increase. Plasma  $\beta$ -HB concentrations have been recognized to be a sensitive tool to detect maternal undernutrition and pregnancy toxemia in sheep. Healthy animals generally have β-HB plasma levels below 0.8 mmol/L, while  $\beta$ -HB concentrations of 0.8 to 1.6 mmol/L could suggest moderate undernutrition (Andrews, 1997). In sheep suffering from pregnancy toxemia  $\beta$ -HB plasma concentrations of more than 3.0 mmol/L are usually measured (Sargison et al., 1994). A vast majority of disorders are characterized by certain changes in the concentration of blood parameters (Ramin et al., 2005). So, for example, blood glucose is the major metabolite used by the sheep fetus and the energy requirements of the ewe increase during late pregnancy due to the rapid growth of the fetus (Firat and O" zpinar, 2002). Serum components are most common biochemical indicators measured routinely for diagnosis or monitoring disease activity; alterations of their concentrations and patterns, although not specific, may be of diagnostic significance in metabolic disorder (Moghaddam and Olfati, 2012). Several investigators have demonstrated the usefulness of serum protein electrophoresis for the initial evaluation of various clinical or pathological conditions in animals (Gojnic et al., 2004; Camacho et al., 2005). Numerous studies have focused on mediators associated with the metabolic changes arising in ewe pregnancy toxemia (Scott et al., 1995; Harmeyer and Schlumbohm, 2006). Yarim and Ciftci (2009) showed that serum concentration of albumin was significantly lower in preeclamptic than in uncomplicated pregnant ewes. The effects of reproductive status on the serum parameters in ewes have not yet been described adequately. Also investigations concerning the effect of the different reproductive stages on the serum parameter values revealed inconsistent data (Ramin et al., 2005; Harmeyer and Schlumbohm, 2006; Yarim and Ciftci, 2009). Thus, the authors of this review recommend that future studies in animal science focus on the important relationship between diagnosis of the pregnancy toxemia and serum chemistry in different gestational stages of ewes.

# TREATMENT

Common treatment for ewes affected with pregnancy toxemia include the oral administration of glycerol or propylene glycol solutions (2 oz. twice a day), intravenous glucose, and, at more than 135 days of gestation, injection of dexamethasone or beta methasone to induce parturition (Radostits et al., 2007), intravenous 5% dextrose drip, 100-300 ml dextrose (50%) bolus IV, B vitamins, remove fetuses (induce labor or c-section) and antibiotics to prevent pneumonia (Gordan, 2012), with the aim of eliminating the metabolic demand for energy, of the gravid uterus. It was therefore hypothesized that hyperketonemia in pregnancy toxemia may also be associated with an inflammatory reaction, and that anti-inflammatory treatment may be effective in treating affected ewes. Based on the results of Zamir et al., (2009) they suggested that flunixin meglumine treatment may provide a means to achieve the full economic potential of high proficiency: ewe and lamb losses due to pregnancy toxemia are reduced and the welfare of the animals is improved. Actually the treatment of pregnancy toxemia in ewes is usually unsuccessful; therefore prevention is of key importance to reduce the occurrence of the disease. The authors of this review also recommend that the presence of significant correlations among serum parameters (glucose, calcium, creatinine, urea, cholesterol, phosphorus and magnesium levels) in pregnant ewes could be useful to compare with values in late pregnant ewes in order to study and treatment of pregnancy toxemia and other abnormal metabolic states.

### PREVENTION

Early and accurate diagnosis of subclinical metabolic disorders, like pregnancy toxemia and ketosis, is important for the dairy sheep industry. An immediate and accurate diagnosis usually increases the possibility for their successive treatment and prevention (Brozos et al., 2011). Commercial production systems are comprised of a variety of nutritional, metabolic, genetic, physiologic, environmental, economic, health, and management factors that singularly or as a group influence the clinical expression of pregnancy toxemia. Recognizing the role management plays in controlling these inputs is crucial to pregnancy toxemia prevention and treatment programs. Also, understanding the normal value serum parameters would be the useful index in the determination of the physiological aspects in non-pregnant or pregnant ewes. These indices may vary depending on factors such as sex, breed, age, steers, season, physical exercise and environmental condition.

Preventing Pregnancy Toxemia (Gordan, 2012):

- Provide adequate energy in ration especially during last 4-6 weeks of gestation.
- Good quality hay with grain supplementation (begins with about 0.5 lbs. per day and increase to 1.5-2.0 lbs per head per day until the time of parturition).
- Avoid abrupt feed changes.
- Avoid stress when possible.
- Provide adequate feeder space.
- Aim for body condition score of 3 to 3+ at lambing.
- Monitor and control parasitism.

Grain is a high source of available energy. Feeding 0.5-1 kg of grain daily along with high quality hay during the last 4-6 weeks of pregnancy will help prevent pregnancy toxemia in ewes (Crnkic and Hodzic, 2012). In the small ruminant intermediary metabolism too, glucose is the most important energy source, and insulin is the major regulator of energy partitioning. Thus, this review recommended that blood glucose and insulin concentrations have to be evaluated during the different gestational stages. Antioxidants may be useful additions to protocols for prevention and treatment of pregnancy toxemia.

### CONCLUSION

Pregnancy toxemia is thought to result from disruption of the ewe's glucose homeostatic mechanism in response to increased nutritional demands of the rapidly developing fetal placental unit. However, further studies are needed to explore the potential role of diagnosis, treatment and prevention of pregnancy toxemia in ewes at abnormal metabolic states. This information could be used by veterinarians to aid in clinical investigation of herds and individual ewes in late pregnancy, and help in the understanding of pathophysiologic changes that occur in these ewes. To finally interpret the glucose data, other parameters of the energy metabolism have to be taken into account.

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