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Biochemical Changes in Pregnancy Toxemia

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Abstract

Pregnancy toxaemia, sometimes referred to as gestational toxaemia, twin-lamb illness, or ovine ketosis, is a metabolic condition that affects pregnant ewes. This article's goal is to highlight potential causes and risk factors for pregnant toxaemia in ewes as well as effective disease control and preventative strategies. Hepatic lipidosis is ultimately brought on by this negative energy balance, which also triggers ketosis and excessive lipid metabolism. Both poorly and well-conditioned sheep may have an excess of ketone bodies; in fact, overweight ewes may be more vulnerable to pregnancy toxaemia. Furthermore, this metabolic ailment can be brought on by circumstances that disrupt feed intake, like storms, transportation, or other illnesses. During the final six weeks of pregnancy, affected sheep typically show signs of weakness and despair. In order to reduce output loss in sheep farming operations, it is crucial to comprehend the causes, pathophysiology, prevention, and treatment of this disease.

Introduction:

Among domestic farm animals, metabolic diseases are most common in dairy cows, pregnant does, and ewes. Other animals only infrequently get these illnesses (Ji *et al.,* 2023). If a poor diet during the dry period exacerbates the continuous nutritional needs of pregnancy, the prevalence of metabolic disorders increases. Ewes are greatly impacted by pregnancy, particularly those who are caring for several lambs (Radostits, *et al.,* 2006). Pregnancy toxaemia, often known as ketosis, is the most common metabolic disorder that affects sheep and goats in the later stages of pregnancy. It often occurs in the latter six weeks of pregnancy, leading to significant financial losses and a high risk of pregnant sheep mortality. It is particularly prevalent in ewes that are extremely fat or have two or more lambs. It is particularly prevalent in ewes that are extremely fat or have two or more lambs. Ketosis is caused by a disturbance in the animal's use of carbohydrates (Bickhardt *et al.,* 1989). As the ewe's pregnancy progresses, her body requires more energy. The rumen's capacity declines as her expanding lambs take up more and more space inside the uterus (Drackley *et al.,* 1989). Because of this combination, the ewe might not be getting enough energy from her food. She will consequently need to break down her own bodily tissues, usually fat, in order to provide energy for her growing lambs. This will release ketones, a dangerous byproduct of fat breakdown, into her bloodstream. Pregnancy toxaemia or

ketosis results from the ewe's body not being able to metabolise the ketones fast enough when this occurs too quickly. Ketosis can also occur when the ewe is overweight because fat takes up room inside the sheep, making it more difficult for the rumen to hold nutrients. Storms, hauling, or other ailments that interfere with feed intake can also cause this metabolic disorder (Freetly and Ferrell, 1998).

Measuring blood glucose and beta hydroxyl butyric acid (BHBA) concentrations is essential for an early diagnosis (Lacetera *et al.,* 2001). Successful treatment for pregnant toxaemia can result from early diagnosis (Andrews, A.1997; Sargison, N. 2007.). Nevertheless, treatment for advanced pregnancy toxaemia is usually unsuccessful (Marteniuk, J and Herdt, T. 1988). Eating disorders, neurological symptoms, blindness, and eventually death are the usual outcomes of pregnancy toxaemia. Therefore, in order to prevent and control the incidence of pregnant toxaemia in ewes as well as to reduce production losses, it is essential to evaluate predisposing conditions. Thus, this study aims to highlight possible causes, risk factors, and practical management and preventative techniques for pregnant toxaemia in ewes.

Etiology: Pregnancy toxaemia is caused by a disturbance in the metabolism of fats and carbohydrates in the last stages of pregnancy (Brozos *et al,,* 2011). This disruption is caused by low blood glucose levels and increased body fat breakdown to compensate for the glucose shortage. Ketones, the toxic metabolites produced by this rapid breakdown of fat, can be detected in the ewe's urine. Because ewes cannot consume enough grain or energy to meet the needs of their developing offspring during the last six weeks of pregnancy, low blood sugar is mostly caused by inadequate nutrition. This is because almost 70% of foetal growth occurs during the last six weeks of pregnancy (Rook, J. 2000).

Overconditioned (BCS 4 or higher) ewes may potentially develop pregnancy toxaemia as a result of abdominal obesity. These plump ewes go into ketosis because they have too much fat to digest and not enough room in their bellies to eat. Because they cannot eat enough to cover their own nutritional needs, let alone the additional burden of expanding foetuses, underconditioned ewes (BCS 2 or less) are especially vulnerable (Freetly and Ferrell, 1998).

Epidemiology Occurrence: It occurs all over the world. The drive to increase lambing percentages and earnings based on feed prices, particularly in lowland flocks that are intensively farmed, has caused the problem to expand. The illness is rare in large-scale industrial systems (Andrews, A.1997). This is partially because sheep breeds used in intensive husbandry are more likely to give birth to twins or triplets. The illness, which mostly affects ewes or does pregnant with twins or triplets, is characterised by low blood sugar. However, sheep breeds in extensive grazing systems often deliver single lambs, and significant outbreaks of pregnant toxaemia are uncommon except under situations of drought or poor pasture management. During the latter six weeks of pregnancy, ewes carrying multiple foetuses are more likely to develop pregnancy toxaemia (Radostits, *et al.,* 2006). Up to 40% of the ewes in a flock may be affected in some years, while many farmers may only deal with a few cases each year (Andrews, A.1997). Within two to ten days, around 80% of cases end in death. The incidence in a flock is determined by the kind and severity of nutritional deficiency as well as the proportion of the flock at risk. It can be very high in starving pregnancy toxaemia as opposed to fat ewe pregnancy toxaemia, which usually happens infrequently.

Clinical disease does not appear for 48 hours in outbreaks that follow management protocols or other stressors, and new cases then appear over several days. In intensively farmed sheep, the disease's natural incidence is about 2% of pregnant ewes; nevertheless, in cases of severe management failures, the majority of late pregnant

ewes may be affected. If therapy is not started early in the clinical course, the case fatality rate is significant. If left untreated, it results in high newborn mortality and 100% ewe mortality. Case mortality rates can be significant even with early treatment (Radostits, *et al.,* 2006).

Risk factors Pregnancy: Inadequate nutrition during late gestation is the main risk factor for pregnancy toxaemia. This is typically caused by the ration's low energy density and the foetal growth's reduced rumen capacity. The disease only affects ewes in the final six weeks of pregnancy, typically in the final month, with the final two weeks of pregnancy seeing the highest incidence. This is due to a sharp increase in the need for metabolisable energy during the final six weeks of pregnancy. Because twin pregnancy makes sheep more vulnerable to hypoglycemia stress and pregnancy toxaemia, it mostly affects ewes carrying twin lambs. For example, ewes carrying twins require 1.9 times more energy than ewes with singles and ewes with triple fetuses require 2.3 times more energy than ewes with singles (Kahn, C. 2005). Pregnancy toxemia may also affect ewes bearing a single large lamb (Schlumbohm, and Harmeyer, 2008).

Body condition: Other risk factors for the disease's start include poor physical health, advanced age, obesity, and low body weight. When obesity is present during late gestation, the uterus expands and deposited fat fills the abdominal cavity. These females struggle to consume enough feed to meet their energy needs due to a lack of rumen space (Pugh, D. 2002). Additionally, ewes in poor physical condition are unable to consume enough food to meet both their own nutritional demands and the energy requirements of their foetuses. This is due to the fact that sensitive thin ewes are consistently fed an inadequate diet, which causes the ewe to mobilise more body fat and produce ketone bodies and hepatic lipidosis as a result of having insufficient energy to fulfil growing foetal demands (Kahn, C. 2005).

Diseases: Pregnancy toxaemia can also be influenced by the presence of other illnesses, such as parasites, foot rot, and foot abscesses. Because of these circumstances, the animal's feed intake is severely reduced (Silk, 2013), resulting in a negative energy balance.

Environmental stress: Stress (acute) syndrome is brought on by environmental stressors like cold and rain, which raise the pregnant ewe's energy requirements (Levalley, 2010) Stress-inducing activities like transportation, shearing, crutching, or drenching may potentially hasten the development of the illness.

Parity: Clinical instances are usually restricted to older ewes and goats in their second or subsequent pregnancies. Due to their limited fertility, the disease is rare in maiden ewes, and its prevalence rises to parity three (Rook, J. 2000).

Breed: Pregnancy toxaemia is significantly more prevalent in highly prolific chosen breeds of sheep and goats (Smith, and Sherman, 1994). Variations in fecundity and management strategies are the main causes of breed variances. For example, compared to Merinos, the disease is more prevalent in British lowland breeds and their crosses. In contrast, British hill breeds are thought to be more resilient to the development of pregnancy toxaemia when the ewe is malnourished; however, this resistance comes at the expense of the lamb's birth weight and has the drawback of increased neonatal mortality. However, there are variations in each sheep's vulnerability that seem to be connected to variations in hepatic gluconeogenesis rates (Radostits, *et al.,* 2006).

Pathology Pathogenesis: To make glucose more accessible to the foetuses, the liver boosts gluconeogenesis in the latter stages of pregnancy. In late gestation, each foetus needs 30–40 g of glucose per day, which accounts for a sizable portion of the ewe's glucose output and is mostly used to support the foetuses rather than the sheep. This is due to the fact that the final six weeks of

pregnancy account for about 70% of foetal growth. In order to ensure sufficient energy in the face of the growing foetuses' demands and the approaching lactation, the mobilisation of fat stores is enhanced in late gestation. However, this enhanced mobilisation may exceed the liver's capacity in a negative energy balance, leading to hepatic lipidosis and consequent deterioration of function (Kahn, C. 2005). The persistent, preferred demands for glucose by the developing foetuses cause ewes with hepatic lipidosis to have an inadequate gluconeogenic response, which leads to hypoglycemia, increased lipid mobilisation, and the buildup of cortisol and ketone bodies. Eighty percent of ewes had high levels of cortisol in their plasma. This could be the result of either decreased liver excretion or increased adrenal output (Ford, 1990). This predisposition's cause is unknown. Twin-bearing ewes are more vulnerable to pregnancy toxaemia because they seem to have more trouble making glucose and eliminating ketone bodies. Excessive lipid mobilisation is linked to the ensuing illness and metabolic alterations (Rook, J. 2000).

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Ketone bodies (BHBA and acetoacetate) are powerful acids that cause metabolic acidosis when they build up in the blood, according to Sargison. According to Schlumbohm and Harmeyer (Schlumbohm, and Harmeyer, 2004), elevated BHBA hinders the metabolism of glucose. This intensifies the onset of ketosis and further inhibits the body's natural generation of glucose. Pregnancy toxaemia appears to be facilitated by the impairment of ketone body elimination in late pregnancy, particularly in ewes carrying twins, as hyperketonemia has multiple negative effects, such as on energy balance and glucose metabolism (Schlumbohm, and Harmeyer, 2003) The encephalopathy that appears in the early stages of the disease is thought to be a hypoglycemic encephalopathy brought on by hypoglycemia.

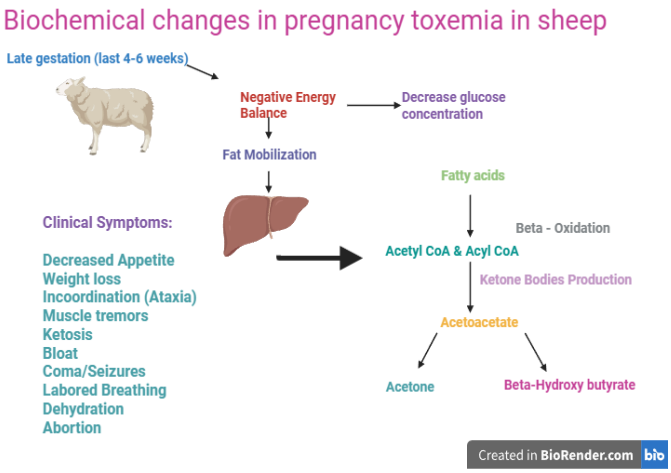
If treatment is not received in the early stages, the encephalopathy and the illness are often irreversible. Although the beginning of indications is unrelated to minimum blood glucose or maximal ketone levels, hypoglycemia and hyperketonemia always precede the onset of clinical signs (Scott, 1995).

Lesions: Common findings include an enlarged adrenal gland and a pale, bloated, friable fatty liver. Furthermore, the afflicted sheep typically has many foetuses in her uterus (Bradford, P. 1996). A decomposing foetus is a sign of premortem death. Ewes that are extremely emaciated may have serous atrophy of the kidney

and heart fat, giving the appearance of starvation (Kahn, C. 2005).

Clinical findings: Separation from the group, failure to rise for feeding in pastoral animals or standing close to the trough with the group of sheep but not eating in housed animals, altered mental state, and apparent blindness—which is characterised by an alert demeanour but a reluctance to move—are the first indications of pregnancy toxaemia. They also exhibit a loss of appetite, lie down, and become lethargic. Affected ewes look dull, wander erratically, and exhibit little fear of people or dogs. Convulsions, tooth grinding, and difficult breathing may eventually occur, along with blindness. When pushed to move, it stumbles into items and presses its head against obstacles.

Many afflicted sheep spend their days lapping the water in water troughs (Radostits *et al.,* 2006). Later on, there are instances of more acute nervous symptoms and noticeable lethargy, but these may be rare and easily overlooked. During these episodes, salivation, lip twitching, and jaw champing are caused by tremors of the head muscles. These are accompanied by a clonic contraction of the cervical muscles that resembles a cogwheel and causes the head to laterally deviate or dorsoflex, followed by circling. The ewe typically has convulsions and falls as the muscle tremor spreads to the entire body. After each convulsion, the ewe rests gently and rises normally, although it is still blind. There is noticeable lethargy during the intervals between convulsions, which may be followed by head pressing, the adoption of strange postures, such as odd limb positions and chin elevation (the "stargazing" posture), poor coordination, and falling when trying to move. The ewe's breath may have a ketone odour. In three to four days, affected ewes typically go recumbent and stay in a deep depression or coma for an additional three to four days. The majority of instances appear one to three weeks prior to lambing. A higher risk of death and more severe disease are linked to onset before day 140 of pregnancy (Kahn, C. 2005).



Diagnosis: Pregnancy toxaemia is diagnosed primarily on clinical signs and history; however, blood work is necessary for a confirmed diagnosis [22]. Individual sheep may exhibit hypoglycemia, elevated urine ketone levels, raised BHBA levels, and often hypocalcaemia and hyperkalaemia as a result of severe ketoacidosis. Low blood glucose levels are indicative of both CSF glucose levels and pregnant toxaemia [20]. Hypoglycemia is not a constant finding, though. Up to 20% of cases have hyperglycemia and up to 40% have normal glucose levels. These led to the hypothesis that hyperglycemia might suggest that the foetuses are dead, whereas hypoglycemia might suggest that the foetuses are alive. According to Wastney *et al.* 1982, there is a noticeable hyperglycemia in terminal cases because foetal death eliminates the fetus's suppressive impact on hepatic gluconeogenesis. BHBA is a more accurate measure of disease severity than blood glucose levels if the diagnosis requires additional confirmation. Elevated levels of non-esterified fatty acids may potentially be a sign of hepatic lipidosis, which impairs liver function (Marteniuk, J and Herdt, T. 1988). Pregnancy toxaemia must be distinguished from other conditions with similar symptoms, such as hypocalcaemia or hypomagnesaemia, in order to make an appropriate diagnosis.

Clinical and analytical results can be used to distinguish between them. Pregnancy toxaemia is characterised by delayed disease progression and death after five to seven days, whereas hypocalcaemia is characterised by rapid disease progression and death after six to twenty-four hours. Pregnancy toxaemia causes elevation of the chin (also known as "star-gazing") with a slow progression to recumbence over two to three days after the onset of initial signs. In contrast, hypocalcaemia causes a rapid progression to recumbence over three to four hours, and sternal recumbence with the head stretched out and chin on the ground with legs folded beneath or stretched out behind the ewe is typical.

Pregnancy toxaemia is characterised by a yellowish, finely speckled liver in post-mortem examinations, although hypocalcaemia typically shows no noteworthy, distinctive post-mortem features. Dosage rates of hypocalcaemia treatment with commercial calcium solutions have little effect on pregnant toxaemia. Ewes often react poorly and slowly to glucose or energy doses; the best results are observed while the ewes are still conscious.

Treatment: Early detection and prompt action to satisfy the affected ewe's energy (glucose) needs are necessary for the successful treatment of pregnant toxaemia. In addition to glucose replacement therapy, therapy necessitates the correction of fluid, electrolyte, and acid-base imbalances. Quick energy sources include oral corn syrup or propylene glycol, which should be administered at a rate of 200 ml four times a day in addition to three to four litres of concentrated oral rehydration fluid (Andrews, A and Wilkinson, J. 1998). When ewe are treated very early in the course of the disease, they usually respond well, but once they are recumbent, their response to medication is poor. Therefore, the rest of the flock should receive treatment if the ewe is already unconscious.

Parenteral therapy: In addition to glucose therapy, isotonic sodium bicarbonate or lactated Ringer's solution should be injected intravenously, and more fluids should be administered via a stomach tube. Although reported results are not outstanding, treatment with recombinant bovine somatotrophin (0.15 mg/kg body weight) in combination with dextrose and electrolytes may result in a shorter treatment period, enhance ewe survival, and increase the viability of lambs born (Burswell *et al.,* 1986).

Oral therapy: Parenteral glucose treatment is supported with oral propylene glycol or glycerin (110 grammes daily). Oral soaking with 160 ml of a concentrated oral rehydration solution that contains 45 g glucose, 8.5 g sodium chloride, 6.17 g glycine, and electrolytes every 4–8 hours has been shown to be successful. Recovery rates are reported to be 55% in advanced cases and 90% in early instances (Burswell *et al.,* 1986). When insulin is added to oral glucose precursors and electrolytes, the survival percentage is much better (87%) than when these treatments are used alone (Henze et al., 1998).

Conclusion: Low blood sugar (glucose) in connection to the fetus's high energy needs is the main cause of pregnancy toxaemia, particularly in pregnant ewes carrying twins. A number of stressors, such as poor nutrition or bad weather, may cause the condition to start. Ewes with two or more lambs are more likely to contract the disease. Ewes who are very skinny or overly obese are also affected by the illness. Clinical signs, history, and clinical testing for low glucose and high ketones are used to make the diagnosis. Early identification and prompt glucose replacement therapy are essential for the successful treatment of pregnant toxaemia. In order to reduce and prevent farm losses, it can be advised to feed high energy concentrates and grains during the final month of pregnancy and to adhere to appropriate management.

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