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Pregnancy Toxemia in Small Ruminants: Clinical, Sonographic, Hematobiochemical and Pathologic Findings

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ABSTRACT

This study was designed to investigate the clinical, ultrasonographic, hematobiochemical, and necropsy findings in sheep and goats with pregnancy toxemia (PT). Forty-eight animals with PT were enrolled. Clinical examination of the diseased animals included hypothermia in 36 animals, 12 with normal rectal temperature, bradycardia in 29, tachycardia in 19, polypnea in 32, and decreased respiratory rate in 16 animals. Thirty animals were presented in sternal position and conscious; of them, 18 were in sternal position but unconscious, and 12 were blind. Seven of the animals in sternal recumbency had nervous symptoms, including opisthotonus, convulsions, and stargazing posture, and 8 were blind. The remaining 18 animals were presented in lateral recumbency with a decreased consciousness. Hepatic sonography showed an overall increased echogenicity and brightness of the liver parenchyma. At postmortem examination, 12 animals had four neonates, two had three and two had two fetuses. The liver was enlarged, yellow and friable. Compared to controls, total leukocytic count and lymphocytes were significantly low. The serum activities of alkaline phosphatase and alanine aminotransferase were significantly lower than controls. Similar, serum concentrations of albumin, calcium and sodium were significantly lowered versus controls. Contrary, serum concentrations of globulin, total bilirubin, glucose, β-hydroxybutyric acid and activity of amylase were significantly higher in diseased compared to controls. In conclusion, this study summarizes the clinical signs as well as sonographic, hematobiochemical and pathologic findings in sheep and goats with PT. We hope our findings will assist in understanding deeply the pathophysiology of PT in these species.

Key words: Goat, Pregnancy toxemia, Sheep, Small ruminants, Ultrasound.

INTRODUCTION

In farm animals, the periparturient period, 21 days before to 21 days after parturition is a very critical stage affecting its heath status and present and future productivity (Tharwat. 2020). If the animal did not pass this phase in a smooth manner, it will suffer several metabolic disorders (Tharwat et al. 2024a). In sheep and goats, pregnancy toxemia (PT) constitutes the most common metabolic syndrome during the final pregnancy stage, with possible significant effects on performance and health of the animals. It is not only a disease of over-conditioned animals but also can affect lean ones, and is typically linked to decreased energy intake and subsequently negative energy balance resulting in mobilization of body fats and proteins (Yarim and Ciftci 2009; Kasimanickam 2016; Mongini and Van Saun 2023). The disease results from disturbance of glucose metabolism of the dam's as a result of elevated nutritional requirements of the rapidly growing fetuses. Varieties of predisposing factors may affect the clinical appearance of PT including metabolic, nutritional, genetic, environmental, physiologic, health, economic and managemental causes (Rook 2000).

Generally, PT occurs with weeks or even days before parturition with an incidence varies from 5-20% with a mortality rate reaching 80% in non-treated cases leading to

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significant financial impacts on the small ruminant's industry (Xue et al. 2019). The disease is mostly observed in animals reared on intensive systems especially in those carrying more than one fetus, and in older multiparous animals (Duehlmeier et al. 2013). PT is characterized by hypocalcemia, hyperketonemia, fatty infiltration of the liver and metabolic acidosis alongside clinical presentations of anorexia, polypnea, ruminal atony, vision loss, depression, drooping ears, and neck and head scoliosis (Lima et al. 2016; Jin et al. 2024).

A clinically significant cardiac damage may occur in animals with PT leading to significant increases in the cardiac biomarkers' cardiac troponin I and creatine kinase-myocardial band and eventually high mortalities (Souza et al. 2020). Even though the PT neonates have high mortalities either on the short or on the long term, generally have decreased weight loss and therefore they always require peri-natal intervention (Weaver et al. 2021). This study was aimed to investigate clinical, sonographic, hematobiochemical and postmortem findings in sheep and goats with PT.

MATERIALS AND METHODS

Animals and experimental design

Forty-eight animals with pregnancy toxemia, (goats, n=32; sheep, n=16), aged 65.5±17.8months and weighed 52.0±14kg, were used. No therapeutic interventions were carried out in either sheep or goats and the course off illness ranged from 1 to 5 days. Ten pregnant healthy animals (goats, n=5; sheep, n=5), in the last trimester of pregnancy were used as a control group for comparisons. Two blood samples, one on EDTA tubes (for measuring hematological parameters) and one on plain tubes (to collect serum) were collected.

Measurement of hematological and biochemical parameters

Total leukocytic count, neutrophil and lymphocyte counts and hemoglobin concentration were measured in EDTA blood samples (VetScan HM5, Abaxis, California, USA). Blood levels of the parameters including total protein (TP), alkaline phosphatase (ALP), alanine aminotransferase (ALT), albumin, globulin, calcium, phosphorus, amylase, total bilirubin (TBIL), blood urea nitrogen (BUN), creatinine, sodium potassium and glucose, were measured in serum samples (VetScan VS2 analyzer, Abaxis, California, USA). Serum concentrations of β-hydroxybutyrate (BHBA) were measured using commercial kits (Human Gesellschaft fur Biochemica und Diagnostica, Wiesbaden, Germany).

Statistical analysis

Data were shown as mean±SD alongside the minimum and maximum values and were compared using Student's *t*-test (SPSS 2017). Values of $P \leq 0.05$ were considered significant.

RESULTS

Clinical examination of the vital signs in diseased animals included hypothermia in 36 animals (37.2±1.9ºC), 12 with normal rectal temperature (39.2±0.6ºC), bradycardia in 29 (50±15 beat/min), tachycardia in 19 (105±10beat/min), polypnea in 32 (35±11breath/min) and decreased respiratory rate in 16 (16±7breath/min). While vital signs in controls included 39.2±0.7ºC, 88±5beat/min, 29±4breath/min for rectal temperature and pulse and respiratory rates, respectively.

During admission, 30 animals were in sternal position and conscious (Fig. 1); of them 18 were in sternal position but unconscious, the head and neck were turned back with absence of menace response and 12 were blind (Fig. 2). Seven of the animals in sternal recumbency had nervous symptoms including opisthotonus, convulsions, stargazing posture and 8 were blind (Fig. 3). The remaining 18 animals were presented in lateral recumbency with decreased degree of consciousness (Fig. 4). Twenty-five of the diseased animals were in the 19th week of pregnancy, 15 in the 20th week and 8 in the 21th week.

A

B

Fig. 1: Sternal presentation of a sheep (**A**) and a goat (**B**) affected with pregnancy toxemia.

A **B**

Fig. 2: Head and neck turned back in 2 goats (**A, B**) affected with pregnancy toxemia. Absence of menace response was also clear in both cases.

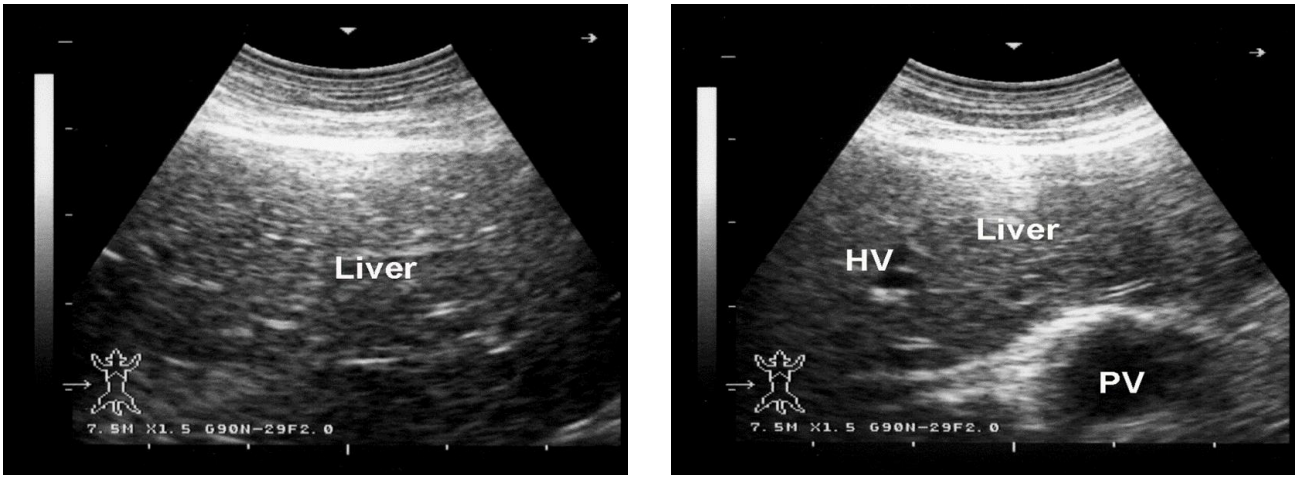
A **B**

Fig. 3: Two goats with pregnancy toxemia presented with nervous symptoms including opisthotonus, convulsions and stargazing posture.

A **B**

Fig. 4: Lateral presentation of a sheep (**A**) and a goat (**B**) with pregnancy toxemia. Both cases were unconsciousness and blind.

Hepatic sonography in 37 diseased animals showed an overall increased echogenicity and brightness of the liver parenchyma. In 16 animals, hepatic blood vessels could not be imaged at all and in other 5, only large blood vessels including portal and hepatic veins were visualized (Fig. 5). Twenty-one of the animals collapsed before and twelve after surgery. In eleven animals, 2 alive neonates for each dam were obtained (Fig. 6) while in other 16 dams, offsprings were dead. At postmortem examination, 12 animals had four neonates, two had three and two had two fetuses (Fig. 7). The liver in all necropsied animals were enlarged, yellow and friable. Giemsa-stained liver impression in 17 animals with PT confirmed severe fatty infiltration (Fig. 8).



A **B**

Fig. 5: An overall increased echogenicity and brightness of the liver parenchyma in a goat with pregnancy toxemia (**A**). Only large blood vessels including portal vein (PV) and hepatic vein (HV) were visualized.

A **B**

C **D**

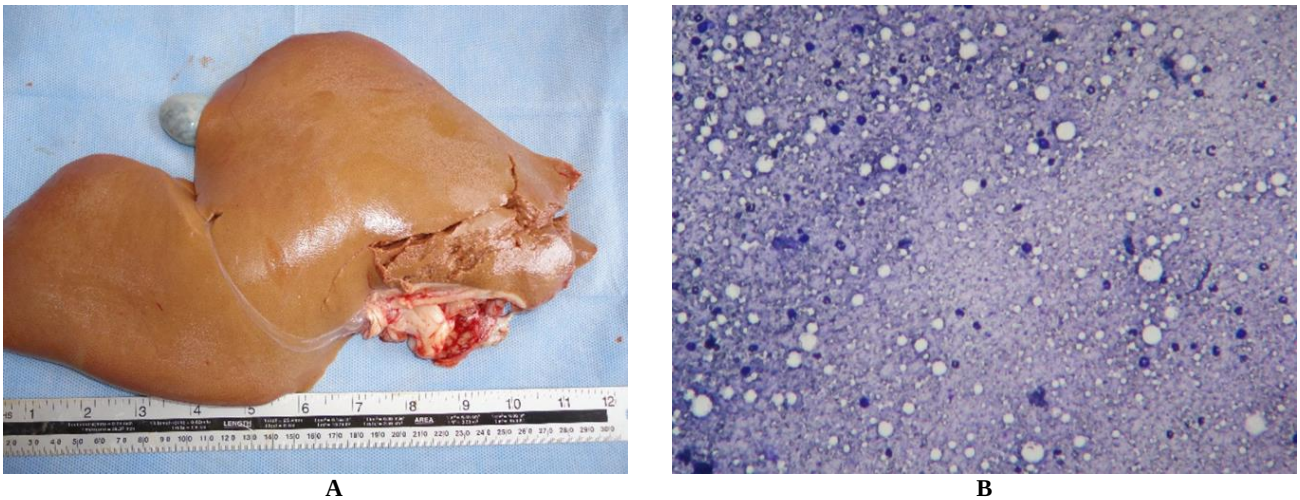
Fig. 6: A sheep and a goat with pregnancy toxemia. Assisting the sheep (**A**) led to parturition of 2 alive lambs (**B**). Assisting the goat (**C**) lead to delivery of 2 alive kids (**D**); however, the dam collapsed immediately after parturition.

The total white blood cells count, neutrophils, lymphocytes and hemoglobin concentration are summarized in Table 1. Compared to healthy pregnant animals, total leukocytic count and lymphocytes were significantly low (P=0.03, P=0.001, respectively). On the other hand, neutrophil count and hemoglobin concentration did not differ significantly between the 2 groups (P=0.9). Table 2 shows the metabolites including TP, ALP, ALT, albumin, globulin, calcium, phosphorus, amylase, TBIL, BUN, creatinine, sodium, potassium, glucose and BHBA. The serum activities of ALP and ALT were significantly lower than controls (P = 0.006, P = 0.008, respectively).

A **B**

C

Fig. 7: Postmortem examination of 3 goats with pregnancy toxemia with 2 (**A**), 3 (**B**) and 4 (**C**) dead kids.



A **B**

Fig. 8: Liver in a necropsied sheep with pregnancy toxemia. It was enlarged, yellow and friable (**A**). Giemsa-stained liver specimen in the same animal confirmed severe fatty infiltration with giant fat cells (**B**).

Table 1: Hematological parameters in goats and sheep with pregnancy toxemia versus controls

	Diseased (n=48)			Controls (n=10)			
Parameters	Means±SD	Min	Max	Means±SD	Min	Max	*P* value
Leukocytes ($\times 10^9$/L)	13.5±5.4	8.36	22.93	19.5±4.7	12.1	24.66	0.03
Neutrophil (×109/L)	6.2±5.0	1.49	17.12	5.9±2.8	2.33	9.03	0.9
Lymphocyte ($\times 10^9$/L)	7.0±4.2	1.37	16.29	15.0±3.7	9.38	18.67	0.001
Hemoglobin (g/dL)	10.7±1.7	8.1	13.1	10.7±1.1	9.8	12.8	0.9

Table 2: Biochemical parameters in goats and sheep with pregnancy toxemia versus controls

	Diseased (n=48)			Controls (n=10)			
Parameters	Means±SD	Min	Max	Means±SD	Min	Max	*P* value
TP (g/L)	66.9±2.8	64.00	72	63.7±5.9	56.00	72	0.1
ALP (U/L)	56±40	23.00	146	143±74	92.00	291	0.006
ALT (U/L)	53±35	11.00	100	12.4±1.5	10.00	14	0.008
Albumin (g/L)	25.1±5.3	18.00	33.0	35.4±3.0	31.00	40	0.0003
Globulin (g/L)	41.6±3.5	34.00	46	28.3±3.1	24.00	32	<0.0001
Ca (mmol/L)	1.6±0.4	1.00	2.23	2.3±0.1	2.19	2.43	<0.0001
Ph (mmol/L)	2.3±0.9	0.76	3.97	2.9±0.7	1.82	3.94	0.1
Amylase (U/L)	42.8±24.3	18.00	90	17.3±0.9	16.00	19	0.01
TBIL (µmol/L)	5.6±1.2	4.00	8	4.5±0.5	4.00	5	0.04
BUN (mmol/L)	9.4±2.5	3.80	12.2	8.1±3.7	3.50	14.3	0.3
Cr (µmol/L)	49.5±19.3	18.00	70	91.5±33.2	51.00	151	0.004
Na (mmol/L)	139.0±2.5	136.00	144	143.0±1.5	141.00	145	0.003
K (mmol/L)	6.4±0.9	4.70	7.6	5.9±0.4	5.20	6.4	0.1
Glu (mmol/L)	5.7±2.4	2.60	9.8	2.9±0.3	2.40	3.3	0.008
BHBA (mmol/L)	6.9±1.4	4.5	9.0	4.4±1.0	2.9	6.0	0.0002

TP, total protein; ALP, alkaline phosphatase; ALT, alanine aminotransferase; Ca, calcium, Ph, Phosphorus, TBIL, total bilirubin; BUN, blood urea nitrogen, CR, creatinine; Na, sodium; K, potassium; Glu, glucose; BHBA, β-hydroxybutyrate.

Similar, serum concentrations of albumin, calcium and sodium were significantly lowered in diseased versus controls (P<0.01). Contrary, serum concentrations of globulin, TBIL, glucose, BHBA and activity of amylase were significantly higher in diseased compared to healthy pregnant animals. Other parameters included total protein, phosphorus, BUN and potassium did not differ significantly between both diseased and healthy animals (P>0.05).

DISCUSSION

Usually, the goats with PT have different presentation findings that may include total loss of appetite, lethargy, recumbency, dropped head, opisthotonos, convulsion, tympany, loss of vision, salivation and teeth grinding (Vasava et al. 2016). In a second study in goats with PT, clinical signs of goats with PT were diverse and included anorexia, recumbency, depression, weakness, lameness, edematous limbs, polypnea, dyspnea, pneumonia, diarrhea, loss of body conditions, dehydration, straining, delayed birth, vocalizing, bruxism, prolapse of the vagina and/or rectum, dystocia, vaginal discharges, tympany and abduction of the fore limbs (Simpson et al. 2019).

Lima et al. (2016) reported that goats with PT were presented with swollen limbs, polypnea, anorexia, static rumen, nervous signs, recumbency, ear drooping ears were the most frequently observed clinical manifestations. In sheep with PT, clinical signs also included anorexia, depression, loss of body weight, recumbency, nervous signs, jaundice, teeth grinding, blindness, dystocia, tympany, and mortality of the dams and fetuses (Mustafa et al. 2023). In a second study in sheep with PT, clinical signs included grinding teeth, anorexia, ataxia and debility (Xue et al. 2019).

In the current report, sheep and goats with PT were admitted with hypothermia in 75% of the animals, normothermic in 25%, bradycardic in 60.4%, tachycardic in 39.6%, polypnea in 66.7% and decreased respiratory rates in 33.3% of the animals. In addition, 62.5% of the animals were admitted in sternal recumbency; 60% of them were comatose with backward deviation of the head and neck, 26.7% were blind, 23.3% had nervous signs. Out of the 48 animals with PT, 18 (37.5%) were presented in lateral position. These findings agree well with earlier studies conducted on goats with PT.

Ultrasonography has been proved effective for early recognition and diagnosis of several thoracic and abdominal disorders in sheep and goats (Tharwat 2021; Tharwat and Al-Hawas 2024; Tharwat et al. 2024b). In this study, interestingly, in 37 (77.1%) of the diseased animals, the liver parenchyma was homogenously bright; of them the hepatic blood vessels could not be imaged at all in 16(48.5%) animals with PT but only the large blood vessels including large branches of the portal and hepatic veins were imaged in 5 out of the 37 (13.5%). On sonograms, the reason why liver appeared bright and blood vessels could not be visualized except in few numbers of diseased animals were clarified during postmortem examination. The liver was found enlarged, icteric and friable on touch and fatty infiltration was confirmed after staining of liver impressions by Giemsa stain; this finding confirms a state of severe negative energy balance in animals with PT. In dairy cows, increased hepatic echogenicity and brightness were also reported in cattle and buffaloes with fatty infiltration (Mohamed et al. 2004; Hayam et al. 2014).

Concerning the hematological alterations, total white blood cells and lymphocytes were significantly lower versus levels in healthy pregnant animals. However, neutrophils and hemoglobin concentration did not differ significantly between diseased and healthy animals. On the other side, Simpson et al. (2019) found neutrophilia in all goats with PT. A temporary physiological stress response due to release of endogenous steroids may be the predisposing factor of observed neutrophilia (Simpson et al. 2019). Neutrophilia was also detected as a physiological condition in pregnant goats and camels during the last week of pregnancy. Neutrophilia was also reported in pregnant women and termed physiological leukocytosis (Paidas and Hossain 2010). The reason why in the current study neutrophilia and leukocytosis were not encountered is the use of a control group consisting of pregnant animals; however other studies used non-pregnant animals as controls.

Several metabolites varied significantly between the group of animals with PT and the controls. The activities of

ALP and ALT and concentrations of albumin, calcium and sodium were significantly lower than controls. However, globulin, TBIL, glucose and BHBA concentrations, and the activity of amylase were significantly higher in diseased versus controls. Other parameters of total protein, phosphorus, BUN and potassium did not differ significantly between both groups. Similar to our findings, Simpson et al. (2019) reported hyperglycemia, hyperbilirubinemia, hypoalbuminemia and hypocalcemia in goats with PT. Hyperglycemia, increased BHBA concentration, hypoalbuminemia, hyperglobulinemia and hypocalcemia were also detected in goats with PT (Jin et al. 2024). However, Vasava et al. (2016) observed significant increases in some serum parameters in goats with PT including significant increases in aspartate aminotransferase, alanine aminotransferase, BUN, creatinine, BHBA, non-esterified fatty acids and significant decreases in glucose and calcium. In goats with PT, it was reported that the level of blood glucose may be used as a good sign of the viability of the fetuses, and hypoglycemic in those with PT may indicate hysterotomy (Lima et al. 2012).

In conclusion, the sheep and goats with PT were admitted with different clinical presentations. All affected animals had recumbent position while first seen; the majority were in sternal followed by lateral positions. Several animals were unconsciousness with deviation of the head and neck backwards, blind and had nervous manifestations. Over two thirds of the diseased animals had bright liver on ultrasonograms, and almost the hepatic blood vessels were difficult to be seen. At necropsy, the liver was enlarged, yellow and friable and Giemsa-stained liver specimens confirmed severe fatty infiltration.

Author contributions

MT: conceived, designed the experiment, carried out the practical work, wrote the manuscript draft and prepared the figures and tables. **AA**: analyzed the hematological and biochemical parameters and carried out postmortem examination. **MM**: revised and edited the manuscript draft. All authors re-read, revised and approved the final manuscript version for publication.

Conflict of Interest Statement

The authors declare that there is no conflict of interest.

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