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RESEARCH ARTICLE

# Determination of Hemato-Biochemical Biomarkers, Associated Risk Factors and Therapeutic Protocols for Pregnancy Toxemia in Beetal Goats

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## Abstract

This study was aimed at evaluating the risk factors, alterations in blood β-hydroxybutyrate (BHB), hemato-biochemical biomarkers for earlier detection of pregnancy toxemia (PT) and comparative efficacy of therapeutic protocols in Beetal goats. A total of (N=100) goats between 120-150 days of gestation were examined. Goats having BHB >3 mmol/L were considered positive for PT by employing Freestyle™ Optium Kit. Risk factors parity, age, body weight, number of fetuses, grazing and housing, were significantly (P<0.05) associated with incidence of PT. Packed cell volume (PCV), WBCs, neutrophils, monocytes and lymphocytes were significantly higher in affected animals. Total protein and albumin were low while ALT, AST, ALP, GGT creatinine and BUN were significantly elevated. Twenty-four diseased goats were divided into two groups. Animals in group A were administered with 10% dextrose and propylene glycol orally, twice a day (BID) for three days. Whereas, in group B aforementioned treatment was supplemented with 0.15 mg/kg/SC recombinant bovine somatotropin (rbST), once a day (OID). Treatment efficacy was 75% and 83.3% in group A and B, respectively. Significant improvement in BHB, hemato-biochemical parameters were observed in goats receiving rbST. This study highlighted the significance of risk factors and hemato-biochemical biomarkers for earlier diagnosis of PT. Treatment with rbST, 10% dextrose and propylene glycol had significant effect on improvement of hemato-biochemical parameters in PT in Beetal goats.

***Keywords:*** *Beetal goats, Hemato-biochemical biomarkers, Pregnancy toxemia, Recombinant bovine somatotropin, rbST, β-hydroxybutyrate*

# Beetal Keçilerinde Gebelik Toksemisi İçin Hemato-Biyokimyasal Biyobelirteçlerin, İlgili Risk Faktörlerinin ve Terapötik Protokollerin Belirlenmesi

## Öz

Bu çalışmada, Beetal keçilerinde gebelik toksemisinin (PT) erken teşhisi için risk faktörlerinin, kan β-hidroksibütirattaki (BHB) değişikliklerin ve hemato-biyokimyasal biyobelirteçlerin değerlendirilmesi ve terapötik protokollerin karşılaştırmalı etkinliğinin analizi amaçlandı. Çalışmada, 120-150 günlük gebe toplam (N=100) keçi incelendi. Freestyle™ Optium Kit kullanılarak gerçekleştirilen analizde β-hidroksibutirat (BHB) seviyesi >3 mmol/L olan keçiler, PT için pozitif kabul edildi. Risk faktörleri paritesi, yaş, vücut ağırlığı, fetüs sayısı, otlatma ve barındırma, PT insidansı ile anlamlı (P<0.05) ilişkili saptandı. Hematokrit değer (PCV), beyaz kan hücreleri (WBCs), nötrofiller, monositler ve lenfositler, hasta hayvanlarda önemli ölçüde daha yüksekti. ALT, AST, ALP, GGT kreatinin ve BUN önemli ölçüde yüksek iken, toplam protein ve albümin düşüktü. Yirmi dört hasta keçi iki gruba ayrıldı. Grup A'daki hayvanlara, üç gün boyunca günde iki kez (BID) %10 dekstroz ve propilen glikol oral yoldan uygulandı. Grup B'de ise yukarıda bahsedilen tedaviye, günde bir kez (OID) 0.15 mg/kg/SC rekombinant sığır somatotropini (rbST) ilave edildi. Tedavi etkinliği grup A ve grup B için sırasıyla %75 ve %83.3 olarak saptandı. rbST uygulanan keçilerde BHB ve hemato-biyokimyasal parametrelerde önemli iyileşme gözlendi. Bu çalışma, PT'nin erken teşhisi için risk faktörlerinin ve hemato-biyokimyasal biyobelirteçlerin önemini vurguladı. Beetal keçilerinde rbST, %10 dekstroz ve propilen glikol tedavisi, PT'de hemato-biyokimyasal parametrelerin iyileştirilmesinde önemli etkiye sahipti.

***Anahtar sözcükler:*** *Beetal keçisi, Hemato-biyokimyasal biyobelirteçler, Gebelik toksemisi, Rekombinant sığır somatotropini, rbST, β-hidroksibütirat*

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## Introduction

Pregnancy toxemia known as gestational ketosis is quite common in ewes and goats during last trimester, due to ever-growing negative energy balance [1]. Small ruminants become extremely susceptible to various metabolic diseases as they come closer to parturition [2]. Pregnancy toxemia often develops during last 4 to 6 weeks of gestation, mainly in pregnancies with more than one fetus [3]. About 60% of fetal growth takes place in last days of gestation period [4]. During this time approximately 33 to 36% of the circulating glucose is directed towards feto-placental unit to satisfy its energy demands [5]. Enormous glucose demand of growing fetuses during pregnancy is fulfilled by the dam. Disparity in fetal glucose demands and supply by dams occurs either due to reduced dietary intake of mother or exponential increase in glucose demands by developing fetuses usually in last trimester, which create negative energy balance and ultimately severe hypoglycemia [6]. Older animals carrying multiple fetuses and having high production under severe stress are most frequently prone to develop pregnancy toxemia [7]. Hyperketonemia and hypoglycemia are the most common biochemical manifestations of this disease. However, biochemical investigations have revealed a marked impact on the functionality of liver and kidney as well [8]. Pregnancy toxemic goats have β-hydroxybutyrate persistently high in the blood, as most of acetoacetate produced in liver cells is consistently reduced to β-hydroxybutyrate by the enzyme hydroxybutyrate dehydrogenase [9]. Unfortunately, PT is endemic amongst all species of goats across the world, causing high morbidities and high mortalities [10]. Absence of the early detection of the disease due to the insufficient information about its pathogenesis and the lack of efficient diagnostic tools are the foremost obstacles in improving our prophylactic as well as therapeutic policies against this disease [11]. Biochemical parameters are integral to early diagnosis of pregnancy toxemia in goats [12]. Affected animals are generally recumbent in 3-4 days, and frequently manifest clinical complications [13]. The glucose, propylene glycol and rbST are being commonly used in treatment therapies of the pregnancy toxemia [14-16]. Whereas, in advance cases the augmentation of treatment therapy with some other compound such as insulin may also be required [16]. Despite vigorous treatment prognosis is generally poor and mortality rates are high in affected animals. Approximately, up to 20% decline in health has been observed in individuals birthed by affected mothers [11]. There is always undue delay in diagnosis of pregnancy toxemia in early stages due to an absence of reliable detection biomarkers of pregnancy toxemia in goats [17]. So, this study was designed, aiming to evaluate the risk factors associated with PT and identify hemato-biochemical biomarkers for early disease detection, alteration in β-hydroxybutyrate (BHB) levels in the blood. A comparative efficacy of rbST supplementation to pregnancy toxemia treatment involving administration of 10% dextrose and propylene glycol was evaluated as well.

## Material and Methods

### *Ethical Considerations*

The designed study was submitted to and approved by animal ethics committee and departmental board of studies (BOS) of Department of Veterinary Medicine, University of Veterinary and Animal Sciences, Lahore.

### *Experimental Animals*

A total of 100 pregnant (N=100) Beetal goats aged between 1-6 years, weighing around 35-55 kg body weight and gestational duration ranging from 120 to 150 days were inducted into this study. Animals showing signs of illness were examined and sampled for pregnancy toxemia from different villages.

### *Ultrasonography*

The pregnant does were subjected to ultrasonography to confirm the stage of gestation and assess the viability of the fetuses. The estimated gestational age of the fetus in weeks was calculated using the formula:

$$Y=4.712+0.445\ X$$

where Y=Gestational age (wks) and X=Fetal parameter (cm) in case of crown rump length and Y=2.675+3.229 X where Y=Gestational age (wks) and X=Fetal parameter (cm) in case of bi-parietal diameter [18].

### *Blood Sampling and Parameters Measured*

Blood samples (3 mL) were aseptically collected in EDTA and non- EDTA coated vacutainers by jugular vein puncture for screening of PT. The blood samples were subjected to analysis of BHB (β-hydroxybutyrate) level in mmol/L via automated Freestyle™ Optium kit for BHBA (Abbot Pharma, Neo-H) [19]. Goats with BHB>3.0 mmol/L were considered as positive for pregnancy toxemia [20]. Hematological parameters were determined from whole blood by using auto hematology analyzer (Rayto, RT-7600™). Whereas, serum samples were obtained from blood collected in non EDTA coated vacutainers and analyzed for serum biochemical parameters by clinical chemistry analyzer (Seamaty, SD1 Sichuan™). Pregnancy toxemic group consisted (N=24) and hemato-biochemical parameters were measured in these animals' pre-treatment. These pregnancy toxemic animals were then subjected to treatment trials for the improvement of clinical signs, increase in fetus's livability and life of dam before and after parturition.

### *Treatment Trials*

Total twenty-four (N=24) pregnancy toxemic goats were equally divided into two groups A and B. Goats in group A were injected with 10% dextrose 500 mL IV, 60 mL propylene glycol orally twice a day, for three consecutive days and while in group B recombinant bovine somatotropin

(rbST) was given additionally at the dose rate of 0.15 mg/kg sc, once daily for three consecutive days [14-16]. Blood samples were taken again from both groups after three consecutive days of treatment and efficacy of treatment was determined on the basis of reduction in BHB in blood and improvement of hematologic and biochemical parameters.

### *Statistical Analysis*

Data regarding prevalence of pregnancy toxemia (PT) was subjected to chi-square analysis with significance level ($P<0.05$). Data regarding hemato-biochemical changes was analyzed through One-Way ANOVA whereas, data regarding comparative therapeutics efficacies was analyzed using paired t-Test, keeping level of significance ($P<0.05$). All the statistical analyses were carried at SPSS version 26.0 (version 26, IBM, Chicago, IL).

## Results

### *Correlation of Risk Factors Associated with Pregnancy Toxemia*

Goats with higher parity and multiple fetuses had more tendency to develop pregnancy toxemia. Goats with 3rd and 4th parity while carrying 3 fetuses experienced highest incidence of pregnancy toxemia at 60.71% and 68.29%, respectively. Similarly, 'age' was also significantly associated ($P<0.05$) with pregnancy toxemia. Therefore, highest percentage 80.0% was seen in goats of age ≤5 years. Higher body weight was positively associated with the development of pregnancy toxemia whereby 41.17% of affected dams weighed between 46-55 kg. In present study, 63.6% goats with pregnancy toxemia were mal-nourished. Whereas, incidence of PT in goats with other concurrent infections was 61.20%. Similarly, 57.80% PT affected animals were self- medicated by the farmers. The 46.20% pregnancy toxemic animals were reared in tethered systems and not allowed to graze. Improper housing played a pivotal role in development of this ailment hence, 57.1% animals positive for pregnancy toxemia were with improper housing. Importance of good sanitary measures was reinforced when 68.7% animals reared in abominable conditions were affected with pregnancy toxemia *(Table 1)*.

### *Correlation of Hemato-biochemical Changes Pre- and Post-treatment*

#### *- Hematological parameters*

Values of total WBCs, packed cell volume, neutrophils, lymphocytes, and monocytes, were significantly ($P<0.05$) higher in pregnancy toxemic goats whereas, red blood cells count (RBCs), hemoglobin (Hb) were significantly ($P<0.05$) lower in pregnancy toxemic animals depicting the hematological disturbances. However, treatment had a positive effect on these parameters leading to normalization of hematological. Whereas, no significant discrepancies were found in other measured hematological parameters as shown *(Table 2, Fig. 1)*.

#### *- Biochemical parameters*

In regard to the biochemical analysis, values of AST, ALT, ALP, and GGT were significantly ($P<0.05$) higher in pregnancy toxemia reflecting the hepatic damages. However, there was considerable improvement in these parameters and were in normal ranges after implication of treatment *(Table 3)*. On the other hand, total protein (TP) and albumin, were also significantly ($P<0.05$) lower in pregnancy toxemic goats. Similarly, BUN and creatinine was considerably higher in the animals suffering from PT which was considerably ($P<0.05$) reduced after treatment *(Table 3)*.

#### *- BHBA (β-hydroxybutyrate)*

In both group A and B, mean value of BHB was significantly declined after treatment. The findings declared, additional use of rbST with 10% Dextrose 500 mL IV and 60 mL propylene glycol is more effective than only dextrose and propylene glycol. However, comparison of treatment groups using t-independent test revealed insignificant difference ($P>0.05$) between both groups. Chi-square analysis of survival rates of dam in both treatment groups revealed insignificant difference ($P>0.05$), which indicated almost equal efficacy of both treatments approaches against pregnancy toxemia in Beetal goats *(Table 4)*.

## Discussion

Pregnancy toxemia is inability of dams to fulfill glucose requirements of developing fetuses [21] Caprine pregnancy toxemia is diagnosed based upon the stage of gestation, number of fetus dam carried, physical signs and hemato-biochemical indices. Current study revealed considerable 35% prevalence of pregnancy toxemia in Beetal goats which was close to 40% [3] whereas, contrary to 88.9% [22]. Association of number of fetuses with pregnancy toxemia was in agreement with previous findings [3]. Failure to cope energy drain in higher number of fetuses stimulated fats metabolism leading to hyperketonemia and pregnancy toxemia [23]. Age of animal corroborates earlier findings [24] that reported older animals to be more susceptible to PT than the young dams. The older animals have comparatively less active basal metabolic rate (BMR) to provide the sufficient energy to developing fetuses [25]. Similarly, as in current study it has been previously established that animals with higher body weight are more prone to PT [26]. Poor feeding and lack of sustained grazing have proven to be significant risk factors for pregnancy toxemia [27]. Malnourishement in pregnant dams produces ketone bodies. These ketone bodies reduce the ruminal motility thereby causing reduced intake and ruminal contractions which further deteriorate body condition [11]. Stress factors

***Table 1.*** *Chi-square analysis of associated risk factors of pregnancy toxemia*

| Variables | Variables Level | Positive/Total | Prevalence% | P-Value |
|---|---|---|---|---|
| Parity number | 1-2 | 08/52 | 15.38 | 0.001 |
| | 3-4 | 17/28 | 60.71 | |
| | 5-6 | 10/20 | 50.00 | |
| | Total | 35/100 | 35.00 | |
| No. of fetuses carrying | 2 | 04/51 | 07.84 | 0.001 |
| | 3 | 28/ 41 | 68.29 | |
| | 4 | 03/8 | 37.5 | |
| | Total | 35/100 | 35.00 | |
| Age(years) | ≤2 | 01/08 | 12.50 | 0.001 |
| | ≤3 | 09/55 | 16.36 | |
| | ≤4 | 10/17 | 58.82 | |
| | ≤5 | 12/15 | 80.00 | |
| | ≤6 | 03/05 | 60.00 | |
| | Total | 35/100 | 35.00 | |
| Body weight | 35-45 kg | 28/83 | 33.73 | 0.001 |
| | 46-55 kg | 07/17 | 41.17 | |
| | Total | 35/100 | 35.00 | |
| Onset of clinical signs/days | 1-2 | 15/56 | 26.79 | 0.052 |
| | 3-4 | 20/44 | 45.45 | |
| | Total | 35/100 | 35.00 | |
| Concurrent infection | Infection | 19/31 | 61.29 | 0.001 |
| | No infection | 16/69 | 23.19 | |
| | Total | 35/100 | 35.00 | |
| Self-medication by farmers | Medicated | 24/81 | 29.63 | 0.020 |
| | Not medicated | 11/19 | 57.89 | |
| | Total | 35/100 | 35.00 | |
| Abortion history | Abortion | 03/04 | 75.00 | 0.087 |
| | No abortion | 32/96 | 33.33 | |
| | Total | 35/100 | 35.00 | |
| Season | Winter | 31/82 | 37.80 | 0.209 |
| | Summer | 04/16 | 25.00 | |
| | Total | 35/100 | 35.00 | |
| Stall feeding/restricted feeding | Stall feeding | 29/73 | 39.73 | 0.103 |
| | No stall feeding | 06/27 | 22.22 | |
| | Total | 35/100 | 35.00 | |
| Grazing | Grazing | 04/33 | 12.12 | 0.001 |
| | Non- grazing | 31/67 | 46.27 | |
| | Total | 35/100 | 35.00 | |
| Housing | Confined | 23/79 | 29.11 | 0.017 |
| | Open | 12/21 | 57.14 | |
| | Total | 35/100 | 35.00 | |
| Feeding quality | Good | 07/56 | 12.50 | 0.001 |
| | Poor | 28/44 | 63.64 | |
| | Total | 35/100 | 35.00 | |
| Space availability | Enough | 09/18 | 50.00 | 0.141 |
| | Overcrowded | 26/82 | 31.71 | |
| | Total | 35/100 | 35.00 | |
| Sanitation | Good | 13/68 | 19.12 | 0.001 |
| | Poor | 22/32 | 68.75 | |
| | Total | 35/100 | 35.00 | |
| Water quality | Fresh/tap water | 26/84 | 30.95 | 0.052 |
| | Canal/pond | 09/16 | 56.25 | |
| | Total | 35/100 | 35.00 | |

*P<0.05 indicates significant difference*

***Table 2.*** *Hematological analysis of different parameters*

| Parameters | Before Treatment | After Treatment | |
|---|---|---|---|
| | Pregnancy Toxemia (Mean±SD) (n=24) | Group A (Mean±SD) (n=12) | Group B (Mean±SD) (n=12) |
| RBCs (x10$^6$/µL) | 13.90±0.12$^a$ | 14.49±0.13$^b$ | 14.40±0.25$^b$ |
| Hb (g/dL) | 9.83±0.29$^a$ | 9.83±0.31$^a$ | 10.25±0.62$^b$ |
| PCV (%) | 44.41±0.11$^a$ | 38.58±0.19$^b$ | 28.16±0.62$^c$ |
| MCV (fL) | 25.00±0.16$^a$ | 24.83±0.17$^a$ | 24.83±0.29$^a$ |
| MCH (pg) | 7.50±0.07$^a$ | 7.56±0.09$^a$ | 7.48±0.11$^a$ |
| MCHC (g/dL) | 34.50±0.63$^a$ | 34.64±0.56$^a$ | 34.79±0.54$^a$ |
| WBCs (x10$^3$/µL) | 16.90±0.24$^a$ | 15.15±0.23$^b$ | 7.31±0.13$^c$ |
| Neutrophils (x10$^3$/µL) | 8.96±0.20$^a$ | 8.21±0.07$^b$ | 7.46±0.10$^c$ |
| Monocytes (x10$^3$/µL) | 0.28±0.02$^a$ | 0.28±0.01$^b$ | 0.15±0.02$^c$ |
| Lymphocytes (x10$^3$/µL) | 8.30±0.17$^a$ | 8.12±0.22$^b$ | 7.21±0.15$^c$ |
| Eosinophils (x10$^3$/µL) | 0.23±0.01$^a$ | 0.20±0.01$^a$ | 0.18±0.008$^a$ |
| Thrombocytes (×10$^9$/µL) | 433±11.54$^a$ | 436±13.30$^a$ | 423±16.06$^a$ |
| Fibrinogen (g/L) | 5.25±0.18$^a$ | 4.87±0.14$^a$ | 5.34±0.11$^a$ |

$^{abc}$ *Different superscripts shows significant variation in the same row*

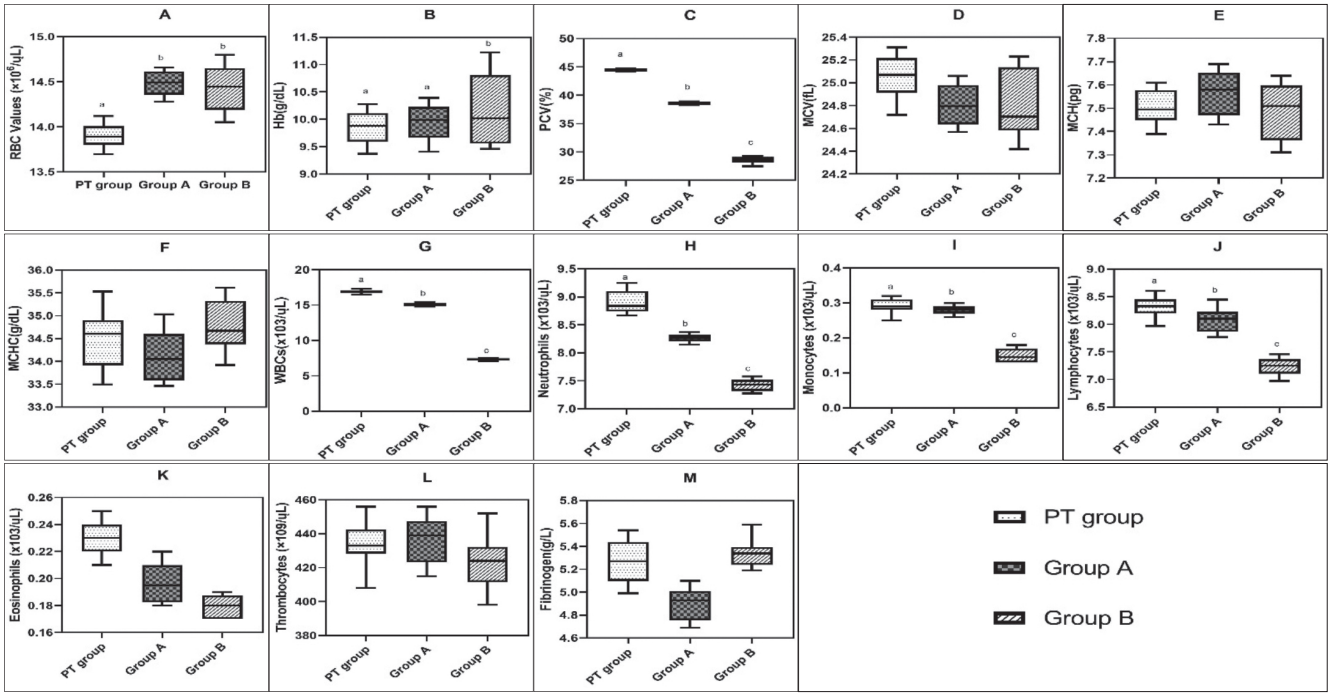


**Fig 1.** Interleaved Box and Whisker plot (Graph Pad Prism Ver.8.4.3) depicting comparative mean±SD values for hematological parameters, whereby significance between pre-treatment (Pregnancy toxemia, PT group) and (post-treatment) group A (10% dextrose 500 mL IV+ 60 mL propylene glycol) and group B (10% dextrose 500 mL IV+ 60 mL propylene glycol + recombinant bovine somatotropin (rbST) at 0.15 mg/kg s/c) are indicated by different superscripts

including concurrent infections, open housing and poor sanitary conditions have also cause decline in feed intake amongst goats leading to a failure in coping with energy requirements of fetuses [28].

Decrease in RBCs and Hb whereas, elevation in PCV in pregnancy toxemic goats indicated electrolyte imbalance which was attributed to stress of starvation, dehydration and kidney failure. These symptoms have been concurrently associated with pathogenesis of caprine pregnancy toxemia [29,30]. In present study decrease in number of RBCs and Hb concentration corroborated previous reports [29,31] while a sharp decline in hemoglobin (Hb) concentration refuted previously published findings in goats. Elevation

***Table 3.*** *Biochemical analysis of different parameters*

| Parameters | Before Treatment | After Treatment | |
|---|---|---|---|
| | Pregnancy Toxemia (Mean±SD) (n=24) | Group A (Mean±SD) (n=12) | Group B (Mean±SD) (n=12) |
| Total Proteins (g/dL) | 4.83±0.25[a] | 6.04±0.23[b] | 7.20±0.22[c] |
| Albumin (g/dL) | 1.98±0.06[a] | 2.43±0.18[b] | 2.85±0.10[c] |
| ALT (IU/L) | 55.75±1.20[a] | 45.91±0.80[b] | 30.08±0.85[c] |
| AST (IU/L) | 306.33±1.35[a] | 246.16±2.13[b] | 153.00±1.71[c] |
| ALP (IU/L) | 414.9±3.46[a] | 349.00±3.23[b] | 173.08±2.99[c] |
| GGT (IU/L) | 65.08±0.93[a] | 39.58±1.01[b] | 29.33±0.54[c] |
| BUN (mg/dL) | 24.58±1.01[a] | 23.16±0.73[a] | 13.54±0.61[b] |
| Creatinine (mg/dL) | 3.93±0.41[a] | 2.92±0.34[b] | 1.69±0.33[c] |

[abc] *The different superscripts show significant variation in the same row*

***Table 4.*** *Efficacy of treatment in group A and B*

| Groups | Before Treatment BHBA (mmol/L) (n=12) | After Treatment BHBA (mmol/L) (n=12) | P-Value | Survival (%) |
|---|---|---|---|---|
| A | 5.008±1.41 | 2.875±1.62 | 0.00019 | 75 |
| B | 5.1±1.33 | 2.08±1.62 | 0.0000008 | 83.33 |
| *p*-value (between treated groups) | | 0.185 | - | 0.615 |

*P<0.05 indicates significant difference*

in PCV (hematocrit) observed by authors was similar to the descriptions of previous studies [29,30,32] but contrary to the findings of Tharwat and Al-Sobayil [31]. MCH, MCV and MCHC varied insignificantly in this study which agreed with the findings of previous study [31].

Leukocytosis and lymphocytosis in pregnancy toxemia could be attributed to the presence of acute and chronic inflammations [33]. Increases in WBCs, neutrophils, monocytes, eosinophils and lymphocytes are in agreement with results as described previously by Abba et al.[29] and Tharwat and Al-Sobayil [31] who postulated that this increase was due to metabolic acidosis (ketoacidosis), infection, localized inflammatory process and tissue necrosis of liver. Neutrophilia could be due to hepatic lipidosis in which exposure of hepatocytes to fatty acids elicits inflammation, increase in oxidative stress, and production of fibrogenic cytokines [32]. Neutrophilia in present findings was in agreement with the description of Smith and Sherman [32] but was contrary to the Tharwat and Al-Sobayil [31]. Lymphocytosis in the present study was similar as described by the previous study [31]. Whereas, lymphopenia in pregnancy toxemic goats was also determined by Abba et al.[29] and Smith and Sherman [32]. Thrombocytes did not show any significant variation in current findings which is similar to the previous study [33]. Similarly, fibrinogen was not affected by pregnancy toxemia and corroborated by the previous findings [34].

Decrease in total protein and albumin recorded was similar as described by the previous study [35,36]. It clearly indicates that adequate quantity of proteins is not being produced by the hepatic system or being lost from the body of diseased animals. This is might be due to increased protein catabolism, decomposing fetuses or terminal kidney failure which causes the decrease in the total protein and albumin [35,36]. The higher levels of AST, ALT, and GGT activities in the pregnancy toxemic, may be attributed to hepatic damage or hepatic lipidosis due to fat mobilization [30,35,37]. These elevated levels of AST, ALT, and GGT are similar to the descriptions of previous studies [30,36,38,39] who found a significantly higher and positive correlation with the rise of ketonemia. In current study the higher GGT level in blood was same as reported by [36] which is an indicator of liver damage in PT in goats [40]. An elevation in the release of alkaline phosphate (ALP) in the circulation from the epithelium of the bile ducts is associated with severe liver damage [41]. In this study elevated level of ALP was similar to the descriptions of previous studies [30,36]. However, current results were contrary to the descriptions of previous studies [35,42] who did not find any changes in blood ALP activity. Higher concentrations of BUN and creatinine may be considered as indicator of involvement of the kidney in caprine pregnancy toxemia due to increased catabolism and severe kidney dysfunction [43]. The increase in BUN and creatinine was similar as reported previously [35,36,44] whereas these findings were not in line with Tharwat and Al-Sobayil [31]. After treatment results show improvement in liver and kidney functioning to prevent the organs from further damages.

Treatment protocols for PT consisted using glucose and other products that trigger glucose utilization [15]. The administration of the i.v. glucose infusion, propylene glycol causes the glycaemia in the blood [15] whereas, rbST triggers glucose utilization via the gluconeogenesis. In current study the therapeutic efficacy of 75%, and 83.3% in both groups was similar to survival rate of 73%, 75%, and 86.7% as described by the previous studies [42,45,46] where i.v. glucose infusion, propylene glycol and rbST was given as treatment protocol [47]. Pregnancy toxemia sometimes might not respond well to a glucose challenge in the advance cases probably due to glucose intolerance caused by decreased insulin levels [48]. However, in animals at the early stages of pregnancy toxemia, treatment with i.v. glucose is useful to reverse the process [14,16,45,46]. Treatment protocols showed better response in the current study probably because of diagnosis of the disease at the early stages and initiation of treatment with dextrose along with propylene glycol and rbST in both groups, which is similar to the descriptions of previous studies [14,16,42,45,46]. Furthermore, propylene glycol treatment was repeated twice daily in this study which subsequently improved the treatment response [26]. Whereas, in the advance cases the supplementation with insulin would be required to enhance the glucose utilization [14,16].

In present study the comparative efficacy of treatment was higher in animals receiving rbST, which is similar to the findings of Anoushepour et al.[44]. Difference in results in both groups indicated that rbST has beneficial effects in the treatment of pregnancy toxemia in goats. So the findings of this study declared that, rbST should preferably be used with dextrose and propylene glycol while treating pregnancy toxemia in goats [45]. However, the treatments regimens may be studied more intensely with other protocols in the Beetal goats to get an ultimate conclusion.

Animals suffering from pregnancy toxemia showed various hemato-biochemical changes which can be used as biomarkers in early detection. Risk factors parity, age, fetuses carried, grazing, housing, were significantly ($P<0.05$) associated. Animals suffering from pregnancy toxemia treated with dextrose, propylene glycol and recombinant bovine somatotropin presented significant decrease in beta hydroxybutyric acid and improvement in other hemato-biochemical parameters which is an indication of successful therapy. Treatment of group A with 10% dextrose 500 mL and 60 mL propylene glycol bid orally for three days expressed survival rate of 75% while group B treated additionally with rbST (0.15 mg/kg) S/C expressed survival rate of 83.3%. Comparison of treatment A and B was non-significant but with higher survival rate of both dams and fetuses in group B. Assumed risk factors have positive association with pregnancy toxemia.

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## Conflict of Interest

There are no conflicts of interest in our present study.

## Author Contributions

YRK, AZD and MI planned, designed, and supervised the research procedure. Data was collected by YRK and AA. Statistical analysis was conducted by AA, KH and AHR. Original draft was written by YRK, RLK. All authors have contributed to the revision and final proof-reading of the manuscript.

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