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Postpartum Insulin Resistance Surrogates in Subclinical Hyperketonemic Dairy Goats: A Longitudinal Comparison with Healthy Herdmates

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ABSTRACT

During the transition phase, dairy goats are highly vulnerable to subclinical hyperketonemia (SCHK). The present work sought to examine how metabolic traits and indirect measures of insulin resistance (sIR) differ between SCHK-affected goats and those in normal health (HEAL) throughout this stage. Twenty Guanzhong dairy goats were categorized into HEAL (n = 10) and SCHK (n = 10) groups according to β-hydroxybutyrate (BHBA) levels in their blood. Samples were drawn from the jugular vein at −3, −2, −1, 0 (kidding), +1, +2, and +3 weeks relative to parturition to determine glucose (GLU) and insulin (INS) concentrations. Indices of sIR were calculated from these measurements. SCHK goats displayed notably higher insulin values during the first three postpartum weeks compared with HEAL goats. At one week after birth, QUICKI, RQUICKI, and RQUICKIBHBA scores declined significantly, whereas HOMA-IR rose in the SCHK group. Increased insulin output in SCHK goats during early lactation seems to help sustain normal glucose levels, contrasting with the response in healthy animals.

Keywords: Dairy goat, Transition period; Insulin resistance; Subclinical hyperketonemia, Surrogate index

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Introduction

The transition phase, defined as the three weeks before and after kidding, is a crucial interval affecting health and reproductive efficiency in dairy goats [1]. This stage involves rapid fetal growth and milk formation, causing a sharp elevation in energy requirements. Because the expanding uterus compresses the rumen, dry matter intake (DMI) drops below normal levels, leading to reduced energy consumption [2]. When energy use surpasses intake, a negative energy balance (NEB) occurs. To compensate, body fat stores are mobilized, producing higher blood levels of nonesterified fatty acids (NEFA) and ketone bodies [3]. Hyperketonemia—characterized by excess ketones in circulation—is a common consequence of NEB [4]. In goats, it is also called pregnancy toxemia or lactation ketosis and often develops in late gestation or shortly after birth [5]. The subclinical variant (SCHK) lacks visible symptoms but increases the likelihood of other production-related disorders such as hypocalcemia or mastitis [6]. SCHK is more frequent than clinical ketosis, with about 10% prevalence in Guanzhong goats in China [7], causing financial losses due to lowered milk yield and disease vulnerability.

Insulin resistance (IR) is considered a physiological adjustment that channels nutrients toward the fetus and mammary gland during the periparturient stage [8]. Several indirect indices of insulin sensitivity (sIR) have been proposed in veterinary and human medicine, derived from glucose (GLU), insulin (INS), β-hydroxybutyrate (BHBA), and NEFA values. These indices include HOMA-IR, QUICKI, RQUICKI, and $RQUICKI_{BHBA}$ [9].

Unlike direct evaluations such as the hyperinsulinemic–euglycemic clamp (HEC), glucose tolerance test (GTT), or insulin tolerance test (ITT), surrogate indices are simpler and less invasive [10]. Such tools have already been applied successfully in dairy cow research [11–13].

While the connection between SCHK and IR has been explored in cattle, comparable data in goats are scarce. Studies in cows reveal that high NEFA or BHBA concentrations reduce glucose uptake in tissues sensitive to insulin [14, 15]. Elevated levels of cortisol, insulin, NEFA, and BHBA in SCHK cows also indicate systemic insulin resistance during transition [16]. These observations confirm a strong link between SCHK and IR, suggesting that IR contributes to SCHK development. However, this association remains insufficiently defined in goats. The current study, therefore, aimed to evaluate changes in sIR indicators and metabolic variables between SCHK and healthy goats throughout the transition period.

Materials and Methods

Animals, location, and study design

This research was carried out from January to March 2019 at the experimental farm of Northwest A&F University in Shaanxi Province, China (106°55′57″ E, 34°48′41″ N). The procedure is outlined in **Figure 1**. Animals were screened and grouped in two phases. In the first phase, 2305 Guanzhong dairy goats were synchronized for estrus in September to ensure February kidding. From these, 96 goats were selected using the following criteria: body condition score (BCS) of 2.75 ± 0.15 (mean ± SEM), primiparous status, similar expected kidding date (first week of February), and absence of medical issues. In the second phase, only goats with single offspring were chosen and divided into two groups based on plasma BHBA: SCHK (n = 10; BHBA = 0.8–1.7 mmol/L) and HEAL (n = 10; BHBA < 0.8 mmol/L) [6, 17, 18].

Animals were kept in free-stall housing from three weeks before to three weeks after parturition. All goats were fed identical total mixed rations (TMR) formulated according to the Nutrient Requirements of Small Ruminants (NRC, 2007). Feed and water were provided freely, and feeding occurred twice daily, at 07:30 and 15:30 h.

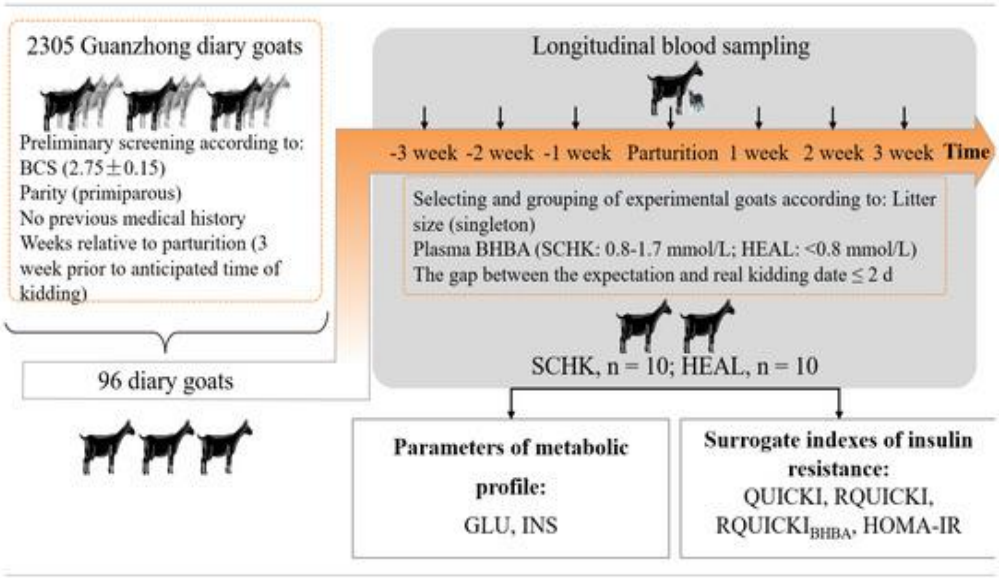


Figure 1. Experimental outline. The study involved two stages: (1) Estrous synchronization was applied to 2305 Guanzhong goats in September to time kidding in February. Of these, 96 were selected based on BCS (2.75 ± 0.15), parity, expected parturition, and good health. Blood was drawn from the jugular vein at −3, −2, −1, 0 (parturition), +1, +2, and +3 weeks relative to kidding using heparinized vacutainer tubes. (2) Goats producing single kids were sorted by BHBA concentration into SCHK (n = 10; 0.8–1.7 mmol/L) and HEAL (n = 10; <0.8 mmol/L). Plasma metabolites were analyzed, and sIR indices were subsequently computed.

Blood collection and laboratory procedures

Jugular venous blood was drawn from each goat at −3, −2, −1, 0 (parturition), +1, +2, and +3 weeks relative to kidding using sodium heparin vacutainers (Becton-Dickinson, Franklin Lakes, NJ, USA). Samples were obtained

in the morning before feeding prepartum, within 24 hours after delivery, and post-milking but prior to morning feed postpartum. Tubes were immediately chilled on ice, centrifuged at 2000 × g for 10 minutes, and plasma was stored at −80 °C until analysis of glucose (GLU), insulin (INS), β-hydroxybutyrate (BHBA), and nonesterified fatty acids (NEFA).

GLU (cat. no. GL8038, GOD-PAP method), BHBA (cat. no. RB1007, enzymatic assay), and NEFA (cat. no. FA115, colorimetric assay) were measured using commercial kits (Randox Laboratories Ltd., Crumlin, UK) with an automated blood analyzer (Hitachi High-Technologies Corp., Tokyo, Japan). Plasma INS levels were quantified with a goat-specific ELISA kit (cat. no. MM-14170, Meimian Biotechnology, Yancheng, Jiangsu, China) and read at 450 nm using a Bio-Rad 680 microplate reader (Bio-Rad, Hercules, CA, USA), following the manufacturer's protocol. Intra- and inter-assay coefficients of variation were 5.0% and 5.3%, respectively.

Calculation of surrogate insulin resistance indices

Indirect measures of insulin resistance (sIR), including HOMA-IR, QUICKI, RQUICKI, and $RQUICKI_{BHBA}$ were computed using standard formulas [9]:

$$HOMA\text{-}IR = [GLU\ (mmol/L) + INS\ (\mu IU/mL)]/22.5 \quad (1)$$

$$QUICKI = 1/[\lg GLU\ (mg/dL) + \lg INS\ (\mu IU/mL)] \quad (2)$$

$$RQUICKI = 1/[\lg GLU\ (mg/dL) + \lg INS\ (\mu IU/mL) + \lg NEFA\ (mmol/L)] \quad (3)$$

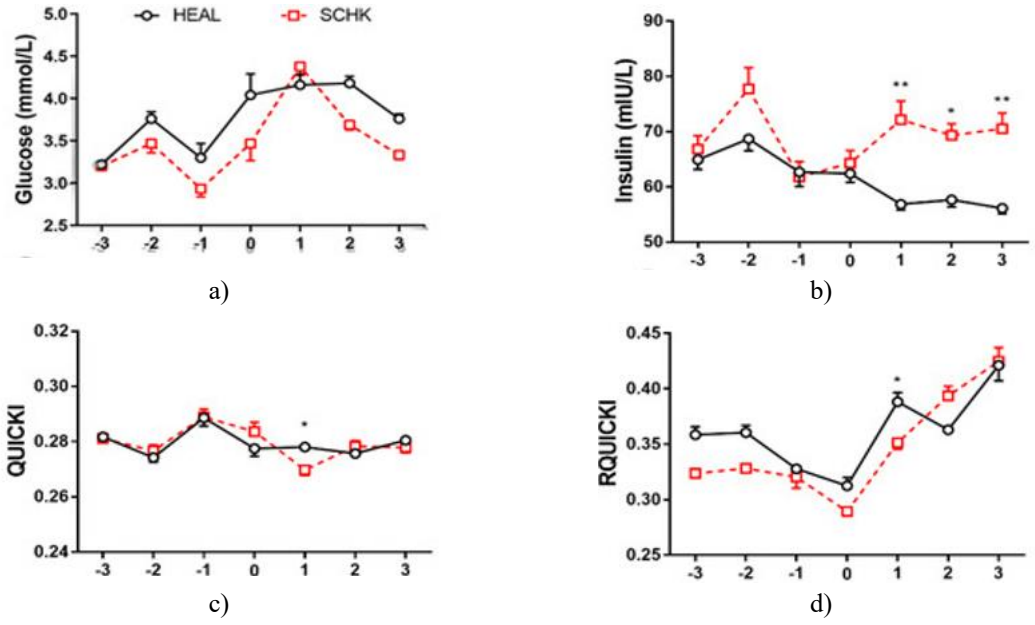
$$RQUICKI_{BHBA} = 1/[\lg GLU\ (mg/dL) + \lg INS\ (\mu IU/mL) + \lg NEFA\ (mmol/L) + \lg BHBA\ (mmol/L) \quad (4)$$

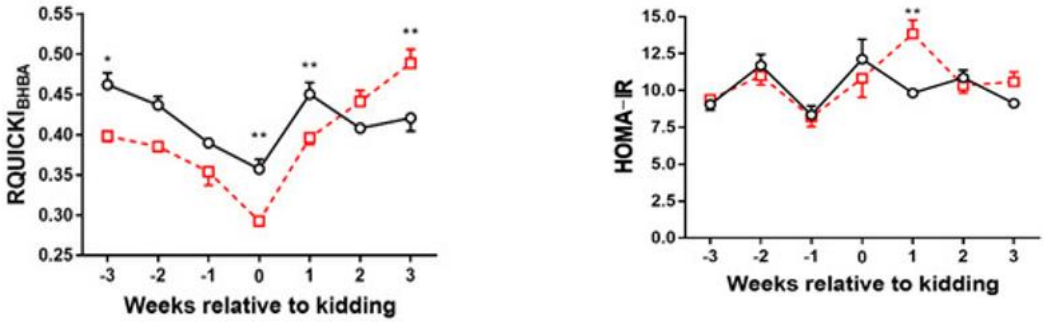
Statistical methods

Data analyses were performed using GraphPad Prism 7.0 (GraphPad Software, La Jolla, CA, USA). Repeated-measures ANOVA with Tukey's post hoc test was applied to determine differences in plasma metabolites and sIR values across time points. Time during the transition period was treated as a repeated factor. All results are presented as mean ± SEM.

Results and Discussion

Plasma glucose levels were slightly higher in HEAL goats than in SCHK goats except at one week postpartum **(Figure 2a**). Insulin concentrations in SCHK goats were significantly elevated compared with HEAL animals during early lactation ($p < 0.05$ or $p < 0.01$) **(Figure 2b)**. At one week postpartum, QUICKI, RQUICKI, and $RQUICKI_{BHBA}$ were significantly lower in SCHK goats ($p < 0.05$ or $p < 0.01$) **(Figures 2c–2e)**, while HOMA-IR was significantly higher ($p < 0.01$) **(Figure 2f)**. The lowest values of RQUICKI and $RQUICKI_{BHBA}$ occurred at parturition.





e) f)

Figure 2. Temporal changes in glucose (a), insulin (b), QUICKI (c), RQUICKI (d), RQUICKI$_{BHBA}$ (e), and HOMA-IR (f) in SCHK versus HEAL goats during the peripartum period. *p < 0.05, **p < 0.01. Data are mean ± SEM (n = 10 per group).

Discussion

Healthy goats showed slightly higher plasma glucose than SCHK goats, consistent with previous findings where HEAL goats had elevated glucose compared with multiparous SCHK goats [19]. Differences in parity and ketone severity could account for variations between studies. Lower glucose in SCHK goats may result from reduced hepatic glucose production caused by high BHBA levels around kidding [2, 20].

Insulin, in contrast, was significantly elevated in SCHK goats during early lactation, matching observations in dairy cows [16]. This elevated insulin response may limit further fat mobilization and prioritize glucose utilization for lactation energy demands [21]. Although SCHK goats had only slightly lower glucose, their insulin was significantly higher, indicating that insulin's effect on skeletal muscle and adipose tissue was reduced—i.e., insulin resistance.

Surrogate indices of insulin sensitivity are widely used in veterinary research [22]. In this study, SCHK goats exhibited lower QUICKI, RQUICKI, and RQUICKI$_{BHBA}$ and higher HOMA-IR at one week postpartum, reflecting reduced insulin responsiveness. However, the use of sIR in livestock remains debated. Some studies have found poor correlation between glucose tolerance test parameters (glucose clearance rate, fatty acid AUC) and insulin resistance in periparturient cows [23], while others found no link between sIR and HEC-derived measurements at the end of the dry period [10]. Further research is needed to validate sIR against direct measures in goats.

Conclusion

Goats affected by SCHK compensate during early lactation by producing higher insulin to maintain plasma glucose levels during the first three weeks postpartum, reflecting decreased insulin sensitivity relative to healthy goats.

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Conflict of Interest: None

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Ethics Statement: None

References

1. Matthews JG. Diseases of the goat: the periparturient goat. 4th ed. Chichester (UK): John Wiley & Sons Limited; 2016.
2. Hayirli A. The role of exogenous insulin in the complex of hepatic lipidosis and ketosis associated with insulin resistance phenomenon in postpartum dairy cattle. Vet Res Commun. 2006;30(7):749-74.

3. Cai C, Kong Y, Wu D, Wang J. Changes of macrominerals and calcitropic hormones in serum of periparturient dairy cows subject to subclinical hypocalcaemia. J Dairy Res. 2018;85(1):12-5.
4. Dore V, Dubuc J, Belanger AM, Buczinski S. Definition of prepartum hyperketonemia in dairy goats. J Dairy Sci. 2015;98(7):4535-43.
5. Marteniuk JV, Herdt TH. Pregnancy toxemia and ketosis of ewes and does. Vet Clin North Am Food Anim Pract. 1988;4(2):307-15.
6. Simões J, Gutiérrez C. Nutritional and metabolic disorders in dairy goats. In: Simões J, Gutiérrez C, editors. Sustainable goat production in adverse environments. Volume 1. Cham (CH): Springer International Publishing; 2017. p. 177-94.
7. Metabolic characteristics of subclinical hyperketonemia and subclinical hypocalcemia in dairy goats [Internet]. [place unknown]: [publisher unknown]; [date unknown] [cited 2025 Nov 12]. Available from: http://www.cnhonneur.net/news/10.html
8. Zamuner F, DiGiacomo K, Cameron AWN, Leury BJ. Endocrine and metabolic status of commercial dairy goats during the transition period. J Dairy Sci. 2020;103(6):5616-28.
9. De Koster JD, Opsomer G. Insulin resistance in dairy cows. Vet Clin North Am Food Anim Pract. 2013;29(2):299-322.
10. De Koster J, Hostens M, Hermans K, Van den Broeck W, Opsomer G. Validation of different measures of insulin sensitivity of glucose metabolism in dairy cows using the hyperinsulinemic euglycemic clamp test as the gold standard. Domest Anim Endocrinol. 2016;57:117-26.
11. Holtenius P, Holtenius K. A model to estimate insulin sensitivity in dairy cows. Acta Vet Scand. 2007;49:29.
12. Rico JE, Bandaru VV, Dorskind JM, Haughey NJ, McFadden JW. Plasma ceramides are elevated in overweight Holstein dairy cows experiencing greater lipolysis and insulin resistance during the transition from late pregnancy to early lactation. J Dairy Sci. 2015;98(11):7757-70.
13. Abuelo A, Hernandez J, Benedito JL, Castillo C. Association of oxidative status and insulin sensitivity in periparturient dairy cattle: an observational study. J Anim Physiol Anim Nutr (Berl). 2016;100(2):279-86.
14. Schoenberg KM, Ehrhardt RM, Overton TR. Effects of plane of nutrition and feed deprivation on insulin responses in dairy cattle during late gestation. J Dairy Sci. 2012;95(2):670-82.
15. Kerestes M, Faigl V, Kulcsar A, Balogh O, Foldi J, Febel H, et al. Periparturient insulin secretion and whole-body insulin responsiveness in dairy cows showing various forms of ketone pattern with or without puerperal metritis. Domest Anim Endocrinol. 2009;37(4):250-61.
16. Youssef MA, El-Ashker MR, Younis MS. The effect of subclinical ketosis on indices of insulin sensitivity and selected metabolic variables in transition dairy cattle. Comp Clin Path. 2017;26(2):329-34.
17. Ramin AG, Asri S, Majdani R. Correlations among serum glucose, beta-hydroxybutyrate and urea concentrations in non-pregnant ewes. Small Rumin Res. 2005;57(2-3):265-9.
18. Sadjadian R, Seifi HA, Mohri M, Naserian AA, Farzaneh N. Variations of energy biochemical metabolites in periparturient dairy Saanen goats. Comp Clin Path. 2013;22(3):449-56.
19. Ismail ZAB, Al-Majali AM, Amireh F, Al-Rawashdeh OF. Metabolic profiles in goat does in late pregnancy with and without subclinical pregnancy toxemia. Vet Clin Pathol. 2008;37(4):434-7.
20. Schlumbohm C, Harmeyer J. Hyperketonemia impairs glucose metabolism in pregnant and nonpregnant ewes. J Dairy Sci. 2004;87(2):350-8.
21. Magistrelli D, Rosi F. Trend analysis of plasma insulin level around parturition in relation to parity in Saanen goats. J Anim Sci. 2014;92(6):2440-46.
22. Hasegawa R, Iwase I, Takagi T, Kondo M, Matsui M, Kawashima C. Insulin resistance: relationship between indices during late gestation in dairy cows and effects on newborn metabolism. Anim Sci J. 2019;90(12):1544-55.
23. Samii SS, Rico JE, Mathews AT, Davis AN, Orndorff CL, Aromeh LO, et al. Effects of body condition score on direct and indirect measurements of insulin sensitivity in periparturient dairy cows. Animal. 2019;13(11):2547-55.