

Importance of hormonal changes during the periparturition period in black Bengal goats

Sukanta Mondal, Archana Minj¹, Mohan Chandra Pathak¹, Devi Nandan Singh¹,
Vijai Prakash Varshney¹

Animal Physiology Division, National Institute of Animal Nutrition and Physiology, Adugodi, Bangalore, Karnataka, ¹Physiology and Climatology Division, Indian Veterinary Research Institute, Izatnagar, Bareilly, Uttar Pradesh, India

Abstract

Background and Aim: The maintenance of pregnancy in livestock requires specific metabolic and functional changes between conception and the end of gestation, mediated through the interplay of hormones. The objectives of this study were to delineate the changes in plasma progesterone, estradiol, triiodothyronine (T₃), thyroxine (T₄), insulin, and cortisol concentrations during periparturient period in black Bengal goats and to elucidate the interrelationship between T₄ and cortisol in building up of the estradiol prior to parturition.

Methods: The blood samples were collected on days -25, -20, -15, -10, and -5 with respect to the date of expected kidding, on the day of kidding (day 0) and also on days 5, 10, 15, 20, and 25 postpartum. Plasma was separated and stored at -20°C until assay of hormones by radioimmunoassay.

Results: Plasma progesterone concentration declined from day -25 abruptly to the day of kidding and remained at basal level up to day 25 postpartum; whereas, plasma estradiol concentration declined abruptly from the day of kidding to a lower level than that of prepartum. Plasma insulin concentration declined ($P < 0.05$) abruptly from day -15 to the day of kidding followed by increase by day 10 postpartum. Circulating cortisol concentrations decreased from day 25 prepartum to the day of kidding, but increased by day 15th postpartum. Plasma T₃ and T₄ concentrations decreased from day 25 prepartum to the day of kidding which increased by day 25 postpartum.

Conclusion: Plasma estradiol was positively correlated with cortisol and T₄ indicating that changes in cortisol and T₄ levels contribute to increase in estradiol prior to delivery and therefore may directly influence the process of parturition.

Key words: Cortisol, estradiol, goat, insulin, progesterone

Received: 28th October, 2013; Revised: 27th December, 2013; Accepted: 18th January, 2014

INTRODUCTION

Black Bengal goats are known to be famous for their fertility, prolificacy, meat, and skin quality as well as adaptability to hot-humid conditions. Problems of slower growth rate, low production of milk, and higher kid mortality^[1,2] hamper full exploitation of productive potential of black Bengal goats. Exploration

of the fundamental endocrine involvement during late pregnancy is essential for development of management strategies for induction of parturition. The interplay of hormones regulates the metabolic and functional changes between mother and conceptus and thus associated with the maintenance of pregnancy in domestic ruminants. During early pregnancy, the growing fetus solely depends on uterine microenvironment for survival and growth as the uterine environment undergoes continual modifications to cope with the needs of the embryo. To meet these needs, the body attempts to reset its endocrine functions including thyroid secretion. There is also a change in body metabolic rate and some of the related biochemical components which are mainly controlled by thyroid hormones and insulin. Changes in nutrients during pregnancy and lactation are governed by thyroid hormones viz., triiodothyronine (T₃) and thyroxine (T₄),

Access this article online	
Quick Response Code:	Website: www.ijcep.org
	DOI: 10.4103/2348-8093.129723

Address for correspondence: Dr. Sukanta Mondal, National Institute of Animal Nutrition and Physiology, Adugodi, Bangalore - 560 030, India. E-mail: sukanta781@gmail.com

and insulin. The decreased levels of progesterone prior to the time of parturition and the increased levels of estradiol and prostaglandins on the day of kidding play a crucial role in spontaneous parturition.

The endocrine changes during late pregnancy and parturition have been reported in various species.^[3,4] Serum progesterone concentration declined immediately before parturition in cow,^[5,6] ewe,^[7,8] pig,^[9,10] and goat.^[11] A rise in glucocorticoid concentrations preceding parturition has been reported in cow,^[12,13] ewe,^[14] and pig.^[15,16] Serum estradiol concentrations have been found to increase in several species before parturition,^[17] including cow,^[18] ewe,^[17] and pig.^[19] Soliman *et al.*,^[20] reported that thyroid hormones increased during late pregnancy in cow. Although a plethora of studies are available on concentrations of various hormones during late pregnancy in other species, information on black Bengal goat is inadequate. The objectives of the study are (i) To characterize the changes in plasma progesterone, estradiol, cortisol, T₃, T₄ and insulin concentrations during late pregnancy and parturition and (ii) to assess the interrelationship between T₄ and cortisol in building up the estradiol peak prior to delivery in black Bengal goat.

MATERIALS AND METHODS

Animals

Five cycling black Bengal goats (aged between 3 and 5 years) were used in the present study. All the animals were maintained using standard farm practices at the goat herd of Physiology and Climatology Division, Indian Veterinary Research Institute at Izatnagar—located at 170 m above the mean sea level in the Indo-Gangetic Plain on [28°22'N latitude and 79°24'E]. The agro-climatic situation is dry and tropical with the highest temperatures occurring from May to July, with a mean monthly temperature of 40°C. The minimum and maximum ambient temperatures ranged from 5 to 35°C and from 25 to 45°C, respectively; while the mean relative humidity varied between 20 and 90%. The rainfall was erratic and mainly concentrated during July-August with a precipitation of 250-600 mm per annum. The animals selected for the study were free from any anatomical, physiological, or infectious disorders and were mated. The pregnant goats were housed in goat pen with a brick floor and fed on a diet of green fodder and concentrate mixture.

Blood sampling

Blood samples were collected once daily from all the goats in heparinized tubes through jugular venipuncture prior to feeding. The blood samples were collected on days -25, -20, -15, -10, and -5 with respect to the date of expected kidding, on the day of kidding (day 0) and also on days 5, 10, 15, 20, and 25 postpartum. Plasma

was separated by centrifugation at 3,000 rpm for 30 min at 4°C and stored frozen at -20°C until assay of hormones.

Assay of hormones

The concentrations of insulin, cortisol, T₃, T₄, progesterone, and estradiol were quantified by the radioimmunoassay kits procured from Immunotech, France. The sensitivity of the T₃ assay was 0.1 nmol/L and the inter- and intra-assay coefficients of variation were 8.6 and 3.3%, respectively. The sensitivity of the T₄ assay was 9.5 nmol/L and the inter- and intra-assay coefficients of variation were 8.6 and 6.2%, respectively. The sensitivity of the insulin assay was 0.5 µIU/ml and the inter- and intra-assay coefficients of variation were 3.4 and 4.3%, respectively. The sensitivity of the progesterone assay was 0.08 ng/ml and the inter- and intra-assay coefficients of variation were 9.0 and 5.8%, respectively. The sensitivity of the estradiol assay was 4.5 pg/ml and the inter- and intra-assay coefficients of variation were 11.2 and 12.1%, respectively. The sensitivity of the cortisol assay was 10 nmol/L and the inter- and intra-assay coefficients of variation were 9.2 and 5.8%, respectively.

Statistical analysis

The data were expressed as the mean ± standard error of the mean (SEM). Data was analyzed for descriptive statistics and significance has been obtained by using analysis of variance (SPSS 16.0, Chicago, IL, USA). Relationship between plasma estradiol and T₄ as well as between estradiol and cortisol was assessed by Pearson's correlation analysis.^[21] The values of different hormones during different days of pre- and postpartum period were compared with that of day 25 prepartum by using paired *t*-test.

RESULTS

The gestation length in the goat varied from 140 to 148 days with a mean of 142.7 ± 2.9 days. The concentrations of insulin, cortisol, T₃, T₄, progesterone, and estradiol are presented in [Figures 1-6].

Plasma insulin and cortisol profiles

In the present study, peripheral plasma insulin concentration was 35.97 ± 7.99 µIU/ml on day -25 and rose to 51.49 ± 6.94 µIU/ml on day -15. The insulin levels then decreased (*P* < 0.05) abruptly to 17.791 ± 1.22 µIU/ml on the day of kidding which increased to 36.92 ± 3.75 µIU/ml on day 10 postpartum [Figure 1]. Plasma cortisol concentration was 59.37 ± 12.91 nmol/L on day 25 before expected kidding. The concentration then decreased (*P* < 0.01) to 29.87 ± 11.14 nmol/L on day 5 prepartum which further increased to 48.04 ± 6.65 nmol/L on the day of kidding. The cortisol concentrations then decreased to 19.87 ± 1.89 nmol/L on day 5th postpartum which increased (*P* < 0.05) to 35.77 ± 8.01 on day 15th postpartum [Figure 2].

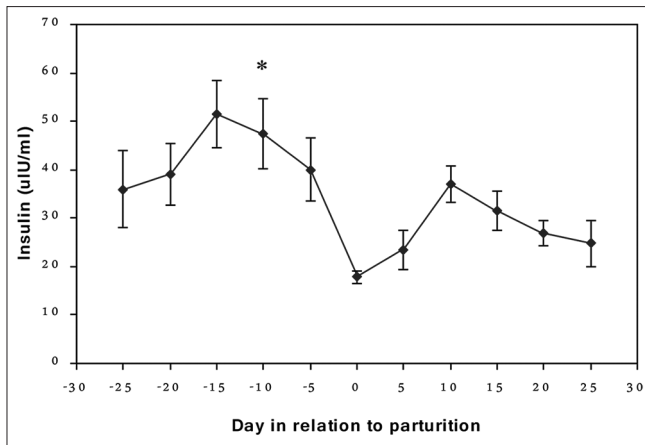


Figure 1: The changes in plasma insulin concentrations during periparturient period in goats. Data are expressed as mean \pm standard deviation (SD). Statistical analysis was done by paired *t*-test. The level of significance depicted for day 10 prepartum are in relation to the concentration of hormone on -25^{th} day (basal value). * $P < 0.05$

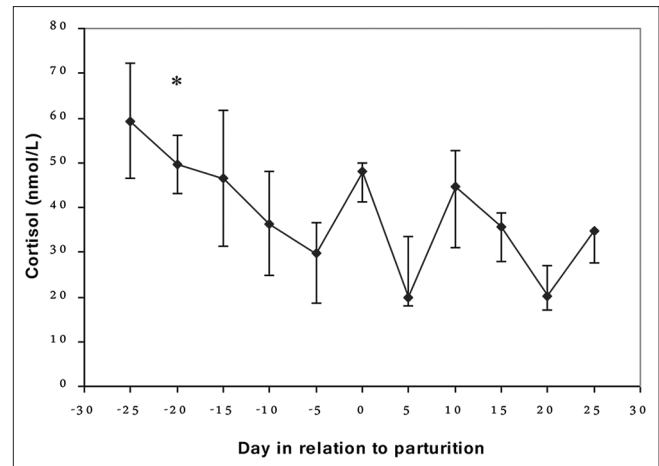


Figure 2: The changes in plasma cortisol concentrations during periparturient period in goats. Data are expressed as mean \pm SD. Statistical analysis was done by paired *t*-test. The level of significance depicted for day 20 prepartum are in relation to the concentration of hormone on -25^{th} day (basal value). * $P < 0.05$

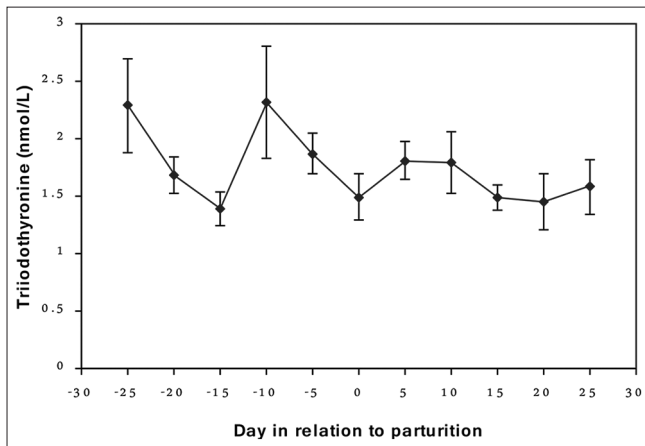


Figure 3: The changes in plasma triiodothyronine (T₃) concentrations during periparturient period in goats. Data are expressed as mean \pm standard deviation

Plasma T₃ and T₄ profiles

The concentrations of T₃ was 2.29 ± 0.41 nmol/L on day 25 prepartum with respect to the day of expected parturition (day 0), declined to 1.39 ± 0.15 on day 15 prepartum and reached to 1.49 ± 0.20 nmol/L on the day of kidding. After kidding the concentrations increased to 1.79 ± 0.27 nmol/L on day 10 postpartum after which concentrations decreased to 1.58 ± 0.24 nmol/L on day 25 postpartum [Figure 3]. Plasma T₄ concentrations decreased from 87.51 ± 13.3 nmol/L on day 25 prepartum through 73.73 ± 2.72 nmol/L on day 15 prepartum to 39.68 ± 5.20 nmol/L on the day of kidding. The concentration rose abruptly after kidding to 70.76 ± 11.47 nmol/L on day 10 postpartum and declined thereafter to 55.36 ± 12.48 nmol/L on day 25 postpartum [Figure 4].

Plasma steroid hormone profiles

Plasma progesterone concentration was 4.95 ± 0.98 ng/ml

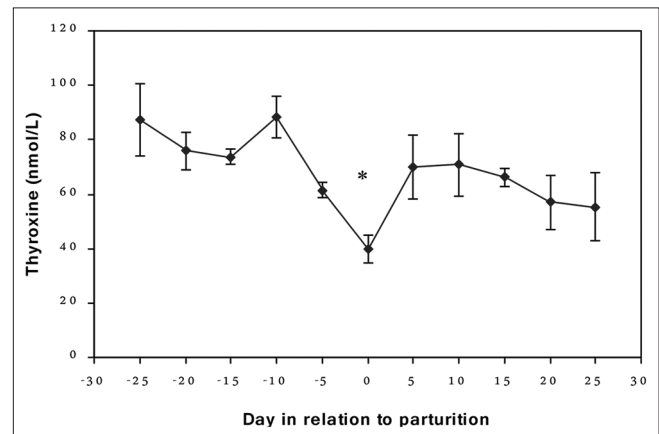


Figure 4: The changes in plasma thyroxine (T₄) concentrations during periparturient period in goats. Data are expressed as mean \pm SD. Statistical analysis was done by paired *t*-test. The level of significance depicted for day of parturition are in relation to the concentration of hormone on -25^{th} day (basal value). * $P < 0.05$

on day -25 which then declined to 3.41 ± 0.14 ng/ml on day 5 prior to parturition, decreasing abruptly to 0.09 ± 0.02 ng/ml on the day of kidding and remained at basal level up to day 25 postpartum [Figure 5]. Peripheral plasma estradiol concentrations decreased from 40.82 ± 5.93 pg/ml on day -25 to 27.56 ± 4.38 pg/ml on day 10 prepartum and then rose ($P < 0.05$) to 50.03 ± 10.13 pg/ml on the day of kidding. The concentrations decreased abruptly after kidding from 24.26 ± 3.32 pg/ml on day 5th postpartum to 16.68 ± 2.43 pg/ml on day 15th postpartum [Figure 6].

Relationship between circulating estradiol and cortisol as well as between estradiol and T₄ levels

The interrelationship between estradiol and cortisol as well as between estradiol and T₄ is presented in Table 1.

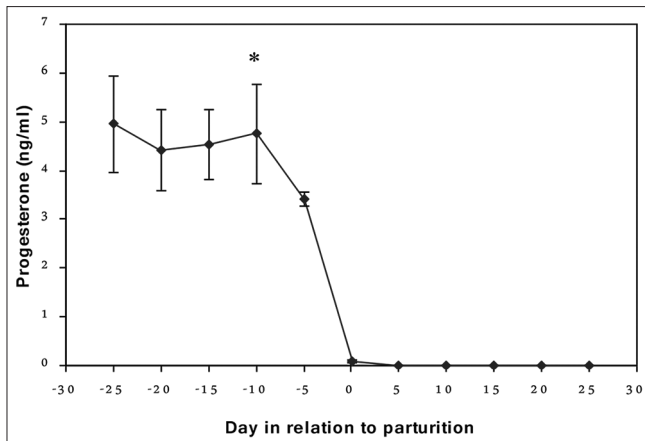


Figure 5: The changes in plasma progesterone concentrations during periparturient period in goats. Data are expressed as mean \pm SD. Statistical analysis was done by paired *t*-test. The level of significance depicted for day 10 prepartum are in relation to the concentration of hormone on -25^{th} day (basal value). * $P < 0.05$

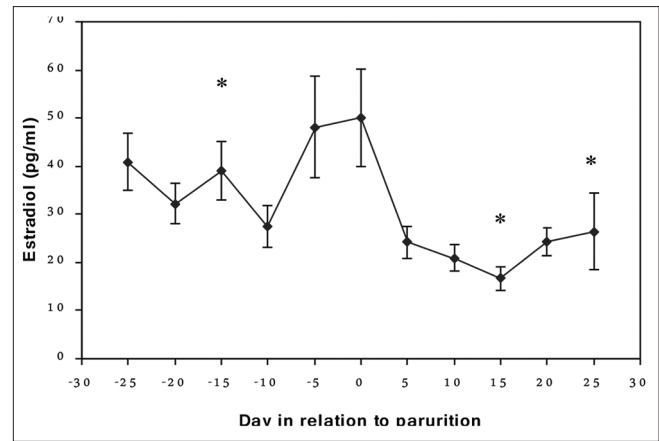


Figure 6: The changes in plasma estradiol concentrations during periparturient period in goats. Data are expressed as mean \pm SD. Statistical analysis was done by paired *t*-test. The level of significance depicted for day 15 prepartum, day 15 and 25 postpartum are in relation to the concentration of hormone on -25^{th} day (basal value). * $P < 0.05$

Table 1: Correlation of level of estradiol with the level of T_4 and cortisol on different pre- and postpartum days

Days	T_4		Cortisol	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
-25	-0.89	<0.05	0.11	<0.05
-20	-0.78	<0.05	0.54	<0.05
-15	0.40	>0.05	0.78	<0.05
-10	0.19	>0.05	-0.79	>0.05
-5	-0.89	<0.05	-0.27	>0.05
0	0.89	>0.05	0.59	<0.05
5	0.51	>0.05	0.20	<0.05
10	-0.20	<0.05	0.39	<0.05
15	0.58	<0.05	0.93	<0.05
20	0.59	<0.05	0.32	<0.05
25	0.58	<0.05	0.37	<0.05

Data are expressed as mean \pm standard deviation. Statistical analysis was done by Pearson's correlation. The level of significance depicted for different days are in relation to the level of estradiol

Estradiol and cortisol levels were positively correlated during most of the days of experimentation except on day 10 and day 5 prepartum. Similarly positive correlation was observed between estradiol and T_4 levels except on day 25, 20, 5 prepartum and day 10 postpartum.

DISCUSSION

To the best of our knowledge, this report represents the first study on the peripheral endocrine profiles during late pregnancy and parturition in black Bengal goat, an indigenous breed of goat. As reported earlier by Khan and Ludri^[22] and Mondal *et al.*,^[23] and also observed in the present study, the decline in plasma insulin concentration around parturition could facilitate the mobilization of nutrients from fat depot for milk synthesis. In an earlier report,^[24] plasma insulin levels have been found to increase from day 84 onwards in pregnant

goats suggesting the crucial role on insulin in partitioning of nutrients to the fetus. The decrease in insulin levels during late pregnancy may be attributed to sharp increase in nonesterified fatty acid (NEFA) concentrations and decrease in glucose concentrations. In contrast, plasma cortisol level increased immediately before parturition in black Bengal goat which is in agreement with earlier studies in cow,^[12,13] ewe,^[8,14] and pig.^[15,16] The secretion of adrenocorticotrophic hormone (ACTH) from fetus increased during last stage of parturition, caused increase in the concentrations of cortisol by stimulating the rapid growth of fetal adrenals. Like cow,^[6,25] ewe,^[7,8] goat,^[23,26] and pig,^[9,10] plasma progesterone concentrations decline before kidding in black Bengal goat. The sudden decrease in progesterone level might be contributing to initiation of parturition by causing a significant change in estrogen-progesterone ratio. However, further studies should be done to substantiate this mechanism. Plasma estradiol levels increased before kidding which are in agreement with earlier reports in cow,^[18,27] ewe,^[14,17] goat,^[12,28,29] and pig.^[9,19,30] Patel *et al.*,^[31] reported that prepartum increase in plasma estradiol is required for uterine contraction that also triggers the release of prostaglandin for contraction of myometrium.

In the present study, plasma T_3 and T_4 concentrations declined during late pregnancy, which is similar to earlier reports in goat^[32] and sheep.^[33,34] Plasma T_3 and T_4 concentrations decrease during late pregnancy due to inhibitory effect of glucocorticoid which rise before parturition; whereas, their increase during postpartum period indicates the enhancement of utilization of nutrients due to stress of parturition. The decline in plasma T_3 and T_4 levels around parturition may be due to transfer of these hormones from placenta to the fetus. Riis and Madsen^[35] reported that decrease in plasma T_3 and T_4 concentrations

reduced the rate of oxidation and the rate of continuous breakdown and formation of protein and fat in mammary tissue. This will also tend to reduce the adverse effects of nutrient deficiency at the onset of lactation. The decrease in the concentration of plasma T_3 on the day of kidding and its subsequent elevation indicates enhanced utilization as a result of increased metabolism due to stress of parturition during which the concentration of cortisol increases rather than being utilized by mammary tissue alone. Decrease in the concentration of plasma T_3 and T_4 on the day of kidding is in agreement with Riis and Madsen^[35] who showed a sudden drop in T_4 at the onset of lactation and reported that low plasma T_4 and high plasma growth hormone concentration favor the mammary gland in the partitioning of nutrients between mammary and non-mammary tissue. In the present study, estradiol was positively correlated with cortisol and T_4 levels during most part of the experimental period. The alteration in thyroid hormone and cortisol levels possibly contribute to increase in estradiol prior to delivery; and therefore, T_4 and cortisol may directly influence the process of parturition.

Limitations of the study

Due to the small sample size of the study animals in the present study, multiple regression analysis could not be done to link the independent contribution of hormonal changes to the parturition mechanism and also we could not establish a direct link between the change of hormones and the process of parturition, by studying the parturition scoring system etc., Therefore, future studies with a large sample size are warranted to substantiate the independent contribution of the hormonal changes to the process of parturition.

CONCLUSION

In conclusion, positive correlation between cortisol and estradiol as well as between estradiol and T_4 during prepartum period suggests that alterations in cortisol and T_4 levels may contribute to the increase in estradiol prior to delivery, which may directly influence the process of parturition.

ACKNOWLEDGMENTS

The authors are grateful to the Director, IVRI, Bareilly for providing the necessary facilities for carrying out the research work. S Mondal was supported by IVRI Senior research fellowship. We thank Director, NIANP for providing necessary facilities for preparing the manuscript.

REFERENCES

1. Devendra C. Studies in the nutrition of the indigenous goat at Malaya and requirement of liveweight gain. *Malaysian Agri J* 1992;46:98-118.

2. Hussain SS. Sustainable genetic improvement of economic traits of black Bengal goats through selective and cross breeding. *BAU Research Program* 1999;10:72-80.
3. Bazer FW, First NL. Pregnancy and parturition. *J Anim Sci* 1983;57:425-60.
4. Wagner WC, Thompson FN, Evans LE, Molokwu EC. Hormonal mechanisms controlling parturition. *J Anim Sci* 1974;38:39-57.
5. Fairclough RJ, Hunter JT, Welch RA, Payne E. Plasma corticosteroid concentrations in the bovine foetus near term. *J Endocrinol* 1975;65:139-40.
6. Hunter JT, Fairclough RJ, Peterson AJ, Welch RA. Foetal and maternal hormonal changes preceding normal bovine parturition. *Acta Endocrinol (Copenh)* 1977;84:653-62.
7. Chamley WA, Buckmaster JM, Cerini ME, Cumming IA, Coding JR, Obst JM, et al. Changes in the levels of progesterone, corticosteroids, estrone, estradiol-17 β , luteinizing hormone, and prolactin in the peripheral plasma of the ewe during late pregnancy and at parturition. *Biol Reprod* 1973;9:30-5.
8. Thompson FN, Wagner WC. Fetal-maternal corticosteroid relationships in sheep during late pregnancy. *J Reprod Fertil* 1974;41:49-56.
9. Molokwu EC, Wagner WC. Endocrine physiology of the puerperal sow. *J Anim Sci* 1973;36:1158-63.
10. Robertson HA, King GJ. Plasma concentrations of progesterone, oestrone, oestradiol-17 β and of oestrone sulphate in the pig at implantation, during pregnancy and at parturition. *J Reprod Fertil* 1974;40:133-41.
11. Thorburn GD, Nicol DH, Bassett JM, Shutt DA, Cox RI. Parturition in the goat and sheep: Changes in corticosteroids, progesterone, oestrogens and prostaglandin-F. *J Reprod Fertil Suppl* 1972;16:61-84.
12. Adams WM, Wagner WC. The role of corticoids in parturition. *Biol Reprod* 1970;3:223-8.
13. Smith VG, Edgerton LA, Hafs HD, Convey EM. Bovine serum estrogens, progestins and glucocorticoids during late pregnancy, parturition and early lactation. *J Anim Sci* 1973;36:391-6.
14. Thompson FN. Feto-placental steroids and parturition in the ewe. Ph.D. thesis, 1973, Iowa State University, Ames.
15. Ash RW, Heap RB. Oestrogen, progesterone and corticosteroid concentrations in peripheral plasma of sows during pregnancy, parturition, lactation and after weaning. *J Endocrinol* 1975;64:141-54.
16. First NL, Bosc MJ. Proposed mechanisms controlling parturition and the induction of parturition in swine. *J Anim Sci* 1979;48:1407-21.
17. Bedford CA, Challis JR, Harrison FA, Heap RB. The role of oestrogens and progesterone in the onset of parturition in various species. *J Reprod Fertil Suppl* 1972;16:1-23.
18. Stabenfeldt GH, Osburn BI, Ewing LL. Peripheral plasma progesterone levels in the cow during pregnancy and parturition. *Am J Physiol* 1970;218:571-5.
19. Guthrie HD, Henricks DM, Handlin DL. Plasma estrogen, progesterone and luteinizing hormone prior to estrus and during early pregnancy in pigs. *Endocrinology* 1972;91:675-9.
20. Soliman FA, Nasr H, Zaki H. Levels of thyroid and thyrotrophic hormones in the blood of Friesian cows at various reproductive stages. *J Reprod Fertil* 1963;6:335-40.
21. Snedecor GW, Cochran GW. In: *Statistical methods*. 6th ed. New Delhi: Oxford and IBH; 1980. p. 45-83.
22. Khan JR, Ludri RS. Changes in blood glucose, plasma non-esterified fatty acids and insulin in pregnant and non-pregnant goats. *Trop Anim Health Prod* 2002;34:81-90.
23. Mondal S, Pathak MC, Varshney VP. Changes in peripheral plasma insulin levels during periparturient period in Black Bengal goats. In: *Proceedings of National Symposium on Recent Trends in Policy Initiatives and Technological Interventions for Rural Prosperity in Small Holder Livestock Production Systems*. India; 2007; p. 147.
24. Bauman DE, Currie WB. Partitioning of nutrients during

- pregnancy and lactation: A review of mechanism involving homeostasis and homeorheosis. *J Dairy Sci* 1980;63:1514-29.
25. Fairclough RJ, Hunter JT, Welch RA. Peripheral plasma progesterone and utero-ovarian prostaglandin F concentrations in the cow around parturition. *Prostaglandins* 1975;9:901-14.
 26. Mondal S, Pathak MC, Singh DN, Varshney VP. Peripheral plasma progesterone concentration during periparturient period in black Bengal goats. In: Proceedings of 40th Annual Meeting of Society for Study of Reproduction, USA; 2007, p. 173.
 27. Hoffmann B, Wagner WC, Hixon JE, Bahr J. Observations concerning the functional status of the corpus luteum and the placenta around parturition in the cow. *Anim Reprod Sci* 1979;2:253-61.
 28. Emanuel L, Krejci P, Pichova D. Czech white breed goat milk production and hormonal during level parturition and lactation. In: Proceedings of 37th Annual Meeting of European Association for Annual Production. Hungry; 1986. p. 174-75.
 29. Mondal S, Varshney VP, Pathak MC. Relationship between plasma estradiol and cortisol concentrations during periparturient period in Black Bengal goats. *Reprod Domest Rumin* 2006;41:118.
 30. Wagner WC, Oxenreider SL. Endocrine physiology following parturition. *J Anim Sci* 1971;32:1-16.
 31. Patel AV, Pathak MM, Mehta VM. Serum oestradiol concentrations around parturition in goats. *Indian J Anim Sci* 1992;62:241-2.
 32. Mondal S, Minj A, Pathak MC, Varshney VP. Peripheral plasma thyroid hormone concentrations during pregnancy in black Bengal goats. *Endocr Abst* 2006;12:100.
 33. Eswari S, Viswanathan S, Leela V, Nayeem MD, Gajendran K. Concentration of serum thyroid hormones during pregnancy, parturition, postpartum and lactation in Madras Red sheep. *Indian J Anim Reprod* 1999;20:116-9.
 34. Okab AB, Elebenna IM, Mekkawy MY, Hassan GA, El-Nouty FD, Salem MH. Seasonal changes in plasma thyroid hormones, total lipid, cholesterol and serum transaminases during pregnancy and parturition in Barki and Rahmani ewes. *Indian J Anim Sci* 1993;63:946-51.
 35. Riis PM, Madsen A. Thyroxine concentration and secretion rates in relation to pregnancy, lactation and energy balance in goats. *J Endocrinol* 1985;107:421-7.

How to cite this article: Mondal S, Minj A, Pathak MC, Singh DN, Varshney VP. Importance of hormonal changes during the periparturition period in black Bengal goats. *Int J Clin Exp Physiol* 2014;1:20-5.

Source of Support: Indian Veterinary Research Institute, (ICAR, New Delhi), **Conflict of Interest:** Nil.

Announcement

Android App



Download
**Android
application**

FREE

A free application to browse and search the journal's content is now available for Android based mobiles and devices. The application provides "Table of Contents" of the latest issues, which are stored on the device for future offline browsing. Internet connection is required to access the back issues and search facility. The application is compatible with all the versions of Android. The application can be downloaded from <https://market.android.com/details?id=comm.app.medknow>. For suggestions and comments do write back to us.