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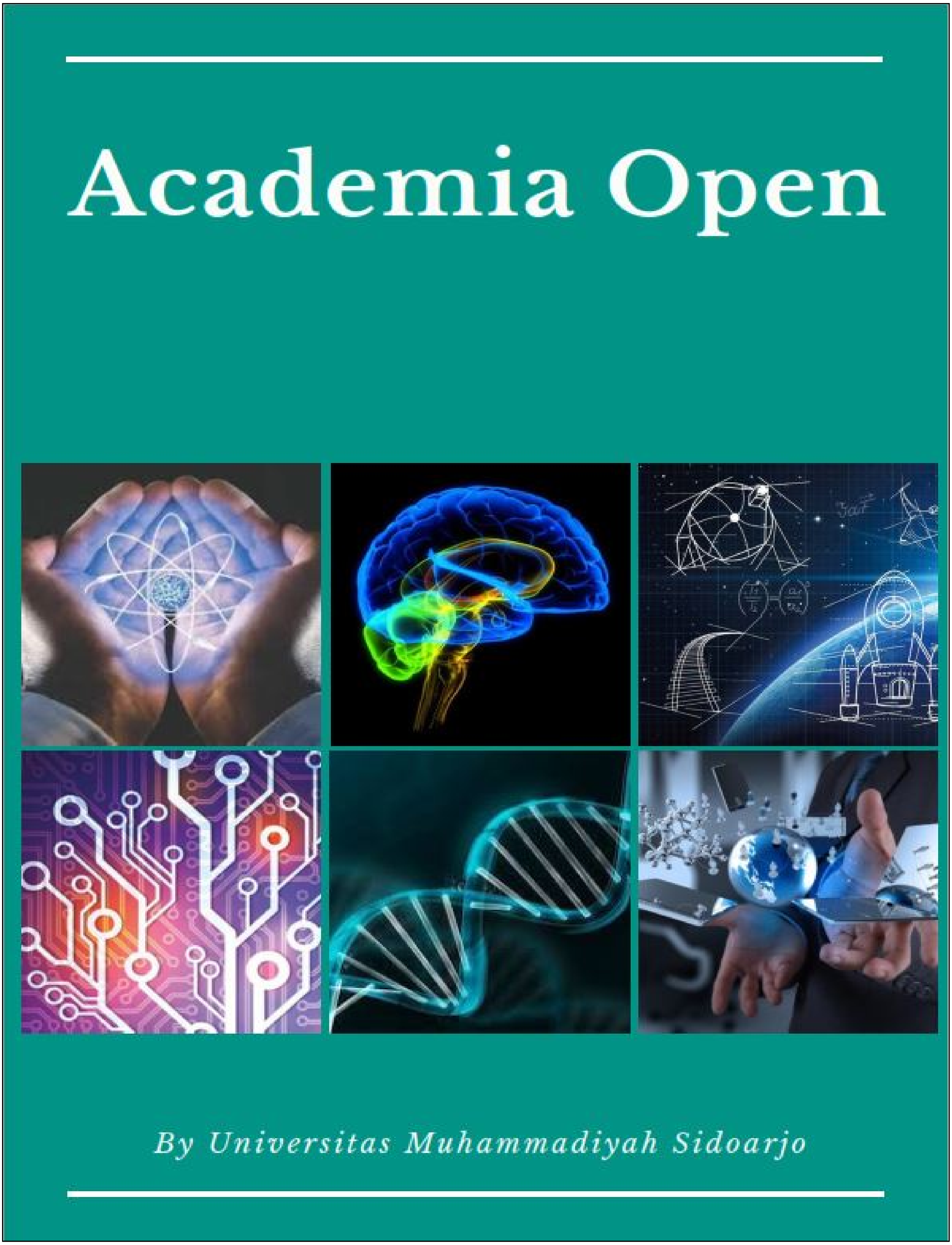

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Uterine and Hormonal Changes Following Pregnancy in Ruminants

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Abstract

General Background: Pregnancy is a pivotal phase in the reproductive cycle of mammals, particularly in ruminants, involving intricate physiological and hormonal coordination. **Specific Background:** Hormonal fluctuations during estrous, pregnancy, and parturition significantly influence uterine and endometrial structure, immune modulation, and mammary development. **Knowledge Gap:** Despite the known involvement of endocrine signaling, detailed insights into uterine transformations post-pregnancy and species-specific hormonal patterns remain limited. **Aim:** This review aimed to examine uterine changes in ruminants after pregnancy, focusing on the hormonal and immunological mechanisms involved. **Results:** It highlights how estrogen and progesterone modulate endometrial dynamics and immune responses; the trophoblast's role in sustaining progesterone secretion through corpus luteum maintenance; and the regulatory cascade triggered by prostaglandin F2α in luteolysis. Notably, cows exhibited higher reproductive hormone levels compared to other ruminants. **Novelty:** The review integrates hormonal profiles with immune function and mammary gland development, offering a comprehensive picture of post-pregnancy uterine remodeling. **Implications:** These findings enhance understanding of implantation biology, support strategies to optimize reproductive efficiency, and inform sustainable dairy and meat production practices in ruminants

Highlights:

- Hormones like progesterone and estrogen drive key uterine and immune changes.
- Trophoblast signals are crucial to sustain pregnancy in ruminants.
- Cows show higher reproductive hormone levels than other ruminants.

Keywords: Uterine Remodeling, Ruminant Reproduction, Hormonal Regulation, Immune Response, Mammary Development

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Introduction

Ruminant are regarded as significant agricultural animals, playing a crucial role in the economies, their productivity is influenced by their nutritional intake, as they provide milk, meat, and hides for leather and fibers [1]. Understanding the hormonal interactions that take place in the uterus during the estrus cycle, pregnancy, and parturition is crucial [2]. A female mammal's primary means of reproducing her offspring and preserving the species' integrity is pregnancy [3]. Changes in the tissue concentration of several hormones, cytokines, enzymes, and growth factors of which hormones are the most significant as well as reproductive organs are all part of this intricately regulated process [4]. The development of the embryo and fetus, the preservation of pregnancy, the birth of a healthy kids, and preparation of the uterus for embryo conception all depend on a variety of hormones. Progesterone and estrogens, however, were the two hormones that were most engaged in pregnancy. The hormones oxytocin, cortisone, relaxin, and prostaglandin which are mostly crucial for parturition are also involved in this process [4] [5]. The reproductive efficiency of camels is suboptimal, the factors contributing to this low reproductive efficiency include the brief breeding season, the delayed onset of puberty, the extended gestation period, and the longer interval between births resulting from extended lactation-related anoestrus [6] [7]. Female puberty is typically marked by the initial onset of estrus. Puberty is the achievement of reproductive capability, involving morphological, physiological, and behavioral maturation [8] [9]. Up until the beginning of parturition, when the endometrium transitions from a progesterone-dominated to an oestrogen-dominated condition, progesterone predominates [10]. Thus, hormone profiles and endocrinological alterations that take place in ruminants during the estrous cycle and various phases of pregnancy are reviewed in this work. The study also highlights the significant uterine immunological alterations that coincide with endocrinological alterations [11] [12]. However, the exploitation of the camel's productive capability is only possible if the reproductive potential can be improved, and this study has increased our understanding of the reproductive biology of the animals [13] [14]. The protrusions on the surface of ovary, which may reflect the presence of developing follicles or yellow bodies, indicating altered reproductive activity. The shape of the ovaries became more irregular and lobulated in their appearance due to the ovarian activity [15]. the purpose of this review assisted in the diagnosis and thus help in obtaining optimal treatment of the diseases. To exploit the recent advances in techniques such as super ovulation and embryo transfer a sound understanding of the reproductive biology of the ruminant. The people trained in this profile should know about the business, computational tools, and statistical analysis and interpretation. Among the objectives of Information Science is to provide a means for making relevant information available to individuals, groups, and organizations involved with science and technology [16].

Literature Review

They experience multiple births, brief gestation periods, and significant reproductive efficiency once they attain puberty. Moreover, nutrition is flexible to seasonal and regional variations and does not necessitate specific meals, Sheep are distinguished by their tiny size, which makes them easy to manage and requires little financial investment to set up breeding initiatives [17] [18]. In addition, there are many births, short pregnancy durations, and reproductive efficiency in reaching puberty. Furthermore, nutrition can adjust to the seasonal and geographical shifts and doesn't require particular foods. The anatomical arrangement of the ovary and ovarian bursa in animals affect the likelihood of their accessibility during clinical examination and predispose to unusual genital disorders. In mammals, during ovarian follicular development, only a restricted number of follicles are chosen for ovulation, while the others experience atresia at different developmental phases [19] [20].

The endometrium's reaction to circulating hormone signals. In cattle, the estrous cycle lasts 18 to 24 days and includes a lengthy luteal phase (14 to18 day), which is distinguished by the existence of the corpus luteum (CL) [18]. Hormones secreted from the hypothalamic-pituitary-gonadal axis cause these cyclical processes, with progesterone (P4) and oestradiol concentrations having the biggest effects on the temporal and spatial alterations in endometrium throughout oestrus cycle. It has been shown that the synthesis of prostaglandin F2-alpha, which can cause luteolysis in sheep, depends on the integrity of the glandular and luminal epithelium being maintained. This discovery suggests that these cells have oxytocin receptors and a mechanism for prostaglandin F2-alpha production [20]. Originally identified as ovine the trophoblast protein-1 (oTP-1). the material/molecule that suppresses the manufacture and/or release of luteolytic PGF2a within cells of the endometrium and prevents corpus luteum retraction is a developmental protein. After it was shown that the oTP-1 belonged to the interferon family, it was subsequently categorized as ovine interferon-tau (oIFN-t), the cytokine oIFN-t acts specifically within uterine endometrium as opposed to systemically, the oIFN-t possesses antiviral, immunosuppressive, antiluteolytic, and maybe antiproliferative qualities. Progesterone receptors in the endometrium. The trophoblast produces oIFN-t in response to granulocyte macrophage colony stimulation factor, which is generated in the maternal uterine endometrium. For the mother to recognize pregnancy, oIFN-t must be secreted from the conceptus trophectoderm 12–15 day in ewe and 14–17 day in the cow and doe post coitus [21] [22].

The previous experiment's results indicated that the ewe's body condition score improved most significantly ($P<0.01$) during flushing. Ewes fed diets containing an energy content of 2.13 Mcal/kgam ME as well as 2.31 Mcal/kgam ME. scored higher on body condition than ewes fed diets having an energetic content of 1.01 Mcal/kg ME (non-flushing). With a calorie content of 2.31 Mcal/kg ME, the ewes' body condition score was 2.31. In other words, raising the feed's energy level can raise the animals' bodily condition rating [8]. After establishing the "maternal recognition of pregnancy," the trophoblast moves on to implantation into the endometrial luminal

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epithelium. Significant alterations in the concentrations of hormones, cytokines, adhesion molecules, enzymes, and growth factors occur during the implantation event; these changes may be essential for the initiation of the feto-maternal bond [23].

Cytokines have a critical role in sustaining pregnancy. Other cytokines, including interleukin1 beta (IL1b), growth of tumors factor beta (TGFb), IL-6, leukemia inhibition factor (LIF), and IL-10, are crucial for embryo growth and development, while IFN-t is important for "maternal recognition of pregnancy." Moreover, IL-6 and LIF are crucial for embryo elongation and placentation [24]. These cytokines are thought to be regulated and interacted with by the reproductive hormones in the uterus [6]. Progesterone is frequently referred to as the "pregnancy hormone" because it is the primary hormone during pregnancy. It keeps the myometrium quiescent, gets the uterus ready for implantation, and stops cyclicity from starting again. In actuality, progesterone, relaxin, prostacyclin, and nitric oxide work together to induce myometrial quiescence during pregnancy. Progesterone has been shown to increase the production of certain endometrial secretions in cows, which are necessary for the healthy development of embryos. Poor embryonic development may result from low progesterone levels in the animals [25].

In both bovines and ovines, progesterone administration promotes embryo development. When progesterone and estrogen work together, the endometrium is changed to a secretory epithelium that may support the conceptus before and after implantation. Throughout first half of pregnancy, the corpus luteum produces progesterone, which the placenta takes over at around 50 day post estrus. The ovaries' subsequent removal does not impair the fetus's development, progesterone level in peripheral plasma rises gradually from the luteal phase level, increases noticeably around 90 day post estrus, increases during 125-day post estrus, and falls in the final days before parturition [26].

The female genital organs can be categorised both functionally and morphologically into the ovaries, situated in the pelvic cavity, and the tubular structures, which include the uterine tubes, uterus, and copulatory organs, the activities of the genital system are the creation and sustenance of the embryo. The alterations in female genital organs are governed by intricate neurological and hormonal mechanisms [27]. The endocrine network plays a significant and crucial role in coordinating the development of the mammary gland (MG) and the animal's reproductive status throughout pregnancy. The reproductive hormones (progesterone, P4, estrogen, E2, and prolactin, PRL) have a direct effect on MG development, whereas metabolic hormones like thyroid hormones have an indirect effect by changing MG's reactivity to reproductive hormones and controlling milk synthesis. Furthermore, in order for these hormones to effectively sustain pregnancy, the endocrine system network (P4, E2, etc.) as well as availability of nutrients (lipids, glucose, and proteins) must continue during this crucial time [28].

Method

This article was prepared using the literature review method with a descriptive-analytical approach. Data were obtained from various scientific sources such as journals, books, and previous research results that discuss histological and hormonal changes in the uterus of large ruminants during the estrous cycle, pregnancy, and parturition. The review includes the role of major hormones such as progesterone, estrogen, oxytocin, and prolactin, as well as microscopic changes in the endometrial, myometrial, and perimetrium layers. In addition, physiological comparisons were made between species such as cows, goats, sheep and camels. Secondary data analysis was also used to support conclusions through statistical results and visualizations such as histograms from previous studies.

Result and Discussion

Another study [29] mention through its effects on implantation, the myometrium, and possibly the uterine cytokine network, the P4 hormone plays a crucial role in both the early and late stages of pregnancy. P4 tended to decline before labor, while E2 increased to promote prostaglandin synthesis. Changes in P4, E2, and PRL levels during the latter stages of pregnancy regulate the construction of the nest and get the MG ready to nurse the infant from the litter. Furthermore, during pregnancy, Insulin-Like Growth Factor-I (IGF-I) plays a significant role in both the mother's metabolism and the growth of the fetus. hence controlling the availability of nutrients needed for the development of the fetus. It is evident from the aforementioned research that a number of hormones work in concert to regulate growth, metabolism, energy balance, and reproductive processes. The endocrinology of bovine reproductive physiology, however, has not gotten much attention [30]. The statistical analysis indicates the measurements of myometrium and follicles in cow was the highest compared to the average parameters for other animals' significance differences (< 0.05) [31] (Histogram 1).

The ovary is a critical endocrine organ that is responsible for the primary production of reproductive steroid hormones in females. As a result, the reproductive system, mammary organ, and feminine behavior are all dependent on a properly functioning. The uterus is a crucial organ for reproduction in mammals. It is crucial for the fertility of females, their health, and that of their offspring. Furthermore, they secrete or transport essential elements for embryonic viability [32]. They can significantly influence the regulation of the estrous cycle during development. Genetic abnormalities or exposure to endocrine disruptors that affect uterine development in the

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fetus and neonate can program adult uterine function, resulting in infertility, cancer, and potentially death. Different diseases of the female genital system can result in disrupted animal production and financial losses [9].

The ovaries of most domestic mammals, with the exception of mares, comprise two different regions: the outer cortex and the inner medulla, encased by a layer of surface epithelium known as germinal epithelium [33]. The cortex is restricted to the deeper zone of the ovary and only extends to the surface at the ovulation fossa. The epithelial layer of the ovulation fossa extends over the remainder of the ovary as the usual tunica serosa. The entire surface of ovary is cover by a single layer of epithelial cells, with the exception of regions that are impacted by ovulation. The nature of these cells varies, ranging from simple squamous to cuboidal or low pseudostratified columnar [34]. The basement membrane anchors the epithelium above the ovarian cortical interstitial, and desmosomes and gap or tight junction complexes provide lateral connectivity The individual follicle in mammalian ovaries comprises an internal oocyte, encircled by granulosal cells, and external layers of thecal cells. The oocyte develops and matures in the presence of follicular fluid and paracrine factors. The differentiation of ovarian tissue commences at 56 days of foetal development, the ovaries are mostly composed of closely clustered cell cords in the cortex and loosely distributed in the medulla [35].

They are superficially covered by germinal epithelium akin to that of cattle. In mammals, during ovarian follicular development, only a restricted number of follicles are chosen for ovulation, while the others experience atresia at different developmental phases, the ovary produces survival factors, in addition to the gonadotropins FSH and LH, that are essential for the successful formation of follicles. the differentiation and proliferation of the myometrium, and the coordinated development of uterine organs are all morphogenetic events that are characteristic of postnatal uterine morphogenesis. The three fundamental histological components of the uterine wall; the endometrium, myometrium, and perimetrium; are defined by the postnatal morphogenetic process. uterine glands, which are either simple or branched coiled tubular glands. The endometrium in goats features non-glandular regions known as caruncles. The perimetrium, is composed of a longitudinal outer layer of smooth muscle and a dense circular inner layer of myometrium, is composed of loose connective tissue containing a variable number of small lymphatic vessels, blood vessels, and nerves, and is externally lined by simple squamous cells of peritoneal mesothelium [36]. The stroma is further divided into stratified compartments, which consist of a highly organised fibroblast zone , a more loosely organised zone in the deeper region (stratum spongiosum), and basal endometrium , as well as blood vessels and immune cells, and the endometrial glands are simple tubular [37].

1. Estrous Cycle Characteristics

The cyclical characteristic of ovarian activity, which enables female to transition from a time of reproductive responsiveness to nonreceptivity and finally establish pregnancy after mating, is exemplified by the estrus cycle. Cattle typically have an estrus cycle of between 18 and 24 days. 16-17 days in ewe and goat, 23-28 days in camel and 16-22 day in gazelle [30]. The luteal phase (14–18 days) and the phase of follicles (4-6 days) are the two distinct phases that make up the cycle. The follicular phase is the time when the corpus luteum dies until ovulation, whereas the luteal phase is the time after ovulation when the corpus luteum forms. The ovulatory follicle undergoes maturity and ovulation during the follicular phase, which results in the release of an oocytes into the oviduct, potentially enabling fertilization [37], mention the reproductive cycle in ewe (Histogram 2).

2. Thyroid Hormones

Compared to mid-gestation, T4 and T3 concentrations rose during the third trimester of pregnancy. There is still a great deal to learn about dairy cows' poor fertility. When ovarian function is manipulated alongside exogenous hormonal manipulation to reduce the antral age of the ovulatory follicle, dairy cow fertility is improved in comparison to cows that receive artificial insemination (AI) after estrus [13].

3. Insulin Like Growth Factor

The concentration of IGF-I decreased ($P<0.05$) from its peak on day 13 to its lowest on day 22 throughout the latter half of pregnancy. This hormone was evidently lower in the third trimester than it was at the middle of pregnancy. In order to decrease maternal anabolic activity and enhance the accessibility of nutrients for the uterus, it is crucial that IGF-I levels be lowered in the latter stages of pregnancy. Due to the decrease in both liver and fat mass, as well as the concurrent expression of IGF-I mRNA, the concentration of IGF-I dropped in the latter stages of pregnancy. Pregnancy is one of the most important stages of a female's life for the survival of her species. Mammalian species go through a highly coordinated process that needs hormones and a reproductive system. Changes in the hormonal makeup of progesterone and estrogen are among the endocrine changes that have a substantial impact on the endometrial structure and the female reproductive immune system [38].

4. Estrogen Hormone

The E2 level gradually rose throughout the second part of pregnancy and continued to rise, peaking on day 28 just before kindling. The E2 level at the 28th day of pregnancy was significantly greater ($P<0.05$) than the levels at days 14 and 21, which did not differ significantly ($P>0.05$). The production of cortisol by the fetal adrenal gland initiates the dominant role of estrogen after parturition by stimulating placenta 17αhydroxylase that converts progesterone to estrogen. This process is closely linked to size of fetus with uterine fluid. Relaxin and estrogen work together to

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loosen up birth canal, making it easier for the fetus to be delivered. The postpartum phase, which lasts from birth to the onset of the first estrus, is marked by the pituitary and hypothalamic hormones interacting to promote endometrial regeneration, uterine an involution, and ovulation cyclicity restart. Breed, nutrition, time of year, lactation, suckling, and suckling intensity all affect postpartum. There are notable variations in the time between the first ovulation and parturition [39].

5. Progesterone Hormone

The level of the progesterone hormone, P4, was progressively raised from the middle of pregnancy to the highest point (4.00 ng/ml) on day 21. This amount at kindle day were then considerably ($P<0.05$) different from that at other gestational days, although being marginally lower two days before delivery. This result is consistent with that of (), who discovered that the P4 level during pregnancy was 3.1 ng/ml.It is also necessary to maintain pregnancy and to keep uterus in a state of inactivity in order to avoid labor starting too soon. Additionally, it facilitates fetal implantation and keeps the pregnancy going. The negative feedback effect of estradiol during parturition may be caused by a decrease in quantity of estrogen receptor in anterior part of the pituitary gland. Reactivity of the pituitary to GnRH is directly related to the quantity and position of estradiol receptors. Following delivery is a critical time for the sheep industry. Human welfare and health are improved by animal farming methods. However, because of the increasing consumer appetite for animal goods, it is difficult to create agricultural items. In order to prevent environmental degradation, there is also social pressure to promote ecologically conscious production [40]. The statistical analysis according into results of [30] indicates the measurements of hormones in cow was the highest compared to that in other animals with significance differences (< 0.05) (Histogram 3), [37] explain the effect the estrus cycle on the uterine hormones in ewe (Histogram 4)

6. Luteal Stage

When the progestogen concentration in the first of two consecutive fecal samples increased by at least 2 standard deviations from the mean concentration in the previous inter-luteal phase, it was considered that the luteal phase had begun. As the sample that came before was the initial sample to meet the previously stated requirements for admission in the succeeding inter-luteal phase, the conclusion of the luteal phase was designated [8].

7. Prolactin Hormone

For prolactin hormone to reach its maximum level, it significantly increased. This amount was much more than that on every gestational day. This growth was prolactin hormonal levels were lower on the day of delivery than on the remaining days of pregnancy, which was the opposite pattern from the other hormones. Pregnant women who were also nursing had lower prolactin levels than pregnant women who were not nursing. Furthermore, they explained these outcomes by pointing to the higher levels of prolactin in the pregnant and lactating animals, which limit prolactin secretion and cause them to consume more feed. For the second stage of mammary gland differentiation, the level of prolactin during pregnancy is crucial. To get mammary gland ready for the release of colostrum and subsequently milk, this phase starts around parturition [40].

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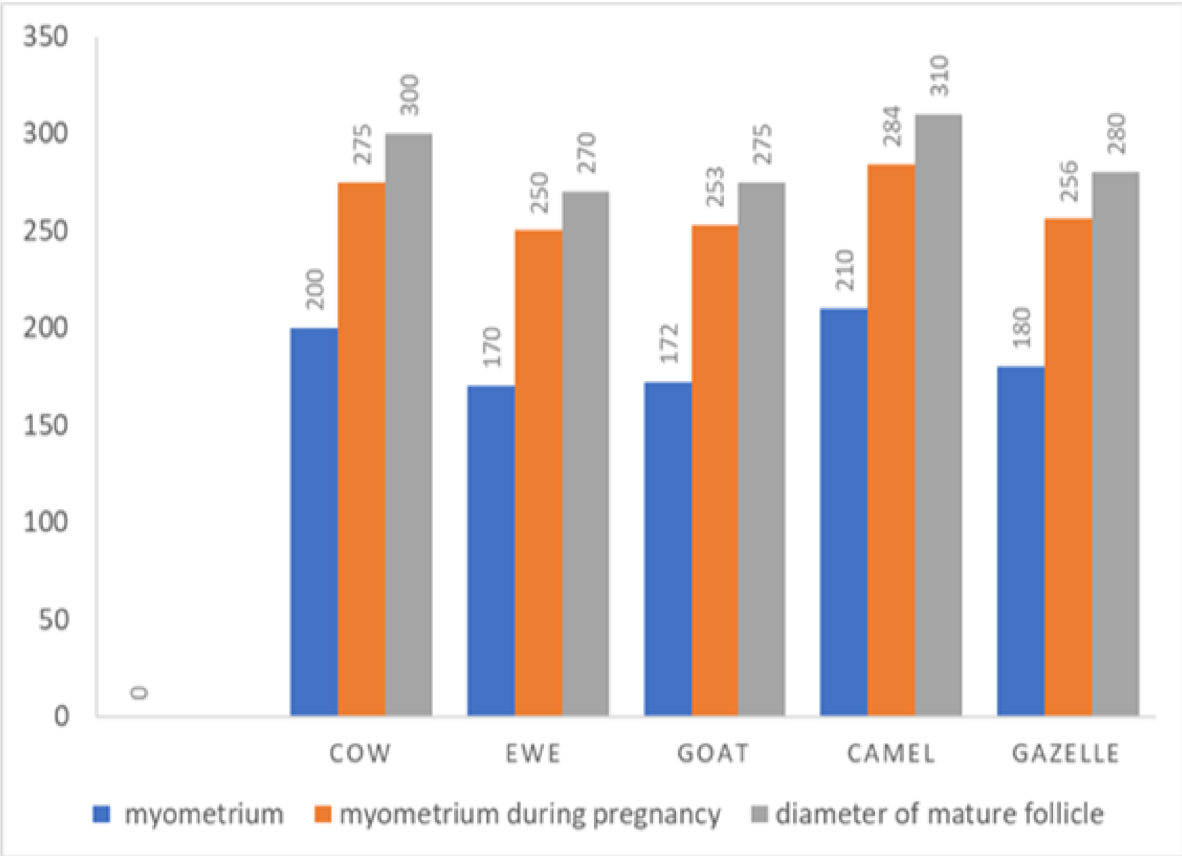

Figure 1. *Histogram Comparative Measurements of Uterus and Ovary Between Study Animals, µm*

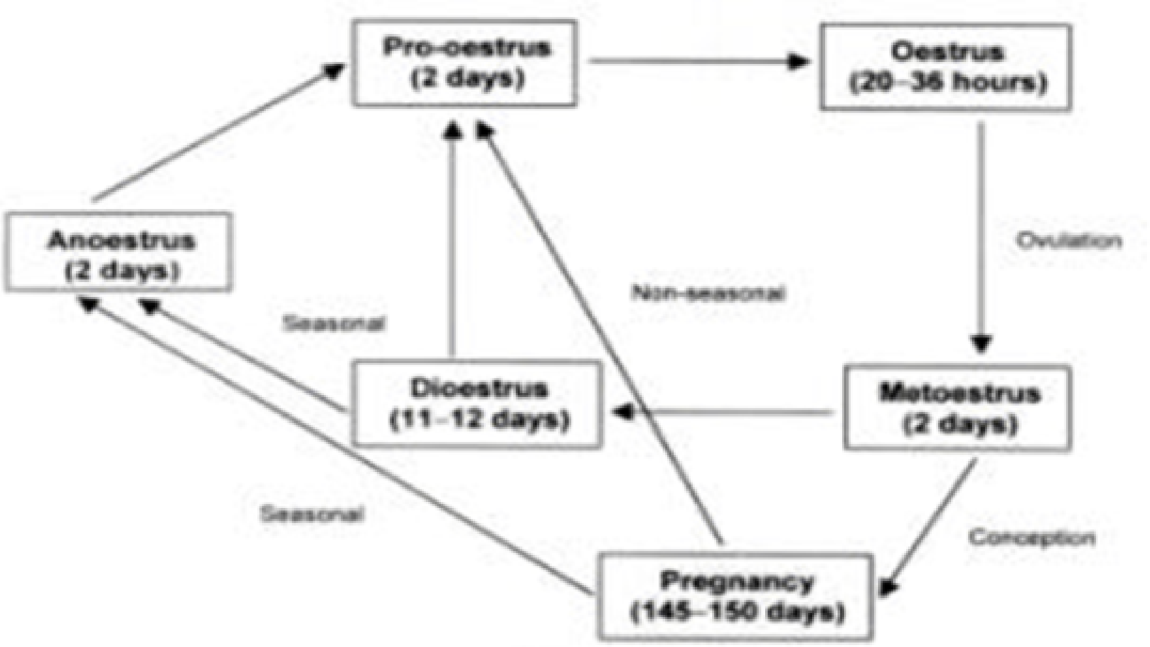

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Figure 2. *Histogram The Reproductive Cycles of Ewe (37)*

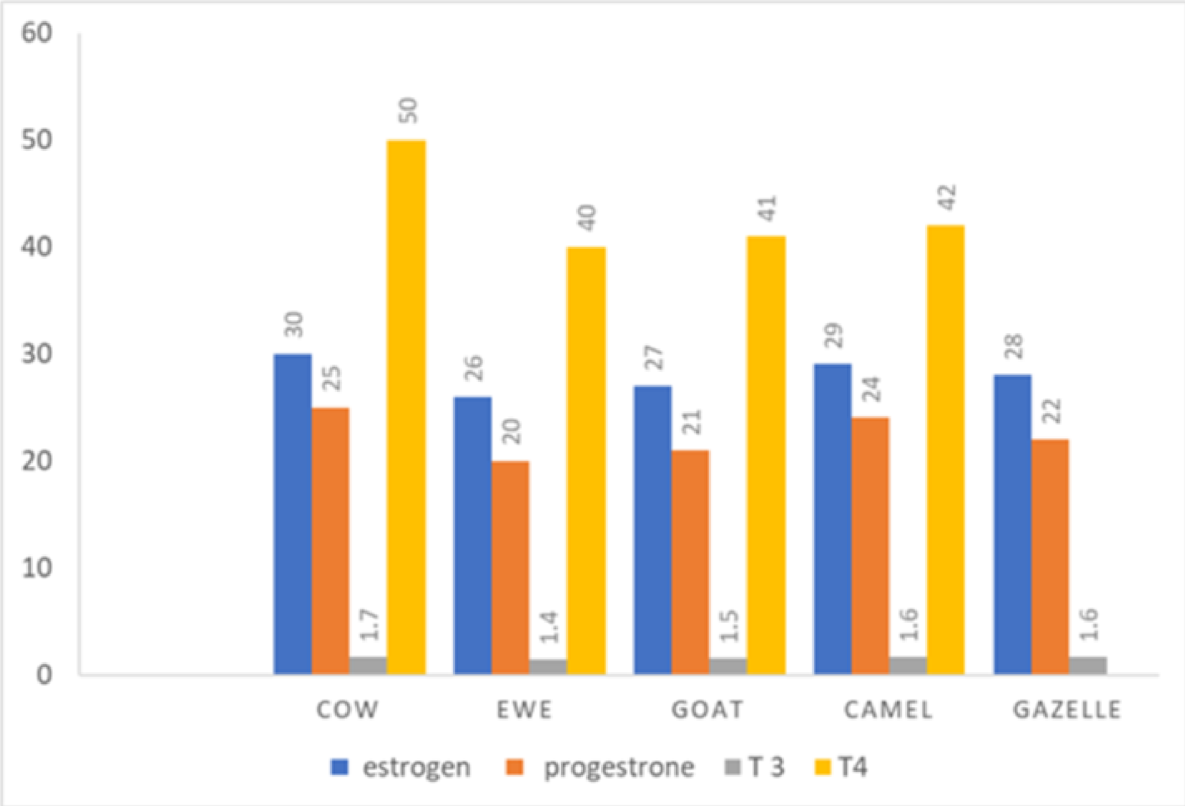

Figure 3. *Histogram Comparative Measurements of Reproductive Hormones, and T3 T4 Between Study Animals, nmol/liter*

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Figure 4. *Histogram Effect the Estrus Cycle on The Uterine Hormones in Ewe (37)*

Conclusion

Animals go through numerous physiological changes during pregnancy, including changes in hormones, Due to present management procedures that forbid two lamb deliveries year, the ewes' aptitude is not being used to its full potential. The research show that sheep can have up to five lambs per pregnancy and a biological maximum of six months each lambing. Sheep's seasonal breeding habits and the length of the postpartum period make it impossible for the sheep producers to do this. While many significant concerns regarding the postpartum period remain unanswered, many others have been well investigated. Life history information for these animals showed a good correlation between peak values in the proportion of secreted oestrogen: progestagen throughout the inter-luteal interval during their estrous cycles, the chance of conception in animals may be influenced by interactions between steroid synthesis and metabolism. Before naturally mating to an intact male, controlled internal release of drugs gadgets were used to synchronize estrous cycles. Peri-ovulatory fecal estrogen levels and the amount of pre copulatory courting behaviors were positively connected with mounting and copulation rates. According to these findings, if estrogen is a reliable indicator of fertility, males will selectively invest their reproductive energy in marrying the most fertile females. This hypothesis was tested by looking at successive stages of the cycle of reproduction finding proof that the most capable corpora lutea would emerge from oocytes as well as follicles produced in an environment with higher levels of estrogen, increasing the likelihood of maintaining pregnancy. Hormone excretion and sexual behavior are related, which lends credence to the idea that men might employ this mechanism to gauge female fertility. This will improve our comprehension of the basic procedures needed for successful implantation, reduce the environmental impact, and increase the efficiency of food production (dairy and meat) in ruminants.

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