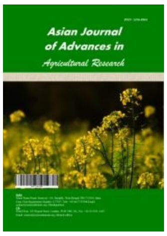

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Risk Factors and Treatment of Postpartum Anestrus in Cattle: The Case of Zebu

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Authors' contributions

This work was carried out in collaboration among all authors. Authors MGM, MM and HI wrote the first draft of the manuscript. Author MGM managed the documentary research. All authors read and approved the manuscript before submission.

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ABSTRACT

This literature review reports on risk factors for postpartum anestrus in zebus and their potential treatments. Prolonged postpartum anestrus is one of the major factors limiting reproductive efficiency in cattle, particularly in *Bos indicus* cows in tropical regions, as it prevents a calving interval of 365 days from being achieved. During anestrus, ovulation does not occur despite ovarian follicular development, as the growing follicles do not reach maturity. This period is very variable and depends on various factors whose importance is relative or, on the contrary, essential. Some are specific to the animal (breastfeeding or food); others relate more to its social environment, season sanitary conditions. Several hormonal treatments have been used to induce ovulation and cyclicity in postpartum cows. Generally speaking, given the inconsistency of the effects or even their lack of practicability, treatments using a single or repeated injection of a gonadotropin-releasing hormone (GnRH) have been gradually abandoned in favour of progestagens. These are administered for 8 to 12 days on a continuous basis in the form of a subcutaneous implant (Crestar®), a vaginal coil (PRID®) or a CIDR. A prostaglandin injection is given two days before the implant is removed. The addition of an ECG treatment at the time of device removal, which increased plasma progesterone concentrations and pregnancy rates in anestrous postpartum suckled *Bos indicus* cows, may be useful to improve reproductive performance. This improvement requires a better understanding of the effect of different risk factors on the recovery of postpartum cyclicity.

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1. INTRODUCTION

Postpartum is the period between calving and new pregnancy. this period includes the waiting and reproduction period, which ideally last 60 and 30 days respectively. Anestrus is said to be physiological in the sense that it occurs during a period in which it is normal not to observe it (prepubertal period and gestation are two examples). If it continues beyond a waiting period of 14-15 months, it becomes pathological [1].

Infertility is one of the characteristics of cattle breeding in Africa, resulting in an increase in the age of first calving and the interval between calvings. It limits the genetic progress and profitability of *Bos indicus* farms. The late resumption of postpartum ovarian activity in Zebu cattle is considered a major obstacle to achieving a calving interval between 12 and 14 months. The profitability of dairy herds depends on the reproductive performance of the animals [1].

Postpartum anestrus is the main factor that negatively affects the reproductive performance of animals bred in the tropics. several factors affect postpartum anestrus, including lactation, pre and postpartum nutritional status, sanitary and environmental conditions and genetic factors [2]. The objective is to obtain one calf per year and a calving interval of 12 months (Stagg et *al.,* 1995). However, tropical cattle have long anestrus, which increases the calving-calving interval, resulting in reduced reproductive performance of the animals [2].

Thus, several hormonal treatments have been used to induce cyclicity and ovulation in *Bos indicus* females. $PGF_{2\alpha}$-based treatments are mainly used in heifers and cows with regular cyclic activity. Other progestin-based products are more indicated in cases of prolonged anestrus after birth (pubertal pathological anestrus) or after calving (postpartum pathological anestrus). Depending on the case, these progestagens may be combined with an injection of $PGF_{2\alpha}$, usually performed two days before removal of the implant or vaginal device. The purpose of this injection is to induce luteolysis of any corpus luteum present. Similarly, an injection of ECG (350 to 500 IU) is given at the end of the progestin-based treatment. This treatment has the effect of promoting follicular growth and ovulation after the withdrawal of the progestin [3].

The objectives of this review are to discuss the impact of postpartum anestrus on the reproductive performance of zebu and to present hormonal treatments that can improve reproductive performance by reducing the duration of anestrus for successful artificial insemination (AI).

2. REPRODUCTIVE PHYSIOLOGY IN *BOS INDICUS COWS*

The differences in reproduction were summarized by Bo et *al,*.2003 Compared to the *Bos taurus*, the zebu is characterized by:

- smaller genital tract dimensions (Study carried out on 500 genital tracts of Azawak, Bororo, Djelli and Goudali zebus taken at the slaughterhouse of Niamey).

- a shorter estrus duration: 10 h (with variations from 13 to 20 h) and less pronounced signs of estrus that appear more during the night, a possible consequence of different environmental conditions (thermal stress). This makes the use of artificial insemination on observed heats very difficult or impossible [5].
- a shorter interval between the onset of estrus and ovulation: 10 to 26 h vs 24 to 38 h in *Bos* Taurus [1]. This would imply a shorter delay between the onset of estrus and the time of ovulation
- a lower liberation of LH at the time of estrus [1].
- comparable follicular dynamics in waves except *that Bos indicus* seems to have a smaller diameter of the dominant follicle (10-12mm) and corpus luteum (17-21mm) [6-8] than *Bos taurus* (14-20mm and 20-30mm, respectively [9] [10] [6].
- a greater number of follicles smaller than 5 mm in diameter Bo *et al.,* 1993
- a smaller diameter of the preovulatory dominant follicle (10 to 12 mm vs. 14 to 20 mm) and of the corpus luteum (17 to 21 mm vs. 20 to 30 mm) which makes palpation more difficult and would imply a more systematic use of ultrasound Bo *et al.,* [6]
- Several studies have characterized the follicular dynamics in Bos indicus [5].

The pattern of follicular growth in Bos indicus is similar to that described in European taurines except that *Bos indicus* appears to have a smaller diameter of the dominant follicle (10-12mm) and corpus luteum (17-21mm; Figueiredo et al., [8] than *Bos taurus* (14–20mm and 20–30 mm, respectively; Ginther et *al.,* [9] Kastelic et *al.,* [10] [6]. These differences have important practical implications as the corpus luteum is difficult to palpate in *Bos indicus*.

3. FACTORS INFLUENCING THE DURATION OF POSTPARTUM ANESTRUS

Prolonged postpartum anestrus is a main factor limiting reproductive efficiency in cattle, particularly in *Bos indicus* cows from tropical regions, because it prevents achievement of a 12 month calving interval. During anestrus, ovulation does not occur despite ovarian follicular development, because growing follicles do not mature [11]. The main factors affecting the duration of postpartum anestrus in cattle are breastfeeding mode and food. Some other factors such as season, social environment and sanitary conditions influences duration of postpartum anestrus.

3.1 Breastfeeding Mode

Breastfeeding contributes to a longer physiological anestrus period. An increase in milk production increases the risk of a negative energy balance and therefore of functional anestrus. Numerous hormonal or zootechnical observations have confirmed the inhibitory effect of udder suckling on the resumption of ovarian activity during the postpartum period [12]. This influence depends not only on the intensity of the mammary stimulus; a cow suckling two calves will most often have a longer anestrus (96 days vs. 67 days) than a cow suckling only one, but also and more importantly on the frequency of this stimulus. Indeed, the duration of anestrus is greater when access to the udder is permanent than if it is limited to one or more daily periods [1]. Suckling is an important factor affecting the recovery of postpartum cyclicity in lactating cows. A cow in continuous contact with her calf will have a longer anestrus than a cow in limited contact with her calf. Thus, the presence of a calf, whether suckling or not, prolongs the anovulatory period after calving [13].

On the hormonal level, breastfeeding results in the effects of lactation include a reduction in GnRH secretion and pituitary sensitivity to the stimulatory action of GnRH. stimulating action of the latter. Weaning is accompanied by an increased secretion of LH, an effect that would nevertheless depend on the level of intake of LH. However, this effect depends on the level of food intake [1].

3.2 Food

Under-nutrition contributes to prolonged postpartum anestrus [14]. The condition score (CS) is a very practical method to evaluate the nutritional status of cows. the estrus cycle is maintained when the CS is greater than or equal to 4. Cows with a CS of 4 have a shorter postpartum anestrus than those with a CS of 3 or 2 [15]. Postpartum anestrus is longer in traditional breeding than in modern breeding, regardless of CS.

Gyawu P. [16] shows that the difference observed between calving/cycling intervals in The Gambia and Ghana can be explained by much greater feeding problems in the former country. in addition, the same author shows that in Ghana, herd management influences the postpartum interval: between two herds located in the same place, a difference in daily grazing time increased the calving-first estrus interval from 86 days (n=25) to 165 days (n=12).

It is also worth noting that Jeannin et *al.,* [17] observed a 60-day delay in the resumption of ovarian activity in The Gambia. the difference with the animals studied by Gyawu is that here, the cows in the village environment were receiving food supplements, thus showing the predominant influence of food on this parameter.

On the hormonal level, the possible mechanism by which under-nutrition may inhibit resumption of postpartum ovarian activity in cows is by the inhibition of hypothalamic GnRH secretion. However, little is known about the specific ways in which information about nutritional state is translated into neuroendocrine signals that affect GnRH secretion [18].

The effects of pre or post-calving feeding on reproduction fall into three types of studies. The first is reserved for effects on follicular growth and luteal activity. The second was devoted to the parameters and performance of reproduction from which they result: anestrus, intervals

Table 1. Size of the genital tract of *Bos indicus* / *Bostaurus (cm)* [4]

Parts of the genital tract	*Bos indicus* Moussa Garba et al. [4]	*Bos taurus* (various sources)
Vulvar vestibule	5,6 ± 1,2	8-10
Vagina length	18,9 ± 3,3	30
Collar length	8,1 ± 2,5	10
Neck diameter	3,4 ± 1,1	< 5
Horn length	21,6 ± 5,2	35 - 45
Horn diameter	1,6 ± 0,5	2.5 - 3.5
Oviduct length	19,1 ± 3,8	30

between calving and 1st insemination, between calving and fertile insemination, fertility index. Finally, the third part of the study focused on describing potential hormonal or biochemical mechanisms.

3.2.1 On follicular growth

Various observations confirm the multiplicity of influences of the energy balance on follicular growth during the postpartum period. thus, the quantitative aspect (moderate or severe) of the energy balance, the effect on the recruitment or the terminal phase of follicular development, the length of the period between calving and the time or energy deficit must be taken into consideration, and the duration of the negative energy balance.

In general, in lactating cows, various studies have shown that chronic undernourishment, i.e., a diet that covers only 60 to 80% of body needs, leads to a daily loss of 500 to 800 g, and would lead in a few weeks to an inflexion of the growth rate of the follicles, to a decrease in the size of the dominant follicles and corpora lutea, to a reduction in the persistence time of the dominant follicles, without modifying the frequency of ovulation or the duration of the cycles [19] [1]. The adoption of a correct diet would induce the progressive reappearance after 50 to 100 days according to the studies of a resumption of normal follicular growth and ovulation.

An ultrasound study showed that lactating cows with a positive energy balance had a higher number of follicles between 10 and 15 mm in diameter [20]. Conversely, a negative energy balance would not prevent follicle recruitment during the first 15 days postpartum [21]. A moderate negative energy balance would therefore affect more the terminal stages of follicular growth [22-24]. A state of undernourishment before or after parturition extends the time at which the dominant follicle reaches its maximum size by 4 to 6 days (10 vs. 14 days). It also delays the time of emergence of the second and third wave of follicular growth by 4 to 6 days. This results in a 3-week increase in the interval between calving and first ovulation (77 vs. 51 days) [18].

3.2.2 On luteal activity

It appears that the first phase of normal luteal activity occurs on average 10 days after the negative energy balance is observed [1]. Progesterone synthesis would be greater in cows with a positive than negative energy balance [25]. This synthesis would also be increased during the 2nd and 3rd luteal phases in animals with a positive energy balance during the 1st week postpartum [26]. Similarly, the number of days between calving and the time of the first increase in progesterone is negatively correlated with the average energy balance during postpartum [27].

3.2.3 On reproductive performance

Most authors recognize that severe (10-20% less than required) and prolonged underfeeding of the cow before and after calving affects ovarian function and contribute to a longer duration of anestrus after calving [28] [29] [30,21]. The negative effect of underfeeding during postpartum has been demonstrated in suckling cows [23] [31]. However, this effect has not been unanimously recognized [32] this effect seems to depend on the antepartum feeding: it is less important in cows that were well fed before calving and more important in those that were underfed before calving [33-34].

3.3 The Season

Tropical climates are varied and often characterized by high temperatures, which are detrimental to the reproductive performance and production of cattle. Heat stress can disrupt the secretion of GnRH and LH hormones, ovulation (delayed peak of LH), follicular growth and that of the dominant follicle, and the expression of heat in cows [35]. Photoperiodism, according to Horta [15] has an influence on the duration of postpartum anestrus. This author found that cows that calved in the dry season had a longer anestrus period than those that calved in the cold season.

The photoperiod acts on the pineal gland (epiphysis) in the brain. During the dark phase, melatonin is secreted. If the nights are long and the days short, the amount of melatonin produced is high. In the so-called 'short-day' species, sexual activity is activated. Melatonin will regulate the suprachiasmatic nucleus which is the main centre of the biological clock in mammals. This intervenes in reproduction via the hypothalamus which secretes more or less GnRH [35].

In northern Côte d'Ivoire, the dry season is long. Maximum fertilisation occurs in transhumant zebu at the time of regrowth of grasses after fire, when their nutritive value is high, in January-February and March-April, giving a kind of natural flushing [35].

In Burkina Faso, at the Bobo-Dioulasso station, with Baule cows kept in good condition, Chicoteau et *al.,* [36] observed seasonal variations with a period less favourable to fertilization in May-June, in the hot and humid pre-pluvious season, during which the quality of the ration is the least good.

In Senegal, the seasonality of zebu reproduction is very marked. Denis and Thiongane [37] studied the ideal breeding season at the Dara Zootechnical Research Centre and in the Ferlo, in northern Senegal, the cradle of the Gobra zebu. Fertile mating is concentrated in the months of August to November, resulting in more births from May to August. In this region the rainy season lasts 3 to 5 months with maximum rainfall in August and September.

Similarly, in The Gambia, the number of births is correlated with the rainfall of the previous month [38].

In Tanzania, zebu breeding performance was linked to seasonal rainfall [39].

3.4 The Social Environment

The presence of a bull favours the return to heat after calving. A bull, even if attached, will have a beneficial effect on the duration of postpartum anestrus. A high concentration of animals introduces the phenomenon of social stress where the dominated animals decrease their food intake. This results in reduced reproductive performance and increased susceptibility to infections and infestations [13].

3.5 Sanitary Conditions

A good sanitary condition remains an essential prerequisite for reproduction. Hygiene conditions allow to limiting the infections of the genital tract which alter the resumption of postpartum cyclicity and therefore the appearance of heat. Any assistance with calving, even if easy, will increase the time taken to resume ovarian activity. Placental retentions, chronic metritis and other acute conditions can influence the duration of postpartum anestrus [13].

4. TREATMENT OF ANESTRUS IN *Bos indicus* COWS

During the last decade, the use of different hormonal protocols to facilitate estrous detection, considered as a major obstacle in cattle reared in tropical conditions, has been the subject of numerous researches and publications. Thus, several treatments (zootechnical and hormonal) are used to induce cyclicity and ovulation in *Bos indicus* females. Most of the hormonal treatments are based on the use of prostaglandin $PGF_{2\alpha,}$ progestagens associated with ECG to improve the reproductive performance of *Bos indicus* females in anestrus.

4.1 Zootechnical Treatments

A reduction in the period of functional anestrus can be achieved by modifying the method of breastfeeding. Early weaning can be done within 30 to 80 days after birth. Breastfeeding can be reduced to one or two daily periods of 30 to 60 minutes for at least 10 days. Finally, a 48-hour weaning period can be applied a few days before the cows are put to breeding. It appears that regardless of the method used, the practice of directed lactation is accompanied by positive effects on reproductive performance such as the interval between calving and first heat or fertilizing insemination or the percentage of pregnancy. However, the improvements observed are more pronounced when the methods are applied to primiparous cows or when the maintenance conditions of the animals are inadequate. Long-term effects on calf growth appear to be minimal [1].

4.2 Hormonal Treatments

Treatments using single or repeated injections of GnRH have been progressively abandoned in favour of progestagens, given the inconsistency of the effects and their impracticality [1].

Various hormonal protocols to induce and synchronise heat have been considered. $PGF_{2\alpha}$-based protocols are mainly used in heifers and cows with regular cyclic activity. Others based on progestagens are more indicated in cases of prolonged anestrus after birth (pubertal pathological anestrus) or after calving (postpartum pathological anestrus). Progesterone (or its analogues) is secreted by the corpus luteum during the cycle and then by the placenta. it is administered for 8 to 12 days in non-cycling females on a continuous basis in the form of a subcutaneous implant (Crestar®; Intervet, 3 mg Norgestomet), a vaginal coil (PRID® Progesterone Intravaginal Device; CEVA; 1.5 g of progesterone) or a CIDR (Control Internal Drug Releasing, 1.3 g to 1.9 g of progesterone). Progesterone-based treatments are most indicated for prolonged anestrus after birth (pubertal pathologic anestrus) or after calving (postpartum functional pathologic anestrus). They allow simulating the luteal phase, thus preventing the appearance of heat and ovulation. The end of the treatment leads to a sudden drop in progesterone levels responsible for the appearance of a peak of LH which provokes ovulation [3].

Prostaglandin $F_{2\alpha}$ (two days before the removal of the implant, to make a possible corpus luteum disappear) or eCG (at the time of the removal of the implant, to stimulate multiple follicular growths, especially if the cows are in anestrus before treatment (300 to 500 IU) can be associated with progesterone. Heat appears 48 to 72 hours after the treatment is stopped. The summary of the characteristics of ECG mentions three major indications: treatment of reproductive disorders, especially in cases of anestrus, synchronization of estrus (in combination with progestagens and $PGF_{2\alpha}$), but also induction of superovulation. After synchronization treatment, approximately 85% of cows express heat between 36 and 60 hours [41-41].

5. CONCLUSION

One of the main causes affecting reproductive performance is the calving interval, which is directly influenced by postpartum anestrus. Duration of postpartum anestrus is mainly affected by the nutritional status and suckling. Adequate nutrition is essential for resumption of postpartum ovarian activity in cattle. Other factors including season, social environment and health conditions may also affect the duration of postpartum anestrus. But tropical cattle have long anestrus, which increases the calving-to-calving interval with a consequent reduction in the animals' reproductive performance [2]. The successful application of artificial insemination in *Bos indicus* cattle not only has to overcome the problem of estrus detection but also has to deal with the problem of nutritionally and suckling-induced anestrous. Hormonal heat synchronization methods are now known and developed in Africa. However, the use of these technologies is still limited and efforts must be made to popularize them, which will undoubtedly have a positive impact on the improvement of livestock. There is still important research to be done to clarify the potential effects of feeding on the dynamics of follicular and luteal growth in the postpartum period.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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