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Overview on Some Factors Negatively Affecting Ovarian Activity in Large Farm Animals

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Abstract: Ovarian activity is a very important function for the furtherance of a species. Many factors were found to affect ovarian activity negatively in farm animals and are related to nutrition, climate, housing, environmental pollution, physiology, health status and other miscellaneous factors. The effect of these adverse factors on ovarian activity in large farm animals was reviewed.

Key words: Farm animals · Ovarian activity · Nutrition · Climate · Management · Pollution · Physiology · Health

INTRODUCTION

The reproductive organs of female farm animals manifest regular cyclic activities between puberty and senescence. These changes entail a complex series of physiological events emanating from the hypothalamus, the pituitary gland and the ovary. The later has two main functions, production of female gametes and secretion of hormones that share in regulation of the reproductive process. Each ovarian cycle begins with follicular growth and maturation, followed by ovulation and the subsequent formation and regression of the corpus luteum (CL). Disturbed ovarian activity is the most prominent cause of reproductive failure and economic losses. It occurs in four clinical forms: silent heat, anoestrus, cystic ovarian disease (COD) and premature luteolysis or persistence of CL [1-3]. It was found that this phenomenon causes great economic losses as the result of fewer days in milk and fewer calves produced per year of life as well as high culling rate mainly due to failure of pregnancy. Understanding the adverse conditions affecting ovarian activity is an important step towards the development of management practices that positively influence the reproductive efficiency of farm animals. This investigation focused on some factors negatively affecting ovarian activity in large farm animals.

1. Adverse Nutritional Conditions: From the practical stand point, in most of the developing countries, adverse nutritional conditions command the greatest attention. Lack of proper nutrition is serious enough to affect ovarian activity and other physiological functions.

1.1-Body condition: Prepubertal severe body weight loss due to diseases of gastrointestinal tract (GIT), chronic systemic diseases, parasitic and toxicological diseases are usually accompanied by delayed puberty and anoestrum. Cows that lost weight before calving had extended post partum intervals compared with cows that gained weight before calving. Only 25% of cows lost weight both before and after calving showed oestrus by 60-80 days after calving vs. 67% of cows in good BCS [4]. Moreover, loss of weight before calving is more detrimental than after calving with a delay of 19 days for every 10% loss of body weight [5]. Reduced Body condition score (BCS)between 90 days before foaling and 90 days after foaling was associated with delayed postfoaling heat, lower pregnancy rates and high incidence of early embryonic death in mares [6]. Buffalo-cows having poor BCS had fewer small and large follicles in their ovaries with low incidence of good quality oocytes [7]. Poor body condition inhibits the secretion of pituitary LH or reduces its pulse frequency. This effect is mediated through glucose level, gonadotropin releasing hormones, (GnRH) pulsatile secretion, opioid peptides, mainly high methionine enkephaline or insulin growth factor-1 (IGF-1) or its binding protein within the hypothalamic pituitary axis [8].

1.2-Underfeeding: Undernutrition is usually related to seasonal fluctuation in availability and quality of feed. It delays puberty in heifers and fillies mainly due to decreased growth rate. Underfeeding caused anoestrus or delayed ovulation in mares and increased the duration of PPA in bovines. Underfeeding led to high incidence of ovarian inactivity, low expression of oestrus and

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ovulation rate [3]. The mechanism whereby undernutrition affecting ovarian activity involves inhibition of both tonic and surge release of GnRH from the hypothalamus. Undernutrition increases the biosynthesis of neuropeptide Y (NPY) and βendorphin and decreases biosynthesis of LH-releasing hormone-messenger ribonucleic acid (LH-RH-mRNA) in the hypothalamus. Such changes reduce the production and release of follicle stimulating hormone (FSH) or LH from the pituitary gland. Also, restricted feeding decreases the concentration of IGF-1 and increases the metabolic clearance rate of growth hormone (GH) and consequently decreases the sensitivity of granulosa cells to FSH stimulation. In the same time, undernutrition reduces the responsiveness of the pituitary to the positive feedback effect of oestradiol from the preovulatory follicles and eliminates the preovulatory gonadotropin surge and suppresses oestrus. Moreover, low level of nutrition is associated with rapid higher level of progesterone, especially after mating and lower rate of embryo survival due to low metabolic clearance rate [9].

1.3-Energy balance: Deficiency of energy is more detrimental to reproduction than deficiency of protein. However, low protein ration reduces the voluntary intake of feed and consequently, animals consume neither adequate energy nor protein [4]. Evidence from cattle revealed that energy deficiency can inhibit ovarian function at pituitary synthesis/release of gonadotropin and at ovarian function [5]. Heifers fed on low energy ration developed smaller dominant ovarian follicles that were associated with a delay of 63 days in attainment of puberty compared with heifers fed on balanced energy. However, the effect of low energy level on puberty is modified by the age of the animals. This effect was apparently more pronounced when feed restriction was applied in the early postnatal phase than in the immediate pubertal phase [9]. Moreover, it was reported that ration deficient in the essential fatty acid linoleic and linolenic delays the onset of puberty due to reduced availability of arachidonic acid required for synthesis of bioactive metabolites and consequently delays the development of both hypothalamic and ovarian components of the reproductive axis [5]. In mature animals, reduced energy intake and negative energy balance (NEB) were associated with decreased maximum diameter of dominant follicle and CL during the last few cycles before the occurrence of anoestrus. Moreover, it lowered plasma oestradiol, reduced LH pulse frequency and amplitude in cows and buffaloes, especially following calving in high yielding animals. Moreover, [10] reported lower total lipids, triglycerides and cholesterol concentrations in the ovarian tissue of cows, buffaloes and she camels suffering from ovarian inactivity as compared to animals with active ovaries. Negative energy balance not only suppresses pulsatile LH secretion, but also reduces ovarian responsiveness to LH stimulation with decreased plasma glucose and insulin values. Insulin is known to stimulate bovine follicular development via influencing the availability of neurotransmitter substrates involved in GnRH secretion. In addition plasma level of IGF-1 is critical to ovarian follicular development and it is low following NEB [9].

1.4-Protein intake: Inadequate protein intakes (<8%) delayed puberty in cattle with a negative correlation between rational protein levels and age at puberty [9]. Ration deficient in protein (<13%) had resulted in weak expression or cessation of oestrus and repeat breeding. Moreover, rations deficient in a single amino acid had slowed growth rate, resulted in a delayed puberty, extended PPA and abnormal fetal growth pattern [11]. Feeding cows from late pregnancy through early lactation on rations containing insufficient rumen degradable protein (RDP) and non-protein nitrogen (NPN), < 13-20% especially in primigravids reduced appetite and food intake and had the same effect of underfeeding with reduced FSH and LH levels. Also, the re-commencement of postpartum oestrous cycle was delayed or suppressed with increased calving to conception interval [12]. Low protein in the ration predisposed to production of abnormal ova, a less favourable uterine environment, insufficient response of ovaries to gonadotropin and/or reduced gonadotropin secretion. Excessive protein intake had been associated with infertility due to a depression in the total soluble sugars of the grass or increased blood urea content. High intake of RDP led to excess rumen ammonia production and was associated with reduction in the pH of the uterine environment. The postpartum breeding performance was low in older dairy cows fed on excessive protein mainly due to increased blood urea concentration. Moreover, high ammonia production in the rumen imposed additional demands of amino acids for its hepatic detoxification [13].

1.5-Overfeeding: Overfeeding in the postweaning period produced heifers that expressed weak oestrous signs, increased embryonic mortalities and lowered pregnancy rates. On the other hand, overfed cows at calving exhibited decreased appetite and developed more severe NEB than cows of moderate condition. As a result over conditioned cows undergo increased mobilization of body fat and accumulated more triacylglycerol in the liver, revealed a longer postpartum interval to first ovulation and reduced fertility. In sheep, over feeding is usually associated with embryo losses [13]. Extremely high nutrition is detrimental to the growth and survival of the embryos in cattle through a decreased plasma progesterone following the high metabolic clearance rate [9].

1.6-Minerals, trace elements and vitamins: Most of readily recognized minerals, trace elements and vitamins deficiency affect the appetite, early postnatal growth, immunocompetency and reproductive performance on a herd basis, especially when mineralized salts is not included in the ration. Deficiency of inorganic phosphorus, iodine, zinc, manganese, vitamin A and β carotene, delayed the development of reproductive organs and attainment of puberty in cows [14]. In cattle, deficiency of calcium, phosphorus, magnesium, copper and zinc iodine, selenium, manganese and cobalt was found to affect ovarian activity. Such deficiencies have been associated with weak, irregular or silent oestrus, poor fertilization, conception, anoestrus or even COD (Selenium and vitamin E). In buffaloes, deficiency of calcium, phosphorus, magnesium, zinc or copper induced anoestrus and ovarian inactivity. In mares, vitamin E deficiency was considered to be a major cause of anoestrus. In sheep, it was found that copper deficiency due to high molybdenum and sulfur lead to stopped signs of oestrus in old ewes and anoestrus during the breeding season. Also, deficiency of phosphorus, iodine, copper and manganese interfered with ovarian activity and disturbed cyclicity in goats [15]. In Egypt, studies on animals, plants and soil trace elements revealed that Egyptian livestock are involved in more than half of the nutritional deficiency diseases caused by trace elements. The most important deficient elements are copper and zinc. Buffalo-cows suffered from minerals deficiency revealed clinical signs of nutritional deficiency as well as anoestrus [16]. Ovarian inactivity in buffalo-cows was associated with low calcium, phosphorus, magnesium, iron, zinc and copper[3]. Phosphorus deficiency decreases appetite, body weight and BCS [4], while zinc deficiency impairs synthesis/ secretion of FSH and LH. Copper, selenium, vitamin E and βcarotene are antioxidants and have a role in protecting the ovarian tissue from dietary polyunsaturated fatty acids peroxidation[5]. Zinc deficiency inhibits steroidogenesis and affects carbohydrate and protein metabolism [14].

1.7-Metabolic disorders: Subclinical ketosis, hypoglycemia, hypomagnesaemia and NEB, delayed uterine involution and ovarian activity leading to long calving interval with greater frequency during the third - fourth lactation and 0-4 months postpartum in bovines. Prolonged feeding on low protein ration in late pregnant dry cow, increased the incidence of metabolic disorders associated with fatty liver [17]. Hypocalcaemia in cows was associated with poor ovarian activity and infertility due to impaired blood flow to the ovaries, reduced energy intake, NEB after reduction of gut motility and impaired uterine contractility[18]. Buffalo-cows suffering from subclinical ketosis, revealed hypoglycemia, delayed uterine involution and PPA with long calving interval [19]. Hypothyroidism was associated with cessation of behavioural signs of oestrus as well as low plasma progesterone level and disturbed the values of some blood metabolites, mainly lipid in buffalo-cows. Low levels of thyroid hormones were associated with a high level of thyroid stimulating hormone (TSH) and suppressed the synthesis, release, ratio and feedback mechanism of both FSH and LH and lead to cessation of ovarian activity [20].

1.8- Oestrogenic/ poisonous plants and feed toxins: Farm animals continuously fed on Berseem clover (*Trifolium alexandrinum*) or soybean showed reduced ovulation rate owing to high content of phytoestrogen and limitation of LH release. Also, reduction of conception rate frequently occurred in cattle grazing in pastures containing oestrogenic plants through maintaining continuous uterine contractility. Feeding on forages containing plants known to be toxic such as Ponderosa pine and Broom Snakeweeds inhibited ovulation with irregular oestrous cycle or total anoestrus in non-pregnant animals. Abortion, retained placenta and prolonged PPA period were recorded in pregnant animals [21]. Nitrate containing plants inhibited ovarian activity via depression of thyroid activity. Acacia contain phenol amines that have reported impact on hypothalamo-pituitary-adrenal axis causing release of cortisol and impaired FSH and LH levels [21]. Chronic Locoweed poisoning caused enlarged ovaries with extensive follicular like-development in prepubertal heifers and it affected normal plasma progesterone and gonadotropin levels [22]. It also, lengthened the oestrous cycle in non-pregnant cattle and induced abortion in pregnant animals [23]. Gossypol found in whole cottonseed and cottonseed meal had a cumulative toxic effect and it reduced the number of follicles in heifers [22]. Heifers fed on concentrate contaminated with fusarium toxins showed ovarian mal-function manifested as low luteal progesterone level [24]. Mohamed [25] reported that aflatoxins contaminated rations adversely affecting ovarian activity and reproduction in farm animals via indirect means such as reduced feed intake, reduced growth or by damaging other vital organs of the body such as kidneys and liver and reduced vitamin A. concentration in the body.

2. Adverse Climatic Conditions:

2.1- Ambient temperature: High ambient temperature or summer heat stress (HS) is a major contributing factor in low fertility among farm animals. It is a world wide problem, which inflicts heavy economic losses and affects about 60% of the world cattle population. Although modern cooling systems are used, especially in dairy farms, fertility remains low [26]. Temperature above the thermocomfort zone of cattle (21-27°C) adversely affected the duration and intensity of oestrus. Heat stressed Holstein heifers (33°C and 60% relative humidity, RH) showed smaller follicles size with low oestradiol level and delayed luteolysis compared to control (21°C and 60% RH) heifers. Moreover, ovarian activity was reduced in cows bred at temperature-humidity index above 72 [27]. The interval between calving and first ovulation was significantly longer for cows calved in summer than those calved in winter. High incidence of embryos mortality and prolonged inter calving interval and huge economic losses were recorded due to HS. In buffaloes, HS during summer had been implicated as a cause of ovarian inactivity[28]. In the same time, very low ambient temperature or extremely cold weather also, depressed oestrous signs and ovarian activity in cows with subsequent reduced fertility due to high adrenaline secretion, loss of energy balance and decreased pulsatile secretion of GnRH [2]. El-Agawany and Hussein [29] reported 25% reduction in oestrous detection rate in Holstein cows due to long daily solar radiation, high ambient temperature and low RH during this period. Summer HS induced ovarian inactivity in buffaloes with significant decreases in glucose, total protein and potassium and increases in urea and sodium concentrations [30]. Also, buffalo cows calved in the hot season had lower reproductive performance than those calved in the cool season. The intervals to the ovulatory oestrus were longer with higher incidence of silent oestrus in the first group as compared to the second group. Moreover, calving intervals were longer for the first group than the second one [31]. Abd El-Rouf [32] observed that during summer, the ovarian activity is depressed in she camels and is manifested by incomplete follicular waves and cessation of oestrus. Heat stress affects ovarian activity via depressed appetite, thyroid activity and BCS, hypoglycaemia as well as increased blood levels of unsaturated fatty acids and keton bodies [33]. Minerals imbalance also occurs due to a reduction in feed intake and increased water loss and reduced pituitary hormone secretion[27]. The dominance of the large follicle is suppressed during HS with decreased steroidogenic capacity, LH and inhibin and production of poor quality oocytes [26]. Moreover, HS directly suppresses GnRH induced LH release [34], especially in cows with low oetradiol level. Increased prolactin secretion has been suggested as a cause of summer ovarian inactivity in both buffalo-cows [28] and she camels[35].

2.2-Photoperiod: Exposure of cows and mares to short photoperiod (PP) or buffaloes and she camels to long PP adversely affecting ovarian activity, especially in seasonal breeders. In cows, exposure to short PP during the second 6 months of life prolonged the age at puberty regardless of season of birth. It was found that long PP was the major seasonal cue that influence puberty in cattle [36]. Days open and calving intervals were both 4 days longer, number of services per conception was 0.07 greater and days at first service was 4.8 greater in herd used no illumination at night compared to herd exposed to dim illumination especially during winter [37]. In mares, Nagy *et al.* [38] observed the occurrence of defined anoestrous periods characterized by ovulatory failure, low plasma progesterone, basal LH levels and gonadal atrophy during the months with shorter PP length (November-March). Photoperiod length is the primary factor that controlling the breeding season in seasonal breeder animals. In buffaloes [39] and she camels [35], an increased PP length was associated with reduced ovarian activity. The proportion of buffaloes exhibited oestrus during the period of long PP was significantly smaller than during the period of short PP (26-vs.74%). While, in she camels, this effect was override by rains fall, nutrition and management and breeding could be occurred throughout the year. Buffalo-cows reveal anoestrus during months of the year with long PP. Injection of melatonin [40] or artificial reduction of PP to 8 hours [41] stimulated the ovarian activity as shown by the occurrence of oestrus, progesterone level, conception and calving rate. Short PP decreases the level of IGF-1, decreases body condition and consequently delays puberty in heifers and PPA in lactating cows [36]. Also, it modulates LH secretion with gonadal atrophy and basal LH level in mares [38]. In short day breeder animals, short PP serves to entrain the endogenous rhythm to produce breeding activity via increased pulsatile secretion of GnRH. The condition is mediated by secretion of melatonin from the pineal gland to transduce photoperiodic message to chemical message. Melatonin is synthesized and released only during the hours of darkness and its production can be inhibited by artificial long PP [1].

3. Adverse Housing Conditions

3.1-Housing system: Any housing arrangement that not allows farm animals to interact safely and freely throughout the day, it would provide less opportunity for appearance of oestrous activity. Cows housed in individual stalls revealed longer PPA period than those housed in-groups. The cervical mucus of cows in oestrus was found to contain pheromone that can reduce the PPA of other cows. The expression of oestrous activity was somewhat low for cows on grooved concrete footing surface or slippery floor. Mounting activity was 3-15 time lower on concrete than on dirt ground surfaces. Cows housed in a tie barn had prolonged PPA period as compared with cows housed in loose byre system. Moreover, the number of inseminations/ conception, service period, calving interval and percentage of cows becoming pregnant by day 120 postpartum were more favorable in loose housed cows compared to tethered cows. It was found that, poor stall and barn design and maintenance commonly contribute to animal discomfort. Uncomfortable cows spend less time eating with reduced feed intake and body condition [42].

3.2-Overcrowding: Prolonged PPA periods had been reported in Friesian cows due to overcrowding, especially at the muddy coinyard. Overcrowded animals find inadequate feed bunk on the manager and have limited willingness for feeding with absence of exercise and decreased body condition and vitality. Also, overcrowding predisposes the interdigital skin to trauma and raises the chance of penetration into the tissues by pathogen abundance in faeces and mud [43].

3.3-Males-females biocontact: It was found that absence of bulls delay the onset of puberty in heifers and also the resumption of ovarian activity in cows following calving. Buffalo-heifers housed away from bulls show signs of puberty with a plasma progesterone level >1.5 ng/ml after a significant older age compared to herdmates exposed to bulls (608 and 549 days, respectively). Also, absence of the vasectomized bulls decreased the incidence of consecutive functional oestrous cycle following both spontaneous and induced oestrus in Italian buffalo-cows. In the same time, the proportion of postpartum suckled zebu cows resumed ovarian activity for bull non- exposed cows was lower than exposed cows by 60-80 days postpartum. In she camels, absence of males during the breeding season led to regression of dominant follicles as male camels play a crucial active role in induction of ovulation with the vital LH surge triggered by copulatory stimulus. Absence of male pheromone inhibits the pulsatile secretion of GnRH from the hypothalamus and consequently of LH release and ovarian inactivity[44].

4. Environmental Pollution

4.1-Pesticides: The greatly increased agricultural uses of pesticides beside their vital role in public health have introduced serious and novel hazards to human and their livestock. Some of these chemicals are stable after application, persist for long years as toxic compounds and become hazardous environmental pollutants [45]. Studies have shown that prolonged exposure to chlorinated hydrocarbons and organic phosphorus compounds (OPC) caused chronic or persistent neurological syndrome, immunosuppressive effects, tumors, abortions and reproductive failure in female farm animals [46]. Impaired ovarian activity and infertility in farm animals were reported following exposure to organochlorines (OC) including chlorophenothan, dichlorophenoxy acetates, hexachlorobenzene, lindane and toxaphene [47]. Tiemann [48] added that dichloro-diphenyl trichloroethan (DDT) pesticides inhibited *in vitro* ovarian cells proliferation and steroidogenesis in cows. In the developing countries, the risk of the pesticides is prominent because of the huge amount used, the lack of proper protective measures during handling and application as well as the loose control on the residues of these chemicals in soil, water and food. Residues of mancopper, diathine M-45 and zinc phosphid pesticides were traced in drainage water, animal fodder and soil of an Egyptian village Also, DDT, dieldrin, eldrin pesticides and their metabolites were detected in drinking water in rural areas, underground water and in Nile water sources and thus such pesticides may find the way to farm animals and induce their adverse effects. In experimental buffaloes, pyrethrins insecticide significantly decreased immunoglobulins level during the oestrogenic phase of the after exposure oestrous cycle. On the other hand, in a survey study at Kafr Shoker village (famous for the huge application of insecticides), the incidence of ovarian inactivity and abortions were high in cows and buffaloes exposed to agricultural pesticides. Residue analysis using thin layer chromatography (TLC) and gas chromatography (GC) confirmed the presence of malathion (TLC) in all exposed animals especially in those suffering from inactive ovaries and abortion, while, dimethoat (GC) was traced in few samples [49].The mechanism whereby pesticides affect ovarian function, is thought to be through a direct cytotoxic action on oocyte meiotic progression and early embryonic development. Also, decreased gonadal progesterone concentration in exposed farm animals after inhibiting of DNA synthesis, cell proliferation and steroidogenesis was reported. In the same time, an indirect action through the pituitary gland with reduced synthesis and release of gonadotropins may be involved as a result of depressed cholinesterase activity[49]. OC acts as weak oestrogens and interferes with oestrogen receptors binding. Some of pesticides are combined with high concentration of heavy metals such as, zinc, copper, lead and cadmium in case of mancopper, diathine M-45 and zinc phosphid pesticides and so its adverse effect become doubled.

4.2-Heavy metals: In the developing countries, whereas agriculture and industry exist side by side, conditions are at their most favourable situation for contamination of air, water and herbage by industrial effluents. Heavy metals are among the most dangerous pollutants that have a tendency to accumulate in different organs and tissues of exposed animals, affect the reproductive function and represent a great hazard on species survival. Lead is considered as one of the most important environmental pollutants and it induces toxic effects even at low levels on nervous, reproductive and endocrine systems [50]. Prepubertal exposure to lead suppressed growth, decreased plasma IGF-1, decreased ovarian folliculogenesis, oestradiol synthesis and delayed puberty in farm animals [51]. Also, lead toxicity induced atrophy of the ovary, reduction of serum progesterone concentration and alteration of uterine hormonal receptors. McEvoy and McEcoy [52] noticed ill thrift and impaired fertility for several months in Northern Ireland cattle after feeding from silo accidentally contaminated with lead ashes from burning old electrical cable. Moreover, lead accumulated from industrial emission in sheep wool and it adversely affected life span and productivity. Cadmium toxicity induced necrosis of preovulatory follicles and damaged the microcirculation in the uterus of exposed animals [53]. Cattle that were grazing on land high in molybdenum showed toxicity with delayed puberty, ovarian dysfunction and anoestrus [11]. Chronic copper and zinc intoxication in sheep from industrial emission caused the accumulation of arsenic, cadmium and lead in their ovaries and uterus with disturbed ovarian activity and increased number of atretic follicles.Inorganic mercury had been reported to block follicular growth and resulted in anoestrus by altering both pituitary gonadotropin and ovarian steroid secretion. In Egypt, Buffalo farms nearby high ways whereas, soil contained moderate to high concentrations of lead and cadmium, revealed reduced incidences of oestrous detection and poor conception rates. Moreover, blood lead and cadmium concentrations were higher in buffalo-cows conceived after 110 days from calving compared to animals conceived after earlier time. Lead and cadmium have a direct gonadotoxic effect as well as an indirect effect (lead) on the hypothalamus and pituitary gland and affect steroidogenesis and disrupt reproductive criteria. In the same time, both metals compete with essential metals mainly zinc and calcium for their binding sites and also, they interfere with sulfhydryl groups, which are essential for normal function of most enzymes [54].

4.3-Air contaminants: Barns that are not designed to allow adequate air exchange depress general health and have a secondary effect on appetite. High levels of air contaminants that are typically found in livestock houses include ammonia, dust, hydrogen sulfide and carbon monoxide cause health problems and indirectly affect ovarian activity [55].

4.4-Radiation: Radiation either from ionized or non ionized source is responsible for complex syndromes that leading to acute and late deteriorations in ovarian activity of exposed farm animals depending upon type and dose of radiation as well as on the duration of exposure. Contamination of feed and forages with radionuclides and their ingestion by farm livestock caused infertility due to a cumulative effect and more progressive functional and morphological changes of ovaries as well as mutation [25].

4.5-Noise: Exposure of Holstein heifers to intermittent noise during the oestrous cycle prolonged the oestrous duration and delayed the ovulation process with absence of the preovulatory LH surge in some animals [56].

5. Adverse Physiological Conditions

5.1-Aging: Food animals are usually slaughtered before senescence, whereas other animals like mares, were reported to cycle less efficiently after 20 year of age with delayed entry into the breeding season, longer follicular phase and fewer ovulations per year[57].

5.2-Suckling: Increased suckling frequency as well as late weaning of calves delayed PPA period and prolonged CI. Moreover, suckling twice daily was sufficient to prolong PPA as much as suckling *ad libitum*. Undernutrition in suckling anoestrous cows tended to prolong the PPA period. However, the negative effect of underfeeding could not completely compensated by supplementation for the positive effect of suckling. In she camels, it was reported that, the first postpartum heat delays from 1-10 months after calving depending upon the intensity of suckling and nutrition status. In mares, true anoestrus with lower than normal LH level was observed during suckling. Suckling delays the release of GnRH from the hypothalamus after calving by stimulating the release of β endorphin and delays the occurrence of postpartum uterine involution as well as the re-commencement of oestrous activity especially in beef cattle[5,58].

5.3-High milk production: High milk production was associated with lower reproductive efficiency in term of depressed ovarian activity and conception rate (52 and 38% for dairy cows producing 6300-6800 and > 10400 kg /year, respectively) with long period of PPA. Also, the increased milk production was significantly correlated with a longer service period and greater number of inseminations/conception in dairy cows [59]. Moreover, milk yield and milk protein at the onset of lactation were negatively correlated with the duration of the service period and the open periods. High milk yield in Holstein cows increased the risk of COD, mastitis and anoestrus. In buffalo-cows, increased milk production was associated with a state of ovarian inactivity and decreased thyroid hormones levels [20]. The effect of high milk production on ovarian activity is as a component of NEB rather than direct effect). Increased utilization of body energy reserves for milk production modulates the patterns of LH secretion, growth hormone (GH), IGF-1 system which have a role in promoting follicular function and serving as a metabolic modulator of ovarian activity during NEB [59].

5.4-Working: Draught stress depressed ovarian activity in cows with decreased hematocrit and hemoglobin content. Underfeeding of animals during the period of draught power provision adversely affecting the condition. Also, It was found that nutritional stress is more important in suppressing ovarian activity than work stress. Moreover, incidence of ovulations without oestrus, short luteal phase and PPA were higher in working compared to non-working cows. Also, in mares, frequent and hard work was found to delay ovulation, especially at the start of the breeding season. However, persistent oestrus in working and racing mares were observed and it is a fairly common complaint due to thin body conformation, low fat and pneumovagina. In Egypt, large farm animals are used more frequently for agricultural work purposes due to the non-availability of mechanization as well as the nature of land fragmentation. Muscular exertion in working animals induced alterations in different blood constituents, disturbed endocrine machinery and suppressed reproductive activity. Working animals were mostly suffered from irregular oestrous cycle, weak oestrous signs, anoestrus and high incidence of brucella infection compared to non-working animals [60].

5.5-Incomplete adaptation to the prevailing environment: Each group of farm animals is adapted to produce well under the conditions prevailing in certain area. So it is not easily and practically to transfer animals from Lower to Upper Egypt suddenly for example and one expects that these animals will satisfactory produce. Incomplete adaptation to the prevailing socioeconomic environment may adversely affect ovarian activity in farm animals. High producing foreign breeds could not be easily adapted to the harsh climatic and poor nutritional status of the desert condition. Also, their low disease resistance especially for blood parasites and their vectors aggravated the condition. These harsh conditions prolonged the prepubertal [2] and PPA [61] periods with expression of weak oestrous signs.

5.6-Postvaccinal reaction: It was found that vaccinations of livestock against the endemic diseases induce postvaccinal reaction in the form of high body temperature, accelerated pulse rate, decreased appetite and temporary cessation of expression of oestrus or weak oestrous signs [1, 11]. Vaccination against thelariasis induced aberrant oestrous cycle in 25% of immunized Friesian heifers due to persistent CL following impaired synthesis of uterine prostaglandine F2α. In Egypt, vaccination of cows against foot and mouth disease (FMD) induced a significant elevation (up to 1.6°C) in rectal temperature with marked increases in plasma progesterone and cortisol levels for a transient period ranging from 36-42 hours following vaccination. Cows exhibited elevated temperature during the first month of gestation returned to oestrus 5-6 days after FMD vaccination and the condition was attributed to thermal stress [62].

6. Adverse Health Conditions

6.1-Problems of parturition and puerperium: Investigations revealed that abnormal calving, dystocia or retained fetal membranes cause marked delay in uterine involution process and ovarian cyclicity, especially in the presence of vaginal discharges, ketosis and NEB [63]. Cows with dystocia, twine birth, metritis, displaced abomasum and COD had more instances of reproductive failure due to disturbed ovarian function at the end of lactation than herdmates without these diseases. Cows with post partum COD revealed cyclic irregularity characterized by either anoestrus or nymphomania [64] with 19 more days to conception after treatment with progesterone releasing intravaginal device [65]. Also, buffalo-cows suffered from obstetrical problems such as vaginal prolapse, placental retention, cervicovaginal lesions and dystocia mainly due to brucellosis showed endometritis, uterine adhesions, repeat breeding and anoestrus. In camels, [66] attributed the poor reproductive performance to the retardation of the cyclic changes in the genital organs during the postpartum period and consequently long calving intervals (24.4± 0.68 months). Ovaries of she camels suffering from postpartum endometritis revealed COD in 30% of the examined cases [67]. In mares, an abnormal puerperal period, particularly with placental retention, was accompanied by a granulocytic reaction in the endometrium, which upset the regeneration of uterine epithelium. This reaction delayed the post foaling oestrus and reduced the chance of conception [68]. Also, luteal persistence due to inadequate secretion of prostaglandin F2α following insufficient uterine involution or infection participated in lactational anoestrus in mares [69]. In Egypt, both dystocia and retained placenta in Friesian cows were associated with cessation of ovarian activity, prolonged calving -conception interval, significant decreases in the serum levels of estradiol-17β, cortisol, βcarotene and selenium and an increased progesterone level [70]. Ahmed [71] isolated *Mycoplasma bovigenitalium* and *Mycoplasma bovis* from buffalo-cows with puerperial disturbance, inactive ovaries and repeat breeding. In the same time, high incidences of isolation of different types of microorganism were recorded in she camels during the postpartum period [72]. In most of cases, the isolation of microorganisms was associated with pathological alterations in the genital organs. The condition was attributed to allergic reaction caused by bacterial toxins and predisposed for prolonged postpartum acyclic period [73]. In goats, prolonged postpartum ovarian activity (as indicated by milk and faecal progesterone analysis) in animals suffered from retained placenta, vaginal prolapse or abortion was obvious as compared with normal kidding group [74]. Problems of calving and puerperium have deleterious effect on the endometrium. Postpartum infection is the most common cause of infertility in cows as it delays uterine involution and prolongs the interval to the first oestrus [75]. Failure of synthesis and release of prostaglandin F2α, disturbed uterine defense mechanism, delayed uterine involution and cessation of ovarian activity usually occur after problems of calving and puerperium. Moreover, disturbance of self-clearance mechanism of the uterus is associated with accumulation of pus in the presence of functional ovarian luteal tissue and anoestrus [39].

6.2-Infection: Studies indicated that the most common etiological agents encounter in abortions, stillbirth and delayed re-commencement of normal ovarian activity after abortion in farm animals are brucella, *Actinomyces pyogenes*, listeria, pasteurella, salmonella, *Haemophilus somnus* and chlamydia in bovine [76], *Strept. equi*, *E. coli*, salmonella and *Staph. aureus* in mares and brucella, listeria, leptospira, mycoplasma, fungus and campylobacter in small ruminants [77]. Postpubertal heifers persistently infected with bovine diarrhea virus (BVD) showed ovarian dysfunction with significant decrease in the number of Graafian follicles, atretic follicles and CL [78]. Bovine pestivirus infection had been associated with significant early reproductive loss including fertilization failure, embryonic mortality and abortion [79]. Infectious bovine rhinotracheitis (IBR) or bovine herpes virus (BHV) induced necrotizing endometritis, oophoritis, local inflammation of CL, decreased progesterone level and abortion in cattle [80]. Infection with blue tongue or rift valley viruses induced viremia, abortion and delayed re-commencement of ovarian activity in cattle [2].

6.3-Parasitic infestation: Field studies indicated that chronic fascioliasis in cows is associated with reduced fertility mainly due to changes in blood metabolites, delayed growth rate and puberty in growing animals and prolonged anoestrous period in mature animals following loss of body condition [81]. Trypanosomoasis in she camels [82] and cows [83] were associated with reduced fertility. In the developing countries, parasitic infestation represents an important cause of direct as well as indirect economic losses in farm animals. Examination of local livestock revealed that cows and buffaloes were positive for fasciola species and suffering from smooth inactive ovaries (21.7 and 69.8%, respectively) and repeat breeding (56.7 and 30.2%, respectively) with loss of body condition [84]. On the other hand, severe infestation with GIT nematodes was associated with low incidences of conception rate and ovarian activity in cows and buffaloes [85]. [84] added that, of the examined animals infested with GIT nematodes, 100% of buffaloes-cows revealing smooth inactive ovaries and 9.10, 62.12 and 28.80 % of cows suffering from smooth ovaries, repeat breeding and endometritis, respectively. Also, 34 and 50% of ewes and does revealed irregular oestrous cycles, respectively. Antibodies against toxoplasmosis were detected in sera of 5.42% of buffalo-cows suffering from chronic endometritis with titer range of 1: 1024-1: 4096. The affection was associated with COD and the condition was attributed to pituitary involvement [86]. Concerning ectoparasites, 14.36% of local Egyptian cattle were positive for ectoparasites, out of these, 12.06% were infested with ticks, 0.93% with lice and 1.39% with mites, the corresponding figures for buffaloes were 70.66, 4.08, 48.21 and 18.3% [87]. Ovarian inactivity may be indirectly occurred following infestation due to, annoyance, stress, anemia and loss of body condition. Parasitic infestation could be considered as a stress factor that depresses body condition, induces anemia, hypoproteinaemia, deficiency of inorganic phosphorus and trace element, transmits diseases and inhibits ovarian function [84].

6.4-Locomotor disorders: Cows with locomotor disorders revealed delayed average interval to conception for 12 days compared with healthy herdmates. On the other hand, the calving to first service intervals (days), calving to conception intervals (days) and number of services per conception were significantly increased from 78.00, 109.60 and 1.73 in normal cows to 102.50, 150.60 and 2.57 in lame cows, respectively [65].

7. Miscellaneous Adverse Conditions

7.1- Skill and capabilities of manager/owner: Insufficient skill and capabilities of the animal manager/owner may adversely affect ovarian activity of his livestock. Application of improper nutritional plane that maintaining reproductive efficiency in various species during the different stages of the reproductive cycle actually will hander ovarian activity. Also, lack of continuous evaluation of animals body condition and selection of suitable animals before breeding may increase troubles at parturition and consequently delayed PPA period. Insufficient oestrous detection, non hygienic interference during parturition and lack of application of programs related to combating of diseases and eradication of parasites, cooperation with supporting services and protection of livestock from drastic climatic conditions are faulty managemental practice depend upon manager skill and adversely affecting fertility and ovarian activity [88].

7.2-Recent technology: Improper application of recent technology such as artificial insemination and embryo transfer in 411 cows induced infertility in 99 of the cases, through ovarian quiescence, COD, catarrhal inflammation of the genital tract, repeat breeding and symptomless infertility in 15, 38, 12, 19 and 16% of the cases, respectively. However, these adverse conditions were not traced in the current literature. In mares, cervical manipulation during non-surgical embryo collection or transfer led to a decrease in cycle length due to increased oxytocin or prostaglandin F2α release and luteolysis. However, this condition was not recorded in surgical method [89].

7.3-Robot milking: Robot milking increased milk production and negatively affected reproduction due to NEB [90].

7.4-Transportation: Transportation of anoestrous postpartum cows had greater adverse effect on ovarian activity as it disrupted LH surge and prolonged the PPA period. Also, transport produced immediate constant increases in adrenocorticotropin hormone (ACTH) secretion and adversely affecting ovarian activity in ewes. It was found that ACTH interferes with the precise timings of reproductive hormones release as well as it reduces the frequency and amplitude of GnRH and LH pulses and deprives the ovary of adequate gonadotropin support leading to its inactivity [91].

7.5-Temperament: Ovarian activity is somewhat depressed in nervous cows due to high adrenaline and low pulsatile secretion of GnRH. In mares, low conception and foaling rates and high incidence of stillbirth were positively correlated with excitability [2].

CONCLUSIONS

Disturbance of ovarian activity is the most prominent cause of reproductive failure and economic losses in farm animals. Currently a lot of factors negatively affect ovarian activity in farm animals, especially in the developing countries, whereas undernutrition, harsh climatic, housing and managemental conditions, diseases as well as pollution are found side by side.

RECOMMENDATIONS

- In order to keep ovarian activity at the maximum possible level to obtain the peak fertility and benefits from farm animals breeding, the following points should be considered:

- Provision of adequate, balanced nutrition and dietary supplementation with fat and minerals mixture especially during the critical periods in the animal life, i.e. prepubertal and postpartum periods should be applied to ameliorate the limitation of intakes and to improve the conception rate.
- Feed ingredients should be obtained and preserved in a stable condition so as to prevent hazardous effects due to contamination or deterioration.
- Protection of livestock from drastic climatic factors especially during summer and in the arid new reclaimed areas should be carried out.
- Application of short photoperiod in housed sheep and buffaloes farms especially before the beginning of the breeding season to overcome sexual inactivity.
- Application of proper stocking density and using intact or vasectomized males for teasing to provide sufficient male stimuli and hasten ovarian activity especially in prepubertal and postpartum animals.
- Construction of farms away from source of severely polluted areas should minimize the risk of exposure to pollutants.
- Animals used for work purposes, suckled and high milk producers should be dietary supplemented to reduce the negative energy balance on ovarian activity.
- Selection of the suitable livestock for breeding in a given area with special emphasis on nutritional requirements, adaptation to climatic factors and resistance to the endemic diseases especially, parasitic diseases.
- Prevention of systemic and reproductive diseases and local medication of lame and mastatic animals to prevent invasion of the causative agent to genital organs.
- The regular postpartum gynecological care would result in significant reduction in the parturition-conception interval, the insemination rate and in percentage of animals culled due to fertility problems.
- Animal managers should pay interest and supervise oestrous detection, early pregnancy diagnosis and culling, adequate record keeping and combating of parasitic diseases and cooperation with support services and continuous training of animal keepers.
- Proper application of artificial insemination and embryo transfer by the specialized personnel.

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