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Review Article

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Hemato-biochemical dynamics: an essential provenance for the reproduction in dairy cows

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Abstract

The present review concentrates on the notion that different blood and blood sera indices play an imperative role in countless biological processes that are significant for reproductive physiology in animals. Specifically, the manuscript describes the necessity of hematological and serum biochemical dynamics in the reproduction of dairy cows. The paper also noticed that reproductive features of dairy cows are disrupted by any digression from the physiologic level of hematological indices including erythrocytes, hemoglobin, platelets and leukocytes and serum biochemicals including glucose, protein, lipid profiles and other essential minerals. Thus, researchers could ensure the accurate interpretation of the consequence of haemato-biochemical dynamics in the reproduction of dairy cows.

Keywords: Biochemicals, Hematology, Reproductive physiology

INTRODUCTION

The essential haemato-biochemical elements with physiological levels are most important to maintain the functional stability of the reproductive tract and any deviation of these elements may harmfully affect the reproductive competence of domestic animals (Sabasthin *et al.*, 2012). Blood is one of the important constituents in the body, which maintains the physiological equilibrium and any disturbance in this equilibrium maintenance will lead to disease or pathological condition which in turn can be known from the changed hematological parameters and these alters in blood parameters are significant pointers of the physiological or pathological condition of the animal (Perumal *et al.*, 2013b). The study of various hematological parameters during various states of reproductive stages is helpful for the detection of various abnormalities in these parameters and able to correlate with problems associated with reproductive dysfunction (Perumal *et al.*, 2013a,c). The facts of blood parameters are very important in diagnosing a variety of pathological and metabolic turmoil that may negatively affect the productive and reproductive appearance of dairy cattle consequent the huge financial losses in dairy industries (Perumal *et al.*, 2013a,c).

Physiological concentrations of blood sera biochemical constituents constantly sustain to confirm the appropriate cellular activities of the animal and, unquestionably, the minerals play an important task in herd fertility (Ceylan *et al.*, 2008). Normal range of biochemical parameters of some sera components collected from cattle is shown in Table 1. At the time of estrus, the blood sera biochemical elements are linked with the fertility condition of cows and the behavior of their reproduction (Amle *et al.*, 2014). Typical concentrations of different blood biochemical parameters are necessary for the regular activity of different systems of the body includ-

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ing reproductive system and deviation from the normal level of these elements is associated with the lack of reproduction and finally reproductive breakdown (Amle *et al.*, 2014; Barui *et al.*, 2015; Noakes *et al.*, 2001). The problematic and diagnosing deficiency conditions of different minerals are describing by the blood picture (Akhtar *et al.*, 2014).

Minerals occupy a basic role in the endorsement of the function of hormones and enzymes at subnormal stage in an incorporated manner, thus control the reproductive activity (Amle *et al.*, 2014). The mineral insufficiency and inequity influenced the ovarian dynamics and act as the causes of lower fertility (Ceylan *et al.*, 2008). Minerals might have a favorable job for the continuation of growth of follicles and pregnancy and fertility collapse might be persuaded by the insufficiency of particular or combined parameters and by the disproportions of the parameters (Ceylan *et al.*, 2008). The nutritional requirements of trace elements are also small but these elements are necessary for the production of numerous proteins and launching of an enormous number of enzymatic reactions, which can significantly influence the reproduction (Hostetler *et al.*, 2003). Reduction of minerals and unbalanced enzymatic reactions due to the insufficiency of nutrition in animals may affect the regular behavior of reproduction (Amle *et al.*, 2014). The crucial trace elements are the constituents of trace metalloenzymes, which are imperative for the construction of bone, metabolism of lipid, utilization of glucose, transportation of iron, synthesis and transportation of DNA (deoxyribonucleic acid) and metabolism of free radical molecules (Jovanovic-Peterson and Peterson, 1996; Hostetler *et al.*, 2003). Through these mechanisms, the trace elements may directly influence the development of the embryo and fetus (Ceylan *et al.*, 2008). Variation in the normal volume of trace elements is associated with many reproductive disorders and the overload or lack of minerals may result in the repeat breeding (RB) in cows (Das *et al.*, 2002). The association between alterations in hormonal and mineral profiles of blood sera results in the deviation in ovarian activities which might be the reason for RB in crossbred cows (Barui *et al.*, 2015). Moreover, the blood sera chemical profiles may designate the condition of nutrition of the trace or essential minerals, which may assist in analysis and supervision of infertility (Amle *et al.*, 2014).

Thus, intend of the present review was to summarize the statements of eminence scholars and scientists on account of the inevitability of haemato-biochemical elements in the reproduction of female animals.

DYNAMICS OF HEMATOLOGICAL ELEMENTS FOR REPRODUCTION IN DAIRY COWS

High concentration of hemoglobin (Hb), packed cell volume (PCV) and total erythrocyte count (TEC) are desirable physiological characters for efficient transport of oxygen (O_2) and carbon dioxide (CO_2) (Ganong, 2001). This is an essential requirement for maintaining the health of animals and thus, cows with a higher concentration of Hb, PCV and TEC were more economical as a result of enhanced reproductive competence (Perumal *et al.*, 2013b). Sabasthin *et al.* (2012) noted that cellular oxygenation of the reproductive system and to the regular estrous cycle is dependent on the concentration of Hb in the circulatory blood. An adequate amount of blood Hb is necessary for the appropriate transportation of O_2 and nutrients to the essential organs at the time of estrus and it was also requisite for metabolic activities of the cells of gonads (Sabasthin *et al.*, 2012). When erythrocytes suffer shear stress in contracted vessels, the erythrocytes discharge adenosine triphosphate (ATP) that can relax and dilate the wall of vessels so that help in usual blood flow in the body (Wan *et al.*, 2008). During the deoxygenating of Hb molecules, erythrocytes discharge S-nitrosothiols, which dilate the blood vessels results in enough blood directing to the areas of the body exhausted of O_2 (Diesen *et al.*, 2008; Perumal *et al.*, 2013b). Specially, erythrocytes are accountable for convey of O_2 to the tissues that lead to more consumption of O_2 to the reproductive tract, which is helpful for better utilization of energy and contraction of smooth muscle that leads to successful fertilization and ultimate good conception rate and that leads to higher fertility rate (Perumal *et al.*, 2013b). Enzymatically, the erythrocytes with normal concentration also secrets the nitric oxide by the use of arginine as substrate (nitric oxide synthetase), which is identical to endothelial cells that may help in the control of tonicity of vessels (Kleinbongard *et al.*, 2006; Ulker *et al.*, 2009). The dilatation of blood vessels of the uterus and other parts of the reproductive tract reasons an augment in the tonicity of horn of the uterus, which favors the movement of gametes towards the site of fertilization and successful conception (Perumal *et al.*, 2013b).

Lower erythrocytic indices in the cycling non-breeding crossbred cows have got to interfere in the normal conception and reproduction and might be contributing to the cause of repeat breeding syndrome (RBS) (Perumal *et al.*, 2013b). The lower level of Hb is

significantly in anestrus cows in comparison to healthy cyclic cows and reducing the Hb concentration might be a reason for repeat breeding (Sabasthin *et al.*, 2012) (Ramakrishna, 1996; ..). It has been noted that there is a significant increase in erythrocytes and leukocytes at the time of estrus in cows (Soliman and Zaki, 1963), but a lower level of Hb is reported in anemia and anestrus than in cycling cows (Mondal and Paul, 2012) (Pariza et al., 2009; ..). The PCV is another indicator of anemia and the PCV is appreciably lower in unhealthy cows likely in anestrus and RB cows (Mondal and Paul, 2012; Kumar and Sharma, 1991) (Islam et al., 1999; ..; ..; Pariza et al., 2009). Moreover, Perumal *et al.* (2013b) noted that TEC, Hb and PCV are lower in RB animals. Normally, the ESR is elevated in animals with chronic infections and malnutrition (Islam et al., 1999).

The platelets are responsible for the production of thrombocytopenia, which is responsible for the production of more prostaglandins ($PGF_{2\alpha}$ and PGE_2) and this prostaglandin helps for ovulation and subsequent contraction of the reproductive tract and fertilization (Woulfe *et al.*, 2008). The platelet number and mean platelet volume width (MPVW) determine the production of prostaglandins, histamine, serotonin and bradykinin, all of these inflammatory factors are responsible for the final stage of ovum maturation and subsequent ovum release and corpus luteum (CL) formation to produce more progesterone (P_4), which will ultimately helpful for successful fertilization and pregnancy (Perumal *et al.*, 2013b). Platelet aggregation via adhesion to vWF-Col VI (von Willebrand factor-interstitial collagen types VI) complexes leads to stimulate the triggering factor that stimulates the thrombotic cascade under high shear stress and in estrus condition that stimulates the release of arachidonic acid and prostaglandins secretion, and the platelet dense and alpha granules are responsible for the metabolism of arachidonic acid, which is essential for collagen-induced discharge of lysosomal enzymes that ultimately are useful for ovulation and fertilization (MacIntyre, 1979). Thus, deficiency of platelets in the blood of dairy cows may impede ovulation and fertilization with or without manifest the estrus signs. Resulting, a lower level of total platelets is responsible for RB in animals (Perumal *et al.*, 2013b).

Simultaneously, the total leukocyte count (TLC) is higher in RB animals (Kumar and Sharma, 1991). Pariza et al. (2009) reported that TLC was higher in anestrus and RB cows, possibly due to bacterial infections. Chronic infection of microorganisms results in endometritis, which is responsible for RB and anestrus (Jahan and Myenuddin, 1996). Microbial infection may influence the leukocytosis, depending on the character of the infectious pathogen, brutality of infection, confrontation of the individual and localization of inflammatory response (Benjamin, 1978). Sabasthin *et al.* (2012) reported that the monocyte concentration is increased in RB buffaloes for the improved phagocytic functions and enhanced demonstration of macrophage activity.

DYNAMICS OF SERUM BIOCHEMICAL ELEMENTS FOR REPRODUCTION IN DAIRY COWS

Glucose: Blood sera glucose influenced the reproduction and simultaneously its lower level reduced the fertility rate as well as the causes of non-cyclicity (Yadav *et al.*, 1995). Serum glucose straightly augmented the production of P_4 by enhancing the rhythm and average volume of luteinizing hormone (LH) or indirectly influences the extended P_4 discharge at the time of early luteal period by rising the concentration of insulin hormone (Richards *et al.*, 1989). Blood glucose concentration may stimulate the pituitary activity, which influences the fertility in animals (Arthur, 1975). Lower energy levels because of hypoglycemia, which may influence the damaged hypothalamo-hypophyseal-ovarian axis and decreased the female gonadal functions and the distorted concentration of glucose may also reduce the luteal functions in RB cows (Joe Arosh *et al.*, 1998). Lower glucose level in blood in the RB cows could be accredited to enhance the peripheral glucose uptake, stoppage of gluconeogenesis or glycogenolysis and endogenous hyperinsulinemia (Mukherjee *et al.*, 2011). Moreover, insufficiency of glucose is linked with the higher frequency of RBS and anestrus (Jani *et al.*, 1995).

Protein: Total serum protein symbolizes the equilibrium between synthesis and catabolism or mechanical loss, and the poor volume of circulatory protein results in insufficiency of certain amino acids, which are essential for the synthesis of proteins (Sabasthin *et al.*, 2012). The protein and amino acids are very important for gonadotropin releasing hormone (GnRH) and LH secretion during the early luteal period of estrous cycle (Mondal and Paul, 2012) (Khan et al., 2010; ..). Decreased concentration of serum protein because of insufficiency of specific amino acids, which are necessary for the synthesis of gonadotropins and ovarian hormones results the turbulence in the synchrony of repro-

ductive hormones in female animals leading to functionless ovaries and a deficiency of protein is linked with the RBS and anestrus (Joe Arosh *et al.*, 1998). Moreover, the globulin an amino acid, acts as a carrier protein for copper (Cu) and the lowered concentration of globulin alter the biosynthesis of certain coenzymes, which hamper the steroid synthesis through the early luteal period of the estrous cycle in RB dairy cows (Khan et al., 2010).

Lipids: Lipid is full of energy reserve and necessary for the maturation of ovum (Dunning *et al.*, 2014). The fat increases postpartum reproduction by improving the energy source of animals, which influences the growth of ovarian follicles and the activity of CL (Hightshoe *et al.*, 1991; Wehrman *et al.*, 1991). The quantity of steroid hormones including sex hormones secretion in the body depends on the accessibility of serum cholesterol because it acts as an ancestor for steroid hormone biosynthesis (Sabasthin *et al.*, 2012). Cholesterol insists on the synthesis of P_4, estrogen (E_2) and androstenedione from avascular granulosa cells due to the pressure of LH surge (Hightshoe *et al.*, 1991). A lower level of serum cholesterol may affect the steroid synthesis in the ovaries which is associated with subnormal E_2 in RB animals than the healthy cyclic animal (Barui *et al.*, 2015). Hence, the prevalence of RB buffaloes could be significant in a herd due to lower serum cholesterol concentration in the RB buffaloes concerning pregnancy and cyclic ones (Sabasthin *et al.*, 2012). Kumar and Sharma (1991) also noticed high frequency of RB and anestrus is linked with insufficiency of cholesterol.

Calcium (Ca): Calcium takes part in pivotal function in the biosynthesis of ovarian hormones through the regulation of gonadotropic hormones and the Ca also sensitizes the reproductive organs through various hormones (Carnegie and Tsang, 1984). Serum Ca illustrates a key role in increase the number and size of preovulatory oocytes and the frequency of ovulation and the Ca regulate the competence of oocytes membrane (El-Shahat and Abo-El maaty, 2009; Amle *et al.*, 2014). The Ca controls the ovulatory process through the influence of gap junctions between the cumulus cells, which results the disturbance of cohesiveness of these cells (Amle *et al.*, 2014). Since, Ca is essential for neuromuscular excitability, muscle contractions and transmission of the nerve impulse at the cellular level, its deficiency may result in reduced tone and contractions of the endometrium, which eventually, may stop the forward movement of sperm and ovum in the reverse direction resulting in the inhibition of formation of zygote and subsequent fertilization (Pandey *et al.*, 2009), resulting repeat breeding being prevalent in the dairy herds. Decreased blood Ca also holds up the uterine involution and enhances the frequency of dystocia, retained placenta and uterine prolapse (Morrow, 1980).

Phosphorus (P): Phosphorus is necessary for conveying the biological energy by the use of ATP and insufficiency of the P may seize the trend of fertilization leading to early embryonic death (EED) and results the RBS and anestrus in animals (Kumar *et al.*, 2010). Lack of P could be the cause of turbulence in ovulation with pituitary-ovarian axis and P insufficient heifers illustrated the reduced conception rate (Bhaskaran and Patil, 1982). Improper Ca-P ratio restrains the course of ovulation by breaking the function of pituitary gland, which affects the reproductive performance (Hurley and Doane, 1989). Inferior inorganic P level has been reported in RB animals, RB buffalo and in RB crossbred cows (Chaurasia *et al.*, 2010; Amle *et al.*, 2014; Akhtar *et al.*, 2014). Furthermore, Bindari *et al.* (2013) also noted that decreased fertility, ingestion of feeds, lactation, ovarian functions, abnormal estrous cycles, augmented frequency of cystic ovaries and delayed sexual maturity have been noticed due to lower P containing feeds.

Copper (Cu): Copper has establishing importance in animals for normal growth, production and reproduction performance (Ceylan *et al.*, 2008). Serum Cu and Zinc (Zn) either singly or in mixture contribute the maintenance of reproductive trend. Biologically the Cu is used as numerous Cu-containing proteins as well as ceruloplasmin and superoxide dismutase, and the Cu acts as a cofactor for enzymes like the amine oxidase, copper-dependent superoxide dismutase, cytochrome oxidase and tyrosinase (Ahmed *et al.*, 2017). The physiological and metabolic activities linked with Cu-enzymes could be spoiled due to Cu insufficiency in animals (Ceylan *et al.*, 2008). The Cu with GnRH has strong effects for the releasing of LH and follicle stimulating hormone (FSH) compared to single GnRH (Michaluk and Kochman, 2007). The Cu takes a serious task in female conception and additional Cu could be used for the correction of subnormal fertility in cows (Ingraham *et al.*, 1987). The delayed or concealed estrus, insufficient ovarian activity, decreased conception, augmented frequency of retained placenta, infertility and EED are the frequent Cu insufficiency symptoms in cows (Hidiroglou, 1979; Graham *et al.*, 1994). Weak

and silent heats, resorption of the embryo, necrosis of the placenta in cows have also been noted due to Cu shortage (Bindari *et al.*, 2013).

Magnesium (Mg): Magnesium insufficiency in RB buffalo has been noted (Das *et al.*, 2009). Though Mg does not play any untiring activity in fertility, yet it is concerned in many enzymatic actions catalyze by ATP associated enzymes (Akhtar *et al.*, 2014). Moreover, Mg stimulates the absorption of Ca and P (Sharma *et al.*, 2004). Mg inequity could stimulate the reproduction secondarily and the lower Ca, inorganic P and Mg levels might be associated with the ovulatory turbulence in RB animals (Akhtar *et al.*, 2014).

Zinc (Zn): The Zn is a vital trace mineral establish to be an important constituent of over 300 metalloenzymes (McCall *et al.*, 2000; Dibley, 2001). Zn metalloenzymes are concerned in almost every biological progression (Maret, 2013). Regulation of gene expression is control by Zn finger proteins, which have an imperative impact on numerous biological activity such as cell division, growth, metabolism, appetite control, immune function and hormone production and it is also concerned with gene expression of steroid hormones receptors (Ahmed *et al.*, 2017). Serum Zn has antioxidant activity as well as antiapoptotic possessions and Zn is necessary for DNA transcription and protein biosynthesis and DNA transcription is a vital fraction for the maturity of germ cells (Ebisch *et al.*, 2007). Further, Zn is necessary for perfect puberty and/or sexual maturity, reproductive performance and beginning of estrus (Bindari *et al.*, 2013). Epithelial integrity of reproductive organs required for the implantation of embryo could be maintained by Zn (Robinson *et al.*, 2006). Biologically Zn is implicated in the arrangement of prostaglandins by controlling of the arachidonic acid cascade (Wauben *et al.*, 1999). The serum Zn also takes a major task in the restoration and upholding of the uterine lining after calving, which is essential for speeding the arrival of usual reproductive activity and estrus (Ceylan *et al.*, 2008; Yasothai, 2014). Zn (and also Cu) diffuses through the uterine epithelium into the whole of the reproductive tract and this diffusion makes osmosis that causes the transport of water out of the epithelium into the whole of the uterus, which helps in the involution of the uterus (Alavi-Shoushtari *et al.*, 2012; Ahmed *et al.*, 2017). It is considered that the minor reduce serum Zn level in cows might be associated with irregular ovarian maturity, disturbances of the estrous cycle, decrease in GnRH synthesis by the hypothalamus and ultimately improper synthesis of FSH and LH, which may lead to reproductive diseases and seize of ovulation (Ceylan *et al.*, 2008). Insufficient Zn concentration in serum might be linked to reducing fertility, fetal mummification, abortion, lower birth weight and extended labor in animals (Kumar *et al.*, 2011).

Iron (Fe): The serum iron (Fe) is concerned for the formation of ferritin results the construction of Hb and myoglobin necessary for the transportation and storage of O_2, which maintain the oxidative enzyme system (Ahmed *et al.*, 2017). The Fe is necessary for the cytochromes and iron-sulfur protein that are components of the respiratory sequence and the insufficient Fe in serum have been linked with the distorted normal activity of the ovary by lessening the growth follicles and pregnancy (Ceylan *et al.*, 2008). Lesser Fe causes anemia and alters the molarity of oviductal fluid results the collapse of fertilization and embryonic death (Kumar *et al.*, 2011; Modi *et al.*, 2013). The Fe deficiency affects the reproduction negatively in the appearance of RBS, results in the amplified the number of inseminations per pregnancy and infrequently results the abortion (Kumar *et al.*, 2011).

Manganese (Mn): Manganese is involved in all metabolic processes in the animal body (Hansen *et al.*, 2006). Serum Mn plays a critical job in the role of specific endocrine glands and reproduction (Bindari *et al.*, 2013). Hansen *et al.* (2006) reported that Mn may act as a cofactor for mevalonate kinase and farnesyl pyrophosphate synthase enzymes that are necessary for the production of squalene, an ancestor of cholesterol. Cholesterol in turn is concerned in the biosynthesis of steroid hormones specially E_2 and P_4 (Bindari *et al.*, 2013). Inactive ovaries, anestrus and poor conception rates are the most common expressions consequent upon the deficiency of Mn (Chesworth, 1992). Deficiency of Mn in serum has also been reported that the causes of defective ovulation and subfertility and thus, reduce the first service conception rates and fertility in ruminants (Lehmkuhler, 2010).

Selenium (Se): Selenium deficiency is associated with reduced fertility (Hidiroglou, 1979). It causes the abortion or weakness of calves and the calves will be unable to stand or suckle. Compromised Se status has been linked with low uterine involution, and poor or silent estrus and sufficient blood Se concentration has reduced the frequency of abortions, stillbirths and periparturient recumbency (Bindari *et al.*, 2013).

Salt: The salt specially, sodium (Na^+) and chloride (Cl^-) deficiencies can influence the digestion and reproductive performance of cows indirectly, and feeding with high potassium (K^+) may hindrance the beginning of puberty and ovulation and hamper the CL formation (Bindari *et al.*, 2013). Smith and Chase (2010) also opined that the diet with superior levels of K^+ or the wide $K^+ - Na^+$ ratio in diets for cows lowers the fertility.

CONCLUSION

In this review study, it should be concluded that the haemato-biochemical activity is essential attribution to the reproduction in female animals including dairy cows. Though the concrete basis is not clear due to a shortage of references, the electrolytes imbalance causing stress may influence the normal reproductive functions in the cows.

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CONFLICT OF INTERESTS

The authors announce that there is no conflict of interests with considers to the publication of this review manuscript.

AUTHORS' CONTRIBUTION

NSJ and MMIH designed the manuscript. MMIH, MH and NSJ acquire part in drafting and critical checking of this manuscript

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