Heat Stress Effects Immunity of Dairy Cattle

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Heat stress (HS) is a complex phenomenon which triggers a variety of animal response mechanisms that have negative impact on livestock welfare and their production. While these negative effects are well established and known to be associated with production responses, growing body of evidence suggests that HS leads to negative effects on the immune response of dairy cattle. The stress response primarily modulates the immune response via the hypothalamic–pituitary–adrenal (HPA) axis but is also likely to shift the adaptive immune function from cell mediated to humoral immunity and thus weakens the animal immune function. While the various management strategies such as providing shade and sprinklers for cows, and nutritional supplementation could be adopted to ameliorate some of the negative effects, further research is required to better understand the impact on production responses because of altered immune status of dairy cattle during HS.

dairy cattle heat stress immune response heifers

1. Introduction

Heat stress (HS) is one of the major factors affecting animal's immune system and their productivity. The earth's climate is gradually evolving and changing. Intergovernmental Panel on Climate Change (IPCC) [1] reported that the earth's temperature has increased by 0.2 °C per decade, with the prediction that the average temperature of the earth will increase by 1.4 °C to 5.8 °C during the 21st century. The thermoneutral zone, a temperature range at which a healthy adult animal can maintain a normal body temperature without the need of using energy beyond its normal basal metabolic rate in dairy cattle ranges from 16 °C to 25 °C [2]. The dairy cattle can maintain their physiological body temperature of 38.4 °C to 39.1 °C in this zone. At the point when an animal crosses its thermoneutral zone, that is surface temperature of 22–25 °C in mild and 26–37 °C in tropical climate environments like India, increased heat gain as compared to loss from the body occurs and the animal's core body temperature starts increasing beyond the normal range resulting in HS [3][4]. Besides ambient temperature, environmental humidity is also an important factor affecting HS's severity. Therefore, Temperature Humidity Index (THI) is a potential measure of HS. Exposure to a THI value of greater than 72 is stressful for dairy cattle and is likely to cause a negative impact on their welfare and production [4]. Similarly, in buffaloes [3], exposure to a THI value of 75 has been reported to cause deleterious effects on their reproductive function. Further, endocrine shifts are visible in cows, especially in prolactin and cortisol levels, when exposed to HS. This increase accommodates the need to increase heat loss [5]. Both hormones are known to affect the immune system. Prolactin [6] and cortisol [7] exert their influence on genes associated with immune responses, notably the heat shock proteins (HSP), which are molecular chaperons and protect cells against the damage caused by increased temperature.

Immune system of animals plays a very important role to overcome various stressors confronted in contemporary production systems [8]. Immune system in calves begins to develop at conception, continues in utero, and matures approximately 6 months after birth [9]. The immune system is of two types: the innate immune system and the adaptive immune system. The innate immune system is independent of exposure to pathogens, while the adaptive immune system is dependent on exposure to pathogens. Both systems work closely together and perform different tasks. Various studies that have examined bovine fetuses at different stages revealed that bovine fetuses had 4 major T cells (associated with immunity) in splenic tissues and the thymus. These T cells were significantly higher in fetal and young calf splenic tissues compared to adults (above 150 days of age), whereas the difference was non-significant for thymus [10].

Critical cellular components of the innate immune response are neutrophils and macrophages [11]. A recent study conducted on functional response of bovine monocyte derived macrophages over thermal and Lipopolysaccharide (LPS) induced stress challenge indicates upregulation of heat shock protein 70 (HSP 70) gene and downregulation of cell signaling, i.e., Toll-like receptor 4 (TLR4) alteration in functional responses like autophagy, phagocytosis, and oxidative ability. Thus, during thermal stress, dairy cattle may be more susceptible to diseases due to dysregulation of macrophage function caused by thermal cum LPS stress [12]. After an in vivo heat challenge, high immune responders (based on their breeding values for antibody and cell-mediated immune responses) outperformed average and low responders in terms of HSP 70 concentration and cell proliferation. Because these results are identical to those obtained during an in vitro heat challenge, it is possible to draw the conclusion that high responders may be more resistant to HS than low and average responders [13].

The innate immune response of the fetal bovine is underdeveloped until gestation. However, as gestation approaches, the functional capacity of innate immune response further decreases due to increased fetal cortisol levels [14]. An acquired immune response consists of antibodies, memory lymphocytes and effector cells. It has been revealed that T lymphocytes and monocytes increased during gestation (from 3 months to the end of gestation). In contrast, B lymphocytes remained low throughout the pregnancy in the spleen as well as peripheral blood [15].

At birth, calves are ‘immunonaive’, i.e., they don’t have immunoglobulins and circulating antibodies [14]. Due to the protective environment in the womb, they do not even have the chance to increase adaptive immunity through experience. The maternal factors during parturition, such as increased cortisol concentration further depress their immune competence, and passive transfer of antibodies from colostrum becomes a necessity at least for the first 2–4 weeks of age [9]. Colostrum is primarily composed of antibodies, cytokines, and cells. Calves that ingest colostrum shortly after birth have significant concentrations of immunoglobulin in serum, whereas colostrum-deprived calves have only trace amounts of immunoglobulin during the first 3 days of life [16].

2. General Effects of Heat Stress on Immunity

2.1. Effects of Heat Stress on Immunity during Pre-Natal Period

Fetal exposure to prenatal maternal stressors during development has consequences that are life-long, affecting the genetic potential of an individual. Research has been conducted on in utero HS during late gestation, affecting immune system during early life and the pre-weaning period [17][18]. During the last week of gestation, pre-natal HS increased the incidence of disease, particularly pneumonia, diarrhea, and omphalitis, in calves. Pneumonia was found to be most strongly associated with pre-natal HS followed by diarrhea and omphalitis. Generally, last week of gestation is the most important week as far as detrimental effects on calves in form of diseases were concerned [19].

Heat stress during the dry period of dairy cows leads to impaired passive transfer of IgG from colostrum during the pre-weaning period [20][21]. There are some studies comparing the quality and quantity of colostrum from cows exposed to hot conditions. According to one such study, the colostrum of cows exposed to high temperatures had lower concentrations of IgG and IgA [21][22]. Conversely, some studies have shown no difference in IgG concentrations [23] or even increased concentration of Immunoglobulins [24].

Overall, the immune competence of calves in post-natal life is negatively affected by HS during pre-natal life through the altered hematological profile and cellular immune status. Total plasma protein levels of the calves suckling colostrum from their heat-stressed dams during gestation were reduced compared to calves suckling thermally comfortable dams [20]. Calves born to heat-stressed dams had higher platelets, higher circulating hemoglobin, higher basophils and circulating acute phase proteins with lower lymphocytes compared to calves born to thermoneutral dams [24]. Maternal HS during gestation can impact the immune status of the calf before weaning. Strong et al. [25] concluded that calves from heat-stressed dams had less expression of tumor necrosis factor alpha (TNF-α) and Toll-like receptor 2 (TLR2) (blood immune markers) and a reduction in lymphocyte percentage as compared to calves from cooled dams.

2.2. Effect of Heat Stress during Post-Natal Period on Immunity

(i) Preweaned calves

There are numerous studies on the effect of HS on lactating as well as dry cows [26][27] and the strategies for the amelioration of HS but pre-weaned calves have not been considered for such HS abatement strategies. In practice, cooling calves are not considered economical as there is no direct effect on the milk production losses. Like mature cows, calves also suffer from HS as it exceeds their ability to dissipate heat. The thermoneutral zone for pre-weaned dairy calves ranges from 10–26 °C [28][29]. Above this temperature, all the energy of the calf is utilized in maintaining body temperature. The thermoneutral zone of different animals depends on various factors like age, size, breed, nutrition, hair coat, behavior, bedding, and weather [30][31].

(ii) Growing heifers

The effects of HS on the immunity of heifers have not been fully studied based on the assumption that heifers are not affected by HS. Nevertheless, the effect of HS on heifers cannot be ignored. Heifers when exposed to high ambient temperatures of 24 °C and above; increase in respiration rate and rectal temperature [32][33][34][35], and heart rate [35][36] have been observed. These observations suggest that heifers are also affected by HS like mature cows. The surface area of heifers increases from 1 to 12 months of age but the ratio of surface area to body weight decreases. Moreover, heat production per unit of body surface area increases with increasing age of the heifer [37]. These observations indicate that the ability of heifers towards heat tolerance and heat dissipation decreases with their age. When confronted with a temperature of 42 °C for 12 h, heifers reduced thymidine (3H) incorporation [38]. However, a three-fold increase in the concentration of HSP 70 was recorded when exposed to 42 °C for 1 h. Breed difference between Angus heifers and Romosinuano heifers in response to HS has been documented [39]. Response of HS post lipopolysaccharide (LPS) concentration of TNF-α was different in both types of heat-stressed heifers as compared to heifers in a thermoneutral environment. The concentration increased in Angus heifers while it decreased in Romosinuano heifers. Moreover, HS post LPS concentration of IFN-γ in Romosinuano heifers increased as compared to Angus heifers where the concentration of IFN-γ decreased. These results indicate potential genetic differences in the impact of HS on the immune status of dairy cattle.

2.3. Effects of Heat Stress on Immunity of Lactating Cows

During summer, an increase in somatic cell count (SCC) and reduction in milk volume and quality have been observed in temperate [40][41] and subtropical areas [42] with the increased THI. It was expected that the total pathogen load should increase as temperature rises, but several variations were found. Lundberg et al. [43] observed that in a herd studied for 12 months, infections such as *Streptococcus dysgalactia* and *Streptococcus uberis* were common during pasture season, i.e., summers and in late housing season, i.e., winters, respectively. The SCC of heat stressed cows was higher as compared to cooled cows [44]. However, the blood plasma concentrations of cytokines and immunoglobulins were lower in heat stressed cows as compared to cooled cows indicating adverse effects of HS on dairy cattle immunity. It was further reported that cooling lactating cows with fans for 8 h per day was found to improve feed intake and milk yield compared to cows under HS. Thus, it can be concluded that that HS abatement strategies may be helpful in eliminating adverse effects of HS.

2.4. Effects of Heat Stress on Immunity of Dry Cows

The dry period is very important for udder health, productivity, and overall health of dairy cattle [45][46][47]. Pre-partem HS increased the incidence of metritis and persistence of uterine diseases in dairy cows independent of vaginal bacteria content [48]. 251 proteins and 224 phosphorylated proteins were found in the lactating mammary glands of cows subjected to pre-partem HS (HS in dry period). These proteins were indicative of increased oxidative stress, reorganization of the mammary gland, and immune dysregulation. Thus, dairy cows may experience reduced milk yield as a result of disrupted mammary function caused by dry period HS [49]. The occurrence of many peripartum diseases can be vigorously monitored and controlled in the dry period [50]. Good dry period management helps in a smooth transition from one lactation to the next by decreasing incidences of ketosis, with no major adverse effects on other health parameters [51]. Incidence rates of clinical mastitis vary in different seasons but are maximum in summers [52]. Mild HS does not affect cell-mediated immunity, colostrum's concentration above protective levels, and passive immunity in dairy cow offspring [53].

Various studies which directly compare HS and cooling show the differences in immune responses. Prolactin signaling in lymphocytes was compared both in HS and cooled environments [54]. Lymphocyte proliferation of cooled cows was more than in heated cows, and they expressed more prolactin receptor (PRL-R) mRNA compared to heated cows suggesting that prolactin signaling affects lymphocyte functions directly. Heat stress abatement during the dry period improves the immune system in dairy cows in their transition period. Neutrophil oxidative burst and phagocytosis in cooled cows were more in comparison to heated cows [55].

3. Effects of Heat Stress on Reproductive Immunology

In dairy cows, HS can have a significant impact on fertility and reproductive processes. Heat stress significantly affects reproductive functions and fertility in dairy cows. Further, it negatively effects gonadotropins Luteinizing Hormone and Follicle Stimulating Hormone (LH and FSH). Although there are some discrepancies in the literature on gonadotropins, most studies show that heat stress reduces LH secretion and its function. For example: follicle tissues from heat stressed cows secreted, lower levels of steroids under gonadotropin stimulation [56]. Under HS, lower concentrations of the GnRH-induced LH surge were found in other studies [57]. Unlike LH secretion, FSH secretion increases under HS.

Heat stress might also cause adverse effects on oocyte maturation and early embryonic development [58]. It can prevent growth of oocytes in many ways. Luteinizing hormone and estradiol's pre-ovulatory surge may be reduced, resulting in cattle with poor follicle maturation and ovarian inactivity [59]. HS reduces degree of dominance of selected follicle, which in turn reduce the capacity of theca interna and granulose cells. Blood estradiol concentration is, thus, reduced in response. The concentration of progesterone in the blood is also affected by HS, which is a major cause of oocyte abnormal maturation and implantation failure [60]. Blood flow to the uterus is reduced during HS, resulting in an elevated uterine temperature. This leads to early embryonic losses and vanquishes development of the embryos [61].

HS also leads to hyperprolactinemia in buffaloes, suppressing gonadotropin secretion and leading to altered ovarian steroidogenesis. Additionally, embryonic survival is reduced when pregnant females are subjected to HS from day 0 to day 7 of their pregnancy [62]. During summers, high mean prolactin concentration was observed in buffaloes as compared to winters. This eventually contributes to poor fertility by lowering gonadal hormone (progesterone synthesis) [63]. Conception rate has been found to decline in dairy cattle above THI 72, and a significant decrease in the conception rates of buffaloes has been observed above THI 75 [64].

4. Amelioration of Heat Stress in Dairy Cattle

4.1. Physical Modification of the Environment to Alleviate Heat Stress

Proper shelter is of utmost importance to protect animals from extreme weather conditions without impacting animal performance in terms of growth, health and productivity. Heat stress can be reduced by using straight forward design principles for animal facilities (such as shape, orientation, the thermophysical characteristics of building materials, ventilation, and opening facilities). However, the focus should be to use economically viable indigenous materials like white galvanized or aluminum roofs, thatch, wood, clay tiles, etc., so farmers can easily adopt those technologies [65].

Shade can be considered a very efficient way to minimize the effects of direct solar radiation on animals, although it doesn't mitigate high relative humidity and ambient air temperature completely [66]. However, building a structure around the shed and planting trees can be extremely helpful in protecting animals from high heat load [67]. The most efficient natural protection of animals from heat load is trees. Artificial structures or buildings are only required if natural shade is not available [68].

In addition to provision of shade, various cooling strategies can be used to lower the body temperature of the cows to maintain flow of heat from core of the body to skin. Evaporative cooling becomes the preferred method of heat loss from animal body when usual methods of heat loss such as radiation and conduction cease to operate as heat gradient is lost once ambient temperature equals the skin temperature.

Both direct and indirect methods of cooling can be used on farm to cool the cows during summer. Direct methods involve misting, sprinkling and fogging systems [69]. Foggers are generally effective in low humidity areas and work on the principle of scattering very fine drops of water which quickly evaporates and immediately cools down the surrounding air [70]. Mist drops are generally larger than fog drops but the working principle is the same. Cooling is done primarily by inspiration of cooled air [70]. Sprinkling on the other hand does not work on the principle of fogging and misting but rather the large water droplets are used to wet the hair coat and skin. Cooling occurs as water evaporates from the hair and skin surface [66].

4.2. Nutritional Interventions to Counter Heat Stress

Nutrition has a major role in alleviating HS. Exogenous antioxidants and salt supplementation in the diet can be effective methods for HS alleviation [4]. It should also be noted that during HS nutritional needs of animals change. Efficient nutritional strategies like increasing nutrient density, ration reformulation which accounts for the reduced dry matter intake, minerals, vitamins and antioxidant supplementation become critical for optimum production in livestock during HS conditions [26]. Nutritional strategies such as chromium picolinate, betaine, and antioxidant supplementation in the diet, as well as changing the rate of starch fermentation, can help animals cope with HS [71]. During HS, changing the diet composition has been reported to encourage increased intake to compensate for low feed consumption [65]. Essential nutrients, particularly amino acids, have been found to be critical for improving production. During HS, oxidative damage occurs, so antioxidant supplementation is one of the primary means to repair damage caused by HS. Antioxidants, both enzymatic and non-enzymatic, protect against oxidative damage produced by HS [4]. Supplementation of sodium and potassium in the form of carbonate and bicarbonate help in regulation of acid–base balance in blood [72]. Several studies have shown that adding Vitamin A, C, E and Zinc in animal feed help in combating HS.

Methionine is an indispensable amino acid (IAA). There has been evidence of an increase in milk yield when dairy cattle are fed appropriately with IAA [73]. Additionally, dairy cows under stress whose diets contain rumen protected methionine (RPM) experience an increase in milk yield [74]. Previous research has shown that during the transition period, when RPM is fed, liver function, oxidative stress, and inflammation improve [75][76][77]. However, there are not much data available on effect of feeding RPM during HS. But supplementation of methionine and arginine during HS to dairy cattle has been shown to improve mammary epithelial cell functions and mammary metabolism [78].

4.3. Enhancement of Immunity as an Abatement Strategy

Enhancing immunity can be a very important stress abatement strategy. Boosting immunity largely depends on nutrition and hence, providing effective nutritional supplements could be considered a significant abatement strategy for HS. Nutrition plays an important role in improving immune status of dairy cows. Buffaloes' cell-mediated immunity has been found to be enhanced by the use of vitamin C and electrolytes [79]. Supplementation of Vitamin A increases pro-inflammatory cytokines such as interleukin 1 (IL-1), TNF-α, IgM, IgG and IgA and thus improves immunity in dairy cattle [80]. Vitamin A also helps in immunoglobulin transport proteins production [81]. Vitamin E along with selenium plays a crucial role in immune function. Vitamin E and selenium supplementation have positive influence on chemotaxis and oxidizing property of neutrophils [82] and phagocytic ability [83].

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