

*Research Article*

# **Role of feeding dietary energy and other nutrients to dairy cows on performance and immune status of dairy cows during the periparturient period**

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Dietary nutrients have big role on immune status and performance of dairy cows during the periparturient periods. Unable to fulfill the nutrients requirement of the cow especially during the transition period predispose the cow to many production diseases like milk fever, subclinical hypocalcemia, ketosis, fatty liver syndrome, retained fetal membranes, metritis, mastitis and displaced abomasum. The objective this review paper was to assess the effect of various dietary nutrients on immune status and production performance of dairy cows during far dry off and transition periods. Feeding different dietary energy, rumen protected amino acids and some micronutrients during the periparturient period play a significant role on energy metabolism and immune status of dairy cows. However, both underfeeding and overfeeding dietary energy during the pregnancy state had negative effect on health status as well as production performance of dairy cows. Under feeding dietary energy during early lactation reduce milk production, immune status and suddenly increase the energy level in diet of the cows lead to sub-acute acidosis. On the other hand overfeeding of dietary energy during the dry period aggravates the negative energy balance in the postpartum cows. It increased the concentration of NEFA in serum of cows in early lactation. Hence, inappropriate feeding of dietary energy during dry off and transition period could not help dairy cow to reduce negative energy balance in the postpartum cows. It also increased the expression of miR-143 gene which regulate the expression of other genes by different mechanisms and increased the expression of miR-378 a non-coding RNA molecule which able to regulate gene expression at posttranscriptional level. Rumen protected amino acids especially methionine and choline are very important for transition cows to alleviate the negative energy balance of cows around calving. Methionine is one of the essential amino acids and has multifunction, it involved in protein synthesis, used as a methyl donor and it also used as precursor of other antioxidant and lipotropic compounds. Feeding this amino acid in the form of rumen protected to dairy cows reduces the degradation methionine in rumen by rumen microbial and increased blood polymorph nuclear leukocyte phagocytosis capacity and oxidative burst activity during the transition period. This showed that supplementation of methionine to transition cow is resulted in better immune response, improve dry matter intake, milk yield and greater in phagocytosis and oxidative burst capabilities upon challenge with lipopolysaccharide.

**Key words:** transition, methionine, oxidative, immune

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## INTRODUCTION

Transition period is a period last 3 weeks before calving to 3 weeks after calving in dairy cows. During this period, various changes are occurred in animal body associated to pregnancy and normal body functions (Drackley, 1999). Different change such as physiological change, metabolic change, immunological change, fetal and mammary gland developmental change are under take to prepare pregnant cow for successful transition from pregnant state to lactation state. But deviation of these change from normal state caused immune suppression around calving and increase the susceptibility of dairy cow to various production diseases such as milk fever, subclinical hypocalcemia, ketosis, fatty liver syndrome, retained fetal membranes, metritis, mastitis and displaced abomasum. To minimize the problem of immune suppression which dairy cows commonly faced around parturition and for successful transition from non-lactation state to lactation state, many attempts have been done to reduce production losses of dairy cows through improve their dry matter intake during the transition period. This review papers mainly focused on various feeding strategies of dairy cows with different dietary nutrients during the dry off and transition periods. Moreover, it mainly focused on recent published articles on feeding of different levels of dietary energy and other nutrients during the dry periods, close up and fresh cow periods in order to improve the immune system, immunity and dairy cows production performance. Immune system is system that involved a collection of cells and molecules to protect the body against infection, malignancy and damaged cells (Drackley, 1999), whereas immunity is reactions by an animal body to foreign substances such as microbes and various macro molecules. As result of different factors, the immune system of the cows around parturition is reduced to protect animals against various production diseases (Drackley, 1999). Although, feeding dietary nutrients to dairy cows during the transition period have huge potential to modulate the immune system of the cows to prepare the animals for immediate response to pathogen challenges, the role these nutrients did not explore well. Hence, this review paper is written to assess the role of different dietary nutrients on immune status, dairy cows production performance, negative energy balance, and dry matter intake of the cows during the periparturient periods.

As methodical approach, this review paper was written through assessing of very recently published articles on high quality, international, and peer reviewed journals. Various research findings on the effect of pre and postpartum feeding of dietary energy levels, supplementing of rumen protected amino-acids and some micro nutrients to dairy cows were reviewed and their role and effect were indicated in this review paper.

## Dietary energy

During the transition period different risk factors such as negative energy balance, inflammation and impaired immune response are highly cause-and-effect related in dairy cows (Esposito et al., 2014). Due to these risk factors the management given to dairy cows during the transition period were focused on reducing negative energy balance or feeding balanced and well formulated ration to transition cows to improve their immunity and dry matter intake (Esposito et al., 2014). Different authors indicated that NEFA and BHB play a significant role on immune status of dairy cows around calving when dairy cows faced some degree of negative energy balance due to reduction in dry matter intake the cows. During this period, dairy cows mobilizing adipose tissue for immediate sources of fuel/energy for different cellular function. Very soon after calving, the concentration of non-esterified fatty acids (NEFA) and beta-hydroxybutyrate (BHB) reached peak level due to lipolysis, this is very known to impair immune cell functions (Buhler et al., 2016). The high level of NEFA in the liver tissue is converted to fatty liver disease due to high mobilization of fat tissue in response to negative energy balance (Gerspach et al., 2017). During negative energy balance, the concentration of NEFA is increased in the liver as a result of mobilization of fatty tissues. Circulating NEFA in the blood can be either utilized by the mammary gland to synthesize milk fat or transported to the liver for further metabolism. During this time, the liver plays a crucial role in the homeostasis of NEFA. There are three primary pathways that metabolized NEFA in the liver is under go. The three pathways are: (1) the metabolized NEFA is oxidized to generate ATP in hepatic mitochondria or peroxisomes to supply energy for liver tissue (2) incomplete oxidation of NEFA is used to produce ketone bodies, including acetone, acetoacetate, and  $\beta$ -hydroxybutyric acid (BHBA), or (3) excess NEFA left in the liver is re-esterification to form triglycerides (TG). The TG can either accumulate in hepatocytes or be transported out of the liver in the form of very-low-density lipoprotein (Grummer, 2008). To minimize the problem of fatty liver disease which is occurred due to mobilization of adipose tissue in response to negative energy balance many attempts have been done through feeding of various nutrients to dairy cows during the transition periods. Some of the feeding strategy that has been used in dairy cow with different level of energy during the far off dry period and close up periods are mentioned in this review paper. Some of these feeding strategies are very useful for dairy industry to minimize the problem of their animals subsequently to reduce the loss of high yielding dairy cows' due to metabolic disorder and other production diseases.

### Feeding of dairy cows with dietary energy levels during the far off period

From 60 to 21 days before calving is known as far-off/dry period in dairy cow, the goals of the far-off include maintaining protein and muscle reserves, maintaining body condition, rejuvenation of the rumen wall, and provision of needed minerals and vitamins. Overfeeding of dairy cows with high energy diet during the far-off period to achieve optimum body condition score at calving and to reduce mobilization of adipose tissue after parturition had negative effect on animal health. Some literature indicated that overfeeding of dairy cows during the far-off period had increased the expression of miR-143 and miR-378 one week before calving. miR-143 is a short RNA molecule and its function is to regulate the expression level of other genes by several mechanisms. miR-378 is one of the small non-coding RNA molecules able to regulate gene expression at posttranscriptional level (Enref.K. et al., 2015). Feeding trial conducted to evaluate overfeeding of grass silage during the far-off dry period combined with concentrate feeding during the close-up dry period did not have adverse effects on the metabolic flexibility of transition dairy cow (Salin et al., 2017). But overfeeding energy in the dry period can affect glucose metabolism and the energy balance of transition cows with potential detrimental effects on the ability to successfully adapt to early lactation (Mann, L.Y., et al., 2016). Overfeeding energy during the entire dry period or close-up period alone did not affect glucose tolerance as assessed by Intravenous Glucose Tolerance Test (IVGTT). Energy uptake during the dry period was associated with changes in periparturient concentrations of glucose, as well as postpartum insulin, glucagon, NEFA, and BHB concentrations. The difference of blood serum concentrations of NEFA between cows overfed energy before calving and high blood concentrations of BHB are likely due to greater negative energy balance postpartum reflected in lower circulating concentration of glucose and insulin and an increase in the total amount of mobilized adipose tissue rather than due to changes in adipose tissue insulin signaling (Mann, Nydam, et al., 2016). Overfeeding of energy during the far off period caused suppression of the adipose tissue before calving. This shows that the response of NEFA was largely driven by basal NEFA concentration. The major factor for directing glucose to the mammary gland is due to low concentration of insulin around calving and this implies the role of peripheral insulin sensitivity is less important (Salin et al., 2017). Similar to study supplementation of concentrate feeds to dairy cows during dry periods did not affect energy intakes, blood glucose, NEFA, and BHB concentrations, and milk yield and milk composition. But it increased papillae surface area in dry periods and but the increased papilla surface

was not maintained into the subsequent lactation (Dieho, B. et al., 2017).

Feeding of dairy cow with 75 and 125 % of estimated requirement of energy before calving to thin (4) body conditioned scored and optimal (5.0) body conditioned scored of dairy cows changed carbohydrate and amino acid metabolism. Feeding these energy level caused a greater and more prolonged negative energy balance after calving in 5 scored body condition scored of dairy cows over fed high energy level before calving (Vailati-Riboni et al., 2016). This showed that feeding of plane of energy level to pre-parturient cow for hepatic function was dependent on body condition scoring of cows. More pronounced transcriptome changes were occurred in thin body condition scored cows in compare to thick body condition scored cows. This showed that thin body conditioned scored cows are more sensitive to pre-parturient feeding energy level than optimally body conditioned scored cows (Vailati-Riboni et al., 2016). Supplementation of concentrate to low body condition scoring cows during dry period had no effect on performance and fertility of cows but it resulted in a higher neutrophil phagocytic index at one week postpartum. Feeding of concentrate to low body condition scored cows also increased the incidence of lameness when compared with feeding of dairy cows only grass silage-diet before calving (Little et al., 2016). The study conducted to evaluate the impact of dietary plane of energy during the dry period on lipoprotein parameter in transition period in dairy cows revealed that high energy diet maintained total cholesterol as compare to lower energy diet but there was no significant increase in LDL fraction of lipoproteins between dietary energy level. In this study it indicated that dry period diet total energy level had a mild impact on lipid parameters (Newman, B. et al., 2016). Another study showed that feeding of different energy level before calving changed the inflammatory state of neutrophils during the periparturient period (Crookenden et al., 2017). However, further study is required to find out the relationship between pre-calving body condition scoring and intake of dietary energy before calving and immune function of transition cows during the whole transition period (Crookenden et al., 2017). Feeding of cow excess energy predicted requirements by approximately 50% during the entire dry period resulted in decreased postpartum basal plasma glucose and insulin, increased glucagon, BHB and NEFA concentrations after calving compared with cows fed a control energy diet during the dry period (Mann, Yepes, et al., 2016). Mann, Yepes, et al. (2016) showed that overfeeding energy to dairy cow during the entire dry period alone did not affect glucose tolerance. Feeding of dairy cows with controlled-energy diet during the dry period decreased the degree of negative energy balance, decreased the number of episodes and degree of hyperketonemia after calving (Mann et al., 2015).

Minimizing of negative energy balance during the transition periods reduces the effect of negative energy balance on immune dysfunction of dairy cows around calving (Little et al., 2017). High energy intake 144% of Metabolizable energy requirement/day followed by gradual restriction of energy intake 119% ME/day did not have adverse effects on the metabolic flexibility of transition cow as compare to control energy intake 100% ME/day throughout the 6 weeks dry period (Salin et al., 2017). Some literature indicated that restriction of feed to under conditioned cows resulted in more liver dysfunction in the cows. Energy demand for milk synthesis is increased in early lactation if nutrient intake is not cope with nutrient requirement reproductive functions such as synthesis and secretion of hormones, follicle ovulation and embryo development may be depressed (Cardoso, 2017).

### **Feeding of dairy cows with different energy level during close up period**

Close-up period is the period lasts the last three weeks before calving. During this time, the cow is preparing to start the next lactation. Feeding of dairy cows during the close up period with different energy levels have an effect on energy metabolism and energy balance cow when the energy demand of cow is very high due to various physiological and hormonal change. Some literature indicated that overfeeding in late pregnancy cow should be limited to under conditioned cows and cows with optimum body condition should be maintained on restricted energy diet (Vailati-Riboni et al., 2017). Feeding of reduced energy density during the close-up period was beneficial in controlling negative energy imbalance before calving and it increased milk yield and dry matter intake and alleviated negative energy balance in postpartum cows (Huang et al., 2014). In other study, feeding of dairy cows with concentrate feeds 4 weeks before calving had no effect on postpartum dry matter intake, milk yield, body tissue mobilization, energy balance, neutrophil or lymphocyte function, health, or corpus luteum activity (Little et al., 2017). Increasing the energy content in total mixed ration of close up cow diet leads to a higher incidence of metabolic disorder after calving (Vailati-Riboni, Farina, et al., 2017). Supplementation of nicotinic acid as energy supply to decrease lipolysis in dairy cows at different parity state showed peak expression of oxidative stress related genes in blood leucocytes before calving (Buhler et al., 2017). Feeding of nicotinic acid to dairy cows which had fed on lower concentrate level feed ration increased prepartal serum superoxide dismutase (SOD) activity, this may be a higher metabolic activity in these animals (Buhler et al., 2017). Supplementation higher dietary energy level induced higher Glutathione peroxidase (GPX) activity and higher expression levels for some

gene and anti-oxidative parameters correlate with energy and metabolic parameters (Buhler et al., 2017). Some study showed that the prevalence of metabolic disorder and negative energy balance is co-occurred during the transition period in dairy cows. The effect of energy density in the close-up period and supplementation of extruded full-fat soybean during the first 4 weeks after calving showed interaction for blood NEFA and bilirubin concentration during early lactation. Ad libitum feeding of high energy diet during the close-up period impaired metabolic status during early lactation and leads to higher plasma level and greater loss of body weight and body condition scoring as compared to low and medium energy diet. Feeding of overfed energy before calving with extruded full-fat soybean postpartum improved postpartum metabolic status and liver function of cows (Zhang Q. et al., 2015). On other experiments feeding extruded full-fat soybean in the first 4 weeks of lactation increased milk yield regardless of prepartum energy diet (Zhang Q. et al., 2015). Diseases incidence is very high in early lactation when the cow is change from pregnancy state to lactation state (Smith et al., 2017). This is because of dairy cows total depend on mobilization of body energy reserves to fulfill their energy deficiency caused by reeducation of dry matter intake a round calving even though the nutrient demands of the cow is increased as a result of fetus development and copious milk synthesis and secretion (Smith et al., 2017). Monitoring of the status of body energy reserves in dairy cow during lactation periods is very important as it is one component of herd health management system. Cows which developed different diseases in the first 30 days of lactation had different characteristics in their physiology and production traits during the changeover and dry periods (Smith et al., 2017). Mastitis, ketosis, uteritis and others diseases are some of production diseases which frequently observed in dairy cows especially during early lactation due to negative energy balance. Different biomarkers indicate the presence of different production diseases in the body animals around calving. From various study conducted it was observed that acute phase proteins, pro-inflammatory cytokines and indicators of oxidative stress may serve as biomarkers of clinical and sub clinical mastitis (Sadek et al., 2017). The expression of SAAs and Haptoglobin indicate the local de novo synthesis of these acute phase proteins within mammary gland tissues (Sadek et al., 2017). Elevated of BHA level which is greater than ( $> 1.2 \text{ mmol/l}$ ) in fresh cow in the first week of lactation indicated significant disease risk and productive losses (Van Saun, 2016). The influence of transition periods on lipid mobilization and paraoxonase-1 (PON1) activity revealed that PON1 significantly positively correlated with total cholesterol but it inversely correlated with NEFA concentration indicating the relationship of PON1 with lipid metabolism and lipomobilization syndrome (Turk et al., 2016). It also

showed PON1 involved in immune-related disorders in dairy cows during the periparturient period (Turk et al., 2016). The study conducted to investigate biochemical change of apolipoprotein B100 and some lipid components showed that the levels of ApoB100, total protein, cholesterol, triglycerides, glucose and thyroid hormones detected in the thermoneutral group significantly exceeded other groups detected in hot environment (Teama, 2016). The study showed that the blood content of NEFA and BHBA were negatively correlated with the level of APOB100 (Teama, 2016). The study conducted revealed that supplementing of glycerol-enriched culture (GY) did not affect the dry matter intake, Net energy intake, body condition scoring change and milk yield. However, it increased milk fat and protein content in early lactation, improve the energy status, increased the enzyme activities and expression of key enzymes Phosphoenolpyruvate carboxykinase (PEPCK-C) in the liver (Teama, 2016). These enzymes are the lyase family which is used in the metabolic pathway of gluconeogenesis. When excess lipolysis is occurred from adipose tissue the susceptibility of dairy cows to different diseased is increased and the lactation performance of the cow is reduced and limited. This lipolysis induces remodeling process with Adipose tissue which is characterized by inflammatory response, cellular proliferation and change in the extracellular matrix (Contreras et al., 2016). This inflammatory response is occurred because of the adipose tissue macrophage is the key component of the inflammatory response during inflammation (Contreras et al., 2016). During transition periods the physiological changes related to parturition, the onset of lactation, extended periods of lipolysis can induce intense Adipose tissue (AT) remodeling with enhanced ATM inflammatory phenotype express that may impair the metabolic function of Adipose tissue in cows (Contreras et al., 2016).

### **Feeding of rumen protected amino acids to dairy cows**

Feeding of rumen protected amino acids to pregnant cows during the transition period is very important to improve the immune status and liver function of the cows. Providing immune modulators to dairy cows around calving is also very useful to improve the liver function and dry matter intake of the animals. The effect of supplementation of methionine or choline as its precursor using an ex vivo whole blood challenge to dairy cows showed that both methionine and choline effectively improved immune function, but supplementation of methionine affected the immune and antioxidant status cow before parturition, increased immune cell antimicrobial functions, lower IL-1beta postpartum, improving postpartum neutrophil and monocyte

phagocytosis capacity and oxidative burst activity. However, supplementation of cows with choline increased monocyte phagocytosis capacity (Vailati-Riboni, Zhou, et al., 2017). Supplementing of transition cows with rumen protected choline and rumen protected methionine promoted energy balance by improving dry matter intake of postpartum cow and it regulating hepatic lipid metabolism, improve postpartum milk yield and enhanced antioxidant capacity and immune function of transition cows (Sun et al., 2016). Feeding of rumen protected Smartamine M with higher energy diet to dairy cow before calving reduce the negative effect of overfeeding of energy diet (Li et al., 2016). Similar result was found between cows fed on over fed energy with or without methionine supplementation in pro-inflammatory response (Li et al., 2016). Recent study revealed that feeding of methionine to dairy cows prevents the negative effect of overfeeding higher energy diet prepartum, increased milk protein and fat percentages, increased the expression of the gluconeogenic gene PCK1 (Vailati-Riboni et al., 2017). Phosphoenolpyruvate carboxykinase 1 (PCK1) is an enzyme which regulate gluconeogenesis. The expression of this gene can be regulated by insulin, glucocorticoids, glucagon, and diet. Feeding this amino acid also increased lipid-metabolism transcription regulator PPARA but it decreased the expression of lipoprotein synthesis enzyme MTTP, lower expression of GSR, and increased expression of the methionine cycle enzymes SAHH and MTR which help in synthesize of methionine endogenously before calving. Supplementing of late pregnant dairy cows with Smartamine M improved hepatic lipid and glucose metabolism it leading to greater liver function and better overall health of transition cow (Vailati-Riboni, Osorio, et al., 2017). Feeding rumen protected methionine to dairy cows increased blood polymorph nuclear leukocyte phagocytosis capacity and oxidative burst activity during the transition period (Zhou et al., 2016). This show supplementation of methionine to transition cow is resulted in better immune response, increased dry matter intake and greater in phagocytosis and oxidative burst capabilities upon challenge with lipopolysaccharides as compare to supplementation of choline (Zhou et al., 2016). In other study feeding of dairy cows with methionine increased monocyte phagocytosis capacity (Vailati-Riboni, Zhou, et al., 2017). But due to extensive microbial degradation dietary methionine and choline in the rumen, the availability of methyl donors of methionine and choline are limited (Girard & Matte, 2005). This indicated that supplementing of rumen bypass methionine and choline is very crucial to increase the bioavailability of these amino acids to dairy cows. Feeding of rumen protected choline to multiparous cows had less cases of subclinical ketosis before calving and after calving as compare to feeding it heifers (Furken & Hoedemaker, 2014). Cows fed on methionine had greater

concentrations of total and reduced glutathione in liver tissue and methionine change liver function, inflammation status and immune response in transition cow (Zhou et al., 2016). This amino acids causes greater in phagocytosis and oxidative burst capabilities of cows during pathogen challenge. Some study showed that feeding of rumen protected choline 60 gram per cow per day to dairy cow during transition period is not sufficient (Zhou et al., 2016). Feeding of the required amount of choline is very useful to explore the function of choline to dairy cows around parturition. In this regard the optimum requirement of rumen protected methionine and choline is needed further study to evaluate their response on immune status of cows (Zhou et al., 2016). Supplementation of cows with rumen protected methionine in the form of MetaSmart or Smartamine M had greater overall plasma oxygen radical absorbance capacity. It increased glutathione and carnitine concentration in the liver, enhanced de novo glutathione and carnitine synthesis in liver and increased antioxidant and  $\beta$ -oxidation capacity (Osorio et al., 2014). The greater decrease of IL-6 after calving in Methionine-supplemented cows indicated a reduction in pro-inflammatory signaling within liver. In other study, lower hepatic phosphatidylcholine is observed in Met-supplemented dairy cows. This is might be associated with greater assembly or export NEFA as very low density lipoproteins from liver (Osorio et al., 2014). The study conducted to assess severity and distribution of hepatic lipidosis in high-yielding dairy cows during the transition periods through evaluation of body condition score, level of NEFA and BHB in serum showed that hepatic lipidosis is associated with long-term histological and metabolic changes in dairy cows (Fiore et al., 2017). Supplementation of rumen protected choline to transition dairy cows increased haptoglobin and insulin concentrations and benefited milk composition (Leiva et al., 2015). Both Methionine and choline have a common characteristic of methyl donors as a result of there is interrelation between methionine and choline (Grummer, 2017). Supplementation of choline is only needed for fat cows to export excess NEFA in the liver as very low density lipoprotein (VLDL) but methionine can prevent fatty liver (Grummer, 2017). Because of the property of choline feeding of choline in the form of rumen protected choline to dairy cow improve liver function by increasing very low-density lipoprotein (VLDL) exportation from liver (Shahsavari et al., 2016). High density lipoprotein, intermediate density lipoprotein, low density lipoprotein, very low-density lipoprotein and chylomicrons are the five major groups of lipoprotein which are made by liver. VLDL is one of these lipoprotein groups which enable cholesterol and fats to move within the water-based solution of the bloodstream. In blood stream this VLDL is converted to low density lipoprotein and intermediate density lipoprotein. When VLDL

involved in transporting of endogenous products the chylomicrons are involved in transporting of exogenous (dietary) products (Dashty et al., 2014). Rumen protected choline also increases gene expression of microsomal triacylglycerol's (TAG) transfer protein and APOB 100 which are required for VLDL synthesis and secretion. Supplementation of rumen protected choline to dairy cows during transition period causes reduction in liver fat and increased milk production (Shahsavari et al., 2016). In other finding supplementation of rumen protected choline increased serum haptoglobin and insulin concentration, change concentration of NEFA in plasma, increase hepatic fat export and decreased risk of metabolic disorders and increased milk yield and milk composition in transition cows (Jayaprakash et al., 2016; Leiva et al., 2015). During transition period, the availability of methionine is limited due to reduction in dry matter take of cow. This reduction in dry matter intake usual leads to severe negative energy balance especially at the onset of lactation, limited lipid metabolism and reduce immune function. Supplementation of methionine during transition period to dairy cows increased blood neutrophil phagocytosis, gives better immune function, lower incidence of ketosis after calving even though it did not decrease liver triacylglycerol (Osorio et al., 2013). Recent study showed that biomarkers identified in dairy cows before the occurrence of diseases increased preventive management, improve animal health and reduce costs in dairy cow production (Crookenden et al., 2016). Supplementation of dairy cow with rumen protected methionine and rumen protected choline improve energy balance by increasing postpartal dry matter intake and regulating hepatic lipid metabolisms, enhanced antioxidant capacity and immune function of transition cows (Zhang et al., 2017). Previous study indicated that supplementation of 40g/cow/day rumen protected lysine to dairy cows during the transition period increased postpartum dry matter intake, and decreased serum free fatty acid, and decreased BHB concentrations. Neither energy nor rumen-protected lysine nor their interaction impacted milk yield, fat or lactose yields (Girma D.D., et al., 2019). In other study, supplementation of 13 g/d of intestinally absorbable lysine caused a general trend to reduced productive performance with little impact on plasma AA concentrations (Robinson, P.H., et al., 2010). Addition of isoleucine, histidine and valine to the lysine complex increased productive performance of the cows, especially milk and milk lactose yield, but had little impact on plasma AA concentrations. Supplementation of a complex of AA was beneficial beyond supplementation of lysine alone, but more research on AA imbalances will be required to determine the effects of supplementation of RP amino acids (Robinson, P.H., et al., 2010).

### Supplementing of dairy cows with micronutrients

Supplementing of micronutrients to dairy cows also play significant role to improve the antioxidant status and subsequently to reduce oxidative stress in dairy cows around calving. Recent research finding indicated that Boron supplementation to pre-partum dairy cows significantly decreased non-esterified fatty acid, Beta-Beta-hydroxybutyrate and triglyceride concentrations in postpartum dairy cow. This indicates that supplementation of Boron is effective in minimizing of negative energy balance, preventing of metabolic disorder and it improve the health of postpartum dairy cows(Basoglu et al., 2017).The effect of parenteral antioxidant supplementation to dairy cows during the dry period on postpartum glucose tolerance is resulted in greater insulin sensitivity after calving and supplementation of antioxidant have played a role in minimizing of the negative effect of negative energy balance(Abuelo et al., 2016). Injection of Vitamins (A, D, E) and trace elements such as Cu, Mn, Se and Zn through intramuscular into dairy cows effectively improve some metabolic and reproductive profile of dairy cows during transition period (Omur et al., 2016). Provision of adequate amount of dietary antioxidant like vitamin E and Selenium proved to be an effective way of controlling the oxidative stress in the transition cow(Omur et al., 2016).

Other finding also indicated that supplementation of antioxidants vitamin E and Zinc to transition cow improved antioxidant activity and decreased oxidative stress in the dairy cows(Maurya et al., 2014).Vitamin E functions as an antioxidant that scavenges free radicals. Subcutaneous injection of trace minerals like selenium, copper, zinc and manganese to the dairy cows before calving at gestation period of 230 and 260 days, and after calving in lactating at 35 days postpartum had increased SOD activity. Moreover, subcutaneous injection of trace minerals to dairy cows that were affected with mastitis had decreased serum SOD activities in the subsequent lactation. However supplementation of trace minerals did not affected leukocyte function (Machado et al.,

2014).Supplementing of Zn, Mn and Cu from amino acid complexes and Co from cobalt glucoheptonate to dairy cow before calving increased polymorph nuclear neutrophilic lymphocyte phagocytosis, antioxidant capacity and increased Co and Cu concentration in liver tissue of postpartum cows(Osorio et al., 2016). Feeding of trace mineral has another advantage in reducing the abundance of some bacteria species. Recent study showed that feeding of dairy cows with Cu and Mn sulfate with Zn glycinate decreased fecal relative abundance of *Treponema* specie in dairy cows. On the other hands, organic Zn has a positive effect on bovine digital

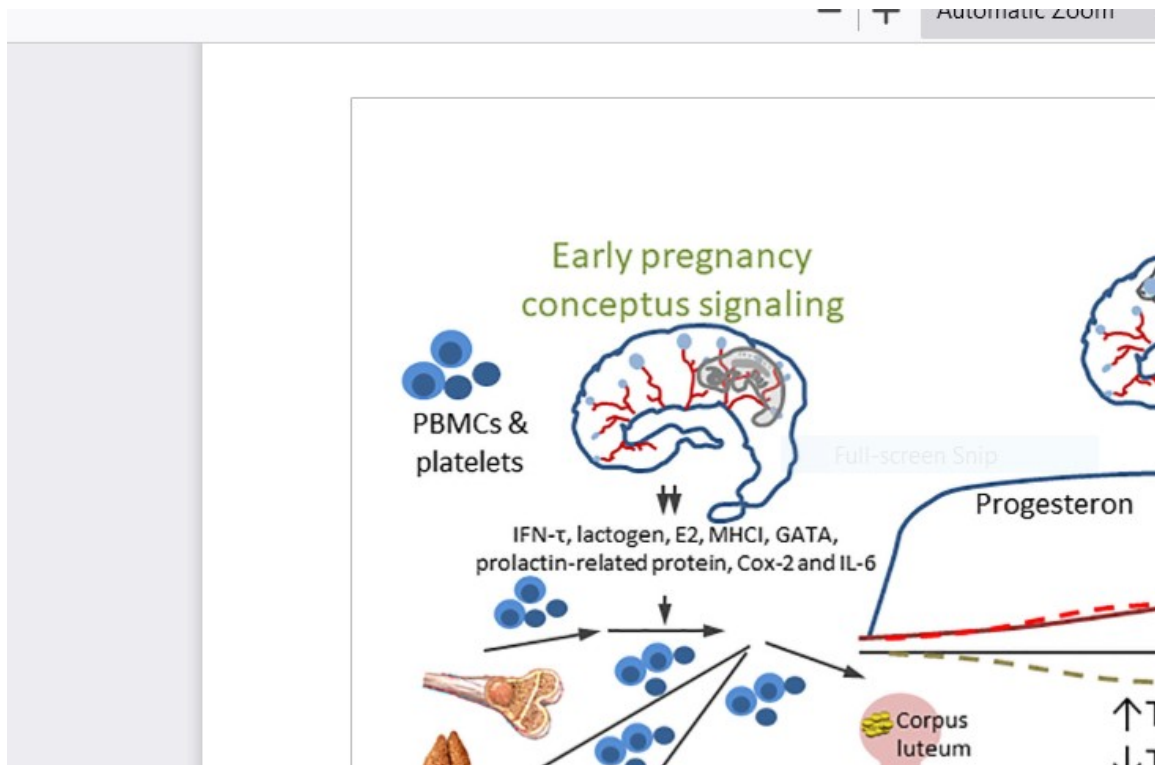
dermatitis. But the mechanism of action how organic Zn supplementation on bovine digital dermatitis is needed various investigations (Faulkner, et al., 2016). The effect of inject able trace minerals contained 300mg of Zn ,50mg of Mn, 25mg of se and 75mg of cu to dairy cows' gestation length of 230 and 260 days under field condition increased the concentration of Se, Zn and Cu in blood serum of cow. The concentration of Ca, Mg, Mo and Zn in serum of dairy cows suffering from retained placenta had reduced as compare to cows without retained placenta. The activities of GPx and SOD did not differ between cows with and without endometritis(Bicalho et al., 2014).Supplementation of selenium to dairy cows especially during the transition periods has beneficial effect on health status of cows. The role of selenium on the health status of dairy cow is through the enzymes of Selenoproteins in which selenium is present as selenocysteine which has a significant role in antioxidant defense and in the formation of thyroid hormones(Mehdi et al., 2013). Selenium stimulates antibody formation and activity of helper T cells, cytotoxic T cells and Natural Killer cells.

Summary of the role micro-and micronutrients on the immune function and other functions in dairy cattle and immune modulation during the pregnancy state is showed in table 1 and figure 1 below.

**Table 1.** Role of micro-and micronutrients in the immune function of cattle

<b>Nutrient</b>	<b>Role in immunity</b>
Fat/energy	Regulates cell mediated immunity and Ab response. Fat-derived fatty acid composition of immune cells, T cell signal and antigen presentation capability.
Protein	Protein/amino acids are required for proliferation and maturity of immune cells. Specific amino acids for instance tryptophan, arginine, and glutamine are required for systemic and gut immune function.
Glucose	Up-regulation of cell proliferation, differentiation, survival, chemotaxis, phagocytosis.
Glutamine	Up-regulation of cytokine and reactive oxygen metabolites (ROM) production, cell division, phagocytosis, CD4 T cell proliferation.
Tryptophan	Activation and maintenance of immune response
Fatty acids	Down-regulation of IgM secretion, cytokine production, cell viability, phagocytosis, diapedesis, antigen presentation, Up-regulation of oxidative burst, necrosis, phagocytosis, cytokine and ROM production, TLR signaling.
Selenium	Maintenance of antioxidant system, enhancement of neutrophil function and neutrophil and macrophage migration.
Zinc	Overall immune function, antioxidant activity, epithelial barrier integrity, nucleic acid and protein synthesis, cell division.
Copper	Overall immune function, antioxidant activity, enhancement of interferon production.
Chromium	Regulation of cell mediated and humoral immune responses, upregulation of blastogenic responses, enhancement of cytokine (IL2, IFN and TNF- $\alpha$ ) production by mononuclear cells, and Ab production.
Iron	Antioxidant defense (essential component of catalase), energy and protein metabolism, oxidation-reduction reactions.
Manganese	Overall immune function, antioxidant protection (integral part of SOD), carbohydrate and lipid metabolism.
Vitamin A,B	Overall immune function, upregulation of lymphocyte proliferation.
Vitamin B	Antioxidant defense, u upregulation of lymphocyte proliferation.
Vitamin D	Antioxidant defense downregulation of inflammation.
Vitamin C	Antioxidant defense downregulation of inflammation
Vitamin E	Lipid soluble antioxidant enhancement of neutrophil function, increase of production of IL 1and major histocompatibility (MHC) class II antigen expression.





## CONCLUSION

Feeding of the required amount nutrients to dairy cow especially during the transition period is very important to balance and fulfill the nutrient requirement of the cow. Failed to balance and unable to fulfill the nutrients requirement the cow during the transition period increased the susceptibility of dairy cow to various production diseases and caused poor transition from non-lactation state to lactation state and reduce the profitability of dairy production. Negative energy balance around calving leads dairy cows to immune suppression and the cows did not withstand or resist to many infectious diseases, metabolic disorders due to reduction in their voluntary dry matter intake around calving. Overfeeding of dietary energy during the dry period increased the concentration of NEFA, BHB in the serum and impaired the immune system of the cows in early lactation. Hence, over feeding of energy during the dry and close-up periods could not help dairy cows to reduce negative energy balance and its effect in postpartum cows. Moreover, feeding of rumen protected amino acids especially methionine and choline improve dry matter intake, immune response and liver functions of cows during the transition period. In general the growth, reproduction, milk synthesis, and metabolic health are all negatively impacted by immune activity; therefore, farm managers must strive to minimize both chronic and acute

infectious or inflammatory insults in order to maximize the potential of dietary formulations.

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