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K Sudha Rani
Assistant Professor, Department of Animal Nutrition, College of Veterinary Science, Garividi, SVVU, Andhra Pradesh, India

K Prabhakar Rao
Assistant Professor, Department of Veterinary Gynaecology and Obstetrics, College of veterinary Science, SVVU, Andhra Pradesh, India

Corresponding Author
K Sudha Rani
Assistant Professor, Department of Animal Nutrition, College of Veterinary Science, Garividi, SVVU, Andhra Pradesh, India

Hematobiochemical profile of a cow during transition period: A review

K Sudha Rani and K Prabhakar Rao

Abstract
Transition period is the period falling between 3 weeks prior to and 3 weeks post parturition. This is the period where the metabolic demand is at its peak for the growth and maintenance of the foetus and lactation during prepartum and postpartum period, respectively. In this context, we aimed to provide the hematobiochemical changes in a cow during transition period.

Keywords: hematobiochemical, cow, transition period

Introduction
Transition cow is generally considered three weeks prepartum until three weeks postpartum. During this period, animals have higher metabolic demands as well as huge stress. Monitoring animal during this period is of prime importance as their immunity is low and they are susceptible for various metabolic disorders like milk fever, ketosis and many more. Hematological parameters are one of the vital sources of information since many decades which helps in monitoring the health status of the animal at individual level or at herd level. Hematobiochemical profile depends of variety of factors such as breed, sex, season, age and physiological stage of the animal. The fast-growing fetus in late gestation can cause reducing the abdominal space and decreased dry matter intake in dam resulting in increasing the pressure on the digestive system and the animal moves to negative energy balance stage (Bell, 1995, Kaufman *et al*., 2017) [6, 33]. During this phase mobilization of the body fat to meet the deficient energy (Drackley, 1999) [14] results in greater accumulation of NEFA, further increases uptake by liver, leads to grater accumulation of triglycerides in hepatocytes. Finally, it leads to fatty liver which increase the risk of postpartum disturbances in cows (Paiano *et al*., 2020, Sheehy *et al*., 2017; Herdt 2000) [51, 64, 25]. Thus, in order to avoid errors in diagnosis, the knowledge of the haemato-biochemical profile during transition period will be helpful in diagnosis and prevention of metabolic disorders.

Hematology
Hematology is highly informative as diagnostic tool in veterinary medicine, not solely but in combination with clinical examination or other diagnostic procedures (Ronald *et al*., 2014) [58]. Investigation of hemogram along with biochemical profiling in prepartum period will be helpful in predicting prepartum cow susceptibility to production diseases (Kevin and Ellen, 2012) [35]. While, Hematological parameters in postpartum period reflect the adoptability of the cow to physiological change i.e. from non-lactation to lactation. The RBC, Hb and immunoglobulin levels are reduced during prepartum period and increases immediately after calving, which is mainly associated with foetal growth (13-15). Joshi *et al.* (2018) [31] reported RBC count increases non-significantly (6.77×106/µL to 6.94×106/µL) on day 7 prepartum as compared to day 15 prepartum (6.87× 106/µL). Oliveira *et al*. (2019) [49] also reported that there was non- significant increase in RBC count (8.78×106/µL to 9.11×106/µL) of Nellore cows from prepartum to parturition. This high production of RBC count may be due to higher metabolic demands of foetus. Always in general RBC count is associated with the need for the oxygen demand, as the oxygen demand increases the amount of RBC count also increases resulting in the release of erythropoietin by kidney tissue. Another elucidation that fits the situation evidenced for the RBC counts at calving is the possible hemoconcentration not only by the reduction in water intake but also by the greater spleen contraction (Van Soest and Blosser, 1954) [72]. Gaven, *et al*. (2010) [20] reported that reduction of RBC count was due to deficiency of iron during prepartum period. Stirnimann *et al*. (1974) [67] also reported that RBC

count was significantly higher until two weeks after calving, than before calving. Wiss and wardrop (2010) [73] reported that this elevation of RBC is due to erythrocytosis at the time of uterine involution and circulatory endocrine changes. Contradictorily, Mehere *et al*. (2002) [45] reported lower values of erythrocyte count in postpartum period non-significantly from day of calving to four weeks postpartum (6.72 ×106/µL vs. 5.90 ×106/µL). This was due to over production of adrenaline due to stress of parturition or higher level of estrogen concentration after parturition and milk production stress.

The physiological mean value of Hb reported earlier in the literature was ranged between 8 and15 g/dl in cattle (Feldman *et al*., 2000) [18]. Oliveira *et al*. (2019) [49] reported that Hb concentration was significantly higher in prepartum (14.43 g/L) when compared to parturition or postpartum (13.45 g/L, 13.34 g/L). This increased hemoglobin level in prepartum is due to increased oxygen flow to gravid uterus for foetal growth (Abud *et al*., 2016) [1] and decreased rate of erythropoiesis (Klinkon, 1993) [38]. Mir *et al*. (2008) [47] reported significantly decreased mean Hb (g/dl) in prepartum period when compared to mid-stage of pregnancy (9.21+0.28 vs. 10.01+0.22). This was due to the dilution of blood which occurs as a consequence of the increase of plasma volume (Singh *et al*., 1991) [65]. Joshi *et al*. (2018) [31] reported that, after calving Hb was reduced significantly from the day of calving to 30 days postpartum (10.87 g/dL vs. 10.15 g/dL). In early post-partum period, lower Hb is due to a decreased rate of erythropoiesis, anemia or increased Hb requirement of mammary tissues for milk synthesis and concomitant rise in blood flow to mammary glands (Kumar and Pachauri, 2000) [40].

Number of WBC in blood is a sign of health status of the animal thus it is an important subset of the complete blood count. Impaired function of white blood cells at the time of calving reduces the immunity (Klinkon, 1999) [39]. Percentages of each white blood cell count are also affected by mammary gland extensive influx of neutrophils into the colostrum around parturition. Kim *et al*. (2005) [37] reported that significant increase in total leucocyte count, lymphocyte and neutrophil percentage in late pregnancy. Elshahawy and Abdullaziz (2017) [17] also reported that WBC count was significantly higher in prepartum period than the postpartum period (12.25 ± 0.46 vs 10.93 + 1.96). Joksimovic *et al*. (2012) [30] stated that significantly higher leucocyte count on the day of parturition (9.26 ± 3.04×109/ L) when compared to 15 days prior to calving (7.16 ± 1.87×109/ L. The highest WBC count was due to elevation is mediated by of serum cortisol level around partition, which stimulates agents for increased neutrophil percent. Klinkon and Zadnik (1999) [39] reported that the lowest mean absolute value for monocytes was constant during pregnancy and decrease slightly in the last month of pregnancy (213+136 vs 224+157).This was due to the migration of monocytes from circulation to tissues and undergo converting macrophages to provide immunity at the time of parturition stress. Schalm and Jain (1986) [62] reported that pregnancy did not affect the number of eosinophil (%), Basophil (%). Joshi *et al*., 2018 [31] reported that platelet count (×10 6/µL) non-significantly decreases at 15 d prior to calving to calving day (320.33+ 21.69 vs 300.67 + 34.81).

RBC indices include mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentrations (MCHC) are helpful in diagnosing different types of anemia. Anemic conditions are inevitable in prepartum animals. Gaven *et al*. (2010) [20] also reported that no significant difference was observed for erythrocyte indices during the prepartum period but iron deficiency might be the cause for a slight non-significant reduction in MCV, MCH.

Gut health (Liver/Kidney/Pancreas)

Gut health comprises a healthy upper and lower gastro intestinal tract. However, other organs like liver, pancreas, spleen are also associated with gut health. A healthy gut contributes to a strong immune system and improves the production of animal. In gut health assessment liver function can be assessed by various enzymes like aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), alanine aminotransferase (ALT). All these liver enzymes suggest the process of lipid mobilization. AST is a hepatocellular leakage enzyme used as a marker efficiently for hepatic lipidosis and catalyzes the transamination of L-aspartate and 2-oxoglutarate to oxaloacetate and glutamate. AST concentration depends on the function of the liver, skeletal muscle and cardiac muscle of dairy cows. The normal activity of AST in blood is 78 to 132 U/L in healthy cattle (Ingvartsen 2006) [27]. Pechova and Halouzka (1997) [52] reported that blood concentration of liver enzymes is positively correlated with the degree of liver infiltration. Van saun *et al*. (2005) [71] reported that the AST level after calving was significantly higher (P<0.0001) in fresh cows than the prepartum period (75.7 vs. 123.2 IU/L). The highest activity of AST was documented during the first week after calving, as lactation progresses AST activity decreases (Etilok *et al*., 2006) [15]. Enrico *et al*., (2005) stated that increase activity of AST during the postpartum period than prepartum period was considered as an indicator for hepatic steatosis (78.54 vs. 118.24 IU/L). During early lactation, 5-10% of high yielding dairy cows suffer from severe hepatosis and 30-40% cows suffer from mild hepatosis. Fat infiltration to liver or injury to the liver tissue increase the level of these enzymes (AST, GGT) that indicate liver injury is generally augmented. When AST concentration reaches higher than 100 IU/L, that indicates hepatic lesions (Bobe *et al*., 2004) [8]. Gonzalez *et al*. (2010) observed negative correlation between AST activity and NEFA values with a significant correlation coefficient (r=-0.46). Ballard *et al*. (2001) [5] reported that using energetic supplementation during transition period in dairy cows had no effect on AST activity during postpartum period (82.2 U/L vs. 79.2 U/L). Mikula *et al*. (2008) [46] conducted a research by top dressing of 400g of glycerol supplementation from 14 d prior calving to till calving. They reported that AST activity was significantly low (P<0.01) in glycerol supplemented group on 56 d lactation (59.5 U/L vs. 89.8 U/L) and on 70 d lactation (40 U/L vs. 93.9 U/L) when compared with control group. There was no significant difference of GGT in control and glycerol supplemented group. Hodemaker *et al*. (2004) [26] conducted a research on peripartal propylene glycerol supplementation in dairy cows. They found that AST activity was not affected by glycerol administration when compared to control group. But they observed increased activity of AST with in physiological range during first 2 wks of postpartum in both groups. This could be due to adjustment of the liver cells turnover rate to the increased metabolic demands during early lactation (Bostedt, 1974) [10]. Seifi *et al*. (2007) [63] reported that AST level was lowest 22 d before calving (46.41 IU/L) when compared to 21 d postpartum (63.30 IU/L). Steen *et al*. (1997) [66] observed that AST level in cows were significantly higher in fatty liver (400 IU/L) and ketosis group

(240 IU/L) when compared with the control group (60 IU/L). This might be the fact that, fatty liver infiltration and liver cells degeneration involve in liver cell membrane damage and destruction cytoplasmic enzyme release and elevated concentration in blood (Lubojacka *et al*., 2005) [43].

Alanine aminotransferase (ALT) activity in cows differs during certain production periods. The normal range of ALT is 11- 40 U/L (Ingvartsen 2006) [27]. In the dry period enzyme activity decreased, but it was still statistically much higher than in the first period of lactation. Generally, the lowest ALT activity was measured during early lactation, while activity increased in the second and third periods of lactation. Tainturier *et al*. (1984) [69] also in their study presented that ALT activity decreased in the seventh and eighth months of pregnancy and that it remained stable until the end of pregnancy, and in the first month of lactation. Stojevic *et al*. (2005) [68] also stated that the activity of ALT decreased in the dry period but it was statistically higher than the first period of lactation (11.84 vs. 8.91 IU/L). They considered that the role of ALT in predicting liver diseases was not significant. Kupczynski *et al*. (2011) [41] conducted an experimental trail by feeding 300 ml of glycerin /d to TMR from 7d prepartum to 3 wk postpartum. They inferred that ALT activity was increased significantly (P<0.05) in treatment group when compared with control group. Bhimte *et al*. (2018) [7] stated that mineral and vitamin supplementation (Zn, Cu, Se and Vit. E) from 28 d prepartum to 56 d postpartum period had significantly lowered the AST, ALT activity in postpartum treatment group when compared to non-supplemented group (P< 0.05). This could be due to reduced DMI around parturition increased the activity of transaminase activity in non- supplemented group, increased transaminase enzyme activity indicated that stress and liver damage status (Sattler and Fürll, 2004) [61].

Gamma-glutamyl transferase (GGT) is a membrane-bound enzyme in organs with accentuated functions in secretion and resorption in body. In the plasma it is vital sign of hepatobiliary system diseases connected with cholestasis and is used in diagnosing liver disease. Its activity is relatively high in livers of cows, horses, sheep and goats (Tenant, 1997) [70]. The normal range of GGT is 6.1- 17.4 U/L (Ingvartsen 2006) [27]. GGT is considered as valuable biomarker of cholestasis or hepatic damage. Moreira *et al*. (2012) [48] stated that GGT concentration level was significantly higher (P>0.05) in the animals with hepatic histopathological injuries (23±14UI/L) compared to those without hepatic damage (18±9UI/L). The GGT values were significant increase (P<0.05) on day 0, at 1st wk after parturition (18.4, 19.1 IU/L) when compared with 1 wk prior to parturition (17.2 IU/L).

Generally serum total protein, albumin and urea are indicators of diet protein intake (Toharmat *et al*., 1999) [70]. As parturition approaches serum total proteins in dam usually decreases. This may be due to the fetus synthesizes all its proteins from the amino acids which are derived from the dam and fetal muscle growth reaching its maximum size at last trimester of pregnancy (Jainudee, and Hafez, 1994) [28]. Albumin is synthesized in the liver; lower serum albumin is indicative of the impaired function of the liver. The reference range of Protein, albumin concentration is approximately5.7-8.1g/Dl and 2.1-3.6 g/DL. Physiological or pathologic conditions can cause shifts in albumin and globulin concentrations and their evaluation is a valuable diagnostic tool (Alberghina *et al*. 2011) [3]. Sateesh *et al*. (2018) [60] also reported that total protein in the prepartum period and at the time of calving was significantly lower (6.58+0.22, 6.75+0.29 g/dl) when compared to the healthy control group and (7.01+0.14 g/dl). A sudden drop in total protein as calving approaches may be due to drain of immune fraction in the form of colostrum. Prodanovic *et al*. (2012) [55] also stated that the average concentration of total protein during 7d prior to calving and on 60 d of lactation (69.59±6.14 g/l to 67.71±8.10) were significantly higher (P<0.001) in comparison with the values obtained during 7d after caving (58.87±3.29 g/l). Yousuf *et al*. (2016) [74] reported a high level of total protein was observed after 2 months of calving when compared with the prepartum period (79.9 g/L vs. 60 g/L). Piccoine *et al*. (2011) reported that albumin concentration was similar thorough prepartum period with a small increase in concentration at calving (2.95 g/DL to 3.15g/dL). The insignificant increase of albumin at calving could be due to higher albumin synthesis by the liver or to a decrease of plasma volume masked by hypoglobulinaemia. Seifi (2007) [63] reported that the lowest albumin was found on d 8 postpartum (29.2 g/L) when compared to 8d prepartum (35.5 g/L) in transition cow. This might be due to decreased synthesis of albumin by the liver or due to loss of albumin into gut or through milk or increased catabolism of albumin. In contrast, Bossaert *et al*. (2012) [9] stated that concentration of albumin decreases around calving and increases in the postpartum period. This might be due to a decrease in the total pool of decreased Ca in prepartum partially linked to albumin concentration (Seifi *et al.*, 2005). Serum globulins also shows a significant decrease during transition period, which associated mainly with the production of colostrum that rich in antibodies that derived from γ-globulins and other immunological changes occurred around parturition (Janku *et al.*, 2011). Khalili *et al*. (2011) [36] conducted a study to evaluate the effect of chromium methionine supplementation on serum biochemistry of cows. They inferred that 5g Cr-methionine supplementation from 5wk prior to parturition till 12 wk postpartum resulted in increase in total protein of serum when compared to control. This could be due to increase of insulin sensitivity to tissues, where insulin is proven at increase synthesis of proteins (Roginski and Mertz, 1969) [57]. In contrast, keglay *et al*. (1997) [34] reported that Cr supplementation had no effect on total protein concentration. Bhimete *et al*. (2018) [7] conducted a research to investigate the effect of antioxidant (Vit. E), minerals (Se, Zn, Cu) and high energy diet supplementation on serum biochemical parameters. They reported that total protein concentration (4.7 vs.5.8 mg/dL) and albumin concentration (3.4 vs. 3.7 mg/dL) was significantly low in non-supplemented group when compared with supplemented group (4.7 vs.5.8 mg/dL) in postpartum period. The lower concentration of serum total protein could be due to reduced DMI, metabolic stress and postpartum NEB which increases utilization of proteins as amino acids due to increased requirements of mammary gland. Whereas, mineral supplementation reduced protein catabolism by mitigating oxidative stress.

An accelerated rate of protein catabolism than the excretion rate of urea in cows causes an increase in urea concentration in blood (Kaneko *et al*., 2008) [32]. Taintuier *et al*. (1984) [69] reported that during pregnancy serum urea concentration remained nearly constant (1.67 - 1.94 mmol/L) after calving increased significantly in the postpartum period (4.40 mmol/L) and returned prepartum range in the second month. Macrae *et al*. (2006) [44] collected blood samples from 35,500 cows and reported that on -10 d of calving 20.5% of cows had low blood urea concentration (<1.7 mmol/L). This reason behind this might be low DMI in prepartum or deficit in effectively rumen degradable protein. In contrast, Piao *et al*. (2015) [53] stated that urea level in blood was increased significantly (P<0.05) from early pregnancy (4 ~ 18.1 mg/dl) to late pregnancy (4.7~17.9 mg/dl). This is due to increased protein intake in the prepartum diet. Gerardo *et al*. (2009) [21] stated that blood urea concentration was significantly lower in the first lactation when compared with the second lactation in both pre and postpartum.

Creatinine in blood is an important marker for kidney function. It is the breakdown product of creatinine phosphate from muscle and protein metabolism. A significantly higher concentration of creatinine was observed in the serum of late pregnant heifers (1.16 mg/dl) compared with primiparous and multiparous dry cows (1.04 mg/dl). This was due to higher relative muscle mass in heifers considering that almost all creatinine is released by the striated muscle (Brscic *et al*., 2015) [11]. Piccione *et al*. (2012) [54] reported that a higher level of serum creatinine in late gestation (1.21 mg/dL) when compared to the second week of lactation (0.99 mg/dL). This might be due to increased serum creatinine level could be attributed to the development of foetal musculature (Roubies *et al*., 2006) [59].

The level of serum/plasma cholesterol was considered as an indirect index of liver function in periparturient cow (Alamouti *et al*., 2009) [2]. In prepartum cow as a result of lipid mobilization free fatty acids reach the liver and re-esterified into triglycerides and subsequently transported as low density lipoproteins. Cholesterol occurs in blood as a part of lipoproteins. Low-density lipoproteins are accountable for transporting the cholesterol to peripheral tissue. The reduction in the serum cholesterol causes the synthesis of low-density lipoproteins from hepatocytes (Bruss., 1997) [12]. Djokovic *et al*. (2015) [13] evaluated that serum cholesterol concentration was low during late pregnancy (3.3 mmol/L) when compared to the mid-lactation period (5.3 mmol/L). Bossaert *et al*. (2012) [9] reported that low cholesterol (1.7mmol/L) at 9d prior to calving, when compared with 21 d after caving (3.7 mmol/L), might be due to inflammatory changes and associated acute phase protein response during this period. High serum cholesterol concentration in prepartum was probably due to decrease catabolism of triglycerides or increased lipolysis. Formigoni *et al*. (1996) [19] conducted a research to evaluate the effect of propylene glycol administration in transition cows. Propylene glycol (300g) was administered directly mixed with the diet from d 10 prior to calving until parturition and diluting in the water on days 3, 6, 9 and 12 days after calving in treatment group and non-supplemented group. Propylene glycol administration increased total cholesterol level significantly (P<0.05) by the treatment at d 25 and 50 postpartum than non-supplemented group (1.63 mg/ml vs. 1.90 mg/ ml). Similar results was obtained by Kupczynski *et al*. (2011) [41] upon glycerol administration (300ml/d) from 7d prior to calving until 3 wk postpartum period significantly increased total cholesterol level (P<0.05) in supplemented group when compared to non- supplemented group (3.02 vs. 1.95 mmol/L) during postpartum period. Significantly high total cholesterol level in treatment group suggests that energy balance was improved by propylene glycol administration. Depression in hepatic total cholesterol synthesis was induced by lower DMI (Reid *et al*., 1983) [56].

Piccione *et al*. (2012) [54] reported that serum triglyceride concentration significantly decreased (P<0.001) when compared prepartum (14.83 mg/dL) to postpartum (9.83 mg/dL). Hormonal changed, lipogenesis, lipolysis is regulated to increase lipid reserve during pregnancy and these reserves are utilized for lactation. Seifi *et al* (2007) [63] reported that triglyceride concentration was significantly low (P<0.001) in postpartum (0.02 mmol/L) when compared to prepartum (0.20 mmol/L). Mammary gland uptake of triglycerides for milk production reduced the serum triglyceride concentration.

Conclusion

Assessment of hematobiochemical parameters during pre-partum and post- partum period gives us and idea about the metabolic health of the animal. Based on these findings one could design proper nutritional manipulations as well as prophylactic treatment strategies to prevent the metabolic disorders and improve the production in dairy animals.

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