The dairy industry in Sudan is based on native breeds, crossbreeds and pure exogenous imported cattle. Development of effective management strategies to alleviate the adverse effects of physiological status and impacts of thermal and nutritional stresses requires basic and applied research work. In dairy cows, the periparturient period presents major physiological challenges as it is affected by metabolic stressors and changes in endocrine status and immune function which result in increased risk of diseases. The objective of this study was to evaluate the physiological changes which occur during the periparturient period in crossbred dairy cows. It was also intended to provide information regarding the potentials of supplementation with vitamins and selenium during the transition period. Twenty-four clinically healthy cows were assigned to 3 groups of 8 cows each, a control group and two treated groups, which received parenterally vitamin E and selenium (Vit. E + Se) or multivitamins: A, D and E (MY). The cows were monitored for 8 weeks before and 4 weeks after calving. The postpartum decrease in body weight of cows was more pronounced in the control group. The calf birth weight was significantly higher in the supplemented groups. PCV and Hb concentration decreased during the periparturient period; cows supplemented with Vit E + Se had higher PCV values during the transition period. The total leukocyte count (TLC), neutrophil and eosinophil ratios increased, whereas lymphocyte ratio decreased at parturition and postpartum period. Supplementation with vitamins and Se decreased TLC, neutrophil and eosinophil ratios and increased lymphocyte ratio. Plasma total protein, albumin and urea levels decreased at parturition, the decrease was more pronounced in the control group. The triglyceride and cholesterol levels decreased at parturition and postpartum period with no effect of supplementation. Plasma Na increased at parturition and decreased postpartum in all experimental groups. Plasma P decreased at parturition and increased postpartum. Plasma Mg decreased at parturition and postpartum in all experimental groups. The activity of transferase enzymes (AST and ALT) increased at parturition with no effect of supplementation. Plasma insulin decreased at parturition in all experimental groups. The information generated could be used in monitoring the nutritional status and health of dairy cows. Antioxidants, including vitamins and Se, could be used to confer protection and enhance immunity of cows, particularly during the transition period, characterized by metabolic stress and immunosuppression.