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Original article

EVALUATION OF SOME METABOLIC PROFILE PARAMETERS IN TRANSITION COWS: THRESHOLDS FOR ESTIMATING POSTPARTUM DISEASES IN AYDIN PROVINCE

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Summary

Erdoğan, S. & K. Ural, 2021. Evaluation of some metabolic profile parameters in transition cows: thresholds for estimating postpartum diseases in Aydin province. *Bulg. J. Vet. Med.,* **24**, No 1, 108–118.

This study aimed to evaluate non-esterified fatty acids (NEFA), beta hydroxybutyric acid (BHBA), magnesium (Mg^{2+}), calcium (Ca^{2+}) and lactate as biological tests for the detection of some metabolic diseases during transition period in selected dairy farms located in Aydın province. Cow-side analysis with body condition score evalutation were performed weekly in at least 12 dairy cattle from each farm from prepartum week 2 to postpartum week 2. According to the prepartum NEFA ≥0.4 mmol/L, postpartum BHBA ≥1.4 mmol/L and Ca^{2+} ≤ 2.0 mmol/L at parturition (day 0) in herd-based evaluation, it was observed that all farms were positively evaluated for negative energy balance and also at risk for subclinical hypocalcaemia. Regarding the threshold value of Mg^{2+} <0.61 mmol/L, subclinical hypomagnesaemia was observed at the I^{st} and II^{nd} farms. It was concluded that prepartum NEFA threshold (0.68 mmol/L), obtained from the receiver operating characteristics statistical analysis could be used for observing some postpartum clinical diseases. It was suggested that it allowed planning and strategic interventions to prevent herd-based diseases in Turkey and will be a precedent for future studies and herd management.

Key words: dairy cattle, metabolic disorders, metabolic profile, threshold value, transition period

INTRODUCTION

Most of the transitional disorders occur due to the inadequacy of certain metabolic elements. In the last weeks of pregnancy, the decrease in dry matter intake and the failure to meet required energy demand (Drackley *et al.,* 2005) resulted in a negative energy balance (NEB) (Leslie *et al.,* 2004; LeBlanc, 2010).

Metabolic profile in transition period is defined as identifying metabolic dynamics of parturition cows to determine metabolic and infectious disease in the herd (Payne *et al.,* 1970). Within this context, concentrations of one of the most emphasised parameters: non-esterified fatty acids (NEFA) and beta hydroxybu-

tyric acid (BHBA) have reflected the magnitude of the amount of fatty acids mobilised from adipose tissues and the oxidation capacity of fatty acids in liver, respectively (Duffield & LeBlanc, 2009; Asl *et al.,* 2011; Chapinal *et al.,* 2012a,b; McArt *et al.,* 2013; Chalmeh *et al.,* 2015). On the other hand many different parameters can be examined within a metabolic profile during the transition period (Seifi *et al.,* 2003; Duffield & LeBlanc, 2009).

Herd based metabolic profiles support the identification of risk factors rather than the diagnosis and can assist the monitoring of subclinical diseases (Oetzel, 2003; Van Saun, 2006; Guyot, 2015). In this aspect, it is important to follow out some biochemical parameters in the transition period in terms of prevention or early intervention of the diseases in the herd (Duffield & LeBlanc, 2009).

There are differences between herd-based evaluation and interpretation of results and individual disease diagnosis although the methods are similar. It is stated that evaluation of samples based on herd rather than individual are more reasonable and feasible for nutrition and management strategies to increase animal welfare (Chapinal *et al.,* 2012a,b). A prior and valuable review indicated that explication of herd analysis regarding metabolic disorders is non-identical within individual testing. Obtained values for individual interpretation could be matched with reference ranges (for healthy cows) of the operator lab (Oetzel, 2003; 2004; 2005; Friedrichs *et al.,* 2012).

This study was aimed to determine the threshold values of some biological blood analytes including NEFA, BHBA, magnesium (Mg^{2+}), calcium (Ca^{2+}) and lactate and evaluate metabolic diseases on herd basis with body condition alteration of transition period in some dairy cattle farms in Aydın province. This is the first study evaluating all of the mentioned parameters together cow-side on herd-based. Also, it was targeted to serve as a model to further studies to be performed with larger populations in our country.

MATERIALS AND METHODS

Animals and farms selection

As a part of the study, three different dairy farms located in Aydın province with 1) ≥250 dairy cattle, 2) freestall housing, 3) total mix ration (TMR) feeding and/or 4) dairy herd improvement programmes were enrolled as described by Ospina *et al.* (2010). A total of 37 clinically healthy primaparous (n=11) and multiparous (n=26) transition cows from different breeds (farms I and II reared Holstein, farm III reared Simmental), body weight and ages (2–8 years of age) were included in the study with at minimum 12 cows in each farm located in Aydın Province, Turkey. On that note, herd-based cow numbers for each farm was determined to be 10–12 cows according to other studies (LeBlanc *et al.,* 2005; Oetzel, 2003;2004; Dohoo *et al.,* 2009). The number of cows in the farms was 500, 450 and 350 respectively. From the total of 37 cows included in the study, 14 were from farm I, 12 from farm II and 12 from farm III.

According to assessment form composed for each farm, animals in all farms with free-stall housing system were fed TMR prepared according to yield and lactation group after milking and milked twice a day (Table 1). TMR was formulated by zootechnicians in the first two farms. Although all animals participated in the study on a volunteer basis with consent from herd owners, ration content and formulations were not available to us.

Table 1. Data of farms

Farm I	Feed stuff	Silage, straw, dry alfalfa, soybean straw, cottonseed, full-fat soybean, wheat, barley and corn grain, oil meal, $CaCO_3$, MgO	
	Feeding type	Total mix ration	
	Feeding hours	Morning (6:30 a.m.)	Evening (3:30 p.m)
Farm II	Feed stuff	Alfalfa, straw, barley pulp, silage, compound feed	
	Feeding type	Total mix ration	
	Feeding hours	Morning (5:00 a.m.)	Evening (4 p.m.)
Farm III	Feed stuff	Silage, grass, straw, alfalfa, concentrated pellet feed	
	Feeding type	Total mix ration	
	Feeding hours	Morning (7:00 a.m.)	Evening (7:00 p.m.)

Each farm was visited weekly starting from the first three weeks of close dry period to fourth week postpartum.

Blood sampling

Blood samples (4 mL) were collected in anticoagulated tubes with both lithium-heparin and K_3EDTA from *Vena coccygea* 6–8 hours after early feeding at prepartum (-2^{nd} and -1^{st} week), parturition (day 0) and postpartum ($+1^{st}$ and $+2^{nd}$ week) periods. Plasma from samples with lithium-heparin was separated by means of mini centrifuge device (Sprout, Healthrow Scientific, USA) within 5 min at 6000 rpm immediately after samples were collected.

BHBA analysis of fresh blood samples with K_3EDTA were performed shortly after taking by cow-side with handheld Vet TD-4235 β-Keto device (Antalya, Turkey) based on the amperometric method. Measurements of other metabolic analytes: NEFA, Mg^{2+}, Ca^{2+} and lactate were done from heparinised plasma with cow-side device Vet Photometer 700 DP (Diaglobal, Germany) at 520 nm wavelength by enzymatic colorimetric spectrometric method. All of the processes were established in the farm with provided optimum temperature conditions.

Body condition scoring (BCS)

After cows were taken to feed fences, the classical BCS were evaluated using a 5-point scoring system as described by Edmonson *et al.* (1989) combined with 0.25 point intermittent scoring system developed by Ferguson *et al.* (1996).

Measurement of fat reserves in the body via palpating and evaluating pointedness and coating of the major three regions (loin, pelvis and tail head) were scored with 1–5 points as per Edmonson *et al.* (1989). Unlike the classical 5-point scoring system, with the other method (Ferguson *et al.,* 1996) evaluation of the fat tissue in the indicated regions was done according to the subclassifications of the two groups determined as 3.0 and above with 0.25 interval points.

Postpartum disease follow-up

In a herd based interpretation, ketosis was determined based on standard data describing the disease – positive ketone test in urine with decreased appetite and milk yield as well as BHBA assessment within study, metritis; decreased appetite, lethargy, decrease in milk yield, higher >39.5 °C body temperature and purulent or red to brown discharge from the vulva until

postpartum day 21 (Sheldon *et al.,* 2006), retained foetal membranes; failure to remove foetal membranes within 24 hours after parturition, mastitis; abnormal milk, hardening or inflammation in the udder (LeBlanc *et al.,* 2002), lameness; restricted movement, difficulty in lying or standing, longer lying times, gait irregularities, changed claw structure (Maas, 2009; Calderon & Cook, 2011). Above mentioned diseases were monitored during 2 weeks after parturition.

Statistical evaluation

Receiver operating characteristics (ROC) curve method was used to define the threshold (cut-off point) values of mentioned biological blood parameters. The area under the curve (AUC) was used in the interpretation of the threshold value for predicting some clinical postpartum diseases. Maximum specificity and sensitivity were used to evaluate the critical threshold in the ROC curve (Greiner *et al.,* 2000). AUC=0.5 was interpreted as noninformative, 0.5<AUC ≤0.7 was accurate, 0.7<AUC≤0.9 was very accurate, 0.9<AUC<1 was highly accurate and lastly AUC=1 was perfect for predicting of diseases (Swets, 1988).

Herd-based interpretation of some subclinical diseases

Herd-based cut-off point and alarm levels of important transition subclinical metabolic diseases comprising ketosis, hypocalcaemia and hypomagnesaemia were determined according to literature data contrarily to our determined threshold values. To determine the NEB, prepartum NEFA cut-off point of ≥0.400 mmol/L and alarm level of >10% (Oetzel, 2003; Cook *et al.,* 2006) with postpartum NEFA cut-off point of ≥0.70 mmol/L and alarm level of >15% were used (Ospina *et al.,* 2013). For herd-based evaluating of the subclinical ketosis (SCK), postpartum BHBA ≥1.4 mmol/L as gold standard measurement along with NEFA, and alarm level of >10% were considered (Oetzel, 2003; Cook *et al.,* 2006). It was stated that cut-off point of Ca^{2+} of ≤2.0 mmol/L indicated subclinical hypocalcemia (SCH) (Oetzel, 2003; Cook *et al.,* 2006), and blood Mg^{2+} <0.61 mmol/L: subclinical hypomagnesaemia (SCM) (Feyter *et al.,* 1986; Goff, 2006). Even as Ca^{2+} analysis of the first postpartum 24–48 hours (Oetzel, 2003) and Mg^{2+} analysis of the first postpartum 12–24 hours (Goff, 2006) were indicated in the literature, we used parturition values (at postpartum first 24 hours) of

Table 2. Cut-off point and alarm levels of subclinical diseases to used herd-based evaluation (Feyter *et al.*, 1986; Oetzel, 2003; Cook *et al.*, 2006; Ospina *et al*., 2013)

Biological parameters	Cut-off point	Alarm level (%)
NEFA (mmol/L)	≥ 0.40 mmol/L (prepartum)	10
	≥ 0.70 mmol/L (postpartum)	15
BHBA (mmol/L)	≥ 1.4 mmol/L (postpartum)	10
Ca^{2+} (mmol/L)	≤ 2.0 mmol/L (postpartum)	30
Mg^{2+} (mmol/L)	< 0.61 mmol/L (postpartum)	20

NEFA=non-esterified fatty acids, BHBA=beta hydroxybutyric acid.

these two parameters on herd-based evaluating of SCH and SCM due to weekly measurements in the study (Table 2).

Lactate was ignored in the evaluation of subclinical diseases due to the lack of literature data and insufficient number of samples to determine the relationship between lactate and subclinical diseases.

The herd-based evaluation of NEB and subclinical diseases comprising SCK, SCH and SCM was performed as positive, negative or borderline in accordance with the proportion of cows below (for SCK and SKH) or above (for NEB and SCK) aforementioned cut-off points with exceeding alarm levels (Oetzel, 2003;2004; Cook *et al.,* 2006).

Ethics Committee approval

This study approved by Adnan Menderes University Local Ethical Committee under certificate number: 64583101/2016/169 and financially supported by Adnan Menderes University, Research Funding Unit (ADÜ-BAP) with project no: VTF-17045.

RESULTS

Biological parameter cut-off points

Cut-off point and standard errors of blood biological tests are shown in Table 3. Maximum specificity and sensitivity evaluated the critical threshold in the ROC curve (Fig. 1). Cut-off point of NEFA with 0.36 mmol/L in prepartum ($P<0.01$) and 0.54 mmol/L in postpartum ($P<0.05$) cows was found to be significantly associated with biomarkers of postpartum clinical disease (Fig. 1, Table 3).

Herd-based interpretation of some subclinical diseases

It was found that prepartum NEFA values were higher than threshold for 12 cows in farm I, 3 cows in farm II and 5 cows in farm III at prepartum week 2 as well as for 9 cows in farm I, 8 in farm II and 4 in farm III at prepartum week 1. Considering the average prepartum NEFA values, it was determined that 10, 7 and 4 cows from farms I, II and III, respectively exceeded the threshold.

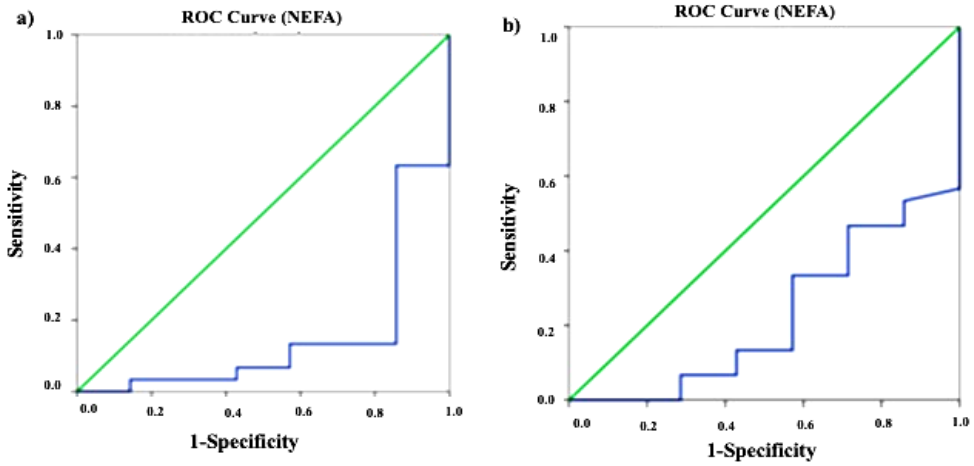

Fig. 1. Cut-off point of non-esterified fatty acids NEFA obtained by ROC analysis; A) prepartum NEFA, B) parturition NEFA ROC curve.

Table 3. Cut-off point (ROC values) and standard errors of the biological tests

Biological parameters	NEFA	BHBA	Ca^{2+}	Mg^{2+}	Lactate	BCS
Prepartum						
Cut-off point (ROC value)	0.36	0.63	1.10	0.31	0.66	3.19
AUC P value	0.004	0.304	0.642	0.068	0.394	0.151
Parturition						
Cut-off point (ROC value)	0.54	0.65	0.12	0.34	0.71	2.88
AUC P value	0.023	0.727	0.427	0.126	0.742	0.112
Postpartum						
Cut-off point (ROC value)	0.27	0.68	2.17	0.30	0.74	2.69
AUC P value	0.601	0.121	0.332	0.404	0.065	0.169

NEFA=non-esterified fatty acids; BHBA=beta hydroxybutyric acid; BCS=body condition score; AUC= the area under the curve.

Considering postpartum NEFA, 5 cows in farm I, 7 cows in farm II and 9 cows in farm III at postpartum week 1 as well as 4, 4 and 8 from farms I, II, and III respectively were found positive for postpartum subclinical diseases. With respect to mean postpartum NEFA values, NEFA concentration of 4, 6 and 8 cows from farms I, II and III were higher than postpartum cut-off points.

According to postpartum BHBA along with NEFA, SCK was found in 2 cows from farm I, 4 from farm II and 1 from farm III at postpartum week 1 and in 5, 4 and 1 cows at postpartum week 2, respectively. For both postpartum weeks, average BHBA levels higher than ≥1.4 mmol/L cut-off point were detected in 3 cows from farm I, 1 cow from farm II and 1 cow from farm III.

It was detected that Ca^{2+} values lower than ≤2.0 were present in 8 cows from farms I and II and 7 cows from farm III. Blood magnesium <0.61 mmol/L was identified in 6 cows from farm I, 11 cows from farm II and one cow from farm III. It was suggested that all 3 farms were at risk for SCH and the presence of SCM in the farms I and II may also be related to inappropriate feed ration and nutrition.

DISCUSSION

The aim of this study was to evaluate the levels of NEFA, BHBA, Mg^{2+}, Ca^{2+} and lactate being biological tests for selected metabolic diseases in dairy cattle herds in Aydın province.

In terms of practical application, individual cow-level cut-off point calculated in different studies (Chapinal *et al.,* 2011; 2012a,b) can be used for evaluating herd-based diseases when cow-level cut-off point exceeded the number of tested animals (Oetzel, 2003; Cook *et al.,* 2006). Although the confidence interval was determined as 95% with appropriate statistical methods, it is reported that lower confidence interval as result of retrospective studies and clinical experiences can be used (Oetzel, 2003; 2004; Duffield & LeBlanc, 2009; Caixeita *et al.,* 2015).

While ROC curve method was used to evaluate the subclinical diseases in our study, herd-based literature data (Oetzel, 2003, Cook *et al.,* 2006; Goff, 2006; Ospina *et al.,* 2013; Caixeta *et al*., 2015) were utilised considering the limited number of animals (37 cows) for interpretation of subclinical diseases.

Regarding elevated NEFA concentrations the prepartum NEFA cut-off point (0.36 mmol/L) obtained in our study was consistent with herd-based value and showed statistical significance (P=0.004). Taking into account that NEFA is a well-known biomarker of NEB in the prepartum period, values exceeding the 0.4 mmol/L cut-off points during last two weeks prepartum (Oetzel, 2003; Cook *et al.,* 2006) might be interpreted as altered levels.

Higher NEFA value (≥0.3 mmol/L) was found to be associated with postpartum metritis and retained placenta (Chapinal *et al.,* 2011). In our study, NEFA values during prepartum and fresh periods were determined to be 0.36 and 0.54 mmol/L, respectively and correlated statistically significantly with some postpartum reproductive diseases including clinical ketosis and lameness. Although one-to-one disease matching cannot be performed due to the limited number of samples (besides unofficial registration), NEFA value alterations at prepartum and postpartum (at herd level) were in accordance with prior studies (Oetzel, 2003; 2004; *Cook et al.,* 2006; Chapinal *et al.,* 2011; 2012a,b; Roberts *et al.,* 2012).

According to literature data based on clinical experience, it was stated that surpassing prepartum NEFA threshold of 0.4 mmol/L and pospartum BHBA of 1.4 mmol/L with 10% alarm level might be suggested in relation with herd level alterations (Oetzel, 2003;2004). Our data showed that the number of animals exceeding the prepartum NEFA threshold of 0.4 mmol/L was significantly higher than the 10% alarm-risk level. In our study, NEFA values during both prepartum weeks were higher as mentioned above. Truly, this was the condition for all three farms presenting NEB at postpartum level.

The Ca^{+2} threshold value used to define herd-based SCH occurring within the first postpartum 48 hours has changed to ≤ 2.1 mmol/L (Chapinal *et al.,* 2012b; Martinez *et al.,* 2012) and ≤2.0 mmol/L (Oetzel, 2003; 2004; Reinhardt *et al.,* 2011; Ospina *et al.,* 2013). It was stated that based on 30% alarm levels for herd-based SCH, herd was at risk if 2–5 animals of 12 cows were below the Ca^{+2} threshold and SCH was diagnosed if more than 5 animals met this criterion (Oetzel 2003; Cook *et al.,* 2006). In our study all farms were positive for SCH based on Ca^{2+} values at parturition. However Ca^{2+} values above the threshold at the first postpartum week were found to decrease. This situation might be related to the return of Ca^{2+} concentrations to normal values after the 4^{th} postpartum day (Melendez *et al.,* 2002).

Another subclinical herd-based evaluated disease – SCM, was diagnosed with cut-off point of <0.61 mmol/L with 20% alarm-risk levels of 12 animals (Feyter *et al.,* 1986; Goff, 2006). Magnesium deficiency in relationship to ration or decreased intestinal absorption (Herdt, 2000; Goff, 2006) has been well described. In this context, when the data in our study are interpreted on the herd basis, the presence of SCM was detected in the first and second farms. It was attributed to decreased absorption of volatile fatty acids because of insufficiently growing ruminal papillae due to not ensured ruminal adap-

tation and lower ruminal pH (Oetzel, 2003), decreased dry matter intake (Bell, 1995; Grossi, 2012) and increased magnesium demands (Piccione *et al.,* 2012), which, in transition period, might influence magnesium absorption. Also, the presence of SCM in both farms was linked to improper ration and feeding (Kronqvist, 2011).

In conclusion, existing studies on metabolic diseases in our country (Avcı, 2012; Akgül, 2014; Çatık, 2015; Özdamar, 2016; Şentürk *et al.,* 2016), were mostly related to prevelance and incidence of SCK on the basis of individual data without herd-based interpretation. It is therefore the first study elucidating metabolic alterations at herd based interpretation on cow side (field study). For this reason, the present study may be a pioneer in determining diseases and risk factors on a herd basis as mentioned before.

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