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A study investigating the relationship between milk urea nitrogen and the reproductive performance of Holstein cows

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ABSTRACT: Since protein is a fundamental component of dairy cows' diet, as well as its metabolites, it is critical to pay attention to milk urea nitrogen (MUN) in order to control the protein concentration in diet because it is one of the most prevalent compounds in milk. Hence, the present research evaluated MUN and its relationship with some reproductive performances and fertility of Holstein dairy cows. There were four groups of data concerning the reproductive and productive performance of large herds of dairy cows in Iran, including group 1) milk urea nitrogen (MUN) less than 12.96 mg/dl; group 2) MUN between 12.96 and 14.35 mg/dl; group 3) MUN between 14.35 and 15.88 mg/dl; and group 4) MUN over 15.88 mg/dl. Initially, a list of each dairy herd involved in Iran's DHI program was prepared, and 30 dairy herds with an excess of 1000 lactating cows were randomly selected. In order to mix the data on reproduction and milk composition, FoxPro 2.6 software was used. A statistical analysis of milk urea nitrogen and other independent variables was conducted through analysis of variance. The aforementioned results regarding the importance of reproduction and pregnancy rate in lactating cows and determining the appropriate concentration of milk urea nitrogen indicate that this parameter could be optimally used to control the protein-to-energy ratio and protein consumption of lactating cows in their diet.

Keywords: milk urea nitrogen (MUN); reproductive performance; fertility; Holstein

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INTRODUCTION

Although having adequate knowledge regarding factors impacting reproductive performance in dairy herds to manage reproduction effectively is imperative, such strategies are better harnessed when coupled with good management and nutritional strategies. As an example, performing higher concentration of protein in the diet of dairy cows will result in some damage to the performance such as a slight decrease in uterine pH, changes in uterine secretions, reduced embryo survival, and impaired embryonic development (Rajala-Schultz et al., 2001; Guo et al., 2004; Hojman et al., 2004). The mean of liver in order to detoxification of performed ammonia in the systemic circulation is production of urea, which is subsequently diffuses or is transported to other fluid pools in the body such as milk in the mammary gland and liquid in the rumen. The urea found in milk, called milk urea nitrogen (MUN), is correlated to BUN (Ruska & Junkens, 2014). The main dietary factors, including CP and energy percentages, affect the amount of urea in blood, plasma, urine, and milk (Roseler et al., 1993), indicating a clear positive correlation between urea and energy balance and possibly with the energy concentration of the milk (DePeters and Ferguson, 1992b; Cizuk & Gebregziabher 1994; Burgos et al. 2010). Monitoring Milk urea nitrogen (MUN) is a useful means for assessing protein nutrition and protein: energy synchronization in dairy cows (Butler et al., 1996; Broderick and Clayton, 1997; Kauffman and St-Pierre, 2001). Furthermore, the index is convenient and noninvasive and may be practical as a management tool to improve production efficiency (Godden et al., 2001a, b; Ayaşan et al., 2011). Existing hypotheses indicate that the higher MUN concentrations will impair either fertilization or embryonic development through either a direct effect of altering the uterine environment (Godden et al., 2001a, b; Garcia-Bojalil et al., 1994) or through an indirect influence on energy status (Godden et al., 2001a,b; Broderick and Clayton, 1997). Nonetheless, there are various recommendations for MUN concentration. For instance, according to Butler et al. (1996), it has been shown that a reduction of about 20% in conception rate in dairy cows will result in an MUN concentration higher than 19 mg/dL. On the other hand, surprisingly, Rajala-Schultz et al. (2001) suggested that an even lower MUN concentration (>15.4 mg/dL) is inversely associated with the rate of fertility in dairy cows. Yet, there is scarce information on the definite MUN concentration at which substantial im-

pairment of reproductive performance occurs. In this case, various fertility parameters, such as days open, also known as calving to conception interval, can easily be determined, which and is an appropriate in monitoring reproductive efficiency. All things considered, however, it is not clear how farmers should use this information or which MUN value is more associated with days open, i.e., if farmers are supposed to use the first MUN analysis after calving, the highest MUN value obtained from calving to conception, or the average MUN analyzed during days open. Thus, this study was performed with the main objective of evaluating the association of monthly MUN concentrations (first, mean, or maximum MUN) before conception and days open in high-producing dairy cows from commercial herds in Iran.

MATERIALS AND METHODS

Data extraction and population of interest

The data regarding production and reproduction performance of dairy cow herds in Iran were obtained from the breeding center of animal science. The list of all the dairy herds participating in Iran's DHI program was prepared at the beginning of the research, and 30 herds with a capacity of more than 1000 lactating dairy cows were randomly selected as representatives of Iran's herds. To measure the data of these herds, the livestock breeding center was referred.

Criteria of Planning

For this purpose, milk records, including MUN and reproduction parameters such as the number of inseminations, the number of births, and the number of were used.

Experimental groups

Mean monthly MUN levels were calculated for each cow during the pre-pregnancy and post-pregnancy periods and divided into four groups.

Parameters

They included insemination per pregnancy, conception rate (fertility percentage), days to first insemination, open days, abortion rate and calving interval.

Statistical model and analyzing of data

Firstly, FoxPro 2.6 software was used to combine the reproductive data (taken from the country's livestock breeding center) with the milk composition data (Alborz milk analysis). SAS software was used for statistical analysis of the data. To analyze the descrip-

tive statistics of the collected data related to the clinical and demographic characteristics of the cows under investigation, ratios, averages and standard deviations were calculated. As binary variables, pregnancy occurrence and non-pregnancy occurrence were scaled as “0” or “1” based on the presence or absence of each condition. A GLM procedure of SAS software (version 9.1) was used to determine the relationship between MUN concentration and births (1, 2 and more). Furthermore, the T-test was used to compare the different ranges of MUN.

RESULTS AND DISCUSSION

Milk urea nitrogen

Figure (1) illustrates the average concentration of milk urea nitrogen. The figure shows that milk urea nitrogen concentrations ranged between 12.15 and 17.50 mg/dl. The highest and lowest concentrations of milk urea nitrogen were related to the 26th herd and the 7th herd, respectively. The average concentration of milk urea nitrogen in pregnant and non-pregnant cows is given in Table (1). During the autumn and winter seasons, both pregnancy and non-pregnancy conditions have lower levels of MUN. Based on Table (1), pregnant cows have a lower average concentration of milk urea nitrogen than non-pregnant cows, but this difference is not statistically significant ($P=0.089$). In the first several weeks after calving,

multiparous cows (MP) have a negative energy balance more easily than primiparous cows (PP) because of insufficient feed intake and high milk production, which may lead to reduced reproductive activities (Gross et al., 2015). According to Jonker et al. (1998), there was a decline in MUN concentration as DIM progressed starting from the second month, which resulted in a similar curve for both MUN and milk yield. In this line, MUN could be augmented as a result of negative energy balance, which a common problem during the period of early lactation (Jorritsma et al., 2003). Additionally, Spicer et al. (2000) have demonstrated that MUN will grow and remain constant, respectively, throughout the first three weeks of lactation and the remaining time. This trend in MUN can be attributed to a number of variables, such as physiological changes and the declining metabolic needs of lactation (Ayaşan et al., 2011). Conversely, lactating cows with positive energy balance perform better reproductively than cows with negative energy balance. In the absence of a negative energy balance, milk urea nitrogen can be used to assess nutritional status and reproductive performance (Raboisson et al., 2017). There may also be environmental factors which contribute to the partial increase in milk urea nitrogen in young cows and heifers with high production, such as stress caused by childbirth and physiological-hormonal changes.

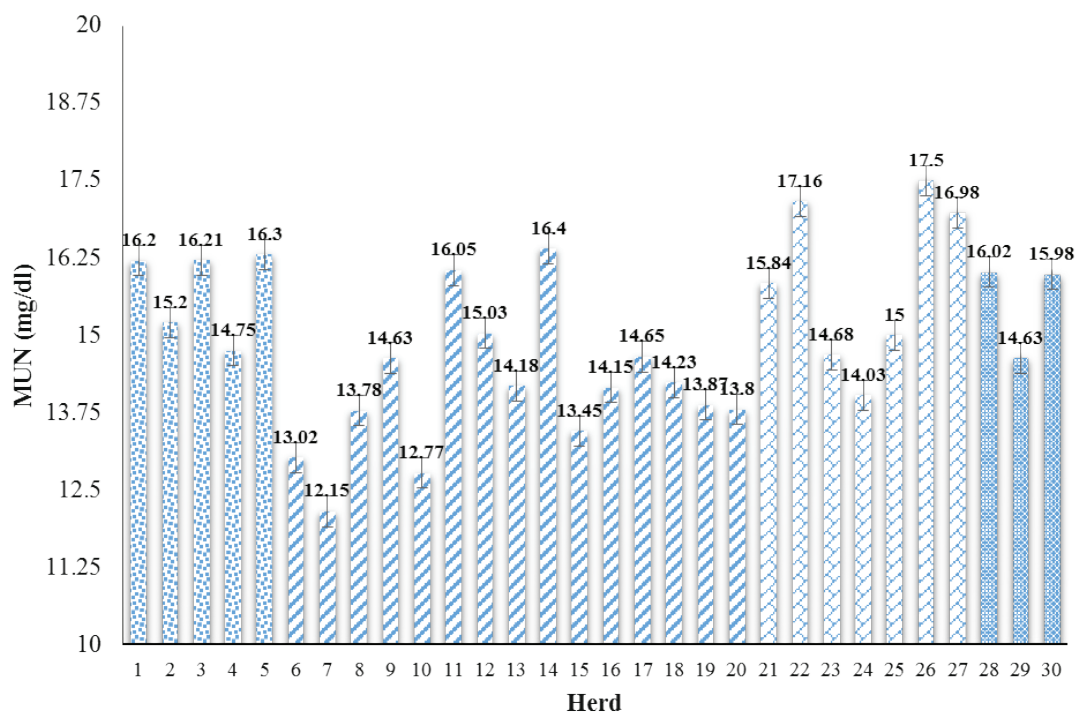


Figure (1) Average concentration of MUN in selected herds

Table 1. Results of logistic regression of selected dairy cows from 2019 to 2022

variable	Odds Ratio	Estimate \pm SE	(95%) Confidence interval	P-Value
MUN (mg/dl)				
MUN \geq 12.96	1	-	-	<0.05
14.38 < MUN < 12.96	2.81	0.13 \pm 1.1	0.1 - 76.55	-
15.88 < MUN < 14.38	1.64	0.08 \pm 0.76	0.0 - 63.90	-
MUN \geq 15.88	1.27	0.12 \pm 1.05	0.1 - 96.16	-
Parity				
1	1	1	-	<0.001
≤ 2	3.22	0.09 \pm 0.20	0.0 - 16.25	-
calving season				
1	1	-	-	< 0.05
2	1.02	0.09 \pm 0.19	0.0 - 14.22	-
3	1.36	0.07 \pm 0.35	0.0 - 26.44	-
4	1.68	0.12 \pm 0.69	0.0 - 51.88	-
Reproductive season				
1	1	-	-	< 0.001
2	1.02	0.09 \pm 0.26	0.0 - 14.23	-
3	2.93	0.12 \pm 0.67	0.0 - 60.76	-
4	3.18	0.66 \pm 0.91	0.0 - 14.79	-

1. 1) Spring; 2) Summer; 3) Autumn; 4) Winter

The possibility of abortion rate (OR) of multiparous (MP) cows increased (OR=2.95). The probability of abortion of cows that gave birth in the summer compared to cows that gave birth in the spring increased (OR=2.11). In general, cows that calve during the summer months are at a higher risk of abortion compared to cows that calve in the winter months (OR=2.11; CI%=0.56-0.95; and $P<0.001$). Two-way interaction between independent variables showed that the interaction between MUN and breeding season was statistically significant ($P\geq 0.01$). The results obtained in this study are consistent with other researchers' reports (Butler et al., 1996; Rangel et al., 2013; Munyaneza et al., 2017; Anand et al., 2019; SM et al., 2021). In the mentioned reports, there has been a remarkable negative relationship between concentration of BUN (>19 mg/dl) and the probability of pregnancy in cows. In accordance with our study, it has been found that changes of seasons and consequently fluctuation in weather condition would be affect the fertility and reproductive characteristics of dairy cows (Rajala-Schultz et al., 2001; Santos et al., 2009). These effects are mostly linked to seasonal variations in photoperiodic stimulation (Dahl et al., 2000) and fed ration quality (Rhodes et al., 2003). Furthermore, dairy producers frequently control the reproductive cycle of their herd such that calves occur during the colder months of the year in order to maximize the rate, as heat stress is more common from

the end of spring to the beginning of fall. In related to the effects of seasonal variations, it has been reported that cows who calve in the spring and winter, are more likely to undergo higher risks of anestrus (Walsh et al., 2007) or postponed postpartum ovulation (Opsomer et al., 2000). Altogether, these are potential explanations for the greatest period of days open observed in those cows that calved in spring. Besides, Godden et al. (2001) report a non-linear negative relationship between milk urea nitrogen and fertility, so that cows with a milk urea nitrogen concentration of 12.6 to 18.2 mg/dl have a lower fertility rate.

Fertility characteristics

Figure (2) illustrates the fertility rate in 4 categories of milk urea nitrogen. As seen in Figure (2), high milk urea nitrogen leads to a lower fertility rate. For instance, high MUN (14.38 mg/dl) compared to low MUN (12.96-38 mg/dl) has significantly reduced the fertility rate ($P=0.033$). In line with the study results, data indicate that there is a remarkable negative relationship between MUN and fertility rate (Butler et al., 1996; Fergousen et al., 1993; Rangel et al., 2013; Munyaneza et al., 2017). In a meta-analytical study, it was stated that MUN more than 19 mg/dl (Butler et al., 1996) or more than 15.4 mg/dl (Rajala-Schultz et al., 2001) in comparison with lower MUN (Raboisson et al., 2017) has significantly decreased the chances of cows being pregnant. Furthermore, Jannah et al.,

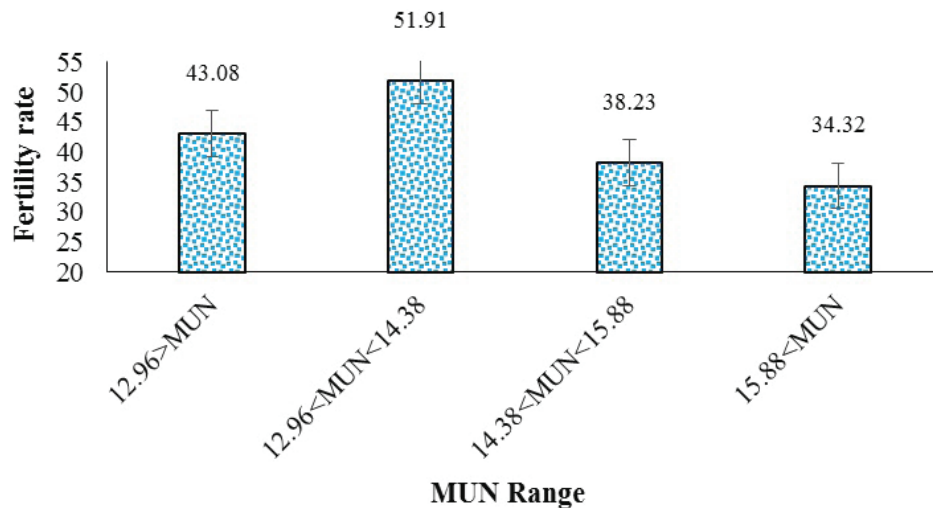


Figure (2) Fertility rate in 4 categories of MUN

(2019) reported a non-linear negative relationship between milk urea nitrogen and fertility. Also, Kananub et al., (2020) found that cows with medium levels of MUN (12.6 to 14 mg/dl) had a higher fertility rate compared to cows with high concentrations of MUN. In general, it has been found that excessive consumption of nitrogen increases the amount of ammonia, urea and other nitrogen compounds in the uterus and blood. These factors affect reproductive efficiency by delaying pregnancy, increasing the number of inseminations per pregnancy and fetal death (Fergousen et al., 1993; Butler et al., 1998; Rangel et al., 2013; Karapetkovska-Hristova et al., 2014; Munyaneza et al., 2017; Bobbo et al., 2020), which were in line with the results of the present study.

Given the strong relationship between MUN and plasma urea nitrogen (PUN), elevated PUN levels may have an impact on the reproductive system. Accordingly, Rhoads et al. (2006) revealed that embryo viability of lactating dairy cows decreased as a consequence of greater levels of PUN. The primary physiological explanation for this effect is that high PUN somewhat modifies the uterine pH (Elrod and Butler, 1993; Elrod et al., 1993; Rhoads et al., 2004). Being a small molecule, urea is capable of diffusing cell membranes of the uterus and reducing the pH level

(Rhoads et al., 2004), eventually impairing embryo development (Ocon and Hansen, 2003). Also, it has reported that other alterations, such as variations in urea concentration, Mg, K, P, and Zn in uterine fluid may also be significant determinants (Jordan et al., 1983). Another theory is that excessive urea in the animal organism is a consequence of extensive liver metabolism to detoxify ammonia absorbed from the rumen, which might worsen the negative energy balance following calving. As a result, there may be irregular cycles and lower reproductive indices (Leroy et al., 2008).

Results of reproductive performances, including days to first insemination (DFS), conception rate (CR), insemination per pregnancy and days open are shown in Table (2). As can be seen, except for days before the first insemination, there is a significant difference in the area of mentioned characteristics between treatments ($P>0.05$). Treatment 4 had the biggest amount related to insemination to pregnancy, days open, and conception rate and the lowest for CR. With CR, however, the highest number has been achieved for treatment 2. It was determined that the high concentration of milk urea nitrogen is somehow equal to having a high interval between calving and first service (78.61 versus 67.13 days). Furthermore,

Table 2. Reproductive characteristics of dairy cows from 2019 to 2022

variable	MUN (mg/dl)				SEM	P-VALUE
	1	2	3	4		
Days to first insemination, d	67.13	69.71	72.35	78.61	11.14	0.78
Conception rate, %	43.08ab	51.91a	38.23 ^{bc}	34.32c	2.23	0.03
Insemination per pregnancy	1.66bc	1.28c	1.78b	2.11a	0.06	0.04
Open days, d	109.20b	125.03b	132.91b	145.44a	13.10	0.05

Table 3. Correlation coefficient of reproductive characteristics with MUN

Variable							
MUN	-						
Days to first insemination, d	0.423	-					
Pregnancy rate, %	- 0.341	-0.421	-				
Insemination per pregnancy	0.375	0.215	- 0.475	-			
Open days, d	0.374	0.364	- 0.321	0.298	-		
Prior to 120 days of DIM, d	-0.564	- 0.364	0.468	- 0.472	- 0.399	-	
Calving Interval, d	0.219	0.395	- 0.456	0.347	0.562	- 0.426	-

there is a significant negative relationship between MUN and conception rate (CR).

What could be concluded from our study is that being inversely affected by measured reproductive parameters by MUN concentrates. The results of the present study are similar to the results obtained from other studies (Doska et al., 2012; Rangel et al., 2013; Raboisson et al., 2017; Jannah et al., 2019; Braga Paiano et al., 2019; Kananub et al., 2020; Souza et al., 2021). Nonetheless, in another study regarding the effect of different levels of MUN on fertility in dairy herds, researchers found that the influence of MUN on reproductive performance may be affected by seasonal changes (Rangel et al., 2013). However, the results of some other studies have indicated that high levels of milk urea nitrogen do not affect the reproductive performance of high-producing cows (Pazzola et al., 2011). In general, it has been found that excessive consumption of nitrogen increases the amount of ammonia, urea and other nitrogen compounds in the uterus and blood. These factors influence reproductive efficiency by delaying pregnancy, increasing the number of inseminations per pregnancy and fetal death (Fergousen et al., 1993; Butler et al., 1998; Rangel et al., 2013; Karapetkovska-Hristova et al., 2014; Munyaneza et al., 2017; Bobbo et al., 2020), which were in line with the results of the present study.

Correlation of reproductive characteristics with milk urea nitrogen

In Table (3), the correlation results between reproductive characteristics and MUN are presented. What stands out from the table is that, there is a positive and significant correlation between the two MUN traits and the days to first insemination and open days ($r=0.423+$; $P<0.05$), and regarding the pregnancy rate and prior to 120 days of DIM there is a negative and significant correlation. However, there were no significant values between insemination ratio per pregnancy ($r=0.375$) and calving interval ($r=0.219$) ($P<0.05$). Various MUN values that impact fertility

have been documented in the literature over time. For instance, Butler et al. (1996) found that dietary protein had a negative impact on fertility in dairy cows, with a MUN content exceeding 19 mg/dL. However, using cows sorted into quartiles for milk urea, Rajala-Schultz et al. (2001) assessed the influence of MUN on fertility in 1,249 dairy cows and found that MUN concentrations more than 15.4 mg/dL resulted in a reduced conception rate compared with lower MUN concentrations. Additionally, according to these investigators, cows with MUN levels below 10 mg/dL prior to conception had a 2.4-fold higher chance of becoming pregnant than cows with levels above 15.4 mg/dL. Recently, the relationship between MUN and some reproductive characteristics has been investigated by a group of researchers (Stoop et al. 2007; König et al. 2008; Mosaferi et al., 2011; Mucha & Strandberg 2011; Rzewuska & Strabel 2014). In this regard, Rzewuska and Strabel (2014) showed that animals with high production values and with medium and lower MUN concentrations have improved fertility traits. Similarly, Mitchell et al. (2005) showed lower MUN during the first and second lactations when examining fertility traits. All things considered, given the disparate findings, it is imperative to study the precise processes by which MUN concentration affects dairy cow fertility.

CONCLUSION

Based on the concentration of MUN in the selected herds according to the seasons, the highest and lowest concentrations of MUN occurred in spring and winter, respectively (MUN range 15.9-16.9 mg/dl and 14.9-2.15 mg/dl). Furthermore, this study found a direct relationship between the parity of the cow and the MUN concentration, so multiparous cows had a higher MUN value (15.88 mg/dl) than primiparous cows.

CONFLICT OF INTEREST

No potential conflict of interest was reported by the author(s).

REFERENCES

- Abdisa T (2018) Review on the reproductive health problem of dairy cattle. *Journal of Dairy & Veterinary sciences* 5(1), 1-12.
- Adamczyk K, Makulska J, Jagusiak W and Węglarz A (2017) Associations between strain, herd size, age at first calving, culling reason and lifetime performance characteristics in Holstein-Friesian cows. *Animal*, 11(2), 327-334.
- Ahammed R, Tasnim M, Halim MA, Sarkar M, Islam MS and Morshed M (2018) A Comparative study on reproductive hormones of repeat breeding and synchronized repeat breeding dairy cows under bathan rearing system at Baghabari milk shed areas in Bangladesh. *IOSR Journal of Agriculture and Veterinary Science* 11(11), 55-60.
- Alabbasi HHH and Hatif SA (2019) The effect of date fruit on puberty and sexual maturity in heifers. *Kufa Journal for Agricultural Sciences* 11(2), 47-54.
- Albarrán-Portillo B and Pollott GE (2013) The relationship between fertility and lactation characteristics in Holstein cows on United Kingdom commercial dairy farms. *Journal of Dairy Science* 96(1), 635-646.
- Anand I, Dhaliwal GS and Chawla PS (2019) High blood/Milk urea nitrogen had deleterious impact on fertility parameters in crossbred cows. *The Indian Journal of Animal Reproduction* 40(1), 42-44.
- Anderson GW and Barton BA (1988) Reproductive efficiency: potential nutrition-management interactions. *Proceedings of Winter Dairy Management Schools, Cornell University, Ithaca, NY, USA*, pp.107.
- Arbel R, Bigun Y, Ezra E, Sturman H and Hojman D (2001) The effect of extended calving intervals in high lactating cows on milk production and profitability. *Journal of Dairy Science* 84(3), 600-608.
- Arunvipas P, VanLeeuwen JA, Dohoo IR, Leger ER, Keefe GP, Burton AS and Lissemore KD (2007) Milk urea-nitrogen negatively affected first-service breeding success in commercial dairy cows in Prince Edward Island, Canada. *Preventive Veterinary Medicine* 82(1-2), 42-50.
- Ayaşan T, Hizli H, Yazgan E, (2011) The effect of milk urea nitrogen on milk composition in Holstein dairy cows. *Eurasian Journal of Veterinary Sciences*, 27 (4), 219-222.
- Beatson PR, Meier S, Cullen NG and Eding H (2019) Genetic variation in milk urea nitrogen concentration of dairy cattle and its implications for reducing urinary nitrogen excretion. *Animal* 13(10), 2164-2171.
- Bertipaglia ECA, Silva RG and Maia ASC (2018) Fertility and hair coat characteristics of Holstein cows in a tropical environment. *Animal Reproduction* 2(3), 187-194.
- Birukawa N, Ando H, Goto M, Kanda N, Pastene LA, Nakatsuji H, Hata H and Urano A (2005) Plasma and urine levels of electrolytes, urea and steroid hormones involved in osmoregulation of cetaceans. *Zoological Science* 22(11), 1245-1257.
- Bisinotto RS, Greco LF, Ribeiro ES, Martinez N, Lima FS, Staples CR, Thatcher WW and Santos JEP (2018) Influences of nutrition and metabolism on fertility of dairy cows. *Animal Reproduction* 9(3), 260-272.
- Bjelland DW, Weigel KA, Hoffman PC, Esser NM and Coblentz WK (2011) The effect of feeding dairy heifers diets with and without supplemental phosphorus on growth, reproductive efficiency, health, and lactation performance. *Journal of Dairy Science* 94(12), 6233-6242.
- Bjelland DW, Weigel KA, Vukasinovic N and Nkrumah JD (2013) Evaluation of inbreeding depression in Holstein cattle using whole-genome SNP markers and alternative measures of genomic inbreeding. *Journal of Dairy Science* 96(7), 4697-4706.
- Bobbo T, Penasa M, Rossoni A and Cassandro M (2020) Genetic aspects of milk urea nitrogen and new indicators of nitrogen efficiency in dairy cows. *Journal of Dairy Science* 103(10), 9207-9212.
- Braga Paiano R, Becker Birgel D and Harry Birgel Junior E (2019) Uterine involution and reproductive performance in dairy cows with metabolic diseases. *Animals* 9(3), 93.
- Broderick GA and Clayton MK (1997) A statistical evaluation of animal and nutritional factors influencing concentrations of milk urea nitrogen. *Journal of Dairy Science* 80(11), 2964-2971.
- Bruckental I, Oldham JD and Sutton JD (1980) Glucose and urea kinetics in cows in early lactation. *British Journal of Nutrition* 44(1), 33-45.
- Burgos SA, Fadel JG and DePeters EJ (2007) Prediction of ammonia emission from dairy cattle manure based on milk urea nitrogen: Relation of milk urea nitrogen to urine urea nitrogen excretion. *Journal of Dairy Science* 90(12), 5499-5508.
- Butler WR (1998) Effect of protein nutrition on ovarian and uterine physiology in dairy cattle. *Journal of Dairy Science* 81(9), 2533-2539.
- Butler WR, Calaman JJ and Beam SW (1996) Plasma and milk urea nitrogen in relation to pregnancy rate in lactating dairy cattle. *Journal of Animal Science* 74(4), 858-865.
- Canfield RW, Sniffen CJ and Butler WR (1990) Effects of excess degradable protein on postpartum reproduction and energy balance in dairy cattle. *Journal of Dairy Science* 73(9), 2342-2349.
- Carlsson J and Pehrson B (1993) The relationships between seasonal variations in the concentration of urea in bulk milk and the production and fertility of dairy herds. *Journal of Veterinary Medicine Series A* 40(1-10), 205-212.
- Carroll DJ, Barton BA, Anderson GW and Smith RD (1988) Influence of protein intake and feeding strategy on reproductive performance of dairy cows. *Journal of Dairy Science* 71(12), 3470-3481.
- Cattaneo L, Signorini ML, Bertoli J, Bartolomé JA, Gareis NC, Díaz PU, Bo GA and Ortega HH (2014) Epidemiological description of cystic ovarian disease in argentine dairy herds: risk factors and effects on the reproductive performance of lactating cows. *Reproduction in Domestic Animals* 49(6), 1028-1033.
- Cowley FC, Barber DG, Houlihan AV and Poppi DP (2015) Immediate and residual effects of heat stress and restricted intake on milk protein and casein composition and energy metabolism. *Journal of Dairy Science* 98(4), 2356-2368.
- Crowe MA, Hostens M and Opsomer G (2018) Reproductive management in dairy cows-the future. *Irish Veterinary Journal* 71(1), 1-13.
- Dallago GM, de Figueiredo DM, de Resende Andrade PC, dos Santos RA, Lacroix R, Santschi DE and Lefebvre DM (2019) Predicting first test day milk yield of dairy heifers. *Computers and Electronics in Agriculture* 166(2), 105032.
- Dash S, Chakravarty AK, Singh A, Upadhyay A, Singh M and Yousuf S (2016) Effect of heat stress on reproductive performances of dairy cattle and buffaloes: A review. *Veterinary World* 9(3), 235.
- Devi P, Debbarma S, Kumar G and Thakur P (2019) Effect of heat stress on reproduction in farm animals and its mitigation: A review. *Journal of Entomology and Zoology Studies* 7(2), 342-345.
- Doska MC, Silva DFFD, Horst JA, Valloto AA, Rossi Junior P and Almeida RD (2012) Sources of variation in milk urea nitrogen in Paraná dairy cows. *Revista Brasileira de Zootecnia* 41(3), 692-697.
- Elrod CC and Butler WR (1993) Reduction of fertility and alteration of uterine pH in heifers fed excess ruminally degradable protein. *Journal of Animal Science* 71(3), 694-701.
- Esposito G, Irons PC, Webb EC and Chapwanya A (2014) Interactions between negative energy balance, metabolic diseases, uterine health and immune response in transition dairy cows. *Animal Reproduction Science* 144(3-4), 60-71.
- Fahey J, Boland MP and O'Callaghan D (2001) The effects of dietary urea on embryo development in superovulated donor ewes and on early embryo survival and development in recipient ewes. *Animal Science* 72(2), 395-400.
- Ferguson JD, Blanchard TL and Chalupa W (1987) November. Protein, fats and fertility in dairy cows. In *American Association of Bovine Practitioners Proceedings of the Annual Conference* pp. 112-117.
- Ferguson JD, Galligan DT, Blanchard T and Reeves M (1993) Serum urea nitrogen and conception rate: the usefulness of test information. *Journal of Dairy Science* 76(12), 3742-3746.
- Gábor G, Tóth F, Özsvári L, Abonyi-Tóth Z and Sasser RG (2008) Factors influencing pregnancy rate and late embryonic loss in dairy cattle. *Reproduction in Domestic Animals* 43(1), 53-58.
- Garcia-Bojalil CM, Staples CR, Thatcher WW and Drost M (1994) Protein intake and development of ovarian follicles and embryos of superovulated nonlactating dairy cows. *Journal of Dairy Science* 77(9),

- 2537-2548.
- Gath VP, Crowe MA, O'Callaghan D, Boland MP, Duffy P, Lonergan P and Mulligan FJ (2012) Effects of diet type on establishment of pregnancy and embryo development in beef heifers. *Animal Reproduction Science* 133(3-4), 139-145.
- Gernand E, König S and Kipp C (2019) Influence of on-farm measurements for heat stress indicators on dairy cow productivity, female fertility, and health. *Journal of Dairy Science* 102(7), 6660-6671.
- Godden SM, Lissimore KD, Kelton DF, Leslie KE, Walton JS and Lumsden JH (2001) Relationships between milk urea concentrations and nutritional management, production, and economic variables in Ontario dairy herds. *Journal of Dairy Science* 84(5), 1128-1139.
- Gonzalez-Recio O, Alenda R, Chang YM, Weigel KA and Gianola D (2006) Selection for female fertility using censored fertility traits and investigation of the relationship with milk production. *Journal of Dairy Science* 89(11), 4438-4444.
- Gross JJ, Kessler EC, Albrecht C and Bruckmaier RM (2015) Response of the cholesterol metabolism to a negative energy balance in dairy cows depends on the lactational stage. *PLoS One* 10(6), 0121956.
- Gunn PJ, Schoonmaker JP, Lemenager RP and Bridges GA (2014) Feeding excess crude protein to gestating and lactating beef heifers: Impact on parturition, milk composition, ovarian function, reproductive efficiency and pre-weaning progeny growth. *Livestock Science* 167(3), 435-448.
- Gustafsson AH and Palmquist DL (1993) Diurnal variation of rumen ammonia, serum urea, and milk urea in dairy cows at high and low yields. *Journal of Dairy Science* 76(2), 475-484.
- Hafez ESE and Hafez B (2013) Reproduction in farm animals. *John Wiley & Sons* pp. 518-522.
- Heins BJ and Hansen LB (2012) Fertility, somatic cell score, and production of Normande \times Holstein, Montbéliarde \times Holstein, and Scandinavian Red \times Holstein crossbreds versus pure Holsteins during their first 5 lactations. *Journal of Dairy Science* 95(2), 918-924.
- Heins BJ, Hansen LB and Seykora AJ (2006) Calving difficulty and stillbirths of pure Holsteins versus crossbreds of Holstein with Normande, Montbéliarde, and Scandinavian Red. *Journal of Dairy Science* 89(7), 2805-2810.
- Henao-Velásquez AF, Múnera-Bedoya OD, Herrera AC, Agudelo-Trujillo JH and Cerón-Muñoz MF (2014) Lactose and milk urea nitrogen: fluctuations during lactation in Holstein cows. *Revista Brasileira de Zootecnia* 43(4), 479-484.
- Hof G, Vervoorn MD, Lenaers PJ and Tamminga S (1997) Milk urea nitrogen as a tool to monitor the protein nutrition of dairy cows. *Journal of Dairy Science* 80(12), 3333-3340.
- Hristova VK (2014) Study of Seasonal Dynamics of Blood Metabolic Profile and Milk Urea Nitrogen (MUN) Level of Cows with Reproduction. *Accelerating the World's Research* 35(5), 36-54.
- Ibtisham F, Nawab AAMIR, Li G, Xiao M, An L and Naseer G (2018) Effect of nutrition on reproductive efficiency of dairy animals. *Medycyna Weterynaryjna* 74(6), 356-361.
- Jannah M, Mustofa I, Utama S, Mulyati S, Safitri E and Al-Arif MA (2019) Identification of estrogen levels in dairy cows based on milk levels and pregnancy rates. *Indian Journal of Public Health Research & Development* 10(12), 320-324.
- Jonker JS, Kohn RA and Erdman RA (1998) Using milk urea nitrogen to predict nitrogen excretion and utilization efficiency in lactating dairy cows. *Journal of Dairy Science* 81(10), 2681-2692.
- Jordan ER and Swanson LV (1979) Serum progesterone and luteinizing hormone in dairy cattle fed varying levels of crude protein. *Journal of Animal Science* 48(5), 1154-1158.
- Jordan ER, Chapman TE, Holtan DW and Swanson LV (1983) Relationship of dietary crude protein to composition of uterine secretions and blood in high-producing postpartum dairy cows. *Journal of Dairy Science* 66(9), 1854-1862.
- Kafilzadeh F and Farivar F (2006) Relationship between pregnancy and blood or milk urea nitrogen in lactating dairy cows. *Iranian Journal of Agricultural Sciences* 37(2), 353-360.
- Kananub S, Pechkerd P, Van Leeuwen J, Stryhn H and Arunvipas P (2020) Evaluation of influence of milk urea nitrogen on reproductive performance in smallholder dairy farms. *Australian Veterinary Journal* 98(8), 375-379.
- Karapetkovska-Hristova V, Tomovska J, Bonev G, Dimitrov S, Dimitrovska G, Presilski S and Ahmad MA (2014) Interrelationship between the milk urea nitrogen level and milk coagulation traits in Holstein-Friesian cows with reproductive disorders in R. Macedonia. *International Journal of Enhanced Research in Science Technology & Engineering* 3(4), 199-207.
- Kohn RA, Kalscheur KF and Russek-Cohen E (2002) Evaluation of models to estimate urinary nitrogen and expected milk urea nitrogen. *Journal of Dairy Science* 85(1), 227-233.
- Kume S, Numata K, Takeya Y, Miyagawa Y, Ikeda S, Kitagawa M, Nonaka K, Oshita T and Kozakai T (2008) Evaluation of urinary nitrogen excretion from plasma urea nitrogen in dry and lactating cows. *Asian-Australasian Journal of Animal Sciences* 21(8), 1159-1163.
- Larson SF, Butler WR and Currie WB (1997) Reduced fertility associated with low progesterone postbreeding and increased milk urea nitrogen in lactating cows. *Journal of Dairy Science* 80(7), 1288-1295.
- Larson SF, Butler WR and Currie WB (2007) Pregnancy rates in lactating dairy cattle following supplementation of progesterone after artificial insemination. *Animal Reproduction Science* 102(1-2), 172-179.
- Law RA, Young FJ, Patterson DC, Kilpatrick DJ, Wylie ARG and Mayne CS (2009) Effect of dietary protein content on the fertility of dairy cows during early and mid-lactation. *Journal of Dairy Science* 92(6), 2737-2746.
- Li HQ, Liu Q, Wang C, Yang ZM, Guo G, Huo WJ, Pei CX, Zhang YL, Zhang SL, Wang H and Liu JX (2016) Effects of dietary supplements of rumen-protected folic acid on lactation performance, energy balance, blood parameters and reproductive performance in dairy cows. *Animal Feed Science and Technology* 213(6), 55-63.
- Linn J (2006) Feed efficiency: Its economic impact in lactating dairy cows. *WCDS Advances in Dairy Technology* 18(19-28), 30.
- Liu J, Li L, Chen X, Lu Y and Wang D (2019) Effects of heat stress on body temperature, milk production, and reproduction in dairy cows: A novel idea for monitoring and evaluation of heat stress-A review. *Asian-Australasian Journal of Animal Sciences* 32(9), 1332.
- López-Gatius F (2018) Approaches to increase reproductive efficiency in artificially inseminated dairy cows. *Animal Reproduction* 10(3), 143-147.
- Maya-Soriano MJ, López-Gatius F, Andreu-Vázquez C and López-Béjar M (2013) Bovine oocytes show a higher tolerance to heat shock in the warm compared with the cold season of the year. *Theriogenology* 79(2), 299-305.
- Mekonnen A, Howie AF, Riley S, Gidey G, Tegegne DT, Desta G, Ashbir G, Gebrekidan B and Harlow C (2017) Serum, milk, saliva and urine progesterone and estradiol profiles in crossbred (Zebu \times Holstein Friesian) dairy cattle. *Animal Husbandry, Dairy and Veterinary Science* 1(3), 63-71.
- Melendez P, Donovan A and Hernandez J (2000) Milk urea nitrogen and infertility in Florida Holstein cows. *Journal of Dairy Science* 83(3), 459-463.
- Mosaferi S, Ettehad S and Kooshavar H (2011) Study on the relationship between milk urea nitrogen (MUN) and fertility in dairy cattle housed in Tabriz. *Veterinary Clinical Pathology the Quarterly Scientific Journal* 2(18), 1233-1245.
- Muller CJ, Potgieter JP, Cloete SWP and Dzama K (2014) Non-genetic factors affecting fertility traits in South African Holstein cows. *South African Journal of Animal Science* 44(1), 54-63.
- Munyaneza N, Niyukuri J and Hachimi YE (2017) Milk urea nitrogen as an indicator of nitrogen metabolism efficiency in dairy cows: a review. *Theriogenology Insight-An International Journal of Reproduction in all Animals* 7(3), pp.145-159.
- Nebel RL and McGilliard ML (1993) Interactions of high milk yield and reproductive performance in dairy cows. *Journal of Dairy Science* 76(10), 3257-3268.
- Negrón-Pérez VM, Fausnacht DW and Rhoads ML (2019) Invited review: Management strategies capable of improving the reproductive performance of heat-stressed dairy cattle. *Journal of Dairy Science*, 102(12), 10695-10710.
- Nilforooshan MA and Edriss MA (2004) Effect of age at first calving on some productive and longevity traits in Iranian Holsteins of the Isfahan province. *Journal of Dairy Science* 87(7), -2135.
- Norman HD, Wright JR, Hubbard SM, Miller RH and Hutchison JL

- (2009) Reproductive status of Holstein and Jersey cows in the United States. *Journal of Dairy Science* 92(7), 3517-3528.
- Ntallaris T, Humblot P, Båge R, Sjunnesson Y, Dupont J and Berglund B (2017) Effect of energy balance profiles on metabolic and reproductive response in Holstein and Swedish Red cows. *Theriogenology* 90(12), 276-283.
- Olivera-Muzante J, Fierro S, Alabart JL, Claramunt M, Minteguiaga MA, Aunchayna G, Errandonea N and Banchero G (2019) Short-term dietary protein supplementation improves reproductive performance of estrous-synchronized ewes when there are long intervals of prostaglandin or progesterone-based treatments for timed ai. *Animal Reproduction Science* 206(3), 78-84.
- Oltenacu PA and Broom DM (2010) The impact of genetic selection for increased milk yield on the welfare of dairy cows. *Animal Welfare* 19(1), 39-49.
- Omur A, Kirbas A, Aksu E, Kandemir F, Dorman E, Kaynar O and Ucar O (2016) Effects of antioxidant vitamins (A, D, E) and trace elements (Cu, Mn, Se, Zn) on some metabolic and reproductive profiles in dairy cows during transition period. *Polish Journal of Veterinary Sciences* 19(4), 34-42.
- Padalia H, Bharti RR, Pundir YPS and Sharma KP (2010) Geospatial multiple logistic regression approach for habitat characterization of scarce plant population: A case study of *Pittosporum eriocarpum* Royle (an endemic species of Uttarakhand, India). *Journal of the Indian Society of Remote Sensing* 38(3), 513-521.
- Payne JM, Rowlands GJ, Manston R and Dew SM (1973) A statistical appraisal of the results of metabolic profile tests on 75 dairy herds. *British Veterinary Journal* 129(4), 370-381.
- Pazzola M, Dettori ML, Carcangiu V, Luridiana S, Mura MC and Vacca GM (2011) Relationship between milk urea, blood plasma urea and body condition score in primiparous browsing goats with different milk yield level. *Archives Animal Breeding* 54(5), 546-556.
- Pongpiachan P, Rodtian P and Ota K (2003) Effects of tropical climate on reproduction of cross-and purebred Friesian cattle in Northern Thailand. *Asian-Australasian Journal of Animal Sciences* 16(7), 952-961.
- Raboisson D, Albaaj A, Nonne G and Foucras G (2017) High urea and pregnancy or conception in dairy cows: A meta-analysis to define the appropriate urea threshold. *Journal of Dairy Science* 100(9), 7581-7587.
- Rahbar R, Sadeghi-Sefidmazgi A, Abdollahpour R and Nejati-Javaremi A (2019) Can post-milking insemination increase conception rate in high-producing Holstein cows under heat stress? A retrospective study. *The Journal of Agricultural Science* 157(3), 254-259.
- Rajala-Schultz PJ, Saville WJA, Frazer GS and Wittum TE (2001) Association between milk urea nitrogen and fertility in Ohio dairy cows. *Journal of Dairy Science* 84(2), 482-489.
- Rangel, A.H.D.N., Soares, A.D., DE Lima, T.C.C., Araújo, T.P.M. and Júnior, D.M.D.L., 2013. Concentration of urea nitrogen in buffalo milk during different seasons of the year in Northeastern Brazil. *Revista Caatinga*, 26(3): pp.99-104.
- Reis Lacerda Medeiros AC (2020) Genetic correlation between milk urea nitrogen and reproductive performance in seasonal grazing dairy cows. *a thesis presented in partial fulfilment of the requirements for the degree of Master of Science (Animal Science) at Massey University, Palmerston North, New Zealand* (Doctoral dissertation, Massey University). pp.94-100.
- Rhoads ML, Rhoads RP, Gilbert RO, Toole R and Butler WR (2006) Detrimental effects of high plasma urea nitrogen levels on viability of embryos from lactating dairy cows. *Animal Reproduction Science* 91(1-2), 1-10.
- Ribeiro ES (2018) Symposium review: Lipids as regulators of conceptus development: Implications for metabolic regulation of reproduction in dairy cattle. *Journal of Dairy Science* 101(4), pp.3630-3641.
- Rodney RM, Celi P, Scott W, Breinhild K and Lean IJ (2015) Effects of dietary fat on fertility of dairy cattle: A meta-analysis and meta-regression. *Journal of Dairy Science* 98(8), 5601-5620.
- Rodney RM, Celi P, Scott W, Breinhild K, Santos JEP and Lean IJ (2018) Effects of nutrition on the fertility of lactating dairy cattle. *Journal of Dairy Science* 101(6), 5115-5133.
- Roseler DK, Ferguson JD, Sniffen CJ and Herrema J (1993) Dietary protein degradability effects on plasma and milk urea nitrogen and milk nonprotein nitrogen in Holstein cows. *Journal of Dairy Science* 76(2), 525-534.
- Roy B, Brahma B, Ghosh S, Pankaj PK and Mandal G (2011) Evaluation of milk urea concentration as useful indicator for dairy herd management: A review. *Asian Journal of Animal and Veterinary Advances* 6(1), 1-19.
- Sadeghi-Sefidmazgi A, Moradi-Shahrabak M, Nejati-Javaremi A, Miraei-Ashtiani SR and Amer PR (2012) Breeding objectives for Holstein dairy cattle in Iran. *Journal of Dairy Science* 95(6), 3406-3418.
- SAS Institute (2001) SAS User's Guide. Version 8.02 ed. SAS Institute Inc., Cary, NC.
- Schaeffer LR, Burnside EB, Glover P and Fatehi J (2011) Crossbreeding results in Canadian dairy cattle for production, reproduction and conformation. *The Open Agriculture Journal* 4(1), 422-428.
- Seroussi E, Shirak A, Gershoni M, Ezra E, de Abreu Santos DJ, Ma L and Liu GE (2019) Bos taurus-indicus hybridization correlates with intralocus sexual-conflict effects of PRDM9 on male and female fertility in Holstein cattle. *BMC Genetics* 20(1), 1-11.
- Sewalem A, Miglior F, Kistemaker GJ, Sullivan PV and Van Doormaal BJ (2008) Relationship between reproduction traits and functional longevity in Canadian dairy cattle. *Journal of Dairy Science* 91(4), 1660-1668.
- Shelton K, Parkinson TJ, Hunter MG, Kelly RW and Lamming GE (1990) Prostaglandin E-2 as a potential luteotrophic agent during early pregnancy in cattle. *Reproduction* 90(1), 11-17.
- Sklan D and Tinsky M (1993) Production and reproduction responses by dairy cows fed varying undegradable protein coated with rumen bypass fat. *Journal of Dairy Science* 76(1), 216-223.
- SM A and Estuty N (2021) Nutritional effects on dairy cattle fertility. *International Journal for Research in Applied Sciences and Biotechnology* 8(4), 71-82.
- Sonderman JP and Larson LL (1989) Effect of dietary protein and exogenous gonadotropin-releasing hormone on circulating progesterone concentrations and performance of Holstein cows. *Journal of Dairy Science* 72(8), 2179-2183.
- Souza FRD, Campos CC, Silva NAMD and Santos RMD (2016) Influence of seasonality, timing of insemination and rectal temperature on conception rate of crossbred dairy cows. *Semina: Ciências Agrárias* 155-162.
- Souza VC, Aguilar M, Van Amburgh M, Nayanjanjale WAD and Hanigan MD (2021) Milk urea nitrogen variation explained by differences in urea transport into the gastrointestinal tract in lactating dairy cows. *Journal of Dairy Science* 104(6), 6715-6726.
- Soydan E and Kuran M (2017) The effect of calving season on reproductive performance of Jersey cows. *Mljekarstvo/Dairy* 67(4), 362-369.
- Spooner MK, Lenis YY, Watson R, Jaimes D and Patterson AL (2021) The role of stem cells in uterine involution. *Reproduction* 161(3), R61-R77.
- Staples CR, Thatcher WW and Clark JH (1990) Relationship between ovarian activity and energy status during the early postpartum period of high producing dairy cows. *Journal of Dairy Science* 73(4), 938-947.
- Starbuck GR, Darwash AO, Mann GE and Lamming GE (2001) The detection and treatment of post insemination progesterone insufficiency in dairy cows. *BSAP Occasional Publication* 26(2), 447-450.
- Summar ML, Koelker S, Freedenberg D, Le Mons C, Haberle J, Lee HS, Kirmse B, Registry TE and Members of the Urea Cycle Disorders Consortium (2013) The incidence of urea cycle disorders. *Molecular Genetics and Metabolism* 110(1-2), 179-180.
- Tillard E, Humblot P, Faye B, Lecomte P, Dohoo I and Bocquier F (2007) Precalving factors affecting conception risk in Holstein dairy cows in tropical conditions. *Theriogenology* 68(4), 567-581.
- Van den Berg I, Ho PN, Haile-Mariam M, Beatson PR, O'Connor E and Pryce JE (2021) Genetic parameters of blood urea nitrogen and milk urea nitrogen concentration in dairy cattle managed in pasture-based production systems of New Zealand and Australia. *Animal Production Science* 114(3), 648-652.
- Vasconcelos JLM, Silcox RW, Rosa GJM, Pursley JR and Wiltbank MC (1999) Synchronization rate, size of the ovulatory follicle, and pregnancy rate after synchronization of ovulation beginning on different days of the estrous cycle in lactating dairy cows. *Theriogenology*

- 52(6), 1067-1078.
- Veen WAG and Bakker YT (1988) The influence of slowly and rapidly degradable concentrate protein on a number of blood parameters in dairy cattle. *Netherlands Journal of Agricultural Science* 36(1), 51-62.
- Walsh SW, Williams EJ and Evans ACO (2011) A review of the causes of poor fertility in high milk producing dairy cows. *Animal Reproduction Science* 123(3-4), 127-138.
- Wathes DC, Taylor VJ, Cheng Z and Mann GE (2003) Follicle growth, corpus luteum function and their effects on embryo development in postpartum dairy cows. *Reproduction Supplement* 61(4), 219-237.
- Wiltbank MC, Souza AH, Carvalho PD, Cunha AP, Giordano JO, Fricke PM, Baez GM and Diskin MG (2014) Physiological and practical effects of progesterone on reproduction in dairy cattle. *Animal* 8(s1), 70-81.
- Wiltbank MC, Souza AH, Giordano JO, Nascimento AB, Vasconcelos JM, Pereira MHC, Fricke PM, Surjus RS, Zinsly FCS, Carvalho PD and Bender RW (2018) Positive and negative effects of progesterone during timed AI protocols in lactating dairy cattle. *Animal Reproduction* 9(3), 231-241.
- Yan L, Robinson R, Shi Z and Mann G (2016) Efficacy of progesterone supplementation during early pregnancy in cows: A meta-analysis. *Theriogenology* 85(8), 1390-1398.
- Yasothai R (2014) Importance of minerals on reproduction in dairy cattle. *International Journal of Science, Environment and Technology* 3(6), 2051-2057.
- Yoon JT, Lee JH, Kim CK, Chung YC. and Kim CH (2004) Effects of milk production, season, parity and lactation period on variations of milk urea nitrogen concentration and milk components of Holstein dairy cows. *Asian-Australasian Journal of Animal Sciences* 17(4), 479-484.