# Factors associated with early and mid-to-late fetal loss in lactating and nonlactating Holstein cattle in a hot climate[1]

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**ABSTRACT:** The purpose of this study was to evaluate associations of lactation, somatic cell count score (SCCS) at breeding, milk yield, lactation number, interval from calving to breeding (days open), number of times inseminated, and season of breeding on fetal loss for lactating Holstein females (both first-parity and multiparous cows) and nonlactating Holstein heifers in a hot climate. Females were palpated between d 40 and 50 of gestation and again at d 70 to 80 to determine pregnancy status. Early fetal loss was defined as a loss that occurred after d 40 to 50 but before d 70 to 80. Mid-to-late fetal loss represented losses after d 70 to 80 but before expected calving. Lactating females had higher early ($P = 0.055$) and mid-to-late fetal loss ($P < 0.05$) than nonlactating heifers. Those lactating females with increased days open experienced greater early ($P < 0.05$) and mid-to-late fetal loss ($P = 0.055$), whereas lactating females with an elevated SCCS encountered greater mid-to-late fetal loss ($P < 0.01$). Milk yield, lactation number, number of times inseminated, and season were not associated with early or mid-to-late fetal loss. For nonlactating heifers, there were no associations between number of times inseminated, season, or age at breeding on early or mid-to-late fetal loss. In conclusion, lactating females were more likely to suffer early and mid-to-late fetal loss than nonlactating heifers. Also, days open and SCCS at breeding were related to ability of lactating females to maintain pregnancy, but there were no relationships between fetal loss and milk yield, lactation number, number of times inseminated, or season.

Key Words: Dairy Cattle, Fetal Loss, Pregnancy

 J. Anim. Sci. 2005. 83:1017–1022

## Introduction

One contributor to infertility in cattle is pregnancy loss during the fetal period that extends from 42 d of gestation until parturition (CBRN, 1972). Based on a compilation of studies by Santos et al. (2004b), estimation of the incidence of fetal loss ranged from 8.3 to 24.0% for lactating dairy cows and 1.5 to 10.2% for dairy heifers. Identification of the factors contributing to fetal mortality could be useful for identifying strategies to decrease these losses. One possible factor is mastitis, which has been associated with loss of pregnancies during the embryonic (Chebel et al., 2004) and fetal period (Risco et al., 1999; Santos et al., 2004a). Other potential causes of fetal loss are the physiological changes associated with high milk production; however, a correlation between milk yield and fetal loss in dairy cattle has not always been observed (López-Gatius et al., 2002; Silke et al., 2002). Similarly, there was no relationship between pregnancy loss during the embryonic period and milk yield (Chebel et al., 2004). Heat stress might also contribute to fetal loss because of its actions to decrease placental function and fetal growth (Collier et al., 1982); such a link has not been described.

Only a limited number of studies have evaluated possible causes of fetal mortality in dairy cattle. The particular importance of factors influencing fetal loss could depend on environment, and little information exists for dairy cattle raised in hot climates. The objective of the present study was to characterize factors associated with rates of early and mid-to-late fetal loss in a herd of dairy cattle maintained in north Florida. It was hypothesized that lactating females would have a higher incidence of early and mid-to-late fetal loss than nonlactating heifers and that early and mid-to-late fetal loss would be higher for females with high milk production, high somatic cell count score (**SCCS**) at breeding, and for those inseminated during the hotter months of the year. We also determined whether the number of times

[1]Supported in part by IFAFS competitive grant 2001-52101-11318 from the USDA Cooperative State Research, Education, and Extension Service. This is Journal Series No. R-10642 of the Florida Agric. Exp. Stn.

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Received December 15, 2004.
Accepted February 10, 2005.

a female is inseminated (a measure of the female's fertility; Chebel et al., 2004) or the interval from calving to conception (days open) is related to the frequency of fetal loss.

## Materials and Methods

### *Animals*

Breeding records for lactating Holstein females (both first-parity and multiparous cows) and nonlactating Holstein heifers were obtained from the University of Florida Dairy Research Unit at Hague, FL (29°46′ N, 82°25′ W), for the period of April 2000 through March 2003 using the PCDART Herd Manager software (v. 7, Dairy Records Management Systems, Raleigh, NC). Lactating females were administered Posilac (Monsanto, Chesterfield Hills, MO) according to manufacturer's recommendations, milked twice daily, and maintained in free-stall barns equipped with sprinklers and fans or misters and fans. Nonlactating heifers were maintained in a variety of facilities with either shade trees or freestanding shade structures covered with shade cloth.

The voluntary waiting period from calving to first insemination was approximately 80 d. For the first insemination after calving, timed AI was performed using the Ovsynch protocol (Pursley et al., 1997) initiated at approximately d 70 after calving and after cows were presynchronized with two injections of $PGF_{2\alpha}$ 14 d apart at approximately 42 and 56 d after calving. Subsequent inseminations for lactating females were conducted at either standing estrus (spontaneous, after injection of $PGF_{2\alpha}$ or following the SelectSynch procedure [Stevenson et al., 2000]) or by timed AI using the Ovsynch procedure. Nonlactating heifers were inseminated beginning at an approximate target weight of 340 kg. Inseminations were performed at either standing estrus (spontaneous) or after injection of $PGF_{2\alpha}$.

### *Determination of Fetal Loss*

Pregnancy diagnosis was performed between d 40 to 50 after insemination using palpation per rectum, and females determined to be pregnant were reconfirmed for pregnancy status by palpation per rectum between d 70 to 80 after insemination. Females that were pregnant between d 40 to 50, but not pregnant between d 70 to 80, were classified as having undergone early fetal loss. Those females determined to be pregnant between d 40 to 50 and again between d 70 to 80, but whose calving date occurred 4 wk or more before their expected calving date (premature parturition), were classified as having undergone mid-to-late fetal loss. The average gestation length for all animals that did not experience fetal loss was 276.1 d, with a range of 253 to 292 d.

### *Description of Potential Factors Associated with Early and Mid-to-Late Fetal Loss for Lactating Females*

The following factors were analyzed for associations with early and mid-to-late fetal loss: SCCS at insemination, average milk yield at the time of insemination (milk yield), lactation number at breeding in which pregnancy was established (lactation number), number of days between the previous calving and the date of breeding that resulted in pregnancy (days open), number of times inseminated until pregnancy was established (times inseminated), and season of the year in which the animal was bred (season). Each cow's milk yield and SCCS were recorded during a monthly test date. Data corresponding to the test date closest to the breeding date at which the female was determined to be pregnant was used for the determination of effects of milk yield and SCCS at the time of breeding. If the breeding date occurred 7 to 21 d between two test dates, the value used for data analysis for milk yield and SCCS at breeding was an average of the test dates before and after the breeding date.

Each of the above-mentioned factors was categorized as described in the following statements. The SCCS was classified as being ≤2.5, 2.6 to 5.0, or >5.0 at the time of breeding. The SCCS is a score calculated by the Dairy Herd Improvement Association based on the raw somatic cell count (**SCC**; a count of the white blood cells [**WBC**] in a milliliter of milk). A SCCS between 0 and 2.5 equates to a SCC range of ≤75,000 WBC/mL of milk, a SCCS between 2.5 and 5.0 equates to a SCC range of >75,000 to ≤400,000 WBC/mL of milk, and a SCCS greater than 5.0 equates to a SCC range >400,000 WBC/mL of milk. Milk yield on the test date closest to the female's breeding date was categorized as <22.7, 22.8 to 34.1, 34.2 to 45.5, or >45.6 kg/d at breeding. Lactation number was organized into first lactation, second lactation, or third or greater lactation. Days open was categorized as <75, 76 to 150, 151 to 300, or >300 d. Categories for number of times inseminated until the establishment of pregnancy were one insemination, two or three inseminations, or four or more inseminations. Season of the year of breeding was classified as cool months (October through March) or hot months (April through September).

### *Description of Potential Factors Associated with Early and Mid-to-Late Fetal Loss for Nonlactating Heifers*

Factors analyzed were the number of times inseminated until pregnancy was established (times inseminated), the season of the year in which the heifer was inseminated (season), and the age of the heifer at the breeding that resulted in an established pregnancy (age at pregnancy). Data for number of times inseminated and season of the year of breeding were categorized as described above for lactating females. Age of heifer at establishment of pregnancy was characterized as ≤15 mo or >15 mo of age.

### *Statistical Analyses*

Data were analyzed by logistic regression with the LOGISTIC procedure of SAS (SAS for Windows, Re-

**Table 1.** Descriptive statistics, adjusted odds ratio (AOR) estimates, and 95% Wald confidence intervals (CI) for differences between lactating females vs. nonlactating heifers in incidence of early and mid-to-late fetal loss

| | Early fetal loss | | | | Mid-to-late fetal loss | | | |
|---|---|---|---|---|---|---|---|---|
| Item | Proportion[a] | AOR | 95% Wald CI[b] | *P*-value[c] | Proportion[a] | AOR | 95% Wald CI[d] | *P*-value[c] |
| Lactating females | 60/950 (6.3%) | 1.79 | 0.99, 3.25 | 0.055 | 33/890 (3.7%) | 3.54 | 1.25, 10.07 | 0.018 |
| Nonlactating heifers | 14/386 (3.6%) | 1.00 | | | 4/372 (1.1%) | 1.00 | | |

[a]Data represent the number of females with fetal loss/total number of females.
[b]Wald $\chi^2$ statistic = 3.70, $P = 0.055$.
[c]Derived from PROC GENMOD of SAS (SAS Inst., Inc., Cary, NC).
[d]Wald $\chi^2$ statistic = 5.63, $P < 0.05$.

lease 8.02; SAS Inst., Inc., Cary, NC) using a backward stepwise logistic model. Variables were continuously removed from the model by the Wald statistic criterion if the significance was greater than 0.20. The full statistical model included main effects and all interactions, except for the days open × times inseminated because these terms are closely correlated; however, no significant interactions were found and the final model included only main effects. The Wald $\chi^2$ statistic was used to determine the significance of each main effect that remained in the reduced model. Effects and classes within a variable were considered to be significant at a level of $P < 0.05$ using the Wald test statistic for each main effect and by the GENMOD procedure of SAS for differences in classes within a variable. Reported *P*-values were obtained from the analysis using GENMOD. The adjusted odds ratio (**AOR**) estimates and the 95% Wald confidence intervals from logistic regression were obtained for each variable that remained in the final statistical model following the backward elimination.

The mathematical model for analysis of early and mid-to-late fetal loss for lactating females included the effects of SCCS, milk yield, lactation number, days open, number of times inseminated, and season. For nonlactating heifers, the mathematical model included number of times inseminated, season, and age at pregnancy. Parity was the only effect in the model to determine differences in early and mid-to-late fetal loss between lactating females and nonlactating females.

## Results

### *Differences in Incidence of Early and Mid-to-Late Fetal Loss between Lactating Females vs. Nonlactating Heifers*

Lactating females had a greater incidence of early and mid-to-late fetal loss than nonlactating heifers (Table 1). The proportion of animals with early fetal loss was 6.3% for lactating females and 3.6% for nonlactating heifers (AOR = 1.79; Wald $\chi^2$ statistic = 3.70; $P = 0.055$). The proportion of animals with mid-to-late fetal loss was 3.7% for lactating females and 1.1% for nonlactating heifers (AOR = 3.54; Wald $\chi^2$ statistic = 5.63; $P < 0.05$).

### *Factors Associated with Early and Mid-to-Late Fetal Loss for Lactating Females*

Descriptive statistics for all factors analyzed are shown in Table 2. The average SCCS for lactating females was 3.02 with a range of 0.01 to 9.25. There was no relationship between SCCS and early fetal loss for lactating females. However, SCCS at insemination was associated with mid-to-late fetal loss (Wald $\chi^2$ statistic = 12.09, $P < 0.01$; Table 3). Specifically, lactating females with a SCCS >5.0 at the time of insemination had a higher percentage of mid-to-late fetal loss (7.3%) than cows with a SCCS <2.5 (2.1%) or 2.6 to 5.0 (4.1%; Table 2).

**Table 2.** Descriptive statistics for the incidence of early and mid-to-late fetal loss for lactating females

| | Early fetal loss | Mid-to-late fetal loss |
|---|---|---|
| Factor | Proportion[a] | Proportion[a] |
| SCCS[b] | | |
| <2.5 | 23/447 (5.1%) | 9/424 (2.1%) |
| 2.6 to 5.0 | 23/339 (6.8%) | 13/316 (4.1%) |
| >5.0 | 14/164 (8.5%) | 11/150 (7.3%) |
| Milk yield | | |
| <22.7 kg/d | 1/50 (2.0%) | 3/49 (6.1%) |
| 22.8 to 34.1 kg/d | 23/369 (6.2%) | 16/346 (4.6%) |
| 34.2 to 45.5 kg/d | 31/423 (7.3%) | 11/392 (2.8%) |
| >45.5 kg/d | 5/108 (4.6%) | 3/103 (2.9%) |
| Lactation | | |
| First | 20/369 (5.4%) | 14/349 (4.0%) |
| Second | 19/259 (7.3%) | 10/240 (4.2%) |
| ≥Third | 21/322 (6.5%) | 9/301 (3.0%) |
| Days open | | |
| <75 d | 5/57 (8.8%) | 1/52 (1.9%) |
| 76 to 150 d | 22/503 (4.4%) | 15/481 (3.1%) |
| 151 to 300 d | 27/273 (9.9%) | 7/246 (2.8%) |
| >300 d | 6/117 (5.1%) | 10/111 (9.0%) |
| No. of inseminations | | |
| One | 16/315 (5.1%) | 10/299 (3.3%) |
| Two to three | 23/336 (6.8%) | 8/313 (2.6%) |
| ≥Four | 21/299 (7.0%) | 15/278 (5.4%) |
| Season | | |
| Cool | 34/655 (5.2%) | 18/621 (2.9%) |
| Hot | 21/236 (8.9%) | 10/225 (4.4%) |

[a]Data represent the number of females with fetal loss/total number of females.
[b]Somatic cell count score.

**Table 3.** Adjusted odds ratio (AOR) estimates and 95% Wald confidence interval (CI) for factors significantly associated with early and mid-to-late fetal loss: days open and somatic cell count score (SCCS)

| | Early fetal loss | | | Mid-to-late fetal loss | | |
|---|---|---|---|---|---|---|
| Factor | AOR | 95% Wald CI | *P*-value[a] | AOR | 95% Wald CI | *P*-value[b] |
| Days open[b] | | | | | | |
| 76 to 150 d vs. <75 d | 1.90 | 0.63, 5.80 | 0.257 | — | — | — |
| 76 to 150 d vs. 151 to 300 d | 2.44 | 1.33, 4.49 | 0.004 | — | — | — |
| 76 to 150 d vs. >300 d | 1.28 | 0.50, 3.27 | 0.604 | — | — | — |
| SCCS[cd] | | | | | | |
| <2.5 vs. 2.6 to 5.0 | — | — | — | 1.52 | 0.56, 4.13 | 0.336 |
| <2.5 vs. >5.0 | — | — | — | 5.43 | 1.97, 14.97 | 0.001 |
| Days open[e] | | | | | | |
| <75 d vs. 76 to 150 d | — | — | — | 1.54 | 0.19, 12.38 | 0.415 |
| <75 d vs. 151 to 300 d | — | — | — | 1.18 | 0.14, 10.20 | 0.443 |
| <75 d vs. >300 d | — | — | — | 4.41 | 0.53, 36.76 | 0.086 |

[a]Derived from PROC GENMOD of SAS (SAS Inst., Inc., Cary, NC).
[b]Wald $\chi^2$ statistic = 8.66, $P < 0.05$.
[c]Somatic cell count score.
[d]Wald $\chi^2$ statistic = 12.09, $P < 0.01$.
[e]Wald $\chi^2$ statistic = 7.60, $P = 0.055$.

Average number of days open among lactating females was 163.8 d, with a range of 53 to 659 d, and days open was associated with both early and mid-to-late fetal loss of lactating females (Wald $\chi^2$ statistic = 8.66 [$P < 0.05$] and 7.60 [$P = 0.055$], respectively; Table 3). In particular, lactating females with days open between 151 to 300 d had a higher incidence of early fetal loss (9.9%) than animals with days open between 76 to 150 d (4.4%; Table 2). For mid-to-late fetal loss, lactating females with days open over 300 d experienced a greater percentage of mid-to-late fetal loss (9.0%) compared with lactating females in the other categories (1.9, 3.1, and 2.8%, respectively, for cows that were <75 d, 76 to 150 d, and 151 to 300 d open; Table 2).

There were no associations of milk yield, lactation number, times inseminated, or season of breeding with the incidence of early or mid-to-late fetal loss. Average milk yield at insemination was 35.6 kg/d (range = 9.3 to 57.3 kg/d), lactation number was 2.2 (range = 1 to 8 lactations), and number of times inseminated was 3.1 (range = 1 to 16 inseminations).

### *Factors Associated with Early and Mid-to-Late Fetal Loss for Nonlactating Heifers*

The descriptive statistics of each factor examined are depicted in Table 4. There were no associations with number of times inseminated, season of breeding, or age at pregnancy on early or mid-to-late fetal loss.

## Discussion

The overall rate of fetal loss (i.e., the sum of early and mid-to-late fetal losses) in the present study was 10.0% for lactating females and 4.7% for nonlactating heifers. These values are comparable to values compiled from the literature by Santos et al. (2004b). In that review, overall rate of pregnancy loss was 10.7% for lactating females (based on a compilation of 10 studies) and 4.2% for dairy heifers (based on five studies). The present conclusion that lactating females are more likely to have increased fetal losses during both the early and mid-to-late periods compared with nonlactating heifers is thus consistent with the literature.

Comparisons of lactating females with nonlactating heifers involve confounded effects of age, lactation status, housing, breeding protocols, and other factors. Of these factors, age and lactation status are the most likely to have caused the difference in fetal loss between cows and heifers. Uterine capacity may be lower in younger animals as indicated by lower birth weights for calves born from primiparous females than for cows at second or third parity (Kertz et al., 1997). Stress associated with lactation could also compromise fetal survival. Increased feed intake associated with lacta-

**Table 4.** Descriptive statistics for the incidence of early and mid-to-late fetal loss for nonlactating heifers

| | Early fetal loss | Mid-to-late fetal loss |
|---|---|---|
| Factor | Proportion[a] | Proportion[a] |
| No. of inseminations | | |
| One | 9/177 (5.1%) | 2/168 (1.2%) |
| Two to three | 3/130 (2.3%) | 2/127 (1.6%) |
| ≥Four | 2/79 (2.5%) | 0/77 (0.0%) |
| Season | | |
| Cool | 7/231 (3.0%) | 3/224 (1.3%) |
| Hot | 7/154 (4.5%) | 1/147 (0.7%) |
| Age at breeding | | |
| ≤15 mo | 12/325 (3.7%) | 4/313 (1.3%) |
| >15 mo | 2/61 (3.3%) | 0/59 (0.0%) |

[a]Data represent the number of females with fetal loss/total number of females.

tion can elevate liver blood flow and metabolism of progesterone during pregnancy (Sangsritavong et al., 2002; Vasconcelos et al., 2003). Luteal progesterone production is needed for the maintenance of pregnancy for the majority of gestation (approximately 200 d; reviewed by Niswender et al., 2000), and the decreased circulating progesterone concentrations associated with increased feed intake during lactation might compromise fetal development and lead to fetal loss. Recently, López-Gatius et al. (2004) demonstrated that 28-d administration of supplemental progesterone to pregnant, lactating cows beginning at d 36 to 42 decreased pregnancy losses at d 90 of pregnancy. Other hormonal changes associated with lactation (e.g., oxytocin release associated with milk ejection) also could conceivably compromise fetal survival.

Another possible cause of increased fetal loss associated with lactation is mastitis. In the present study, cows with high SCCS near the time of insemination were more likely to experience mid-to-late fetal losses. Similarly, cows diagnosed with mastitis during the first 45 d of gestation were 2.7 times more at risk of abortion within the following 90 d of gestation compared with cows without mastitis (Risco et al., 1999). A separate study found that mastitis was associated with increased rate of abortions independent of the timing of the first clinical mastitis occurrence during lactation (Santos et al., 2004a). Given that cows that experience mastitis near insemination are also likely to experience mastitis later in lactation (Elvinger et al., 1991; Sargeant et al., 1998), it is not clear at which stages of pregnancy physiological changes induced by mastitis could interfere with maintenance of pregnancy. Among the potential consequences of mastitis that could affect fetal survival are increased secretion of $PGF_{2\alpha}$ (Hockett et al., 2000) and an increase in circulating concentrations of cytokines, such as tumor necrosis factor-$\alpha$ (Perkins et al., 2002), which has been implicated in pregnancy loss in mice (Gorivodsky et al., 1998). Note, however, that changes in blood concentrations of cytokines are not always observed in mastitis (Lehtolainen et al., 2004).

As seen previously (López-Gatius et al., 2002; Silke et al., 2002), differences in milk yield were not associated with rate of fetal loss among lactating females. Such a result would indicate that the difference in fetal losses between lactating cows and nonlactating heifers is related more to age than to lactation status, or that stresses of lactation causing fetal loss are not the result of the metabolic demands of lactation (which would increase with increasing milk yield), but rather other consequences of lactation independent of milk yield (such as hormonal changes and mastitis).

In the present study, increased days open at the time of pregnancy establishment was associated with increased fetal losses. The reason for this relationship is unclear because there was no relationship between number of times inseminated and fetal losses. In other studies, there were no relationships between calving to insemination interval or days open and pregnancy loss by d 84 to 90 of gestation (Silke et al., 2002; López-Gatius et al., 2004). One contribution to days open would be the occurrence of undocumented pregnancy losses, and it is possible that the relationship between days open and fetal loss seen here represents repeatability of fetal loss. The fact that the number of times inseminated did not affect pregnancy loss would imply that the ability of a cow to establish pregnancy is not related to the ability to maintain that pregnancy in the fetal period. The lack of a strong relationship between pregnancy establishment and fetal survival is not unexpected given the large number of environmental determinants of cow fertility.

It was hypothesized that heat stress during the course of gestation compromises fetal loss and that one result would be an effect of breeding season on rates of fetal loss. This hypothesis was based on decreases in placental blood flow and size in sheep (Alexander et al., 1987; Bell et al., 1987), as well as reductions in placental hormone secretion and fetal growth caused by heat stress in cattle (Collier et al., 1982). In contrast with our hypothesis, there was no association of season of breeding with rates of fetal loss. Interpretation of this result is made difficult by the fact that heat stress occurs throughout much of the year in Florida, and gestation in the bovine is 9 mo. Thus, all females experienced heat stress at some point of gestation and the lack of a seasonal effect could reflect either a lack of effect of heat stress on fetal survival or effects of heat stress on pregnancy loss occurring at several stages of gestation.

In conclusion, lactating females were more likely to have increased early and mid-to-late fetal loss than nonlactating heifers. Increased fetal losses were associated with increased days open for lactating females, and the occurrence of mastitis was associated with mid-to-late fetal loss. Although season of breeding was not associated with fetal loss, it cannot be determined whether heat stress has no effect on fetal survival or that compromising effects of heat stress on pregnancy loss were obscured by the occurrence of heat stress at various points during gestation in most animals.

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