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Theriogenology

Association of postpartum diseases occurring within 60 days after calving with productivity and reproductive performance in dairy cows in Fukuoka: A cow-level, retrospective cohort study

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ABSTRACT. Peripartum disorders in dairy cows negatively influence their productivity and reproductive performance. However, only a few reports have clearly indicated the influence of such disorders on the productivity and reproductive performance at a local-area or cow-level in Japan. This study aimed to elucidate the influence of diseases occurring within 60 days after calving on subsequent productivity and reproductive performance. Accordingly, a wide-area database on dairy production was used for epidemiological analysis; subsequently, multivariable analysis was performed to investigate the association of such diseases with productivity or reproductive performance in 6,545 cows from 178 farms in Fukuoka. We used 305-day energy-corrected milk (305 ECM) as an index of productivity and conception and culling as indices of reproductive performance. With regard to causality, mixed-effects model was used for analyzing the association between disease and productivity, and Cox proportional hazard model was used for analyzing the association between disease and reproductive performance. Compared to the disease absence group, the disease presence group demonstrated significantly lower 305 ECM [−154 kg; 95% confidence interval (CI), −229 to −79] and risk of pregnancy [hazard ratio (HR), 0.85; 95% CI, 0.80–0.91] and higher risk of culling (HR, 1.36; 95% CI, 1.17–1.59). These results indicate that, in Fukuoka, dairy cows affected by diseases within 60 days after calving exhibit lower productivity and reproductive performance. Therefore, proper dairy cow management during the peripartum period to prevent diseases during early lactation may maintain or improve productivity.

KEY WORDS: dairy cow, epidemiological analysis, peripartum period, productivity, reproductive performance

The Japanese archipelago stretches from north to south and has a few different climatic zones, ranging from the subtropical areas of the south to the subarctic areas of the north. About 67% of the land in Japan consists of mountains, and thus, the self-sufficiency rate for grass production is very low. Moreover, this rate varies from region to region. Dairy cow productivity and reproductive performance are influenced by many environmental factors, such as climate and geography [15, 23]. Therefore, it is important to consider each area's characteristics and farming background. In Japan, Holstein Friesians account for 98% of the total number of dairy cattle (about 1.35 million) the country, and more than half of these cattle are raised in Hokkaido Prefecture in northern Japan [35]. Thus, national data is not necessarily suitable as a reference for all dairy-producing regions because the records of Hokkaido Prefecture have the largest impact on national information. Therefore, it is important to make up the regional information using the

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data to improve dairy farming in each specific region.

Peripartum disorders in dairy cows negatively influences productivity and reproductive performance. Maizon *et al*. showed that days open increased in cows with dystocia, stillbirth, retained placenta, metritis, or other diseases occurring during the first 45 days after calving [33]. Giuliodori *et al.* reported that peripartum management influences subsequent reproductive performance, which is one of the most important factors influencing efficient dairy management [17]. High culling rate can sometimes be viewed as a sign of management failure [12]. Reportedly, the farmer's management style and attitude significantly contribute to the variation in farm performance [5]. Stable and efficient farm management are essential for the maintenance or improvement of productivity and reproductive performance. Koketsu [30] reported that it is essential to make decisions on the basis of evidence from production records to control productivity. Demographic, reproduction, production, and health factors are determinants involved in the administration of a farm enterprise [25]. Epidemiological observational studies are suitable for analyzing the factors that hinder productivity or reproductive performance [36]. There are several reports about Japanese Black cows [28, 29, 41]; however, very few reports have concretely elucidated such factors using dairy cows from a local prefectural unit in Japan.

In dairy cattle, improper transitional period management after calving causes negative energy balance, decreased milk production, increased cow morbidity, delayed uterus recovery, and reduced reproductive potential [3, 4, 16, 22]. Therefore, proper feeding and management during the transitional period may improve postpartum productivity and reproductive performance in dairy cows. Additionally, the incidence of common clinical diseases is closely associated with calving, with the high-risk period being within 30 days after calving [18, 27, 39]. The highest rates of culling occurred near parturition in the first 60 days in milk [6, 24]. Fetrow *et al*. analyzed culling history on dairies, and indicated that the turnover rates in subsets of the total population in the first 60 days of lactation was often useful for recognizing farm management [13]. Therefore, this study focuses on monitoring the incidence of diseases in dairy cows during the first 60 days of lactation as an index for peripartum management in the dairy farm.

In our previous herd-level study, we focused on elucidating the importance of herd management during dry period [19]. We suggested that during dry periods in Fukuoka, appropriate dairy herd management, which aims to prevent increases in the culling and death rates during early lactation, may maintain or improve reproductive performance. However, our previous study had limitations because it was a herd-level, cross-sectional study carried out over a period of only 1 year. Further studies at an individual cow level for a longer period, using the database created in our previous study, are warranted to elucidate key management points for improving productivity and reproductive performance of dairy herds in this area. Moreover, few longitudinal studies analyzed dairy productivity and reproductive performance in detail, in Japan. We replaced transition or dry period management problems with diseases occurring within 60 days after calving, and verified the hypothesis that, in Fukuoka, productivity and reproductive performance are low in dairy cows because of the occurrence of diseases within 60 days after calving, using a retrospective cohort study design at cow level.

MATERIALS AND METHODS

Study area

Fukuoka (coordinates: 33° 35′ N and 130° 24′ E) is a prefecture in Kyushu, Southern Japan. Fukuoka has a subtropical climate with humid summers and relatively mild winters. Most dairy farmers in Fukuoka rely on imported livestock feed, and the self-sufficiency rate of grass is very low. Additionally, Fukuoka was divided into three different areas on the basis of productivity background (Northwest, Northeast, South).

Data collection and processing

This study was carried out according to the guidelines for the care and use of laboratory animals at Obihiro University of Agriculture and Veterinary Medicine. For our previous study, we used a database created using data from three organizations, Dairy Cooperative Association, Livestock Improvement Association of Japan (LIAJ), and Federation of Agricultural Mutual Relief Association [19]. Dairy Cooperative Association manages herd-level productivity information, while LIAJ manages cow-level productivity and reproductive information. Lastly, the Federation of Agricultural Mutual Relief Association manages disease information of individual cattle. For the present study, we extracted records on dairy farms from April 1, 2012 to March 31, 2014, which included records of 178 out of 274 dairy farms in Fukuoka. The profile of the 178 farms was as follows: mean number of cows, 43 ± 25 (average ± standard deviation); parity, 2.8 ± 0.4; and individual milk yield per day, 23.5 ± 3.0 kg. Cow data for this study were collected from the database for cows calved from April 1, 2012 to March 31, 2013 as the section criterion. If a cow had calved twice during this period, records of the first calving were used. From the initially selected 6,776 cows, 231 cows that were culled within the first 60 days after calving were excluded, as groups at 60 days after calving were set; thus, 6,545 cows were finally included in the study. The cows were followed up for 330 days after calving.

Variables

Independent variable:

This was defined by the presence or absence of a disease within 60 days after calving. On the basis of this variable, cows were classified into two groups: disease presence (2,758 cows) and disease absence (3,787 cows) groups.

Dependent variables:

Three hundred and five-day energy-corrected milk (ECM). When days in milk (DIM) exceeded 305, ECM was calculated from the measured value.

When DIM ranged from 240 to 305, ECM was calculated from the estimated value. When DIM were <240, ECM data were excluded from analysis. ECM was expressed as the amount of energy in milk based on milk weight, with fat and protein contents standardized to 3.5 and 3.2% [7], respectively, using the following formula:

3.5/3.2 ECM=(0.327 × milk in kg) + (12.95 × milk fat in kg) + (7.65 × milk protein in kg).

Pregnancy. In this study, days open is the interval between calving and artificial insemination (AI) dates for the cows that conceived within 300 days of calving. For survival analysis using Cox proportional hazard regression model, the follow-up period was 200 days from calving and the endpoint was the point when AI led to pregnancy.

Culling. The number of cows that were culled within 300 days after calving was calculated in this study. For survival analysis using Cox proportional hazard regression model, the follow-up period was 300 days from calving and the endpoint was culling.

Confounding variables:

The following six confounding variables were used: parity (1, 2, or ≥3), calving season (Spring: March–May, Summer: June–August, Autumn: September–November, or Winter: December–February), area (Northeast, Northwest, or South), herd size (<30, ≥30– <50, or ≥50), and stall type (tie stall, free stall, or free barn) for fixed effect and farm (n=178) for random effect. In this case, we categorized herd size on the basis of quartile point of the annual average number of cows in the farms.

Statistical analysis

The outcomes were described using summary statistics. For univariable analysis, the comparison means of a continuous variable between two groups were evaluated using χ^2 and Cochran–Armitage trend tests using data from analysis of variance and contingency table analysis among groups. For multivariable analysis, when the outcome was a continuous variable, such as 305 ECM, a general linear mixed regression model was used to assess the effect using estimated values (EV) and 95% confidence intervals (CIs). When the outcome was a categorical variable, that is, time-to-event such as pregnancy or culling, Cox proportional hazards regression model was used to assess the relative risk as hazard ratios (HRs) and 95% CIs. Interaction effects between two categorical independent variables were included in all models, but insignificant interactions were removed from the final models ($P \geq 0.05$). Values were considered statistically significant at $P<0.05$. All statistical analysis were performed using SAS version 9.4 (SAS Institute Japan Ltd., Tokyo, Japan).

RESULTS

In this study, the percentage of cows with diseases within 60 days after calving was 42%. The major categories of diseases in the disease presence group were perinatal (34%), udder (18%), and metabolic (17%) diseases; metabolic diseases included milk fever, mastitis, and ketosis, respectively.

Tables 1, 2, and 3 show the mean, median, and distribution (standard deviation, lower and upper quartiles) of three dependent variables, respectively. The percentage of cows for which 305 ECM was calculated was significantly higher in the disease absence group than in the disease presence group (89% vs. 86%); however, the 305 ECM value was similar in both the groups ($P=0.580$). Similarly, the percentage of pregnant cows with days open within 300 after calving was significantly higher in the disease absence group than in the disease presence group (80 vs. 77%). However, this parameter was significantly lower in the disease absence group than in the disease presence group (median: 125 vs. 136 days). The percentage of cows that were culled within 300 days after calving was significantly lower in the disease absence group than in the disease presence group (9 vs. 14%), whereas the days to culling after calving were similar in both the groups ($P=0.349$).

The distribution of disease occurrence within 60 days after calving in the category groups of each confounding variable is shown in Table 4. Parity, area, herd size, and stall type showed significant differences among category groups. Moreover, with regard to rank order categories, disease occurrence tended to increase with an increase in parity ($P_{trend}<0.001$) and a decrease in the herd size ($P_{trend}=0.002$).

The relationship between disease occurrence within 60 days after calving and 305 ECM was analyzed using general linear mixed regression model with six confounding variables (Table 5). On the basis of the independent variable, 305 ECM of 89.0% of the cows in the disease absence group and 85.7% of those in the disease presence group were calculated. 305 ECM value was significantly lower [−154 (95% CI: −229 to −79) kg] in the disease presence group than in the disease absence group.

The relationship between disease occurrence within 60 days and conception within 200 days after calving was analyzed using Cox proportional hazards regression model with six confounding variables (Table 6). On the basis of the independent variable, the percentage of cows that conceived within 200 days after calving was 63.7% in the disease absence group and 59.1% in the disease presence group. The disease presence group demonstrated significantly lower fertility (HR: 0.85, 95% CI: 0.80–0.91) than the disease absence group.

The relationship between disease occurrence within 60 days after calving and culling within 300 days after calving were analyzed using Cox proportional hazards regression model with six confounding variables (Table 7). With regard to the independent variable, the percentage of culling cows that conceived within 300 days after calving was 8.7% in the disease absence group and 13.7% in the disease presence group. The disease presence group demonstrated significantly higher risk of being culled (HR: 1.36; 95% CI: 1.17–1.59) than the disease absence group.

Table 1. Summary of 305-day energy-corrected milk (305 ECM)

Disease group	N	n	n/N (%)	305 ECM (kg)					$P^{a)}$
				Mean	SD	Lower quartile	Median	Upper quartile	
Absence	3,787	3,371	89[b)]	9,800	1,753	8,630	9,712	10,911	0.580
Presence	2,758	2,364	86	9,844	1,882	8,569	9,729	10,985	

a) One-way analysis of variance. b) χ^2: P<0.001.

Table 2. Summary of days open within 300 days after calving

Disease group	N	n	n/N (%)	Days open (days)					$P^{a)}$
				Mean	SD	Lower quartile	Median	Upper quartile	
Absence	3,787	3,044	80[b)]	139	68	84	125	185	<0.001
Presence	2,758	2,121	77	148	67	93	136	195	

a) One-way analysis of variance. b) χ^2: P<0.001.

Table 3. Summary of days to culling within 300 days after calving

Disease group	N	n	n/N (%)	Days to culling (days)					$P^{a)}$
				Mean	SD	Lower quartile	Median	Upper quartile	
Absence	3,787	329	9[b)]	180	68	116	188	234	0.349
Presence	2,758	379	14	176	69	113	173	237	

a) One-way analysis of variance. b) χ^2: P<0.001.

Table 4. Disease occurrence within 60 days after calving in the category groups of each confounding variable (n=6,545 cows)

Variable	Category	N	Presence n (%)	Absence n (%)	P	P-trend
Parity	1	1,912	652 (34.1)	1,260 (65.9)	<0.001	<0.001
	2	1,648	626 (38.0)	1,022 (62.0)		
	3≤	2,985	1,480 (49.6)	1,505 (50.4)		
Calving season	Spring	1,265	535 (42.3)	730 (57.7)	0.535	
	Summer	1,626	707 (43.5)	919 (56.5)		
	Autumn	1,831	751 (41.0)	1,080 (59.0)		
	Winter	1,823	765 (42.0)	1,058 (58.0)		
Area	Northwest	2,242	962 (42.9)	1,280 (57.1)	0.038	
	South	3,307	1,413 (42.7)	1,894 (57.3)		
	Northeast	996	383 (38.5)	613 (61.5)		
Herd size[a)]	<30	1,129	502 (44.5)	627 (55.5)	0.003	0.002
	30≤ to <50	2,455	1,076 (43.8)	1,379 (56.2)		
	50≤	2,961	1,180 (39.9)	1,781 (60.1)		
Stall type	Tie stall	4,308	1,844 (42.8)	2,464 (57.2)	0.003	
	Free stall	826	303 (36.7)	523 (63.3)		
	Free barn	1,411	611 (43.3)	800 (56.7)		

P: χ^2, P-trend: Cochran–Armitage trend test. a) Mean number of cows.

DISCUSSION

In this retrospective cohort study on dairy cows in Fukuoka, our results suggest that the incidence of diseases within 60 days after calving is significantly associated with a decrease in the productivity and reproductive performance after adjustment for parity and other potential confounding variables.

Energy-corrected milk was calculated and used as an index of cow productivity. In a similar study conducted on dairy cows in France, the incidence of disorders was found to negatively influence the length of productive life [1]. The incidence of common clinical diseases is closely associated with calving, with the high-risk period being within 30 days after calving [18, 27, 39]. Cows experiencing postpartum hyperketonemia are at a higher risks of subsequent low milk production than clinically healthy

Table 5. Relationship between disease occurrence within 60 days after calving and 305-day energy-corrected milk as determined general linear mixed regression model

Variable	Category	N	n	n/N (%)	EV	95% CI	*P*
Independent variable							
Disease	Absence	3,787	3,371	89.0	0	-	-
	Presence	2,758	2,364	85.7	−154	−229–−79	<0.001
Confounding variables							
Parity	1	1,912	1,819	95.1	0	-	-
	2	1,648	1,502	91.1	1,135	1,043–1,228	<0.001
	3≤	2,985	2,414	80.9	1,537	1,453–1,621	<0.001
Calving season	Spring	1,265	1,097	86.7	0	-	-
	Summer	1,626	1,436	88.3	−280	−387–−174	<0.001
	Autumn	1,831	1,644	89.8	−28	−131–77	0.604
	Winter	1,823	1,558	85.5	58	−47–163	0.277
Area	Northwest	2,242	1,973	88.0	0	-	-
	South	3,307	2,875	86.9	−209	−537–119	0.211
	Northeast	996	887	89.1	−95	−509–320	0.654
Herd size[a)]	<30	1,129	994	88.0	0	-	-
	30≤ to <50	2,455	2,144	87.3	606	274–937	<0.001
	50≤	2,961	2,597	87.7	1,172	676–1,668	<0.001
Stall type	Tie stall	4,308	3,770	87.5	0	-	-
	Free stall	826	728	88.1	−19	−676–638	0.955
	Free barn	1,411	1,237	87.7	68	−480–616	0.808

Farm for random effect was added as a confounding factor in this model. EV: estimated value. 95% CI: 95% confidence intervals for estimated value. *P*: probability of the reference category in the variable. a) Mean number of cows.

Table 6. Association between disease occurrence within 60 days after calving and days open as determined by Cox proportional hazard regression model

Variable	Category	N	n	n/N (%)	HR	95% CI	*P*
Independent variable							
Disease	Absence	3,787	2,411	63.7	1.00	-	-
	Presence	2,758	1,630	59.1	0.85	0.80–0.91	<0.001
Confounding variables							
Parity	1	1,912	1,303	68.1	1.00	-	-
	2	1,648	1,052	63.8	0.87	0.80–0.94	<0.001
	3≤	2,985	1,686	56.5	0.71	0.66–0.77	<0.001
Calving season	Spring	1,265	698	55.2	1.00	-	-
	Summer	1,626	1,058	65.1	1.36	1.23–1.50	<0.001
	Autumn	1,831	1,193	65.2	1.39	1.26–1.53	<0.001
	Winter	1,823	1,092	59.9	1.27	1.15–1.40	<0.001
Area	Northwest	2,242	1,468	65.5	1.00	-	-
	South	3,307	1,966	59.4	0.89	0.78–1.01	0.079
	Northeast	996	607	60.9	0.94	0.79–1.11	0.454
Herd size[a)]	30	1,129	649	57.5	1.00	-	-
	30≤ to <50	2,455	1,517	61.8	1.13	0.98–1.30	0.085
	50≤	2,961	1,875	63.3	1.22	1.01–1.48	0.042
Stall type	Tie stall	4,308	2,652	61.6	1.00	-	-
	Free stall	826	515	62.3	0.94	0.74–1.20	0.608
	Free barn	1,411	874	61.9	0.95	0.77–1.17	0.617

Farm for random effect was added as a confounding factor in this model. HR: hazard ratio, 95% CI: 95% confidence intervals for hazard ratio. *P*: probability of the reference category in the variable. a) Mean number of cows.

cows [11, 34]. Therefore, we evaluated the association between disease occurrence within 60 days after calving and 305 ECM. ECM estimated using univariable analysis was not significantly different between both the groups (*P*=0.580). Nevertheless, the percentage of cows for which 305 ECM could be calculated was greater in the disease absence group than in the disease presence group. These results may have been due to the lack of adjustment for the confounding factors. As seen in Table 4, the group with

Table 7. Association between disease occurrence within 60 days after calving and days to culling after calving as determined by Cox proportional hazard regression model

Variable	Category	N	n	n/N (%)	HR	95% CI	*P*
Independent variable							
Disease	Absence	3,787	329	8.7	1.00	-	-
	Presence	2,758	379	13.7	1.36	1.17–1.59	<0.001
Confounding variables							
Parity	1	1,912	53	2.8	1.00	-	-
	2	1,648	123	7.5	2.79	2.02–3.85	<0.001
	3≤	2,985	532	17.8	7.04	5.29–9.35	<0.001
Calving season	Spring	1,265	147	11.6	1.00	-	-
	Summer	1,626	152	9.3	0.76	0.61–0.96	0.020
	Autumn	1,831	172	9.4	0.67	0.54–0.84	<0.001
	Winter	1,823	237	13.0	1.00	0.81–1.23	0.973
Area	Northwest	2,242	214	9.5	1.00	-	-
	South	3,307	396	12.0	1.29	1.06–1.56	0.011
	Northeast	996	98	9.8	1.01	0.77–1.33	0.919
Herd size[a)]	<30	1,129	119	10.5	1.00	-	-
	30≤ to <50	2,455	302	12.3	1.15	0.91–1.45	0.248
	50≤	2,961	287	9.7	1.06	0.78–1.43	0.709
Stall type	Tie stall	4,308	499	11.6	1.00	-	-
	Free stall	826	89	10.8	0.95	0.68–1.32	0.749
	Free barn	1,411	120	8.5	0.64	0.47–0.87	0.004

Farm for random effect was added as a confounding factor in this model. HR: hazard ratio, 95% CI: 95% confidence intervals for hazard ratio. *P*: probability of the reference category in the variable. a) Mean number of cows.

a parity of ≥3 demonstrated the highest incidence of diseases. This may be because the milk yield and culling rate increase with an increase in parity [32]. Considering the results of univariable analysis, the differences between the groups can be attributed to the fact that the parity of majority of the cows was ≥3 in disease presence group, but it was 1 or 2 in the disease absence group. Multivariable analysis with confounding variables showed a significantly lower 305 ECM (EV, −154 kg) in the disease presence group than in the disease absence group. In a comprehensive assessment of 305 ECM using both univariable and multivariable analysis, disease occurrence during early postpartum period negatively affected subsequent milk production.

In the present study, days open and days to culling after calving were used as indices to assess reproductive performance. Univariable analysis for days open, a dependent variable, demonstrated a significantly higher number of days open in the disease presence group than in the disease absence group. Multivariable analysis also showed that fertility was lower in the cows of the disease presence group than those of the other group (adjusted HR, 0.85). Univariable analysis for culling, another dependent variable, demonstrated no significant difference between the two groups within 60 days after calving (*P*=0.349). Furthermore, this parameter was analyzed using Cox proportional hazards model, which was adjusted for the confounding factor and judged on the basis of the estimated value. Culling was found to be significantly higher in the disease presence group than in the disease absence group (adjusted HR, 1.36). Overall, these results indicate that, in Fukuoka, dairy cows with diseases occurring within 60 days after calving show lower productivity and reproductive performance. Dubuc *et al*. reported that postpartum diseases frequently occurred in Canadian dairy herds, and alarm levels determined using median herd prevalence of postpartum diseases were identified as risk factors for poor reproductive performance and increased culling [8]. Among postpartum diseases, displaced abomasum and milk fever are known as risk factors for culling [2, 8, 21, 26]. Furthermore, hyperketonemia is known to increase the likelihood of displaced abomasum [11, 34]. Therefore, cows experiencing postpartum hyperketonemia have a higher risk of early culling and poor reproductive performance than healthy cows [34, 37, 40, 42]. Peripartum disorders impair reproductive performance, and they have been identified as risk factors for subsequent culling in dairy herds [3, 21, 38]. Retained placenta is a well-known risk factor for metritis and endometritis [31]. Consequently, it negatively affects reproductive performance [10, 14, 20]. By itself, retained placenta is known to have no effect on culling [9, 21, 26]; however, some studies point to this condition as a risk factor [2, 8]. In the present study, the only independent variable was the occurrence of diseases during the early postpartum period. Our results are consistent with those of previous studies conducted in other countries and to the best of our knowledge, identify a concrete quantified relative risk for the first time in Fukuoka, Japan.

We should consider the following limitations when interpreting our data. First, the sample population may not be a representative of all the cows in Fukuoka, because the data were mainly collected only from the member farms of Livestock Improvement Association of Japan. Second, the period for collecting samples (1 year) may be short, and disease occurrence and productivity may not be constant each year in dairy cows. Finally, the adjustment of confounding factors may be insufficient; calving condition, milk yield, and calving-to-calving interval could generate a bias in the determination of reproductive performance or productivity. Nevertheless, we analyzed corrected data from three organizations supporting dairy farms, and further studies including more data are warranted to improve our understanding of this subject.

In conclusion, multivariable analysis with six confounding factors were performed considering different backgrounds of the cows and the influence of disease occurrence during early postpartum period on subsequent productivity and reproductive performance was elucidated. Additionally, we could obtain more applicable results by analyzing farm data from local areas. Such information would facilitate the development of an advisory tool for farms in which dairy cows frequently suffer from postpartum diseases. To design a concrete strategy to improve productivity and reproductive performance in dairy cows, further long-term research investigating the influence of individual postpartum diseases will be needed.

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