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Modelling the Effect of Metabolic Diseases on Lactation Curves of Vrindavani Cattle

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ABSTRACT

Metabolic diseases are the disease related to disturbance of one or more metabolic processes in the dairy animals due to nutritional imbalances or inefficient farm management. Metabolic diseases are reported worldwide irrespective of geographical and climatic conditions. The present study aims to find the best fitted model that describes the lactation behaviour of Vrindavani cattle (Crossbred Cattle) in diseased and healthy condition. Five standard lactation curve models i.e. Incomplete Gamma function (WD), Linear decline model (CL), Wilmink model (WL), Mixed log model (ML) and Mitscherlich x Exponential (ME) were fitted on DTDMY data of primiparous healthy and diseased Vrindavani cattle maintained at cattle and buffalo farm, ICAR-IVRI, Izatnagar. The goodness of fit were judged by MSE, MAE, R^2, AIC and BIC. The Durbin-Watson and Shapiro-Wilk test was used to test the presence of autocorrelation and normality of residual respectively and the repeated measures analysis was used to study the effect of metabolic diseases on the milk production of dairy animals. The result shows that the ML and WD models were best fitted to describe the lactation pattern of healthy and diseased Vrindavani cattle. The milk production varied significantly from healthy to diseased condition ($p<0.001$) and the decrease in milk production of Vrindavani cattle due to metabolic disease was 34.42%.

Keywords: *Goodness of Fit, Lactation Curve, Nonlinear Model, Metabolic Disease, Repeated Measures ANOVA*

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INTRODUCTION

Agriculture sector is a backbone of the rural economy. Apart from providing food and nutritional security, agriculture and allied sectors provide 58 percent employment to rural population. At the time of independence, India's economy is purely agriculture based and the contribution of agriculture and allied sector in gross domestic product was approximately 50 percent. In the present scenario, the agriculture and allied sectors continuously growing at 4.1 percent and gross domestic product is expected to be 17.3 percent during 2016-17 based on Gross Value Added at 2011-12 prices [12].

Food and nutritional security in present scenario are major issues among the scientific community, beside this there is an insignificant increase in agricultural product due to huge degradation of natural resources and adverse climate change. However, a continuous increase is reported in dairy sector with an annual growth of 6.27 percent. Crossbred cattle (26 percent) are one of the major contributors to the dairy sector [3]. At present, India ranked first among the milk producing country with annual milk production 155.5 million tonnes and per capita availability of milk is around 337 grams per day in 2015-16. Milk production per animal in India is still very low and the huge milk production is due to a large number of dairy animals [1].

Lactation curves provide a better insight to the dairy management system and defined as a graphical representation of milk production over a lactation period. The initial milk production, the rate by which lactation curve reaches to peak, the rate of declination of lactation curve and peak production are the four major components of lactation curve. A number of linear and nonlinear functions have been proposed to describe the lactation behaviour of dairy animals. Catillo *et al.* studied and concluded that the Parity, lactation length and calving season have significant effects on the lactation curve of dairy animals [7]. However, the present of disease condition (Milk fever, retained placenta, ketosis, and mastitis) also affected the lactation curve. Hostens *et al.* proposed that the metabolic disease, milk production increased at faster rate and declined at slower rate as compared to cows that encountered one or more metabolic problems [15].

Dairy cattle require micro-nutrient and macro-nutrient in the form of minerals (feed and fodder or some minerals supplements) in their diet for optimal productivity. In case of milch dairy animals, the minerals contents of output (milk production) exceeds input due to the nutritional imbalances and deficiencies, or poor management of feeding programs for dairy cows and lead to negative energy balance. However, dairy animals balanced the requirements by mobilization minerals from its body reserves for a shorter period but continuous imbalances develop into production related problems known as metabolic diseases. Metabolic or postpartum metabolic diseases in dairy animals are due to negative energy balance and can be eliminated by providing balanced nutritional diet and proper farm management. Ostergaard *et al*. studied the impact of metabolic disease and concluded that there was a negative correlation between the incidence of disease and the dry matter intake result in the decrease milk production [20].

Metabolic diseases are reported worldwide irrespective of geographical and climatic conditions. The incidence rate of postpartum metabolic disease has been found to be very low in an organised farm. The incidence rate of postpartum metabolic diseases was high in crossbred cattle with respect to indigenous cattle and buffaloes. However, the incidences of postpartum metabolic diseases are found to be more in multiparous animals than primiparous dairy animals. The incidence of different postpartum metabolic disease was low i.e. 4.9% for Ketosis [21] and 1.6% for Milk fever [13] but the impact of disease on milk production was high. Hostens *et al.* used Nonlinear Milk Bot lactation model to estimate the effects of metabolic diseases and estimated the incidences of milk fever, retained placenta and ketosis was 4.8%, 3.6% and 8.3% respectively in the first 30 DIM [15]

Metabolic diseases lead to an economic burden due to reduced milk production, veterinarian or medicine cost, discarded milk and sometimes death of animals. Kelton *et al.* estimates the economic loss per cow in North USA and concluded that the impact of the postpartum metabolic disease was significant and per animals losses range from $145 (for ketosis) to $334 (for milk fever) [16]. Bareille *et al.* studied the impact of metabolic disease and concluded that the reduction in milk production and feed intake was 4.1–25.7 kg and 6.7–14.7 kg dry matter respectively [5]. Bar *et al.* 2005 estimate the production loss was 142 kg for multiparous cow with parity and three and above [4].

In view of the above discussion, the present study is systematically designed in accordance with the aims to compare five standard lactation curve models and their predictive ability in dairy animals in the postpartum metabolic disease condition.

MATERIAL AND METHODS

Source of Data

The present study aims to model the effects of postpartum metabolic disease on the lactation curves of dairy animals. For the study, 39419 DTDMY data of multiparous Vrindavani cattle (crossbred cattle) were collected from Cattle and Buffalo farm, LPM section (ICAR-Indian Veterinary Research Institute, Izatnagar). The data regarding season of calving, age at 1st calving, parity and incidence of disease were also collectedfrom record book maintained at the farm over a period of 10 years (2005-2014).

Standard Lactation Curves Model

Incomplete gamma model [26]

$$Y_t=at^be^{-ct}$$

Linear decline model [8]

$$Y_t=a-bt-ae^{-ct}$$

Exponential lactation curve model [25]

$$Y_t = a + be^{-kt}+ ct$$

Mitscherlich x Exponential [22]

$$Y_t = a(1-be^{-ct})\, e^{-dt}$$

Mixed log model [14]

$$Y_t = a +b(t)^{1/2} + c\ln(t)$$

where, *"a"* is scale parameter or milk yield at the beginning of lactation, *'b'* is a parameter represent rate of change from initial production to maximum yield, *'c'* is a parameter represent rate of change from maximum yield to the end of lactation, *'d'* is a parameter related to maximum milk yield, *'ln'* is the natural logarithms and *'k'* is the constant equal to 0.065.

Estimation of parameters of non-linear lactation curve model

Five standard lactation curve models *i.e.* Incomplete gamma model (WD), Linear decline model (CL), Exponential lactation curve model (WL), Mitscherlich x Exponential (ME) and Mixed log model (ML) were selected to describe the lactation pattern of dairy animals suffered from the postpartum metabolic disease. These five nonlinear functions were fitted by nonlinear regression to the DTDMY data described above using PROC NLIN statement of the statistical package SAS 9.3 version. Parameters of the linear model are estimated by minimizing the objective function, *i.e.* residual sum of squares but, for non-linear functionestimate of parameter are obtained by an iterative procedure. In this study, the Levenberg–Marquardt algorithm [17, 18] was used to estimates of the parameters of each of the lactation curvesalong with standard error.

Goodness of Fit

The goodness of fit provides a statistical measure of how well the regression line approximates the real test day data points. There are many model selection and model evaluation criterion present in the literature out of which, Coefficient of determination (R^2), Mean square error (MSE), Mean absolute error (MAE) were used to select the best-fitted model and Akaike's Information Criteria (AIC) and Bayesian information criterion (BIC) was used to evaluate the best model. Residuals obtained by these functions were plotted graphically.

Coefficient of Determination (R^2)

$$R^2 = 1 - \frac{\text{Residual sum of square}}{\text{Total sum of square}}$$

Mean Square Error (MSE);

$$MSE = \sum_{i=1}^{n} \frac{(O_i - P_I)^2}{n}$$

Mean Absolute Error (MAE)

$$MAE = \sum_{i=1}^{n} \frac{(O_i - P_I)}{n}$$

Akaike's Information Criteria (AIC)

$$AIC = 2P - 2\ln(L)$$

$$AIC = n\log_e MSE + 2P$$

Bayesian Information Criterion (BIC)

$$BIC = n\log_e(MSE) + P\log_e(n)$$

where, 'n' =No. of experimental observation, 'O' = Observed value, 'P' = predicted value, 'K' is the number of parameters in the model and 'L' is the maximized value of the likelihood function for the model. The value of R^2 close to 1 represents the best-fitted model. The preferred model is one which has a minimum value of MSE, MAE, AIC or BIC value.

Examination of Normality assumption of residuals (Errors)

Residuals or errors are defined as the difference between the observed and predicted value of the response. For modeling and regression analysis, there are two assumptions *viz.*

a) The errors are independently and identically distributed *i.e.* $\varepsilon \sim N(0,1)$
b) The errors have constant variance.

Durbin-Watson test was used to test the assumption regarding the independence of residuals *i.e.* no autocorrelation [11]. Shapiro-Wilk test and Kolmogorov-Smirnov test was used to test the assumption regarding the normality of the residuals [23, 24].

Repeated Measurement analysis to study the effects of postpartum metabolic disease on milk productionof dairy animals

$$y_{ij} = \mu + D_i + ID(D)Random + W_j + (DW)_{ij} + \varepsilon_{ij}$$

where, y_{ij}= Observed value of the response variable for i^{th} disease (i=1,2) at j^{th} week (j=1,2,...44); μ = General mean effect; D_i=Effect of i^{th}disease; P_j = Effect of j^{th}week; *ID(D)Random* = Random term; ε_{ij} = Error term.

RESULTS AND DISCUSSION

The incidence of postpartum metabolic disease was more in crossbred cattle. In crossbred cattle, the incidence was mostly observed in third or more parity animals. The effects of season on the incidence occurrence were non-significant. However, a significant reduction was reported in the milk production due to the incidence of disease. The summary of milk production (Table 1) shows that the peak production (kg), total production (kg) and Day in milk (day) were significantly reduced in Vrindavani cattle after the incidence of postpartum metabolic disease.

Table 1: Summary of Total milk production, lactation length and peak production of dairy animals in healthy and diseased condition

Vrindavani Cattle	Total production	Lactation length	Peak production
Diseased Vrindavani	2116.44±0.15	204.43±16.43	12.88±0.99
Multiparous Vrindavani	3368.07±0.17	295.18±2.50	19.13±0.56

Vrindavani cattle is a synthetic crossbred strain of cattle developed at ICAR-IVRI with 25-50 percent indigenous (Haryana breed) and 50-75% exotic inheritance (Jersey, Holstein Friesian and Brown Swiss). Vrindavani is prolific milk producer with 3368 kg (305 days) total production and 19.13 kg/day peak production. Due to the high exotic inheritance of Vrindavani cattle are more susceptible to adverse climatic and disease condition with respect to indigenous cattle and buffaloes. The postpartum metabolic disease has significant effects on the milk production of Vrindavani cattle. The observed DTDMY data and predicted DTMYD by the best-fitted model (ML for healthy and WD for diseased) of healthy and diseased Vrindavani cattle are represented graphically (fig. 1).

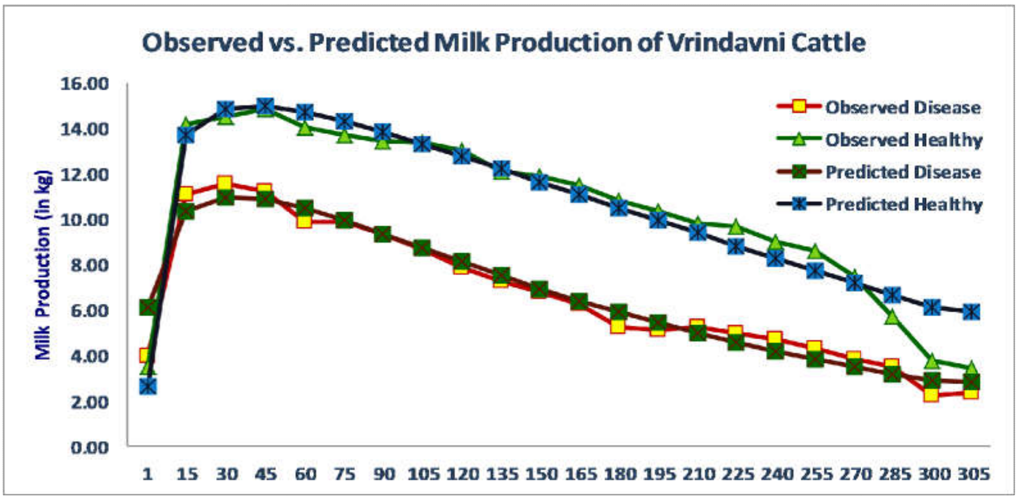

Figure 1: Observed vs. predicted milk production of Vrindavani cattle in disease and healthy condition

The estimate of the parameters of different model, various measure of goodness of fit, predicted total production and predicted peak production were separately mentioned for diseased (Table 2) and healthy Vrindavani cattle (Table 3). In case of diseased Vrindavani cattle, the lactation behaviour was best explain by WD (MSE = 0.188; R^2 = 0.974; AIC=-504.1) followed by CL (R^2 = 0.966), ML (R^2 = 0.967) ME (R^2 = 0.967) and least fitted by WL (R^2 = 0.943). Almost all lactation curve models accurately predicted the peak production and total production. Whereas, ML (MSE = 0.454; R^2 = 0.949; AIC=-234.5) was the best-fitted model to describe the lactation pattern of healthy Vrindavani cattle followed by ME (R^2 = 0.942), CL (R^2 = 0.936), WL (R^2 = 0.935) and least fitted by WD model with R^2 = 0.927. All models accurately predict the total production but underpredicted the peak production by 3.60 kg/day (CL) to 4.28kg/day (WD).

Test for independence of residuals

Durbin-Watson test statistic used to access, whether the residuals are correlated or independence. The table value of upper DW statistic critical value is d_U = 1.82541 (n=305; p=3; α=5%) and 1.83204 (n=305; p=4; α=5%) whereas the lower critical value is d_L = 1.79901 (n=305; p=3; α=5%) and 1.79236 (n=305; p=4; α=5%). There was significant autocorrelation present between residuals produced by different lactation curve models fitted on the DTDMY data of dairy animals in diseased as well as healthy conditions. If the DW statistic is more than d_U then it represents positive autocorrelation among residuals, whereas then residuals are negative autocorrelation if DW statistic is lower than d_L. Durbin-Watson test statistic values for different model in diseased and healthy dairy animals are mentioned (Table 4-5) and graphically represented by the plot of residuals against days (fig. 2-3).

Table 2: Estimated value of parameter of different lactation curves model of diseased Vrindavani cattle along with different measures of goodness of fit

Model	Parameter	Estimate	SE	MAE	MSE	R^2	AIC	BIC	PY(P)	TP(P)
CL	a	11.876	0.064	0.420	0.251	0.966	-415.1	-403.9	11.17	2115.13
	b	0.031	0.000							
	c	0.247	0.011							
ML	a	6.047	0.221	0.408	0.239	0.967	-429.9	-418.7	10.82	2116.48
	b	-1.418	0.023							
	c	3.685	0.097							
ME	a	11.915	0.065	0.410	0.242	0.967	-424.3	-409.4	11.11	2116.45
	b	0.824	0.046							
	c	0.032	0.000							
	d	0.200	0.015							
WL	a	12.254	0.092	0.519	0.416	0.943	-261.3	-250.1	10.58	2116.47
	b	-5.013	0.297							
	c	-0.033	0.000							
WD	a	6.163	0.144	0.345	0.188	0.974	-504.1	-492.9	10.97	2112.30
	b	0.230	0.007							
	c	0.007	0.000							

(SE = Standard Error; MAE = Mean Absolute Error; MSE = Mean Squared Error; R^2 = Coefficient of determination; AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion; PY (P) = Predicted Peak Yield; TP(P) = Predicted Total Production)

Table 3: Estimated value of parameter of different lactation curves model of multiparous Vrindavani cattle along with different measures of goodness of fit

Model	Parameter	Estimate	SE	MAE	MSE	R^2	AIC	BIC	PY(P)	TP(P)
CL	a	16.653	0.100	0.567	0.568	0.936	-166.7	-155.6	15.53	3364.73
	b	0.035	0.001							
	c	0.166	0.007							
ML	a	4.550	0.305	0.486	0.454	0.949	-234.5	-223.4	14.98	3368.04
	b	-1.937	0.031							
	c	6.149	0.133							
ME	a	16.862	0.106	0.536	0.520	0.942	-191.3	-176.5	15.38	3368.09
	b	0.763	0.033							
	c	0.036	0.001							
	d	0.114	0.007							
WL	a	17.370	0.108	0.561	0.579	0.935	-160.8	-149.6	15.11	3368.09
	b	-10.214	0.350							
	c	-0.038	0.001							
WD	a	6.862	0.233	0.587	0.651	0.927	-125.0	-113.9	14.85	3372.53
	b	0.265	0.010							
	c	0.005	0.000							

Table 4: Test for the presence of autocorrelation and normality of residual in Vrindavani cattle suffered from metabolic disease by different models

Model	Durbin-Watson	Kolmogorov-Smirnov		Shapiro-Wilk	
	Statistic	Statistic	Sig.	Statistic	Sig.
CL	0.246	0.079	0.000	0.976	<.0001
ML	0.348	0.085	0.000	0.968	<.0001
ME	0.246	0.077	0.000	0.969	<.0001
WL	0.167	0.069	0.001	0.945	<.0001
WD	0.334	0.064	0.004	0.942	<.0001

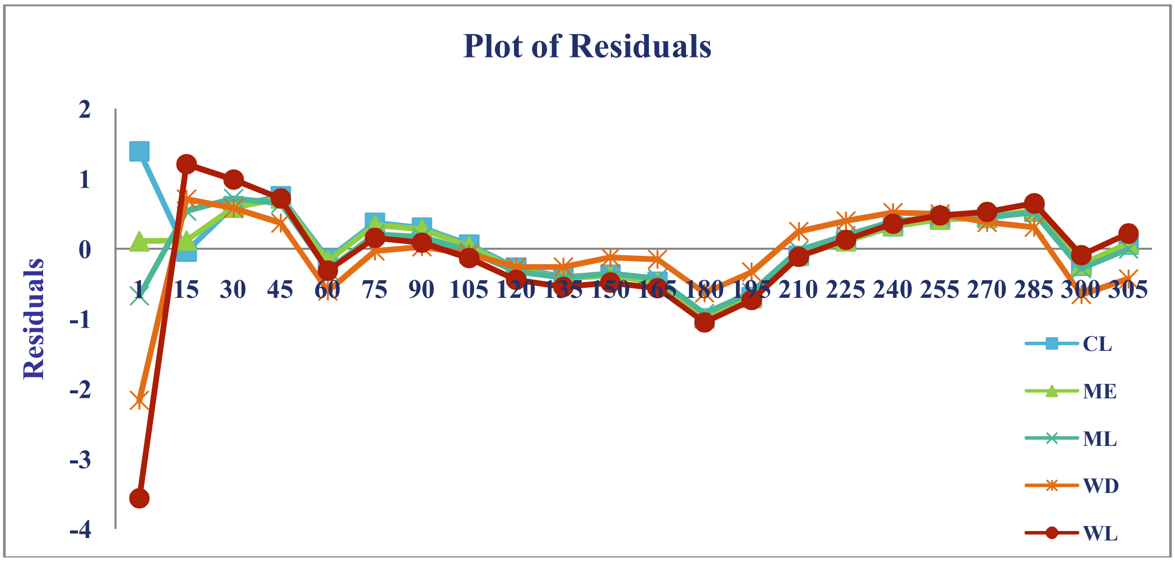

Figure 2: Residual plot in case of Milk production of diseased Vrindavani cattle

Table 5: Test for the presence of autocorrelation and normality of residual in multiparous Vrindavani cattle by different models

Model	Durbin-Watson	Kolmogorov-Smirnov		Shapiro-Wilk	
	Statistic	Statistic	Sig.	Statistic	Sig.
CL	0.136	0.126	0.000	0.906	<.0001
ML	0.146	0.090	0.000	0.912	<.0001
ME	0.161	0.109	0.000	0.906	<.0001
WL	0.169	0.071	0.001	0.927	<.0001
WD	0.131	0.102	0.000	0.909	<.0001

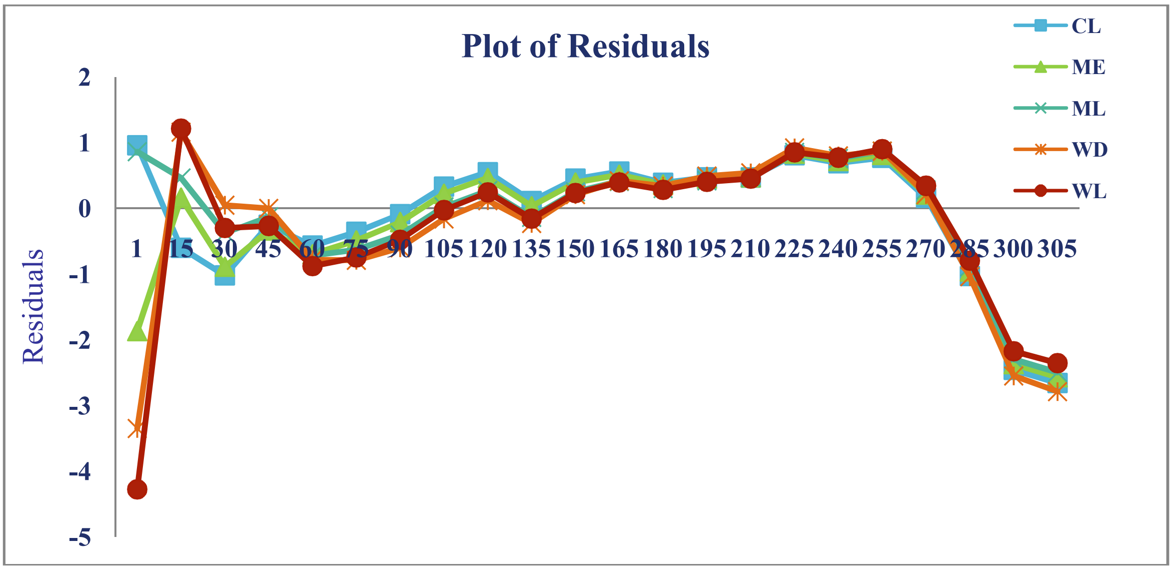

Figure 3: Residual plot in case of Milk production of healthy Vrindavani cattle

Effects of postpartum metabolic disease on milk production of dairy animals

Therepeated measure ANOVA was used to estimate the effect of postpartum metabolic disease. In case of Vrindavani cattle, the effect of postpartum metabolic disease was significant ($p<0.05$). The effects of period (week) and interaction of disease incidence and period was also significant ($p<0.001$) (Table 6). The present result was supported by study of Drackley and Appuhamy *et al.* [2, 10]. However, some studies also concluded that the metabolic diseases have an insignificant effect on milk production [6, 9].

Dairy animals undergo several changes from heifer to cow, the change may be due to several hormonal, metabolic and physiological changes. Change may be due to farm to farm or nutritional practices, which often lead to an increased incidence of diseases during this timeframe [19]. In the present study, the average production of healthy and diseased Vrindavani cattle was 11.29 kg/day and 8.21 kg/day respectively and the reduction in milk production due to disease was 27.28 percent (Table 7) and the incidence of postpartum metabolic disease produces overall negative impact on the dairy industry. The present study was supported by the study of Appuhamy *et al.,* where he concluded that the reduction in milk production due to incidence of post-partum metabolic disease in HF and Jersey cattle was 10.5% approximately [2].

Table 6: Repeated measure ANOVA for effect of disease on milk production of Vrindavani cattle

Tests with respect to Random Effects					
Source	**SS**	**MS Num**	**DF**	**F ratio**	**Prob > F**
Disease	65.6901	65.6901	1	7.2477	0.0071*
Vrindavani & Random	31243.4	452.803	69	49.9584	<.0001*
Week	36665.3	852.681	43	94.0774	<.0001*
Disease*Week	1211.82	28.1819	43	3.1093	<.0001*

Table 7: Effect of disease on milk production of Vrindavani cattle

Least Squares Means Table			
Level	**Least Squares Mean**	**S.E**	**Mean**
Diseased Vrindavani cattle	9.560110 ^{a}	0.13584106	8.2073
Healthy Vrindavani cattle	10.081116 ^{b}	0.08282642	11.2960

CONCLUSION

The ML and WD model was the best-fitted model to describe the lactation pattern of Vrindavani cattle in healthy and disease condition respectively. The effect of postpartum metabolic disease was significant on the milk production and 27.28 percent reduction in milk productiondue to disease.The study was based on data collected from an organised farm where better management conditions are provided to dairy animals. So, the result regarding reduction in milk production may vary in field condition. The impact of metabolic disease must be reduced by proper feeding and management practices.

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