The use of dijkstra mechanistic model for genetic analysis of the lactation curve characteristics and their relationships with age at first calving and somatic cell score of Iranian dairy cows

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ABSTRACT. The objective of this study was to estimate lactation curve parameters with Dijkstra mechanistic model and to evaluate genetic and phenotypic relationships between the parameters and the average somatic cell count in primiparous cows. The finding indicated that heritability estimates for partial milk yield (PMY1, PMY2 and PMY3), total 305-day milk yield (TMY305), decay parameter (λ2), age at first calving (AFC) and peak yield (PY) were moderate while the heritability of persistency (PS%), average somatic cell score (AVGSCS), time to peak yield (TP), initial milk production (λ0), specific rate of cell proliferation at parturition (λ1), and specific rate of cell death (λ3) were quite low. Genetic correlations between both AFC and PS% traits with average somatic cell scores was negative (-0.047 and -0.060) but low positive genetic correlation were between partial milk yields (PMY1 and PMY3) while negative genetic correlation (-0.06) was obtained between TMY305 and AVGSCS. Differences between TMY305 of cows with less than 100000 cells mL-1 and cows with >1,500,000 cells mL-1 was approximately 708 Kg and is equivalent to 8% loss of milk yield/cow during lactation period and also loss of persistency (11.1 %) was shown for the extreme classes of SCC in this study.

Keywords: genetic parameters; milk yield traits; persistency; somatic cell count.

Introduction

Milk production, reproduction performance and udder health are the most important traits in dairy cattle breeding programs. Relationship between these traits could have a major impact on dairy cattle production costs. Lactation curve refers to a graphic representation of milk production and lactation time starting at calving. One of the main mathematical models suggested for studying the lactation curve are mechanistic models like Dijkstra function. This model was developed to describe the growth pattern of the mammary glands during pregnancy and lactation.

Somatic cell count (SCC) is one of the critical traits that is an indicator of mastitis or mammary infection in heifers and dairy cattle (Jeretina, Škorjanc, & Babnik, 2017). Much research have been carried out to estimate phenotype and genetic parameters of SCS and its relationship with the other traits (Yamazaki et al., 2013; Chegini et al., 2015; Archer et al., 2013; Haile-Mariam et al., 2003; Strapakova et al., 2016). Schutz, Hansen, Steunenagel, and Kuck, (1990) reported that SCS is high at the beginning of lactation and decreases gradually until 5 to 6 weeks of the lactation and after that it remains nearly constant or increases linearly in primiparous and multiparous cows towards the end of the lactation. Different estimates of SCS heritability in whole lactation have been reported in the literature for the first lactation. Reents, Dekkers, and Schaeffer (1995) and DeGroot et al. (2007) reported that heritability of SCS in the first lactation were 0.09 and 0.04 respectively but the findings of Miglior et al. (2007) and Samore et al. (2008) showed that SCS heritability were 0.19 and 0.18 in Holstein primiparous cows. Evaluation of SCS heritability during the course of the lactation using random regression models by ZavadiLOva et al. (2011) showed an increase from 0.08 to 0.11 in Holstein cows. Average heritability of SCS was found to be lowest at the beginning and highest at the end of lactation in different studies (Elsaid et al., 2011; Yamazaki et al., 2013). Negative genetic correlation was reported between SCS and persistency by Haile-Mariam et al. (2005). Also Yamazaki et al. (2013) found that
SCS increases along with increasing milk yield in early lactation of primiparous cows. Moreover, Archer et al. (2013) reported a negative correlation between SCS in the first month of milk production and cumulative milk yield (a unit increase of SCS was associated with 482 Kg decrease of total milk yield). In this study a mechanistic model was applied for fitting the lactation curve (Dijkstra model) for better understanding the association between SCC, age at first calving (AFC) and biological lactation curve parameters in Iranian Holstein cows.

**Material and methods**

The data consisted of 274340 test day records of milk yield from 30,470 primiparous cows in 220 Iranian Holstein dairy herds which calved between 2012 and 2016 and collected by The Animal Breeding Center of Iran. Outliers and out of range production and reproduction records were deleted from the analysis. Records of days in milk (DIM) <5 and >305 days were eliminated. AFC ranged between 18 to 36 months and the number of test day records per cow was from 8 to 10 and cows with daily milk production lower than 2 Kg day⁻¹ were discarded. In order to make a normal distribution, the average number of SCC (AVGSCC) of different test days during lactation was transformed to average number of SCS (AVGSCS) using the following formula (Ali & Shook, 1980):

\[
AVGSCS = \log_2(SCC/100000) + 3
\]

Mechanistic function of Dijkstra was applied for mathematical description of the lactation curve (Dijkstra et al., 1997). This model is based on a set of different parameters representing cell proliferation and apoptosis in mammary glands. The mechanistic model was superior to Wood, Wilmink and Rook functions for describing the lactation curve with significant parameter estimates and the lowest residual mean square (Val-Arreola, Kebreab, Dijkstra, & France, 2004). The mechanistic model and some functions that predict peak yields (PY), time to peak (TP) and TMY305 are as follow (Nasri et al., 2008):

\[
Y_t = \lambda_0 \exp \left( \frac{\lambda_1}{\lambda_2} (1 - \exp^{-\lambda_2 t}) - \lambda_3 t \right)
\]

\[
TP = \lambda_2^{-1} \ln \left( \frac{\lambda_1}{\lambda_3} \right)
\]

\[
PY = \lambda_0 \left( \frac{\lambda_3}{\lambda_2} \right) \lambda_2 \exp(\lambda_1 - \lambda_3 / \lambda_2)
\]

\[
TMY305 = \lambda_0 \int_0^{305} \exp \left[ \frac{\lambda_1}{\lambda_2} (1 - \exp^{-\lambda_2 t}) \right] - \lambda_3 t
\]

where: \(\lambda_0=\) initial milk production, \(\lambda_1=\) specific rate of cell proliferation at parturition, \(\lambda_2=\) decay parameter and \(\lambda_3=\) specific rate of cell death.

Dijkstra function was fitted to the test day records of individual cows using an iterative nonlinear curve fitting procedure (PROC NLIN of SAS software) (Statistical Analysis System [SAS], 2004) with Marquardt algorithm strategy. Moreover, estimated partial milk production from the first, second and third 100 days of lactation plus total 505 days milk yield (PMY1, PMY2, PMY3 and TMY305) were also calculated for each animal using PROC SQL of SAS. For the phenotypic analysis of PMY1, PMY2, PMY3, TMY305, and persistency traits, a general linear model was applied:

\[
Y_{ijkm} = \mu + HYS_i + AVGSCC_j + b(AFC)_k + e_{ijkm}
\]

where

- \(Y_{ijkm}\) = observation traits (\(\lambda_0, \lambda_1, \lambda_2, \lambda_3, TP, PY, PMY1, PMY2, PMY3, TMY305 and persistency)
- \(HYS=\) fixed effect of herd-year-season of calving;
- \(b=\) quadratic regression coefficient of the trait on age at first calving;
- \(AFC=\) covariate effect of age at first calving in month (18, ..., 36);
- \(AVGSCC=\) fixed effect of different somatic cell count classes (k=1, ..., 11);
- \(e_{ijkm}=\) random residual effect.
Somatic cell counts were categorized into 11 groups shown in the Table 1.

### Table 1. Different somatic cell count classes used in this study.

| Class | AVGSCC (<100/mL) |
|-------|----------------|
| 1     | <100           |
| 2     | 100-200        |
| 3     | 200-300        |
| 4     | 300-400        |
| 5     | 400-500        |
| 6     | 500-600        |
| 7     | 600-700        |
| 8     | 700-800        |
| 9     | 800-1000       |
| 10    | 1000-1500      |
| 11    | >1500          |

Calculation of persistency (PS %) was based on Johansson and Hansson formula (Johansson & Hansson, 1940) as follow:

\[
PS\% = \frac{PMY3}{PMY1} \times 100
\]

Genetic analysis (calculation of heritability and genetic correlation) of the traits was carried out by simple univariate and bivariate animal models using a restricted maximum likelihood method implemented in WOMBAT program (Meyer, 2007). The model and distributional properties were assumed are as follows:

\[
y = X\beta + Za + e
\]

\[
E \left[ \frac{y}{e} \right] = \begin{bmatrix} x\beta \\ 0 \\ 0 \end{bmatrix}
\]

\[
\text{VAR} \left[ \frac{a}{e} \right] = \begin{bmatrix} A\sigma^2_a & 0 \\ 0 & I\sigma^2_e \end{bmatrix} = \begin{bmatrix} G & 0 \\ 0 & R \end{bmatrix}
\]

where \( y \) were a vector of dependent variables, \( \beta \) is a vector of fixed effects (herd- year- season of calving and AFC as a covariate), \( a \) is a vector of additive genetic values of animals, \( e \) is a vector of random residual effects, \( \sigma^2_a \) is the additive genetic variance, \( \sigma^2_e \) is the residual variance, \( X \) and \( Z \) are incidence matrices for fixed and random effects.

### Result and discussion

Average lactation milk yield and SCS in primiparous cows was presented in Figure 1. The initial milk yield begins with 24.2 Kg and increased to 37.1 Kg in peak yield which was around 70 days of lactation and then gradually decreased till the end of lactation. The estimates of AVGSCS ranged from 1.94 to 3.06 for primiparous Holstein cows and the number of somatic cells is high immediately after parturition but drops rapidly during the first three weeks and reach minimum in the second month of lactation.

![Figure 1. Average milk yield and AVGSCS during lactation stages.](image)

The highest fluctuation in AVGSCS was shown during the first 100 days of lactation and then steadily increased till the end of lactation. Based on the study of Barkema et al. (1999) somatic cell count is high after...
parturition and then decreases to normal level within 4-5 weeks after calving. Koc et al. (2008) showed that the lowest SCC was in the second and third lactation months of turkey Holstein dairy cows. The high somatic cell count at the beginning of lactation is due to the high immunoglobulin content in the colostrum (Saloniemi et al., 1995) or high risk of intra-mammary infection from environmental pathogens (Detsilleux et al., 1997).

Although one of main factor for flatness of lactation curve in primiparous compare to multiparous cows is smaller increase in SCS during the first lactation. So it indicates that the pattern of SCS during different lactations can change the shape of lactation curve too. These trends in SCS and milk yield are similar to the result of previous studies (Jamrozik & Schaeffer, 2012; Weller et al., 1992; Yamazaki et al., 2013). Descriptive statistics of different parameters related to the Dijkstra model plus age at first calving, AVGSCC and AVGSCSC are presented in Table 2. Initial milk yield predicted by Dijkstra equation is more accurate than the Wood model because initial milk in the Wood model forced to be zero which is not acceptable biologically in mechanistic models (Nasri et al., 2008). In our study overall mean of initial milk production ($\lambda_0$) or product of the number of differentiated parenchyma cells was $16.27\pm12.11$ which was lower than those reported by Nasri et al. (2008) for Holstein cow (20.7) but it was higher than reported of Val-Arreola et al. (2004) (15.1) and Dijkstra et al. (2010) (14.5) for Mexican and England Holstein dairy cow respectively.

### Table 2. Some descriptive statistics for estimated parameters and the variables obtained from the mechanistic model in dairy cows.

| parameters | Average | SD  | Min   | Max   |
|------------|---------|-----|-------|-------|
| $\lambda_1$ | 16.27   | 12.11 | $9\times10^{-4}$ | 50.14 |
| $\lambda_1$ | 0.18    | 0.21 | $4\times10^{-3}$ | 1.55 |
| $\lambda_2$ | 0.06    | 0.05 | $4\times10^{-4}$ | 0.35 |
| $\lambda_3$ | 0.05    | 0.12 | $3\times10^{-4}$ | 1.53 |
| TP (day)   | 71.2    | 22.1 | 30.02 | 109.3 |
| PY (Kg)    | 36.91   | 5.69 | 11.65 | 62.65 |
| PMY1       | 3217.57 | 525.90 | 780.07 | 5446.99 |
| PMY2       | 3596.62 | 540.90 | 1115.95 | 5551.63 |
| PMY3       | 3038.99 | 643.34 | 571.20 | 5583.09 |
| TMY305     | 9653.18 | 1572.52 | 2938.92 | 15864.77 |
| PS%        | 94.79   | 16.77 | 10.95  | 155.76 |
| AVGSCC     | 173579.11 | 232199.21 | 14500.0 | 2722571 |
| AVGSCS     | 2.30    | 1.10  | 0.20  | 7.58  |
| AFC(month) | 25.41   | 2.43  | 18.33 | 36.43 |

$\lambda_1$- initial milk production, $\lambda_2$- specific rate of cell proliferation at parturition, $\lambda_3$- decay parameter and $\lambda_4$- specific rate of cell death, PY- peak yields, TP-time to peak, milk yield production from 5-100 (PMY1), 101-200 (PMY2), 201-305 (PMY3), total 305 days milk yield (TMY305), persistency (PS%), average SCC (AVGSCC) and average SCS (AVGSCS).

The difference in initial milk yield may be attributed to herd management, genetic group or even the parity in dairy cows (Chegini et al., 2015). The average rate of cell proliferation and death ($\lambda_1$ and $\lambda_3$) 0.18 and 0.03 respectively. These parameters estimate per week for primiparous cows in the study of Dijkstra et al. (2010) were 0.52 and 0.017 respectively. The higher average cell proliferation rate indicating faster in secretory cell numbers in dairy a cow which is low in the first lactation compare to the subsequent parities. In contrast, the specific rate of cell death is lower than cell proliferation which means higher number of secretory cell number for production of milk yield and higher persistency as well. Predicted peak yields (PY) and time to peak (TP) are two important parameters in each lactation curve model. In Dijkstra model the highest milk yield (36.91 kg) was observed after the second months of lactation (71 days). The PY and TP estimated was higher than reported in literature for Holstein dairy cattle (Nasri et al., 2008) while Cunha et al. (2010) reported PY and TP using Dijkstra model for low, medium and high milk production farms. These amounts for the first lactation numbers were 15.10 kg and 25 days, 17.69 kg and 77 days and 29.90 kg and 77 days respectively. Val-Arreola et al. (2004) and Cunha et al. (2010) reported that Dijkstra model overestimate TP compare to other lactation model and this model is prefer for the lactations whose time to peak occurs on a day farther from the beginning of lactation. Based on Val-Arreola et al. (2004) and Nasri et al. (2008) estimation of maximum milk yield using Dijkstra equation is accurate. The PY and TP in the study of Nasri et al. (2008) were 40 kg and 29 days respectively which were completely different with the results of this study. This difference in PY and TP could be due to the management of herd and high environmental temperature in Iran. Estimation of total 305-days milk yield and partial milk yields (PMY1, PMY2 and PMY3) using mechanistic model are 9653.18, 3217.57, 3596.62 and 3038.99 kg respectively. In this study the proportion of PMY1, PMY2 and PMY3 from TMY305 are 33.33%, 35.18% and 31.48% respectively which

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means that the highest and lowest total milk yield attributed to the second and third 100 days of lactation. The average persistency was 94.97% which indicate that milk production in PMY3 and PMY1 are similar. Persistency of milk yield in this study was higher than those of Cakilli and Gunes (2007) for Brown Swiss cows (59.91%). The average number of somatic cell count and AFC are 173579±232199 cells mL⁻¹ and 25.41 month respectively. The AVGSCC± SD in this study was lower than the study of Chegini et al. (2015) (245100±543800 cells mL⁻¹) but higher than finding of Haile-Mariam et al. (2003) (119700±507600 cells mL⁻¹). The role of average number of somatic cell count on causing clinical or subclinical mastitis is extremely important. So monitoring of SCC in dairy herds for the health of the cows and the quality of the milk yield is critical.

Heritabilities

Heritabilities of different mechanistic parameters plus genetic and environmental correlations of these parameters with AVGSCS are presented in Table 3. The point heritability estimates of main lactation curve parameters are low except for decay parameter (λ₃).

| Parameters | h² | AVGSCS | rₑ | rₑ |
|------------|----|--------|----|----|
| λ₀         | 0.02±0.01 | -0.09±0.04 | 0.35±0.01 |
| λ₁         | 0.02±0.01 | 0.07±0.00 | 0.02±0.01 |
| λ₂         | 0.21±0.05 | -0.09±0.01 | 0.40±0.01 |
| λ₃         | 0.05±0.01 | -0.06±0.15 | 0.04±0.01 |
| TP         | 0.02±0.01 | -0.25±0.01 | -0.05±0.01 |
| PY         | 0.18±0.02 | 0.07±0.10 | -0.09±0.06 |
| AFC(month) | 0.16±0.02 | -0.04±0.01 | 0.05±0.01 |
| PMY1       | 0.15±0.02 | 0.08±0.02 | -0.07±0.01 |
| PMY2       | 0.18±0.02 | 0.13±0.03 | -0.16±0.01 |
| PMY3       | 0.13±0.01 | 0.06±0.04 | -0.18±0.02 |
| TMY305     | 0.19±0.02 | -0.05±0.01 | 0.16±0.02 |
| PS%        | 0.07±0.01 | -0.06±0.01 | -0.12±0.01 |
| AVGSCS     | 0.09±0.01 | -0.08±0.01 | -0.12±0.01 |

λ₀ – initial milk production, λ₃ – decay parameter and λ₅ – specific rate of cell death, PY – peak yields, TP – time to peak, milk yield production from 5-100 (PMY1), 101-200 (PMY2), 201-305 (PMY3), total 305 days milk yield (TMY305), persistency (PS%), average SCS (AVGSCS) and average SCC (AVGSCS).

Few research have undertaken on the estimation of the parameters of a mechanistic function. Difference between heritabilities, reported by researchers, attributed to differences in statistical models, different data structure and genetic variation between populations, variation of the breeds in different environmental conditions, estimation methods, type of the lactation curve function and effects used in the model as well (Makgahlela et al., 2007). The heritability of peak time (0.02) is absolutely lower that peak yield (0.18) in this study. This is different with the result of Farhangfar and Rowlinson (2007) who founded 0.1and 0.3 heritability for peak time and peak yield respectively in Iranian primiparous Holstein cows using the Wood incomplete gamma function. Also heritability estimates for TP (0.099) and PY (0.259) in the study of Chegini et al. (2015) were similar to the result of Farhangfar and Rowlinson (2007).

The lower heritability of TP and PY indicates that there is considerably lower genetic variation in these parameters in mechanism model compared to the empirical function like incomplete gamma function. Heritability of AFC, PS % and AVGSCS in this study are 0.17, 0.072 and 0.092 respectively (Table 3). The estimation of heritability for persistency measure and AVGSCS are low but AFC has moderate heritability. Low to medium heritability amount of different persistency measures were reported by Atashi et al. (2006) and Boujenane and Hilal (2012). Considerable variations in heritability of AFC are reported in different studies. The estimate of heritability of AFC obtained in the study of Nilforoooshan and Edriss (2004) in Iranian Holstein was 0.086 but the estimate of AFC heritability in our study was lower than finding of Makgahlela et al. (2007) and Goshu et al. (2014) which calculate it 0.24 and 0.53 respectively. These variations indicate that there was wide genetic variation for AFC in different cattle population under various management systems. The heritability estimates of partial (PMY1, PMY2, PMY3 and TMY305) ranged from 0.13 to 0.19. The highest heritability was showed in PMY2 and TMY305 respectively (0.187 and 0.195). Heritabilities of these traits in the study of Chegini et al. (2015) were 0.16, 0.29, 0.27 and 0.29 respectively and the highest heritability was obtained in the second parts of lactation. Moreover, in both studies,
heritability of total 305-d milk yield and the second 100 day period are similar. Heritability of persistency which depends on the definition of the trait, range from low to high value in different studies. The lower level of milk production at the end compare to the beginning of lactation affects the estimate of persistency heritability. Heritability of AVGSCS in this study was low (0.092) (Table 3). Heritability estimates for AVGSCS in different studies ranged from 0.03 to 0.17 (Chegini et al., 2015; Odegard et al., 2003; Carlen et al., 2004). Based on different researches, this variation in heritability can be attributed to several factors like differences in trait definition, statistical models, populations and estimation methods (Rupp & Boichard, 1999; Zavadilovaet al., 2011).

**Genetic and environmental correlations**

The range of genetic and environmental correlations between lactation curve parameters with AVGSCS are between -0.25 to 0.15 and -0.18 to 0.33 respectively (Table 3). Negative genetic correlation between $\lambda_0$ and AVGSCS indicate that cows with higher initial milk yield have lower mean somatic cell score. In other words increasing somatic cell counts in the beginning of lactation and causing health problem like mastitis, decrease initial milk yield in dairy cows (Dijkstra et al., 2010). Low positive and negative genetic correlation among $\lambda_1$ and $\lambda_3$ with AVGSCS was obtained in this study (0.079 vs. -0.067). The positive genetic correlation between the rate of cell proliferation at parturition and AVGSCS indicate that cell higher proliferation increase slightly somatic cell count in dairy cattle and negative genetic correlation of specific rate of cell death with AVGSCS demonstrate that higher apoptosis of mammary cell glands decrease the number of somatic cell counts in primiparous Holstein cows.

Peak time and peak yield are two important characteristics of lactation curve and genetic correlations of AVGSCS with these traits are -0.251 and 0.078, respectively. Based on this study, the more importance of genetic relationship of somatic cell counts on peak time compare to peak yield is obvious in primiparous Holstein cows. It means that cows with higher somatic cell count show earlier peak time during first lactation. So selection of cows with lower somatic cell count and consequently latter peak time, make flatter lactation curve and more resistant to subclinical mastitis. Moreover, the low genetic correlation between peak yield and somatic cell counts suggested that these traits are influenced by less similar genes. Chegini et al. (2015) reported that the genetic correlation between peak time and peak yield with average somatic cell count and Ln Somatic cell score are -0.23±0.15, 0.07±0.12 and -0.19±0.12, -0.02±0.09 respectively.

Negative genetic correlations between both AFC and PS% traits with average somatic scores (-0.047 and -0.060) was obtained in this study (Table 3). This negative genetic correlation between AFC and AVGSCS was reported in the study of Chegini et al. (2015). There are many studies that estimate the genetic correlation of SCSs and persistency in dairy cattle with different methodologies (Yamazaki et al., 2013; Haile-Mariam et al., 2003; Strapakova et al., 2016; Harder et al., 2006). Cows with high mean somatic cell counts tend to have low yield persistency in different lactations. Based on the result of Yamasaki et al. (2013) selection of cows with higher persistency might help to diminish SCS in the later stage of the first and second lactations. Our result with in agreement with the finding Haile-Mariam et al. (2005) who reported unfavorable and low genetic correlation between somatic cell count and persistency (-0.050). Negative genetic correlation between somatic cell count and persistency in primiparous Holstein cows was -0.23 in the study of Yamazaki et al. (2015) and -0.123 in the study of Strapakova et al. (2016) indicated that the genetic correlation between these traits is low to moderate based on persistency measures, method of data analysis and population structure.

Low positive genetic correlation observed between partial milk yield (PMY1, PMY2, and PMY3) and AVGSCS but genetic correlation between AVGSCS and 305-day milk yield was negative (Table 3). In the study of Chegini et al. (2015), genetic correlation between mean log, somatic cell count with 305-day milk yield, the first, second and third 100-day milk yield was -0.08, 0.03, -0.08 and -0.16 respectively. Negative genetic correlation (-0.084) between SCS and milk production in Chinese Holstein cattle was reported by Guo et al. (2010). Based on the finding of Koivula et al. (2005) negative genetic correlation between SCC milk yields is due to high somatic cell count which damage to the udder texture and this led to lower milk yield especially in latter parities. Mrode et al. (1998) and Rupp and Boichard (1999) reported favorite positive genetic correlation between SCC and milk yield. Also Kheirabadi and Razmkabir, (2016) founded that genetic correlation between milk yield and SCS ranged from 0.006 to 0.139 and with an average of 0.07 while environmental correlation between milk yield and SCS was negative in Iranian Holstein cows. Small
positive genetic correlation between these traits suggested some antagonism between increasing milk yield and decreasing SCS. But Sharma et al. (2016) explained that positive unfavorable genetic correlation between milk yield and high somatic cell count (clinical mastitis) indicate that genetic improvement of milk yield is accompany with increasing genetic susceptibility to mastitis.

In our study the sign of environmental and phenotypic correlations are similar (negative). Dadpasand et al. (2013) mentioned that this situation resulted from optimum hygiene and management practices which can support increasing milk yield and controlling SCS. In a different study Jatta et al. (2012) showed that genetic correlation between milk yield and lnSCC was 0.26 using bivariate animal model methodology which means that high somatic cell count observes in high producing cows and the consequence is high rate of mastitis in these animals. The reason of change in genetic correlation from low positive to negative is due to high positive and negative genetic correlation between these traits in early and at the end of lactation respectively (Haile-Mariam et al., 2001).

Mean estimated breeding value (EBV) for SCS and 305-d milk yield was -0.012(SE =0.0035) and 18.369 (SE= 2.398) respectively (Figure 2). Based on this figure, during these years, average EBV 305-day milk yield increased from 11.5 in the first year and increased till 2015 and then gradually decreased. The mean EBV SCS decreased slightly from 0.111 in 2012 and reached -0.187 in 2016 in our dataset. Decreasing EBV SCS between 2012 and 2016 indicate the better health status of dairy cows and better management and environmental control to maintain high milk production and less mastitis susceptibility.

Phenotypic trends

Least square means of SCC in various AFC was shown in Figure 3. The maximum number of somatic cell obtained in 18 months (266720 cells). Based on the results, with increasing AFC from 18 to 22 months, average number of SCC decreased (the lower value observed in 22 months of calving) and from 22 to 26 months a steadily trend was observed in least square means of SCC and average SCC gradually progress till 36 months of calving. The change in least square means of SCC during consecutive AFC showed as a polynomial function with the relatively high coefficient of determination (0.77). Cubic regression quantified this progress as -34000 cells mL⁻¹ during AFC 18 to 36. The reason of finding of negative polynomial coefficient related to high amount of SCC before 22 months of calving in primiparous Holstein. Cows calving at younger age (18 to 21 months) were expected to have higher SCC in the milk while calving between 22 and 26 months resulted to minimum SCC, so with respect to SCC, AFC between 22 till 26 months could be the optimum calving time for Iranian primiparous Holstein. Niforooshan and Edriss (2004) suggested that the optimum AFC in Holstein for maximum profit and 305-d milk yield should be 23 to 24 months of age. In the study of Eastham et al. (2018) they reported that the lowest SCC was observed in AFC of 21 months (72,764 cells mL⁻¹) and SCC increased steadily till 41 months of calving with the highest least square mean of 99,558 cells mL⁻¹.
It seems that factors that affect increasing SCC such as udder infection, incomplete milking, hygienic problems, keeping sick cows with healthy cows and any other stress (Alhussien & Dang, 2018) are more harmful on younger heifers calved before 22 months. In an opposite study reported by Juozaitiene and Juozaitis (2005) they found that there is no significant relationship between AFC and SCC in Lithuanian Black-and-White cattle. Least square means of cumulative milk yield in the first, second and third 100 days of lactation plus total 305-day milk yield and persistency in different SCC groups are presented in Figure 4 and 5.

In general, the results showed a negative phenotypic relationship between SCC and milk yield production or persistency which observed in many studies (Rupp & Boichard, 1999; Durr et al., 2008; Archer et al., 2013). Changes in PS% as increasing SCC are significant in dairy cows. The least square mean (LSM) of persistency in completely healthy cows is 95% (SCC< 100,000 cells mL⁻¹) and gradually decreased to minimum amount when SCC> 1,500,000 in cows with high mastitis (83.9%). As mentioned in the last paragraphs, different studies showed that high SCC had considerable but negative impact on persistency in both primiparous and multiparous cows.

Figure 3. Least square means (+SE) of SCC (×1000ml) for different first calving ages.

Figure 4. Least square means of the first (PMY1), second (PMY2) and third (PMY3) 100 days of lactation in different SCC classes.
The least square means of PMY2, PMY3 and TMY305 decreased slightly as the number of SCC increased in primiparous cows. Least square means of milk yield for PMY1 in the first class of SCC is around 2965 kg and decreased gradually to 2,895 kg in the last class of SCC. The extreme LSM of milk yield for PMY2 and PMY3 are 3,133 to 2,889 kg milk production respectively.

The different of LSM for the first and last class of SCC in PMY1, PMY2 and PMY3 are 70, 244 and 396 kg respectively. This is in agreement with finding of Hagnestam-Nielsen et al. (2009) who denoted that the most extensive milk loss related to increase in SCC was observed in late lactation. Also LSM of TMY305 decreased from 8918 (95% CI=8,838-8,918 kg) in the first class of SCC to 8,210 (95% CI=7,859-8,561 kg) milk in the last class. It has been suggested that cows with SCC less than 100,000 cells mL\(^{-1}\) are healthy and are not to be infected by pathogens (Hand et al., 2012). With respect to this assumption, a large number of dairy cows in Iran suspected to suffer from mastitis during the first lactation and it could be a major factor in diminishing milk yield in Iranian dairy cows.

Estimation of 305-day milk yield and persistency for healthy cow were 8918 kg and 95.52% respectively. Also least square means of milk loss in cows with 400,000 to 500,000 cells mL\(^{-1}\) and >1500000 cells mL\(^{-1}\) classes were 378 and 708 kg respectively which equal to 8% loss of milk yield/cow during standard lactation period. As high producing primiparous cows are more susceptible to mastitis, it is predicted that elevation of SCC had a worse effect on milk loss in multiparous cows.

Consequently daily milk loss of SCC at 400,000 to 500,000 cells mL\(^{-1}\) ranged from 0.7 to 2.0 kg in primiparous Swedish Holstein cows. Another study showed that daily milk loss at 400000 cells mL\(^{-1}\) varied between 0.8 to 3.1 kg in primiparous cows (Horter & Seegers, 1998). With respect to high level of SCC in Iranian Holstein cows, low heritability of AVGSCS and negative relationship between this trait and other economic performance which resulted to high mastitis probability, the following recommendations are appropriate:

1- Regular udder health monitoring is an essential component for prevention of subclinical and clinical mastitis. 2- Management factors like type of housing, bedding and stall maintenance and manure handling also have a critical influence on high rate of SCC which is an index of udder health and 3- regular estimate of genetic parameters for SCC using advance models like random regression test day model for increasing the accuracy of selection against mastitis in dairy cattle in Iran.
Conclusion

Genetic parameters of Dijkstra mechanistic model and their relationship with average somatic cell count were investigated in this study. The heritability of somatic cell count is low and unfavorable correlation was obtained between this trait and lactation parameters. Low genetic correlation between average somatic cell score and partial or 305-day milk was obtained in this study and critical negative phenotypic trend was shown between milk yield performance and persistency with somatic cell count. Somatic cell count is relatively high in Iranian dairy herds and therefore it is important that seek a selection programs to decrease somatic cell count and improve mastitis resistance in all parities. Proper milking techniques and management, monthly control of SCC in dairy cows, and increase the profitability of production system are needed to reduce SCC in dairy cattle farms.

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