ORIGINAL ARTICLE

Relationship between inbreeding and milk production traits in two Italian dairy sheep breeds

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Funding information
Regione Autonoma della Sardegna, Grant/Award Number: CRP 61608

Abstract

The effects of inbreeding in livestock species breeds have been well documented and they have a negative impact on profitability. The objective of this study was to evaluate the levels of inbreeding in Sarda (SAR, $n = 785$) and Valle del Belice (VdB, $n = 473$) dairy sheep breeds and their impact on milk production traits. Two inbreeding coefficients (F) were estimated: using pedigree (F_{PED}), or runs of homozygosity (ROH; F_{ROH}) at different minimum ROH lengths and different ROH classes. After the quality control, 38,779 single nucleotide polymorphisms remained for further analyses. A mixed-linear model was used to evaluate the impact of inbreeding coefficients on production traits within each breed. VdB showed higher inbreeding coefficients compared to SAR, with both breeds showing lower estimates as the minimum ROH length increased. Significant inbreeding depression was found only for milk yield, with a loss of around 7 g/day (for SAR) and 9 g/day (VdB) for a 1% increase of F_{ROH}. The present study confirms how the use of genomic information can be used to manage intra-breed diversity and to calculate the effects of inbreeding on phenotypic traits.

KEYWORDS
genomic information, inbreeding depression, mixed model, runs of homozygosity

1 | INTRODUCTION

The main cause of inbreeding occurrence in livestock populations is the increase in average relationships among animals due to the implementation of breeding programmes (Leroy, 2014). This is particularly true for the Mediterranean farming system of sheep, in which natural mating is the common practice and the exchange of rams among flocks is quite unusual. This leads to an increase in inbreeding within the population and a consequent decrease in variability. However, there are different ways to control the inbreeding levels within a breeding programme, such as the use of the optimum contribution selection (e.g., Wang et al., 2017). Selection increases the frequency of homozygous regions in the genome, which promotes genetic progress by increasing the frequency of favourable alleles. At the same time, it can decrease the genetic diversity, and increase the frequency of some

unfavourable alleles in the population, potentially having a negative impact on the phenotypic values for some productive and reproductive traits. This negative consequence of inbreeding is known as inbreeding depression, that is, a general reduction of animal fitness and performance, together with an increased frequency of genetic defects (Charlesworth & Charlesworth, 1999; Curik et al., 2001). Therefore, it is important to control the level of inbreeding in a population under artificial selection to avoid the negative impact of inbreeding depression. Inbreeding depression can be estimated using the individual inbreeding coefficient (F), defined as the probability that both alleles at any locus within an individual are identical by descent. Values of F have been traditionally computed from the pedigree information (F_{PED}; Lynch & Walsh, 1998). However, pedigrees can contain several errors (Legarra et al., 2014; Weller et al., 2004) or they may not even be recorded (Mészáros et al., 2015). A pedigree error rate of approximately 10% was reported in the Mexican Holstein population (García-Ruiz et al., 2019). This problem is exacerbated in some situations as, for example, the semi-extensive sheep farming systems, where relationship recording is hampered by the limited use of artificial insemination and the simultaneous presence of more rams in the same flock (Hayes & Goddard, 2008). Larger unknown fatherhood rates were reported for Latxa (around 50%) and Manech/Basco-Béarnaise (around 20%) sheep populations (Legarra et al., 2014). To overcome these limitations (i.e., missing and wrong pedigree recording), we can make use of new technologies such as genotyping the animals using high-throughput single-nucleotide polymorphism (SNP) platforms. These new technologies provide an alternative for an accurate estimation of relationship and inbreeding when pedigree recording is difficult (e.g., extensive, or semi-extensive farming systems in which matings are not registered). Once the animals are genotyped, several metrics can be derived from the genomic information. For instance, Runs of Homozygosity (ROH), that is, contiguous stretches of homozygous genotypes that occur in an individual due to parental transmission of identical haplotypes (Gibson et al., 2006), are becoming a widely adopted genomic tool to study the genetic structure of populations (Macciotta et al., 2021; Mastrangelo et al., 2018). They have been used to detect selection signatures, and deleterious mutations (e.g., Sumreddee et al., 2019), to develop association studies with production traits (Cesarani et al., 2021), and to study the temporal framework of inbreeding events (Gibson et al., 2006). In particular, the ROH-based inbreeding coefficient (F_{ROH}) is considered a powerful method of detecting inbreeding effects among several alternative estimates of inbreeding (e.g., Bjelland et al., 2013; Keller et al., 2011). Inbreeding depression at genome wide (Martikainen et al., 2017) or chromosomal (Martikainen et al., 2018) levels was estimated using F_{ROH} coefficients in Finnish Ayrshire cattle. Martikainen et al. (2017) suggested that the total homozygosity levels may not reveal all the harmful effects of inbreeding on fertility, whereas F_{ROH} values at chromosome levels were associated with the lengthening of the interval from first to last inseminations (Martikainen et al., 2018).

Previous studies have already investigated the inbreeding effects on production traits in sheep breeds (Barczak et al., 2009; Dorostkar et al., 2012; Kiya et al., 2019). Most of these analyses on sheep were carried out using pedigree-based inbreeding coefficients and growth traits (Gholizadeh & Ghafouri-Kesbi, 2016). More recently, genomic and pedigree inbreeding depression was estimated for semen traits in the Basco-Béarnaise dairy sheep breed (Antonios et al., 2021), whereas inbreeding depression from homozygous regions was studied for litter size in six different sheep breeds (Tao et al., 2021a).

Although selection intensity in the populations studied here is low, they have been historically selected for milk production and, therefore, some signals of inbreeding depression are expected. Therefore, in this work, the level of inbreeding and the inbreeding depression on milk production traits in two Italian dairy sheep breeds was estimated using pedigree and genomic information.

2 | MATERIALS AND METHODS

Animal Care and Use Committee approval was not needed as data were obtained from pre-existing databases.

2.1 | Sampling, genotyping, and quality control

A sample of 785 and 473 ewes of Sarda (SAR) and Valle del Belice (VdB) dairy sheep breeds, respectively, were used for this study. SAR is the largest Italian sheep breed with about 3 million animals (Casu et al., 2022); VdB is the main breed reared for milk production in Sicily, the biggest Italian Island, with about 154,000 heads (www.vetinfo.it). SAR animals were sampled in 45 flocks spread throughout the Island of Sardinia, whereas VdB animals came from four different flocks.

Animals were genotyped with the Infinium Ovine SNP50 v1 BeadChip (Illumina Inc.). Markers were mapped on the 4.0 version of the *Ovis aries* assembly. Since all genotyped animals were females, SNPs mapped on OAR 27 were also considered in this study. Quality control was performed within each breed with the following parameters: call rate greater than 0.975, minor allele frequency greater than 0.01, p-value for the deviation from the

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Hardy–Weinberg equilibrium greater than 0.01. Moreover, call rate for each ewe was greater than 0.95. Only the SNPs in common between those that passed the quality control within each breed were considered. In the end, all animals and 38,779 SNPs were retained for the analyses.

2.2 | Phenotypic data

For all genotyped ewes, daily milk production traits (i.e., kg of milk per day, MY; fat percentage, FP; and protein percentage, PP) were available (Table 1). The average values for SAR were 1.75 ± 0.44 (MY), 5.96 ± 1.41 (FP), and 5.44 ± 0.71 (PP). VdB showed lower MY (1.39 ± 0.54), but larger fat (6.95 ± 1.05) and protein (5.73 ± 0.66) percentages. As reported in Table 1, most of the records came from multiparous ewes in both breeds. As far as the lactation stage was concerned, VdB had more data at the beginning of lactation, whereas SAR had more data in the central part of the lactation.

TABLE 1 Basic statistics of the analysed dataset and inbreeding coefficients (F) estimated in the two sheep breeds using pedigree (F_{PED}) and genomic data (F_{ROH})

	Sarda	Valle del Belice
Data, n		
Primiparous	168	177
Pluriparous	617	296
DIM class 1	73	360
DIM class 2	214	68
DIM class 3	435	35
DIM class 4	63	10
Traits		
Milk, kg/day	1.75 ± 0.44	1.39 ± 0.54
Fat, %	5.96 ± 1.41	6.95 ± 1.05
Protein, %	5.44 ± 0.71	5.73 ± 0.66
Inbreeding[a], %		
F_{PED}	5.3 ± 6.44 (265)	15.3 ± 8.1 (250)
F_{ROH1}	8.63 ± 4.24 (785)	10.87 ± 6.38 (473)
F_{ROH2}	7.21 ± 4.21 (784)	9.52 ± 6.38 (473)
F_{ROH4}	5.66 ± 4.02 (782)	7.88 ± 6.23 (472)
F_{ROH8}	3.64 ± 3.51 (757)	5.86 ± 5.76 (454)
F_{ROH16}	2.41 ± 2.84 (496)	4.63 ± 4.71 (315)
F_{ROH1-2}	1.41 ± 0.33 (783)	1.36 ± 0.48 (473)
F_{ROH2-4}	1.57 ± 0.55 (784)	1.67 ± 0.74 (473)
F_{ROH4-8}	2.14 ± 0.98 (781)	2.26 ± 1.05 (470)
$F_{ROH8-16}$	2.07 ± 1.40 (738)	2.68 ± 1.85 (448)

[a]Mean $\pm$ *SD* refers to values of animals with inbreeding different from 0 reported in parenthesis.

2.3 | Inbreeding estimation

Two different inbreeding coefficients were estimated: (i) pedigree inbreeding (F_{PED}), calculated using the official pedigrees of the two breeds through inbupgf90 (Misztal et al., 2014); (ii) ROH-based inbreeding (F_{ROH}), computed as the ratio between the sum of consecutive ROH length per animal and the genome length covered by SNPs.

F_{ROH} was computed with the following equation:

$$F_{ROH} = ROH_{TOT} / L_{TOT}$$

- where ROH_{TOT} is the sum of all the ROH found in an individual and L_{TOT} is the total genome length covered by SNPs.

F_{ROH} at the chromosome level was computed as:

$$F_{ROH} = ROH_{CHR} / L_{CHR}$$

- where ROH_{CHR} is the sum of the ROH in the chromosome and L_{CHR} is the length of the chromosome covered by SNPs.

The pedigree of SAR included a total of 633,317 animals, with no missing parents. The SAR genotyped animals were offspring of 399 different rams (1.97 ± 1.54 daughters per ram) and 749 different ewes (1.05 ± 0.24 daughters per ewe). The SAR-genotyped ewes showed an average number of generations equal to 3.82 ± 1.05, with a pedigree completeness index of 0.78 ± 0.19. As far as the VdB, the pedigree included a total of 5,861 animals with 60 and 576 missing sires and dams respectively. The genotyped females descended from 31 sires and 399 dams. The VdB-genotyped ewes had on average 4.05 ± 1.27 available generations, with a pedigree completeness index of 0.67 ± 0.37.

Consecutive ROH were detected using the R package detectRUNS (Biscarini et al., 2018), for each breed separately, with the following criteria: minimum 15 homozygotes SNPs, minimum ROH length of 1 Mb, maximum gap among consecutive SNPs of 1 Mb, no heterozygote or missing markers allowed. According to different minimum ROH length size, five different F_{ROH} coefficients were estimated using subsequent lengths: (i) F_{ROH1}, using ROH >1 Mb; (ii) F_{ROH2}, using ROH >2 Mb; (iii) F_{ROH4}, using ROH >4 Mb; (iv) F_{ROH8}, using ROH >8 Mb; (v) F_{ROH16}, using ROH > 16 Mb.

According to Lozada-Soto et al. (2021) and Mulim et al. (2022), to better discriminate between recent (long ROH) and old (short ROH) inbreeding we computed the following classes: F_{ROH1-2}, using only ROH ≥1 Mb and

ROH <2 Mb; F_{ROH2-4}, using only ROH ≥2 Mb and ROH <4 Mb; F_{ROH4-8}, using only ROH ≥4 Mb and ROH <8 Mb; $F_{ROH8-16}$, using only ROH ≥8 Mb and ROH <16 Mb.

2.4 | Inbreeding depression estimation

The extent of inbreeding depression was estimated separately by breed through the following mixed-linear model:

$$y = \text{herd} + \text{parity} + \text{month} + \text{DIM} + \text{sampling} + \text{inbreeding} + \text{animal} + e \quad (1)$$

where y was the considered milk trait (i.e., kg of milk per day, MY; fat percentage, FP; and protein percentage, PP); herd was the random effect of the herd (45 levels and four levels for SAR and VdB respectively); parity was the fixed effect of parity (two levels: primiparous and multiparous); month was the fixed effect of lambing month (six and nine levels for SAR and VdB respectively); DIM was the fixed effect of days in milk (four levels: 1 = DIM ≤150; 2 = DIM >150 and DIM ≤200; 3 = DIM >200 and DIM ≤250; 4 = DIM >250); sampling was the random effect of the sampling month; inbreeding was the considered inbreeding coefficients (i.e., F_{PED} and the different F_{ROH}); animal was the random additive genetic effect; e was the random residual effect. The extent of inbreeding depression at chromosome level was also investigated by fitting the chromosome-wide ROH-based coefficients: in this model, the inbreeding coefficients computed within each chromosome were used instead of the one computed using the whole genome. The animal effect was modelled using the genomic relationship matrix built according to method 1 proposed by VanRaden (2008).

Phenotypes for SAR animals were sampled within the only year (2014), whereas for VdB the phenotypes were retrieved from 2005 to 2012. For this reason, the mixed model for VdB also included the year as fixed effect. The mixed-linear models were performed using the SAS PROC MIXED (SAS Institute Inc., 2013). The significance of the inbreeding effect was established through the F test.

3 | RESULTS AND DISCUSSION

3.1 | Inbreeding estimation

For SAR, the average F_{ROH1} was 8.63 ± 4.24%, with a maximum value of 34.87%, whereas the average F_{PED} value was 5.3 ± 6.4%, considering only the animals with inbreeding above 0, or 1.8 ± 4.5%, considering all animals in the analysis (Table 1). For VdB, the average F_{ROH1} and F_{PED} values were 10.87 ± 6.38% (max

36.96%) and 15.3 ± 8.1 (8.1 ± 9.6% considering all animals) respectively. As expected, in both breeds, average F_{ROH} values decreased as the minimum ROH length increased, with VdB showing constantly higher values than SAR. This decreasing trend is justified by the lower number of ROH detected as the minimum length increases. F_{ROH1} values estimated in the present study for SAR are in agreement with other reports in Sarda dairy sheep (Cesarani et al., 2022), but they are higher than those estimated for Sarda dairy rams (4.1%; Cesarani et al., 2019). The difference with the coefficients estimated in males can be identified in the use of different numbers of SNP by Cesarani et al. (2019) and the consideration of ROH mapped on chromosome OAR27 in the present study. A total of 2,687 ROH (6% of the total) were found in OAR27 in SAR ewes. ROH on this chromosome showed the largest average length, together with ROH on OAR19. Thus, homozygote regions of OAR27 significantly contributed to the F_{ROH} values of SAR animals. A slightly lower F_{ROH1} value was estimated in VdB (8.4 ± 6.1% vs. 10.9 ± 6.4% of the present study) by Mastrangelo et al. (2017), who computed ROH in a very similar dataset but using different software and different parameters (e.g., minimum number of 40 SNPs). Mastrangelo et al. (2018) reported ROH-based inbreeding estimates for both breeds analysed in this study: while F_{ROH1} estimate for VdB (9.9 ± 7.7%) was similar to the one computed here, the value for SAR (4.1 ± 3.5%) was half of the one estimated in the present work. Besides a different number of SNPs and animals considered in their study, in Mastrangelo et al. (2018), the sexual OAR27 was excluded and different settings were used to define ROH. Lower inbreeding coefficients were estimated in other sheep breeds such Lacaune (F_{ROH} = 0.04, and F_{PED} = 0.03; Rodríguez-Ramilo et al., 2019) and Latxa Cara Rubia (F_{ROH} = 0.03, and F_{PED} = 0.02; Granado-Tajada et al., 2020). However, consistent with our results, Nosrati et al. (2021) found F_{ROH} values ranging from 0.9% to 22% in Southwest European sheep breeds.

Table 2 shows the correlations among the different inbreeding coefficients within each breed. In SAR, moderate correlations were observed between F_{PED} and F_{ROH} and they increased with ROH length. This pattern was already reported in sheep (e.g., Rodríguez-Ramilo et al., 2019) and cattle (e.g., Hidalgo et al., 2021). It is interesting to note the negative, even if not significant, correlation between F_{PED} and the five F_{ROH} coefficients found for VdB. According to the theory and to the reports available in the literature, this result was quite unexpected; however, this negative correlation confirmed the poor quality of the available pedigree for the VdB breed and the higher reliability of the genomic-based inbreeding (Biscarini et al., 2020). Several

TABLE 2 Correlations (above diagonal) and their significance (below diagonal) among pedigree (F_{PED}) and genomic (F_{ROH}) inbreeding coefficients

	F_{PED}	F_{ROH1}	F_{ROH2}	F_{ROH4}	F_{ROH8}	F_{ROH16}	$F_{ROH1\text{-}2}$	$F_{ROH2\text{-}4}$	$F_{ROH4\text{-}8}$	$F_{ROH8\text{-}16}$
Sarda										
F_{PED}		0.44	0.45	0.43	0.44	0.47	0.07	0.13	0.21	0.31
F_{ROH1}	***		1.00	0.99	0.96	0.86	0.11	0.45	0.65	0.82
F_{ROH2}	***	***		0.99	0.96	0.87	0.03	0.43	0.64	0.82
F_{ROH4}	***	***	***		0.98	0.90	−0.01	0.31	0.63	0.82
F_{ROH8}	***	***	***	***		0.94	−0.04	0.26	0.44	0.8
F_{ROH16}	***	***	***	***	***		−0.10	0.17	0.33	0.55
$F_{ROH1\text{-}2}$	***	***	NS	NS	NS	NS		0.27	0.13	0.07
$F_{ROH2\text{-}4}$	***	***	***	***	***	***	***		0.35	0.34
$F_{ROH4\text{-}8}$	***	***	***	***	***	***	***	***		0.49
$F_{ROH8\text{-}16}$	***	***	***	***	***	***	NS	***	***	
Valle del Belice										
F_{PED}		−0.08	−0.08	−0.09	−0.09	−0.08	0.01	0.04	−0.01	−0.08
F_{ROH1}	NS		1.00	0.99	0.96	0.91	0.04	0.30	0.57	0.81
F_{ROH2}	NS	***		0.99	0.97	0.92	−0.04	0.26	0.56	0.82
F_{ROH4}	NS	***	***		0.99	0.94	−0.11	0.14	0.51	0.82
F_{ROH8}	*	***	***	***		0.97	−0.15	0.07	0.37	0.80
F_{ROH16}	NS	***	***	***	***		−0.15	0.03	0.28	0.62
$F_{ROH1\text{-}2}$	NS	NS	NS	*	***	***		0.58	0.21	0.11
$F_{ROH2\text{-}4}$	NS	***	***	***	NS	NS	***		0.48	0.14
$F_{ROH4\text{-}8}$	NS	***	***	***	***	***	***	***		0.47
$F_{ROH8\text{-}16}$	NS	***	***	***	***	***	*	***	***	

***$p < 0.001$; **$p < 0.01$; *$p < 0.05$; NS $p \geq 0.05$.

authors have described a high F_{PED}-F_{ROH} correlation when a deeper number of described generations are available in the pedigree (Ferenčaković et al., 2013a; Marras et al., 2015; Purfield et al., 2012), suggesting that the correlation between these parameters increases with the pedigree depth. In addition, it should be highlighted that pedigree relatedness is estimated from statistical expectations of the probable IBD genomic proportion, whereas genotype-based estimates show the actual relatedness among individuals and can provide greater accuracy on relatedness (Visscher et al., 2006). As expected, the five F_{ROH} coefficients computed with subsequent ROH lengths were largely and positively correlated with each other. In SAR, $F_{ROH1\text{-}2}$ showed no significant correlations with F_{ROH4}, F_{ROH8}, F_{ROH16} and $F_{ROH8\text{-}16}$. Correlations among the classes (i.e., $F_{ROH1\text{-}2}$, $F_{ROH2\text{-}4}$, $F_{ROH4\text{-}8}$, $F_{ROH8\text{-}16}$) were low to moderate in both SAR (from 0.07 to 0.40) and VdB (from 0.11 to 0.58).

Similar correlation estimates among F_{PED} and F_{ROH} found for SAR were reported for Basco-Béarnaise, Manech Tête Rousse, and Lacaune (Rodríguez-Ramilo et al., 2019) or Laxta (Granado-Tajada et al., 2020) sheep breeds. Inbreeding coefficients are related to selection

intensity and population structure and their accuracy depends on the reliability and completeness of data (Gorjanc et al., 2015; Yang & Su, 2016). However, the latter has a stronger impact on F_{PED} which strongly depends on depth and completeness of pedigree. The high dependency of F_{PED} on the quality of data is confirmed by the average F_{PED} value highlighted in this study: the very high standard deviation is due to coefficients equal to zero for some animals that have an incomplete or shallow pedigree. In particular, underestimated pedigree-based inbreeding coefficients can be caused by pedigrees with a large number of missing ancestors (Barczak et al., 2009). On the contrary, to estimate inbreeding coefficients using genomic information (e.g., ROH) there is no need to have known relatives of animals and therefore they can be estimated also in populations in which pedigree is not accurate or not even recorded. Moreover, several studies showed that inbreeding based on ROH provides a better measure of individual inbreeding than using pedigree information (Ferenčaković et al., 2013b; Forutan et al., 2018). Thus, F_{ROH} has been largely adopted as inbreeding coefficient to study depression phenomena in cattle (e.g., Doekes et al., 2019; Hidalgo et al., 2021; Pilon et al., 2021), sheep

(Antonios et al., 2021; Tao et al., 2021a) and goat (Luigi-Sierra et al., 2022).

3.2 | Inbreeding depression estimation

Different studies on cattle showed that genomic estimates of inbreeding can be used instead of pedigree estimates to calculate the effects of inbreeding on milk production traits (Bjelland et al., 2013; Pryce et al., 2014). However, investigations in sheep using genomic data have been mainly focused on fertility and growth traits, instead of on milk production traits.

The estimates of inbreeding depression from the mixed model analysis always exhibited a negative sign even if coefficients for FP and PP were not statistically significant (Table 3). Values are expressed as the change in the phenotype for a 1% increase in inbreeding coefficients.

Both F_{PED} and all F_{ROH} (except for F_{ROH1-2}, F_{ROH2-4} and F_{ROH4-8}) were significantly associated with MY in SAR breed. F_{ROH2-4}, related to relatively old inbreeding, was significantly and negatively associated with PP in SAR. The only coefficients with significant effects on MY in VdB were the F_{ROH} computed using subsequent lengths (i.e., F_{ROH1}, F_{ROH2}, F_{ROH4}, F_{ROH8}, F_{ROH16}) and F_{ROH4-8}. At the chromosome level (Table S1), nine autosomes showed signals of inbreeding depression. Significant coefficients were estimated in SAR on OARs 3, 21, and 26 for MY and OARs 6 and 26 for PP respectively. The significant signals for VdB were found on OARs 1, 2, 11, and 25 (MY) and on OAR18 (FP). Raadsma et al. (2009) carried out a meta-analysis on quantitative trait loci (QTL) affecting milk traits in sheep. These authors reported regions significantly affecting milk production in four chromosomes highlighted in the present study. In particular, these authors found two regions on OAR2, six regions on OAR3, one region on OAR6 and two regions on OAR25 associated with fat, protein or milk production. Chromosome 6, significant for PP in SAR, is well-known to present important QTL affecting milk production traits in sheep and cattle (e.g., Arnyasi et al., 2009; Diez-Tascón et al., 2001; Kucerova et al., 2006). Moreover, Usai et al. (2019) found on OAR6 three significant regions in a genome-wide analysis carried out in Sarda dairy sheep. Two of these regions were identified by only one SNP each, whereas the third one included 802 SNPs. The latter was a long region (36.2–105.2 Mb) significant for both fat and protein contents; within this interval, the authors found the strongest signal for protein content. In this same position, a QTL for protein content was reported also for Churra sheep. Interestingly, the inbreeding coefficients estimated in OAR26 showed a negative effect for both MY and PP in SAR breed. In this chromosome, a QTL associated with the udder attachment, which could

be associated with milk production traits, has been found in Spanish Churra dairy sheep (Gutiérrez-Gil et al., 2008).

The negative effect of inbreeding depression showed a reduction in MY ranging from 6 to 10 g/day (for SAR) and from 9 to 11 g/day (for VdB) for a 1% increase in inbreeding coefficients. This would correspond to a decrease of 1.3–2.1 kg and 1.9–2.3 kg in 210-day lactation in SAR and VdB respectively. Due to the lack of estimates of genomic inbreeding depression on milk production traits in sheep, our results were compared to reports in cattle. Bjelland et al. (2013) reported a decrease in total milk yield to 205 day postpartum of 20 kg per 1% increase in F_{ROH} in Holstein cattle. Moreover, Doekes et al. (2019) found that an increase of 1% in F_{ROH} in Dutch Holstein-Friesian dairy cattle resulted in a 36.3 kg decrease in 305-day milk yield. These authors reported an average milk production of 8,091 kg and, thus, the milk loss associated with inbreeding depression represents less than 0.5% of the total yield. In our case, the milk loss is on a percentage slightly higher: a loss of about 2 kg represents 0.8% of the average milk yield (250 kg) of Italian dairy sheep.

Since ROH length is an indicator of the age of inbreeding—short ROH is associated with old events, whereas long ROH with recent events (Howrigan et al., 2011; McQuillan et al., 2008)—the five F_{ROH} coefficients computing using subsequent lengths indicate the effect of old and recent inbreeding. For the three traits in both breeds, the coefficient estimated for F_{ROH16} was the largest, indicating a more negative effect of recent inbreeding compared to the old one. The more unfavourable effect of recent inbreeding is in agreement with a recent study on Basco-Béarnaise dairy sheep breed on semen motility traits (Antonios et al., 2021). These authors reported coefficients of −0.905 and −1.534 for ROH$_{Total}$ (using all ROH) and $F_{ROHRecent}$ (ROH > 17 Mb) respectively. Tao et al. (2021b) reported larger negative effects of F_{ROH} computed using only longer ROH (i.e., associated with recent inbreeding) for body weight in Qira black sheep: −0.60 (0.18) and −0.84 (0.40) kg for 1% increase in F_{ROH} estimated using ROH between 5 and 20 Mb and >20 Mb respectively. Recently, the effects of F_{ROH} on litter size were analysed in six sheep breeds: Wadi, Hu, Icelandic, Finnsheep, Romanov, and Texel (Tao et al., 2021a). These authors found negative estimates (and significantly different from zero) for F_{ROH} computed using only regions between 4 and 8 Mb, or higher than 8 Mb, in Hu sheep breed. On the contrary, Doekes et al. (2019) stated that no clear differences between old and recent inbreeding were found in inbreeding depression for yield, fertility, and udder traits in Dutch Holstein–Friesian dairy cattle. Moreover, a negative effect of both total (i.e., based on ROH with a minimum length of 4 Mb) and recent (i.e., based on ROH with a minimum length of 17 Mb) F_{ROH} was reported

TABLE 3 Inbreeding depression and standard errors for milk production traits using pedigree (F_{PED}) and genomic data (F_{ROH})

	Milk (kg/day)	Fat (%)	Protein (%)
Sarda			
F_{PED}	−0.006 (0.002)*	−0.007 (0.009)[NS]	−0.006 (0.005)[NS]
F_{ROH1}	−0.007 (0.003)*	−0.005 (0.011)[NS]	−0.007 (0.006)[NS]
F_{ROH2}	−0.007 (0.003)*	−0.005 (0.011)[NS]	−0.008 (0.006)[NS]
F_{ROH4}	−0.007 (0.003)*	−0.005 (0.011)[NS]	−0.007 (0.006)[NS]
F_{ROH8}	−0.008 (0.003)*	−0.005 (0.013)[NS]	−0.008 (0.007)[NS]
F_{ROH16}	−0.010 (0.004)*	−0.014 (0.017)[NS]	−0.013 (0.009)[NS]
F_{ROH1-2}	−0.031 (0.032)[NS]	0.057 (0.123)[NS]	0.034 (0.069)[NS]
F_{ROH2-4}	−0.022 (0.021)[NS]	−0.033 (0.080)[NS]	−0.099 (0.044)*
F_{ROH4-8}	−0.005 (0.012)[NS]	−0.014 (0.005)[NS]	−0.007 (0.025)[NS]
$F_{ROH8-16}$	−0.016 (0.008)*	−0.015 (0.032)[NS]	−0.000 (0.002)[NS]
Valle del Belice			
F_{PED}	−0.377 (0.236)[NS]	−0.036 (0.462)[NS]	−0.138 (0.282)[NS]
F_{ROH1}	−0.010 (0.004)**	−0.006 (0.007)[NS]	−0.002 (0.004)[NS]
F_{ROH2}	−0.009 (0.004)*	−0.006 (0.007)[NS]	−0.003 (0.004)[NS]
F_{ROH4}	−0.009 (0.004)*	−0.005 (0.007)[NS]	−0.003 (0.004)[NS]
F_{ROH8}	−0.009 (0.004)*	−0.008 (0.008)[NS]	−0.002 (0.005)[NS]
F_{ROH16}	−0.011 (0.005)*	−0.015 (0.009)[NS]	−0.006 (0.006)[NS]
F_{ROH1-2}	−0.018 (0.045)[NS]	0.048 (0.088)[NS]	0.090 (0.053)[NS]
F_{ROH2-4}	−0.042 (0.029)[NS]	−0.056 (0.058)[NS]	−0.022 (0.035)[NS]
F_{ROH4-8}	−0.050 (0.021)*	0.041 (0.042)[NS]	−0.016 (0.025)[NS]
$F_{ROH8-16}$	−0.015 (0.012)[NS]	0.012 (0.024)[NS]	0.008 (0.014)[NS]

***$p < 0.001$; **$p < 0.01$; *$p < 0.05$; [NS]$p \geq 0.05$.

on semen motility by Antonios et al. (2021). Several authors reported that this result can be explained considering the 'purging effect' (Doekes et al., 2019; McParland et al., 2009; Pryce et al., 2014). Inbreeding arising from a distant common ancestor should have less effect on fitness compared with inbreeding from a recent common relative because natural selection over long periods of time should act to purge deleterious alleles from the population (Holt et al., 2005). However, it should be pointed out that very short ROH (e.g., <1 or 2 Mb) are likely to be false positive.

The small number of signals of inbreeding depression can be associated with the generally limited magnitude of the selection pressure in sheep compared to cattle. The population structures of both breeds are not organized in large half-sib families, as in the case of the dairy cattle populations, and genetic connections among flocks are rather poor because of the limited exchange of rams and the scarce use of AI. Moreover, the lack of significance for coefficients of the mixed model can be likely attributed to a lack of statistical power due to the

small sample size. Also, poor quality of the data, especially for the pedigree in VdB as confirmed also by the negative correlation between F_{PED} and F_{ROH} values, could have had an effect. In fact, animals are mainly raised on semi-extensive farms, and the pedigree registration is often not accurate because the matings are not under the control of the farmers. However, there is a general lack of significance in most of the papers analysing the inbreeding depression in cattle and sheep. For example, Antonios et al. (2021) studied the effect of eight different inbreeding coefficients on three different traits but found significance just for 5 out of 24 coefficients tested. Also, Tao et al. (2021a) found significant inbreeding depression for just one of the six analysed sheep breeds, whereas only 11 out of 28 were significant in Tao, Liu, et al. (2021). Finally, Hidalgo et al. (2021) analysed the inbreeding depression in the Romosinuano cattle breed, and they found negative coefficients for both pedigree-based and ROH-based inbreeding; however, only two coefficients, the F_{PED} computed for ungenotyped animals, were significant, whereas the other six inbreeding coefficients computed for genotyped animals were not significantly different from zero.

4 | CONCLUSIONS

In this study, we have reported the estimates of inbreeding and inbreeding depression on milk production traits in two local genetic resources (Sarda and VdB sheep) using pedigree and genomic information. In both breeds, average F_{ROH} values decreased as the minimum ROH length increased, with VdB showing constantly higher values than Sarda. In Sarda, moderate correlation was observed between F_{PED} and F_{ROH} and it increased with ROH length. The negative correlation reported for VdB confirmed the poor quality of the available pedigree for the breed and the higher reliability of the genomic-based inbreeding.

Both F_{PED} and all F_{ROH} were significantly associated with MY in the SAR breed, whereas the only coefficients with significant effects on MY in VdB were the F_{ROH} computed using subsequent lengths. Although the magnitude of the inbreeding depression measured by the F_{ROH} is rather small, the effect is not negligible with the current inbreeding level (about 1.5–2.3 kg of milk loss over the whole lactation of 210 day for a 1% increase in the inbreeding coefficient). The present study confirmed how the use of genomic information instead of pedigree estimates can be also used to monitor inbreeding, manage intra-breed diversity, and calculate the effects of inbreeding on phenotypic traits. Minimizing inbreeding would be expected to augment economic gain by increasing milk yield.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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