ESTIMATING LETHAL EQUIVALENT OF THE PANNON WHITE RABBIT POPULATION APPLYING GENERALISED LINEAR MIXED MODELS

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ABSTRACT

The closed Pannon White rabbit population has long and complete pedigree making it highly suitable for inbreeding studies. Survival of rabbit kits at birth is modelled as a binary variable applying generalised linear mixed models (GLMM) based on the log link function. Modelling was performed taking into account the inbreeding coefficient of the kit, inbreeding coefficient of the dam, season of parturition, parity of the dam and animal. Based on the monthly averages of the survival of rabbit kits at birth the analysed period (1992-2017) was divided to two periods (1992-1997 and 1997-2017). Altogether 22718 kindling records were analysed. The estimated regression coefficients for the inbreeding coefficients of the kits and for the dams were -0.20±0.27 and -0.41±0.36 and 0.05±0.08 and -0.01±0.09 in the first and second periods, respectively. This corresponds to the lethal equivalent of 0.2 in the first period, which disappeared in the second period. Due to the large standard errors, the results were not significant.

Key words: generalised linear mixed models, binomial regression, lethal equivalent, survival rate at birth, Pannon White rabbits

INTRODUCTION

Inbreeding which is the mating of related animals is an inevitable consequence of selection in a closed population, especially when the breeding animals are selected based on best linear unbiased predictors (i.e. breeding values). The consequence of mating related animals is that the proportion of homozygous loci is being increased to the expense of the heterozygous ones. This phenomenon can be quantified by the inbreeding coefficient that provides the probability that the two alleles at any locus in an individual are identical by descent (Malecot, 1970). It is well known that inbred progenies are often affected by inbreeding depression that is the reduced fitness because of lower survival, mating and/or reproduction in the progeny of related individuals compared to the progeny of unrelated animals (Hedrick and García-Dorado, 2016). The Pannon White rabbit population was developed at the Kaposvár University. Due to its closed condition, the Pannon White rabbit population is highly suitable for inbreeding related studies. The lack of immigration makes possible to have a complete pedigree. The applied circular mating scheme is also advantageous from the aspect of the inbreeding rate (Nagy *et al.*, 2010). According to our knowledge, the influence of inbreeding on survival rate in rabbits has not yet been investigated. It therefore was decided that in the present study the survival rate at birth would be investigated.

MATERIALS AND METHODS

Animals and experimental design

The Pannon White rabbit population was developed at the Kaposvár University from the late 1980 and the Hungarian Authorities recognized it as a rabbit breed in 1992. It has been selected as a closed population ever since. Generations are overlapping and the reproduction rhythm is 42 days long. Nagy *et al.* (2010) describe population foundation and management in detail. Analysis was based on the pedigree and kindling records that have been collected continuously between 1992 and 2017. The analysed dataset consisted of 22.781 kindling records. In order to calculate litter inbreeding coefficients, dummy progeny were created according to the unique combinations of does and related mating bucks.

Pedigree Analyses

The pedigree was analysed applying the GRAIN software (Doekes *et al.*, 2019) calculating the inbreeding coefficient of the dam (F_d) and of the litter (F_l) defined as the probability that the two alleles at any locus in an individual are identical by descent (IBD). Coefficients were calculated by the stochastic method "gene dropping" using 1.000.000 iterations.

Statistical Analysis

The effects of inbreeding on the survival of kits at birth - which was treated as a binomial response trait - was examined applying generalised linear mixed models (GLMM). Fitting GLMM models were performed by means of pedigreemm R software package. Based on the monthly averages of the survival of rabbit kits at birth the analysed period be split to two main periods (1992.12-1997.08 and 1997.09-2017.11, respectively). Further statistical analyses were performed for these two periods separately. The applied model was developed using the pedigree and contained the parity number (combined into four groups: 1, 2, 3-10, ≥11) and season (summer: between 15/06 and 15/09, other: rest of the year) of kindling as fixed effects. Collinearity was tested by calculating correlation between dam and litter inbreeding coefficients and by Generalised Variance Inflation Factor GVIF. In the first and second periods, the correlation coefficients between dam and litter inbreeding coefficients were 0.02 and 0.67, respectively. The calculated GVIF values for the same periods were 1.00, 1.00, 1.86 and 1.89, respectively. Thus, no sign of collinearity between the dam and litter inbreeding coefficients was found. Based on the different inbreeding coefficients or their equivalents, the model was the following: $\log[p(\text{survival})] = \text{parity} + \text{season} + F_d + F_l + \text{year-season} + \text{animal}$. The estimates of the litter inbreeding it directly provides the number of lethal equivalents (LE) which can be defined as the number of deleterious genes per gamete, when combined in a homozygous state, would result in the death of an individual (Hoeck *et al.*, 2015).

RESULTS AND DISCUSSION

Looking at the evolution of the Wright inbreeding coefficients (Table 1) continuous increasing tendencies were observed both for the dams and for the litters. The number of records where F_d and F_l were higher than 20% was only 73 and 131, maximum values of F_d and F_l were 33% and 34%, respectively. Due to the closed population structure, all F_d and F_l values were higher then zero after 2011. However, even in the last examined year 2017 the average F_d and F_l values were relatively low (11.4% and 11.9%, respectively). These values are lower than that of the result of a half-sib mating showing the low inbreeding rate of the Pannon White rabbit population. Examining inbreeding depression it was observed that during the first period the increasing litter inbreeding had a negative estimate (although it was not significant) for the survival rate at birth (Table 2). On the contrary, positive estimate could be detected for dam inbreeding (not significant). The importance of treating both litter and dam inbreeding simultaneously was emphasized by Falconer (1960) who noted that litter inbreeding might reduce the viability of embryos while dam inbreeding may have an effect on the fertility of the females. In our previous study (Nagy *et al.*, 2013) analysing the same rabbit population the litter inbreeding negatively affected number of kits born alive while dam inbreeding significantly increased number of kits born dead which latter effect may be connected to uterine capacity.

Table 1: Descriptive statistics of the dam and litter inbreeding coefficients

Inbreeding coefficient of the dam			Inbreeding coefficient of the litter		
Year	mean	standard deviation	Year	mean	standard deviation
1992	0.00	0.00	1992	0.00	0.00
1997	0.01	0.02	1997	0.01	0.02
2002[a]	0.02	0.02	2002[a]	0.03	0.02
2007	0.05	0.04	2007	0.06	0.03
2012	0.08	0.03	2012	0.09	0.02
2017	0.11	0.03	2017	0.12	0.03

Table 2: Effects of the explanatory variables on the survival rate of the kits

First period 1992-1997			Second period 1997-2017		
Factor	estimate	SE	Factor	estimate	SE
Intercept	-0.07	0.01	Intercept	-0.06	0.01
F_d	-0.41	0.36	F_d	-0.01	0.09
F_l	-0.20	0.27	F_l	0.05	0.08
PARITY [T.2]	0.02	0.02	PARITY [T.2]	0.02	0.01
PARITY [T.3]	0.02	0.01	PARITY [T.3]	0.01	0.01
PARITY [T.4]	0.03	0.02	PARITY [T.4]	0.01	0.01

SEASON: summer vs. other; PARITY [T.2]: parity 1 vs 2; PARITY [T.3]: parity 1 vs 3; PARITY [T.4]: parity 1 vs 4;

According to Kennedy *et al.* (2014), using the unstandardized version of their model the estimated effect of F_l on the survival rate at birth provides directly the number of lethal equivalents per gamete (B). We believe Kennedy *et al.* (2014) could not obtain LE directly as they used logit link function. In our case, using the log link function the received value for the period of 1992-1997 was 0.2 giving directly the estimated lethal equivalent. This value is within the range estimates of B regardless to the analysed species (Ralls *et al.*, 1988). In our study, the survival rate at birth is an early life-stage trait that explains the relatively low value of LE. In studies related to different bird species there was a clear tendency that the magnitudes of the estimated lethal equivalents increased with the age until survival was monitored. When survival rates were followed until 1-2 years or until recruitment, different authors (Hoeck *et al.*, 2015; Kennedy *et al.*, 2014) reported higher LE (B=3.4-6.9) compared to the study of Gruber at al. (2010) analysing the early life-stage trait of hatching rate (B=0.17). It has to be mentioned that the estimated lethal equivalents of the different studies were not always directly comparable as they used different methodology. In a recent study, Nietlisbach *et al.* (2019) used computer simulation in order to compare the different methods estimating LE. According to their results, exponent maximum likelihood and GLM log-link methods were unbiased while GLM logit-link method resulted overestimated LE-s especially if the true value of LE was high. On the contrary, Armstrong and Cassey (2007) reanalysed the lemur dataset of Kalinowski and Hedrick (1998) and they reported that the logit-linear models gave a better fit to the data than log-linear models proposed by Nietlisbach *et al.* (2019). It has to be noted that the estimated effect in the first period was not significant, but according to Nietlischbach *et al.* (2019), the significance level using the log-link is questionable because standard confidence intervals are typically too high.

CONCLUSIONS

Based on the results Pannon White rabbit population did not show any significant inbreeding depression related to dam and litter inbreeding. The estimated lethal equivalent also was not significantly different from zero. Thus, it can be concluded that at present the Pannon White rabbit population does not possess substantial inbreeding load.

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