Risk factors for intrapartum stillbirth in piglets born from cloprostenol-induced farrowing sows

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Abstract

The present study aimed at examining the association between different risk factors and intrapartum stillbirth in piglets born from cloprostenol-induced farrowing sows. This study enrolled 898 piglets born within 77 Landrace x Yorkshire sows subjected to farrowing induction using cloprostenol at day 114 of gestation. Generalized Linear Mixed Models were used to determine important indicators for intrapartum stillbirth at the piglet level. Investigated risk factors included parity, gestation length, litter size, birth order, piglets’ gender, birth interval, cumulative farrowing duration, birth weight, crown-rump length, body mass index, ponderal index, and birth weight deviation. The stillbirth rate was 5.3%. Intrapartum stillbirth accounted for 79.2% of all stillbirths. Body conformation traits (birth weight, birth weight deviation, body mass index, and ponderal index), birth order, and cumulative farrowing duration were important indicators for intrapartum stillbirth. Birth order (OR = 1.24; 95% CI = 1.13–1.37), birth interval (OR = 1.01; 95% CI = 1.01–1.02), birth weight deviation (OR = 0.78; 95% CI = 0.69–0.88), and ponderal index (OR = 0.95; 95% CI = 0.91–0.99) were selected in the model that best explained the variation of stillbirth (marginal R² = 0.31, conditional R² = 0.54). Results of this study highlight the importance of body size and shape, birth order, and birth interval in prediction of the intrapartum stillbirth of piglets born from cloprostenol-induced farrowing sows.

Introduction

Over recent decades, the development of management, nutrition science, and genetic selection has increased litter size considerably (Rutherford et al. 2013; Koketsu et al. 2017). Unfortunately, an increase in litter size results in an increased number of low birth weight piglets (Koketsu et al. 2017) and an elevated stillbirth rate (Nam and Sukon 2020a; Nam and Sukon 2020b; Nam and Sukon 2021).

Piglets that died after day 109 of gestation and before births are defined as stillbirths (Gugjoo et al. 2012). About 10–15% of stillbirths occur before the onset of parturition (prepartum stillbirth) and 67%–75% of stillbirths occur during delivery (intrapartum stillbirth) (Sprecher et al. 1974; Leenhouwers et al. 2003). Prepartum stillbirths characterize by normal appearance at the time of expulsion, while intrapartum stillbirths have a normal colour of abdominal organs and non-aerated lungs (Leenhouwers et al. 2003). Intrapartum stillbirths are the results of asphyxia and dystocia (Roongsitthichai and Olanratmanee 2021). Many factors have been identified as the cause of the intrapartum stillbirth such as large litter size, high parity, long/short gestation length, high birth order, low birth weight, long birth interval, and long cumulative farrowing duration (Baxter et al. 2009; Vallet et al. 2010; Vanderhaeghe et al. 2011; Langendijk et al. 2018; Nam and Sukon 2020a; Nam and Sukon 2020b; Nam and Sukon 2021).

Farrowing induction is used to minimize labour requirements over the weekend and to increase farrowing supervision, thereby reducing stillbirth (Kirwood 2015). The induction of farrowing can be done with the application of prostaglandins or its analogues, alone or in combination with oxytocin (Decaluwé et al. 2014) or carbetocin (Boonraungrod et al. 2018) 24 h after prostaglandin administration. Prostaglandins can be administered with a single dose (Vallet and Miles 2017) or two doses, 6 h apart to decrease the variation of gestation length (Tospitakkul et al. 2019). Most of the induction programmes are conducted at day 114 of gestation (Otto et al. 2017; Boonraungrod et al. 2018; Tospitakkul et al. 2019; Hlová et al. 2020), some are utilized earlier (Cassar et al. 2005; Foisnet et al. 2011).

Among prostaglandin products, cloprostenol was used most frequently (Otto et al. 2017; Vallet and Miles 2017; Boonraungrod et al. 2018; Tospitakkul et al. 2019). Risk factors for stillbirth in piglets born within non-induced farrowings have been investigated, however, such information in prostaglandin-induced farrowings is limited. Therefore, knowledge in risk factors associated with intrapartum stillbirth under farrowing induction may be valuable for swine farm industry where the use of farrowing induction is still in reluctance. The aim of the present study was to determine the risk factors for intrapartum stillbirth in piglets born from cloprostenol-induced farrowing sows.

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Materials and methods

Animals and housing

This study was conducted at a commercial swine farm in Bacnhin province in the North of Vietnam during 13th October 2020 and 9th January 2021. The herd has a breeding capacity of 600 sows. Pregnant sows were daily fed 2.0–3.0 kg of industrialized gestation feed. In the first 84 days of gestation, sows were fed gestation diet which had a metabolizable energy of 3000 kcal/kg, and 14% crude protein. From day 85 to farrowing sows were fed lactation diet which had a metabolizable energy of 3200 kcal/kg, and 16.5% crude protein. The ingredients of diet make up were soybean meal, animal protein, rice, rice bran, corn, wheat bran, casava root, amino acids, vitamins, and minerals. Sows were allocated in individual crates sized 180 cm in width and 220 cm in length. Sows were provided water ad libitum through a bite nipple drinking system. The temperature in the gestation and farrowing rooms was controlled by using fans and water sprinklers. Vaccination against classical swine fever, Aujeszky’s disease, foot and mouth disease, porcine reproductive and respiratory syndrome, and porcine parvovirus was used in all sows. About 5–7 days before the estimated farrowing date, batches of 70–80 sows were removed to 3 farrowing rooms which had similar conditions. Each farrowing room had about 25–30 sows that were allocated in individual farrowing crates. Sows were fed 1.5, 1.0, and 0.5 kg of feed on days 111, 112, and 113 to farrowing. Farrowing was induced by an injection of 175 mcg cloprostenol sodium (HAN-PROST, Hanvet, Vietnam) into the vulva at 7 am on day 114 of gestation. The farrowing induction which has been routinely practiced in this farm since 2017 was conducted every 3 weeks. During the parturition 1–2 farm workers were responsible for farrowing supervision in each room.

Data collection and definitions

Data were collected from sows that started farrowing during working time (7AM-17PM) by farm workers who were trained for data collection. Because several sows might farrow in the same time, they were randomly chosen to be enrolled into the study. This ensured that collection of all required information of such sows was possible. Moreover, for the certainty of prostaglandin effect on farrowing only sows that started their farrowings at least 8 h after cloprostenol injection were used in the study. In total, data of 1004 piglets born within 77 Yorkshire x Landrace crossbred sows were recorded. The parity number of investigated sow ranged between 1 and 8 with 16, 17, 4, 3, 20, 13, 3, and 1 sows in parity 1, 2, 3, 4, 5, 6, 7, and 8, respectively. Parity, gestation length, litter size, birth order, birth interval, cumulative farrowing duration, crown-rump length, birth weight, and piglet’s gender were recorded. Gestation length was the interval between the date of first insemination and the date of farrowing. Litter size included live-born, stillborn, and mummiﬁed piglets. Birth weight was measured using a digital scale. The crown-rump length was measured using a tape measure. The measurement of birth weight and crown-rump length was conducted immediately after mucous removal and lasted for about 40 s. Body mass index and ponderal index were calculated from birth weight and crown-rump length measurements via the following equations: birth weight (kg)/(crown-rump length, m)² and birth weight (kg)/(crown-rump length, m)³, respectively. Birth weight deviation (BWD, kg) was the difference between the birth weight of a given piglet and the average birth weight of all stillborn and live-born piglets in that litter (Canario et al. 2006). Stillbirth was examined immediately after birth and categorized into three types (1) non-fresh stillborn piglets were those with partly brown skin colour; (2) prepartum stillborn piglets were those with no sign of skin degeneration but showing the brick-red colour of abdominal organs; and (3) intrapartum stillborn piglets were those with normal colour of abdominal organs and non-aerated lungs (Leenhouters et al. 2003). Mummiﬁed piglets were those with brown/black skin.

Statistical analysis

Descriptive statistics were calculated based on all available and complete data from 77 sows and 1004 piglets (Table 1). For risk analysis, firstborn, mummiﬁed, non-fresh, and prepartum stillborn piglets were removed leaving 898 piglets. To account for the dependency of the data, multilevel logistic regression was conducted through Generalized Linear Mixed Models (GLMMs) to determine potential risk factors for intrapartum stillbirth. The dependent variable was intrapartum stillbirth (binary outcome). The independent variables were divided into two levels of factors. Level 1 (piglet level) factors contained birth order, birth interval, cumulative farrowing duration, piglet’s gender, birth weight, crown-rump length, body mass index, and ponderal index. Level 2 (sow level) factors contained parity, gestation length, and litter size. All independent variables were treated as continuous variables in the analysis. The model was built as: 

$$\text{logit(Pr}(Y_{ij} = 1)) = \alpha_0 + \alpha_0 + \gamma_i \cdot X_{ij} + \gamma_j \cdot Z_{ij} + \gamma_m \cdot Z_{mj} (\text{Austin and Merlo 2017}).$$

$Y_{ij}$ was the binary response variable measured on the $i$th piglet within the $j$th sow ($Y_{ij} = 1$ was the occurrence of the stillbirth). $X_{ij}$ through $Z_{mj}$ denoted the k predictor or explanatory variables measured on the piglet. $Z_{ij}$ through $Z_{mj}$ denoted the m predictor variables measured on the $j$th sow. $\alpha_0$ was the
regression coefficient for k predictor or explanatory variables measured on the piglet. \( \beta_m \) was the regression coefficient for m predictor or explanatory variables measured on the sow. Only \( \alpha_g \) was a random intercept for sow specific effect. Other explanatory variables in the model were treated as fixed effects. Three multilevel logistic regression models were fitted, but only a final model was reported. The first model (Model 1) was a null model which did not contain any piglet or sow factors. It included only sow-specific random effects to model between-sow variation in intrapartum stillbirth. The second model (Model 2) included all piglet factors and all sow factors. The third model (Model 3) was the final model and included only significant factors that best explained the variation of intrapartum stillbirth. The variance of random effects including \( \tau^2 \), and variance partition coefficient (VPC) or intraclass correlation (ICC) were calculated (Austin and Merlo 2017). The final model was reached through the following steps. Firstly, univariate GLMMs were performed to identify the importance of all single risk factors. All factors significant at a \( P < 0.1 \) were retained for multivariate GLMMs. The most significant factor (based on \( p \)-value and the lowest Akaike information criterion (AIC)) was then coupled with other significant factors and these couples were analyzed in different multivariate GLMMs. The most significant GLMM containing 2 independent factors was then added with other significant factors to look for the most significant model containing 3 independent factors. This procedure was repeated until the addition of an independent factor resulted in neither a decrease of the AIC value nor a significant value of the added factor. To avoid multicollinearity of independent variables, Spearman’s correlation was used to quantify the relationship among significant variables concerning intrapartum stillbirth (IBM SPSS Statistics for Windows, Version 22.0, Armonk, NY: IBM Corp). In addition, variance inflation factor (VIF) was used to determine multicollinearity or confounding factors in the model. Hosmer-Lemeshow goodness of fit test was run to check if the expected outcome matched the observed outcome. The regression coefficients from univariate and multivariate (the final model) models were converted to odds ratio for ease of interpretation. All tests were conducted in RStudio Desktop 1.4.1106. A \( P \) value <0.05 was considered significant.

### Results

In total, 77 litters from 5 farrowing batches and 1004 piglets were recorded. Among the litters, 28 out of 77 (36.4%) litters had at least one stillborn piglet. Twenty-one piglets (2.1%) were classified as mummies, and 53 piglets were stillborn accounting for 5.3%. Intrapartum stillbirth accounted for 79.2% of all stillbirths. Farrowing duration, birth interval, crown-rump length, and birth weight were 249.9 ± 122.9 min (72–859), 19.3 ± 31.4 min (0–370), 267 ± 26 mm (150–335), and 1473 ± 377 g (400–2435), respectively (Table 1).

Regarding correlations between significant explanatory variables concerning intrapartum stillbirth, body mass index vs. ponderal index, birth weight vs. birth weight deviation, and birth order vs. cumulative farrowing duration had strong correlation coefficients (Spearman’s rho = 0.883, 0.780, and 0.705, respectively). All other correlation coefficients were week (Spearman’s rho <0.312).

Univariate GLMMs analyses showed that parity, birth order, birth interval, cumulative farrowing duration, birth weight, body mass index, ponderal index, and birth weight deviation were all associated with intrapartum stillbirth (Table 2). By contrast, gestation length, litter size, crown-rump length, and piglet’s gender were not associated with intrapartum stillbirth.

The final multivariate GLMM that best explained variation of intrapartum stillbirth in piglets was presented in Table 2. The selection order of independent factors was birth order, birth weight deviation, birth interval, and ponderal index. Birth order, birth interval positively correlated with, whereas birth weight deviation and ponderal index were negatively associated with intrapartum stillbirth. The final multivariate GLMM had a \( p \)-value <0.001. The marginal R2 and conditional R2 of the final model were 0.31 and 0.54, respectively. Hosmer-Lemeshow goodness of fit test showed a good fit between expected and observed outcomes (\( p = 0.637 \)). The variance inflation factors for birth order, birth weight deviation, birth interval, and ponderal index were 1.12, 1.23, 1.10, and 1.05, respectively, which showed that there was no confounding factors within selected ones.

### Discussion

The stillbirth rate of piglets in the present study (5.3%) was quite similar to that (4.4–5.8%) previously reported in natural farrowings (Baxter et al. 2008; Baxter et al. 2009; Nam and Sukon 2021). In another study, Boonraungrod et al. (2018) also found that the stillbirth rate in the induced farrowings ranged from 4.0–4.7%. The present stillbirth rate was, however, lower than the results (8.8–9.8%) recently reported in cloprostenol-induced farrowings (Tospitakkul et al. 2019).
and this difference may be attributable to the variation in herd condition.

Many previous studies have elucidated the association between dozen of factors and stillbirth in different conditions (reviewed by Vanderhaeghe et al. (2013)). However, the understanding of risk factors influencing intrapartum stillbirth in piglets born from prostaglandin-induced farrowing sows is inadequate. The present study highlighted the importance of birth order, birth interval, ponderal index, and birth weight deviation in the explanation of variation of stillbirth in piglets born from cloprostenol-induced farrowings. The importance of these factors in spontaneous farrowings were also reported in previous studies (Baxter et al. 2009; Langendijk et al. 2019; Nam and Sukon 2020b; Nam and Sukon 2021). Therefore, this study indicated that risk factors for stillbirth in piglets might be, to some extent, similar across farrowing conditions. There are increasing evidences of the importance of body conformation indices in the explanation of stillbirth in piglets (Baxter et al. 2009; Nam and Sukon 2020b; Nam and Sukon 2021). Birth weight (Baxter et al. 2009) and birth weight deviation (Canario et al. 2006) were found to be negatively associated with stillbirth in which birth weight deviation was reported to be more important than individual birth weight in explaining the stillbirth (Canario et al. 2006). That finding was in agreement with the result of the present study. Piglets with low birth weight deviation had low birth weight. Also, piglets with low body mass index and ponderal index were small and disproportionate and might be suffered from uterine growth retardation (Paules et al. 2019). Small piglets have lower haemoglobin concentrations in comparison with their heavier littermates (Zaleski and Hacker 1993). Also, they might experience substandard nutrition and acquire inadequate neuro-development (Wise et al. 1997; Roelofs et al. 2018). Therefore, these piglets are more prone to death during parturition (Baxter et al. 2009; Nam and Sukon 2020b; Nam and Sukon 2021). Selection for lean growth might result in higher birth weight but less maturity characterized by less body fat at birth (Herpin et al. 1993). Meanwhile, body mass index and ponderal index measure the fatness of piglets rather than sole birth weight. Hence, ponderal index and body mass index are considered more important than birth weight concerning stillbirth as showed in this study and others (Herpin et al. 1993; Baxter et al. 2009; Nam and Sukon 2020b; Nam and Sukon 2021).

The positive associations between stillbirth and birth order, cumulative farrowing duration, and birth interval have been reported in several previous documents (Baxter et al. 2012; Langendijk et al. 2018; Udomchanya et al. 2019; Nam and Sukon 2020b; Nam and Sukon 2021). Fetal expulsion is the result of the active movement of piglets (Taverne and van der Weijden 2008) and uterine contraction (Mota-Rojas et al. 2007). The former activity spends oxygen and energy provided from blood. The latter action causes interruption of blood flow to the placenta resulting in asphyxiation characterized by reduced piglet’s heart rate, increased lactate, and lowered pH of fetal blood (van Dijk et al. 2008). Increased birth order results in an increased number of series of uterine contractions and predisposes piglets to cumulative hypoxia and stress. Also, prolonged cumulative farrowing duration exacerbates the effect of birth order on stillbirth (Langendijk et al. 2018). Furthermore, Vallet et al. (2010) found a positive association between stillbirth of piglets and their own birth interval instead of a significant effect of birth intervals of previous piglets on stillbirth of subsequent piglets. Such findings suggest the importance of birth interval when the piglets actively manage to travel through the birth canal especially the thick and inherent long swine cervix.

The effect of gestation length on stillbirth is controversial. Some authors reported an increased stillbirth rate in either short gestations. i.e. <114 days (Vallet et al. 2010; Nam and Sukon 2020a; Nam and Sukon 2020b; Nam and Sukon 2021) or long gestations. i.e. >116 days (Nam and Sukon 2020b) or >117 days (Nam and Sukon 2021) while others did not find any association between gestation and stillbirth (Canario et al. 2006; Udomchanya et al. 2019). Piglets born from short gestations may be less mature and lighter (Zaleski and Hacker 1993) while those born from prolonged gestations may be affected by placental aging (Maiti et al. 2017). In this study, the non-significant association may be the result of less variation of gestation length in induced sows which varied between 114 and 118 days. Also, no correlation between birth weight and gestation length existed in this study (Spearman’s rho = 0.039, P = 0.244).

The positive association between litter size and stillbirth was demonstrated in several previous studies (Borges et al. 2005; Vanderhaeghe et al. 2010; Nam and Sukon 2020a; Nam and Sukon 2020b). The increased stillbirth rate in large litters may be the result of decreased birth weight and increased farrowing duration (van Dijk et al. 2005). Non-significant effect of litter size in this study was not due to the large variation of litter size when it was treated as a continuous rather than a categorical variable as in other studies (Borges et al. 2005; Nam and Sukon 2020a; Nam and Sukon 2021). An explanation for the non-significance may be that the litter size in this study is smaller when compared with that in a study where a significant effect was found (13.2 vs. 15.8) (Nam and Sukon 2020b).

The effect pattern of parity on stillbirth is different among studies. Some authors found a positive correlation (Borges et al. 2005; Vanderhaeghe et al. 2010; Vanderhaeghe et al. 2011; Pandolfi et al. 2017; Nam and Sukon 2020b), others reported increased stillbirth in first parity (Canario et al. 2006; Nam and Sukon 2020a). Increased stillbirth in later parity may be attributable to long farrowing duration (Borges et al. 2005) and that in first parity may be due to small birth canal size (Canario et al. 2006). In this study, the positive association between parity and intrapartum stillbirth may be attributable to the association between parity and other independent variables such as litter size, birth weight, and cumulative farrowing duration. Indeed, in this study parity positively correlated with litter size (Pearson correlation = 0.32, P < 0.001) and cumulative farrowing duration (Pearson correlation = 0.093, P = 0.005), while negatively correlated with birth weight (Pearson correlation = −0.116, P < 0.001).

Conclusions

This study indicates that under the condition of cloprostenol-induced farrowings, birth order, birth weight deviation, birth
interval, and ponderal index of piglets are important factors influencing the stillbirth of piglets. The data suggest that increasing birth weight deviation and ponderal index of piglets should be the target for genetic selection to reduce intrapartum stillbirth. Furthermore, the importance of birth order and birth interval in intrapartum stillbirth prediction implies the need for supervision, especially at the second half, of farrowings.

Ethical approval
This study was waived from the animal care and use committee of Vietnam National University of Agriculture because all procedures done on animals have been routinely practiced in the investigated farm, and the study did not involve in sample collection.

Disclosure statement
No potential conflict of interest was reported by the author(s).

Data availability statement
The data presented in this study are available on request from the corresponding author.

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