

SUPPLEMENT REVIEW

The challenge of large litters on the immune system of the sow and the piglets

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Abstract

The use of hyperprolific sow lines has increased litter size considerably in the last three decades. Nowadays, in some countries litters can reach up to 18–20 piglets being a major challenge for the sow's physiology during pregnancy, parturition and lactation. The increased number of piglets born per litter prolongs sensibly the duration of farrowing, decreases the piglets' average weight at birth and their vitality, increases the competition for colostrum intake and can affect negatively piglets' survival. This review aims to describe how large litters can affect the immune system of the sow and the piglets and proposes measures to improve this condition.

KEYWORDS

birthweight, colostrum, duration of farrowing, immunoglobulins, intrauterine growth retardation, pig

1 | INTRODUCTION

In the European pig production, there has been a steady increase in litter size during the last three decades (Baumgartner, 2012; Kemp, Da Silva, & Soede, 2018). Only during the period from 1990 to 2010, litter size is on average increased from 11 to 14 piglets born per sow per litter, with some countries reaching an average of 16 piglets (Baumgartner, 2012). Nowadays, when raising hyperprolific sow lines, it is not uncommon to have litters up to 18–20 piglets (Björkman, Oliviero, Rajala-Schultz, Soede, & Peltoniemi, 2017; Kemp et al., 2018; Kobek Thorsen, Aagaard Schild, Rangstrup-Christensen, Bilde, & Juul Pedersen, 2017).

This increasing number of piglets is a major challenge for the sow physiology during pregnancy, at parturition and during lactation. There is a negative correlation between the number of pig fetuses and the growth of the individual fetuses; similarly, a high number of fetuses is connected with reduced uterine blood flow per foetus (Pere & Etienne, 2000). This reduced utero-placental blood flow and/or angiogenesis may be associated with a pathologic condition known as intrauterine growth retardation (IUGR) (Reynolds et al., 2006). In hyperprolific sows, lack of space in the uterus has also been indicated to be a main reason for reduced foetal growth (Vallet, McNeel, Miles, & Freking, 2014; Vonnahme, Wilson, & Ford,

2002). In late pregnancy, foetal weight decreases linearly from the utero-tubal junction (smaller uterine lumen diameter) towards the cervix (Che et al., 2016).

Observations made in many studies in the last 26 years show an increase in the duration of farrowing when litter size increases (Figure 1). This can affect negatively the sow by increased duration of this painful process, inflammation of the uterus and risk for retained placentas (Björkman et al., 2017; Ison, Jarvis, Hall, Ashworth, & Rutherford, 2018; Kaiser et al., 2018). Large litters are difficult to manage also during lactation, because sows can have on average 14–16 teats (Labroue, Caugant, Ligonesche, & Gaudré, 2001); however, not all teats may be active. Andersen, Nevdal, and Bøe (2011) suggest that without manipulation of litter size and without human help, the number of piglets a sow is able to successfully wean is no more than 10 to 11.

Large litters have a direct impact also on piglets at birth. The higher is the number of piglet born in a litter, the lower is the piglet birthweight (Figure 2) and the higher is the variation in piglet birthweight within the litter (Akdag, Arslan, & Demir, 2009; Beaulieu, Aalhus, Williams, & Patience, 2010; Matheson, Walling, & Edwards, 2018; Quesnel, Brossard, Valancogne, & Quiniou, 2008; Smit et al., 2013). A greater number of piglets born than the available teats at the sow's udder, a lower birthweight and a greater birthweight

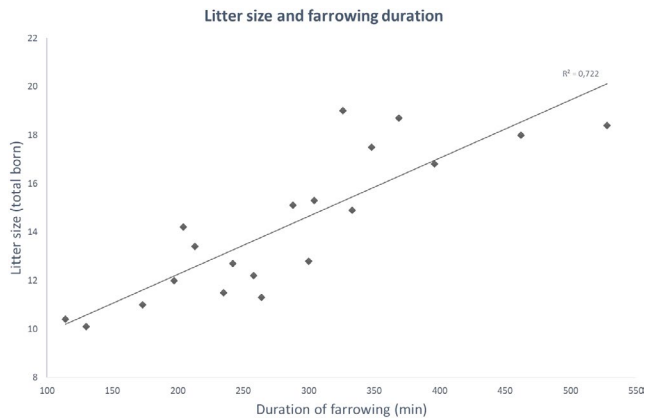


FIGURE 1 Relationship between litter size and the duration of farrowing in 20 studies from 1992 to 2018 (Björkman et al., 2017, 2018; Canario, Roy, Gruand, & Bidanel, 2006; van Dijk, van Rens, van der Lende, & Taverne, 2005; Feyera et al., 2018; Gu et al., 2011; Guillemet et al., 2007; Hales, Moustsen, Devreese, Nielsen, & Hansen, 2015; Hansen, Hales, Weber, Edwards, & Moustsen, 2017; Kobek Thorsen et al., 2017; Madec & Leon, 1992; Oliviero, Heinonen, Valros, & Peltoniemi, 2010; Oliviero, Kothe, Heinonen, Valros, & Peltoniemi, 2013; Oliviero et al., 2008; Olsson, Botermans, & Englund, 2019; van Rens & van der Lende, 2004; Tummaruk & Pearodwong, 2015; Van Wettere, Toplis, & Miller, 2018; Yun et al., 2018; Zaleski & Hacker, 1993)

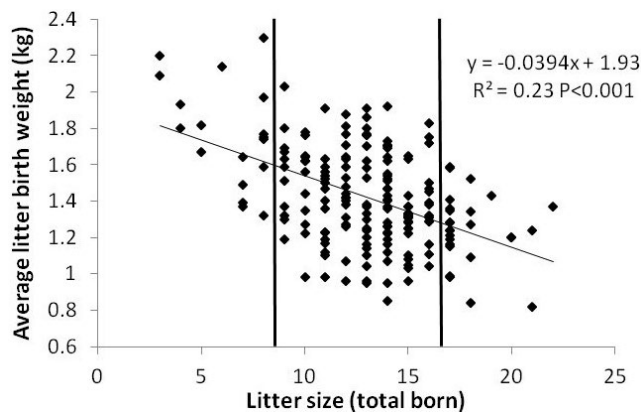


FIGURE 2 Relationship between litter size (total born) and the average piglet birthweight by litter (from Smit et al., 2013; Animal, Cambridge press, supplementary material)

variation all increase the piglets' competition for colostrum intake (Declerck, Sarrazin, Dewulf, & Maes, 2017). Similarly, lower birthweight and long farrowing duration are associated with lower piglet vitality at birth, which can delay the access to the udder (Hoy, Lutter, Wähner, & Puppe, 1994; Islas-Fabila et al., 2018).

In large litters, an increased number of piglets born with signs of intrauterine growth retardation (IUGR) is also reported. These piglets have an extremely lower birthweight and lower vitality (Amdi et al., 2013; Matheson et al., 2018). A reduced colostrum intake in the first 24 hr of life has negative effects on the piglet survival (Devillers, Le Dividich, & Prunier, 2011).

The neonate piglets are born with functionally mature innate immunity, without the protection of immunoglobulins because of

the epitheliochorial nature of the porcine placenta and with polarized Th2-type immunity. The Th2-type immunity is mediated by high levels of progesterone and Th2 cytokines produced in the maternal-foetal interface. Neonate piglets must acquire maternal immunoglobulins from ingested colostrum for passive immune protection, before they will adequately produce own immunoglobulins at approximately 3–4 weeks of age (Rooke & Bland, 2002). The aim of this review is to describe how large litters can affect the immune system of the sow and the piglets, and to propose measures to improve this condition.

2 | HEALTH AND WELFARE IMPLICATIONS OF THE LARGE LITTER SIZE OF TODAY

As already pointed out, there are a number of physiological changes observed along with the constant increment of the litter size of the sow. Some of these changes may cause direct adverse effects on the health and welfare of the sow and her piglets that livestock producers should be aware of. The risk of crushing is one such major adverse effect. As the birthweight of the piglet has been decreasing, the relative size difference between the sow and her newborn piglet has increased, which is one known factor for increased crushing. In a crushing event, the newborn may be instantly killed, or it can survive with varying degrees of tissue damage, which may cause severe pain and suffering for it (Pandolfi, Edwards, Robert, & Kyriazakis, 2017; Yun et al., 2018).

Another such major factor is illustrated in Figure 1 increasing duration of farrowing along with the increasing litter size. Parturition is known to be a painful process in large mammalian species (Algers & Uvnäs-Moberg, 2007; Taverne & van der Weijden, 2008), and increasing its duration directly increases the suffering of the sow and stress of newborn piglets (Algers & Uvnäs-Moberg, 2007; Jarvis et al., 1997; Langendijk, Fleuren, van Hees, & van Kempen, 2018; Oliviero, Heinonen, Valros, Halli, & Peltoniemi, 2008). Langendijk et al. (2018) showed that the longer the foetus stayed in the uterus during the second stage of parturition, the higher was the risk of stillbirth, crushing and adverse effects on the physiology of the newborn piglet.

In addition, this increment in the duration of the process of farrowing increases the risk of birth complications and occurrence of diseases *post-partum* (Björkman, Oliviero, Kauffold, Soede, & Peltoniemi, 2018; Björkman et al., 2017; Peltoniemi, Björkman, & Oliviero, 2016). Therefore, if there is an urge to further increase the litter size in the pig, these adverse effects should be kept in mind. Scientific evidence is now suggesting to slow down the rapid increase in litter size, allowing the sow to adapt to the changes seen in anatomy, physiology and pathology associated with the current development.

3 | IMMUNITY OF SOWS DURING PREGNANCY, AT FARROWING AND DURING LACTATION

The humoral and cellular factors of maternal immunity in swine were reviewed by Salmon, Berri, Gerdt, and Meurens (2009). An increase

in production of mammogenic hormones, including oestrogen, relaxin and prolactin, accelerates mammary gland (MG) growth rapidly after day 75 of gestation. Cellular and humoral factors regulate the homing of lymphocytes into the mammary gland: T cells during pregnancy and B cells during lactation, respectively. The expression of addressin MadCAM-1 directs gut-derived, $\alpha 4\beta 7$ -positive, activated effector T cells into the MG. The expression of addressin is regulated by an oestrogen-responsive element.

During lactation, chemokine CCL28 is produced by epithelial cells of the MG, and together with the expression of MadCAM-1 on the luminal side of endothelial cells, $\alpha 4\beta 7$ -bearing, gut-derived B cells and IgA lymphoblasts are directed into the MG where they develop into plasma cells producing secretory dimeric IgA (sIgA). Since these cells were originally stimulated in the gut, they now produce sIgA of the same specificity as gut IgA, into milk. This is the basis of the so-called entero-mammary immune link (Salmon et al., 2009).

The passive mucosal protection of neonate piglet is dependent on the continuous supply of maternally sIgA. In milk, sIgA would give a local protection to the suckling neonatal piglet's intestine as long as there is milk intake, giving them time to develop their own immune responses. IgA production is influenced by intrinsic genetic factors in the foetus as well as extrinsic environmental factors during the post-natal period. At birth, piglets are exposed to new antigens through maternal colostrum/milk as well as exogenous microbiota (Levast, Berri, Wilson, Meurens, & Salmon, 2014).

Natural infections and vaccination form a basis of immunoglobulin production against the pathogens. Antigenic stimuli direct the adaptive immune responses and further the formation of immunoglobulins and respective memory lymphocytes. Produced immunoglobulins reflect antigenic stimulation of the maternal system and are transferred to neonate piglets via colostrum. Immunoglobulins from plasma are concentrated into colostrum, with most of colostrum produced before farrowing, and transient and mature milk after farrowing (Theil, Lauridsen, & Quesnel, 2014).

Immunoglobulins are transported from the blood using a special FcRn-receptor-mediated system: FcRn expressed by the epithelial cells mediates IgG molecule transfer from plasma into mammary gland and colostrum (Schnulle & Hurley, 2003). Porcine colostrum is characterized by very high levels of IgG (30–70 g/L) and rich mixture of bioactive molecules like growth factors and enzymes. The level of IgG may be four times higher than the level of IgA and IgG in the serum of the sow.

The composition of colostrum changes during the first 24 hr, and 34–36 hr after parturition, the secretion is termed transient milk until 10 days and milk after that (Theil et al., 2014). In addition to the transfer of humoral immunity, cellular components of colostrum, mainly lymphocytes, can enter the systemic circulation and secondary lymphoid organs of the neonate (Nechvatalova, Kudlackova, Leva, Babickova, & Faldyna, 2011). Colostrum also contains a lot of cells, a relatively high percentage of these cells being lymphocytes (15%–25%). Bandrick, Ariza-Nieto, Baidoo, and Molitor (2014) demonstrated that colostrum lymphocytes (CD4+, CD8+, $\gamma\delta$ T cells)

were selectively transferred into piglet blood. However, the specific mechanism for transportation through the neonatal enterocytes is not known at a molecular level.

The function of these cells in the neonate is still unclear, even though it was suggested that they may have an influence on the innate and adaptive immune responses (Bandrick et al., 2014). Hlavova, Stepanova, and Faldyna (2014) found out that the colostrum T-cell subpopulations expressed markers consistent with an effector memory phenotype, indicating that these were antigen-experienced cells. The phenotype of colostrum T and NK cells suggested a role in mucosal immunity and potentially in transfer of passive immunity from sow to piglet.

Maternal nutrition plays a vital role in foetal development, early development of neonates, and lactation and regulates the lifetime productivity of offspring (Zhang et al., 2019). Nutritional feeding strategies include feed additives, such as organic acids, short- and medium-chain fatty acids, probiotics, prebiotics and certain specific carbohydrates. After parturition, maternal nutrition continues to regulate growth and development of piglets, including development of immune system (Salmon et al., 2009).

4 | IMMUNITY OF THE NEWBORN PIGLETS UNTIL WEANING

At birth, the porcine foetus possesses elementary level of immunological competence, especially innate immunity, but adaptive immunity is naive due to the type of placentation (Sinkora & Butler, 2009). Since epitheliochorial placenta does not allow transfer of maternally derived antibodies or immune cells to the foetus, piglets are dependent on innate immune protection and uptake of maternally derived passive immunity (Quesnel, Farmer, & Devillers, 2012; Rooke & Bland, 2002).

Gut closure of neonate piglet occurs 24–36 hr after birth, barring the absorption of immunoglobulins. Failure of piglets to achieve an adequate intake of colostrum is the primary cause for the majority of piglet deaths occurring within the first days of the post-natal period (Quesnel et al., 2012). There is clear evidence that colostrum and milk intake influence piglets' gut development and maturation of their immune system (Salmon et al., 2009; Turfkruyer and Verhasselt, 2015).

Lactocrine signalling properties of colostrum and milk are believed to be critical for optimal neonatal developmental events and to enhance the capacity of neonates to sense, respond and adapt to the circumstances into which they are born (Bartol et al., 2013). Gene expression pathways involved in tissue development, functions and immunity are also activated in the small intestine and influenced by sow milk composition and consumption when gilts were fed with yeast-mannan-rich fraction during gestation and lactation (Grauagnard et al., 2015). Ogawa et al. (2016) demonstrated that colostrum ingestion during the first 24 hr plays a significant role in early post-natal development of both mucosal and systemic immunity of piglets.

5 | LARGE LITTER SIZE AND SOW IMMUNITY

As described in Figure 1, large litters imply longer duration of farrowing. Indirectly this can affect the sow's passive immunity output, since sows producing low colostrum yield tended to have a longer birth interval during the early process of parturition (Quesnel, 2011). It is feasible to consider that when more piglets are born, quantitatively larger amount of immunoglobulins needs to be transported from the sow blood circulation to the colostrum.

During the lactation phase, immunoglobulins are also produced locally by mammary gland plasma cells, sIgA being the major form of immunoglobulin in milk (Salmon et al., 2009). The process of production of immunoglobulins implies the use and synthesis of large-size proteins (Drori & Tirosh, 2011). A considerable energy expenditure is necessary to maintain such prolific production of immunoglobulins (Woof, 2013). The maintenance of such energy-demanding process might be intensified in sows having large litters, where the total amount of colostrum and milk requirement is higher. It is therefore of high importance to have the right body condition of the sow at farrowing, and to have targeted feeding strategies to improve the production of immunoglobulins and to support increased protein turnover.

A number of piglets higher than the available udder nipples may be connected with increased mammary lesions, like skin wounds or deeper ulcers caused by the piglets' teeth that can be infected by environmental bacteria (Hultén et al., 2003; Martineau, Farmer, & Peltoniemi, 2012). Therefore, during lactation of large litters, persistent skin lesions or deep granulomatous infections can serve as an increased challenge for the immune system of the sow, with increased local activity of macrophages, lymphocytes and plasma cells (Hultén et al., 2003).

6 | LARGE LITTER SIZE AND PIGLET IMMUNITY

Pig placenta conformation does not allow exchange of immunoglobulins between maternal and foetal blood in uterus; therefore, at birth, piglets need to acquire adequate amount of colostrum to absorb passively IgG and IgM (Rooke & Bland, 2002). At the same time, IgG content in the colostrum declines rapidly after the start of parturition (Figure 3).

The recommended amount of colostrum needed per piglet is at least 200 g to minimize the mortality and 250 g for good body weight gain (Quesnel et al., 2012). Since the amount of colostrum offered is limited by the sow own production, there is a possibility that in large litters, some of the piglets may suffer lack of colostrum. Similarly, because in large litters the energy needed for appropriate growth of the piglets may be limited by the available colostrum and milk, some of the piglets will stay underweight.

Lessard et al. (2018) studied the influence of birthweight and milk intake within the first 16 days of life on the activation and the

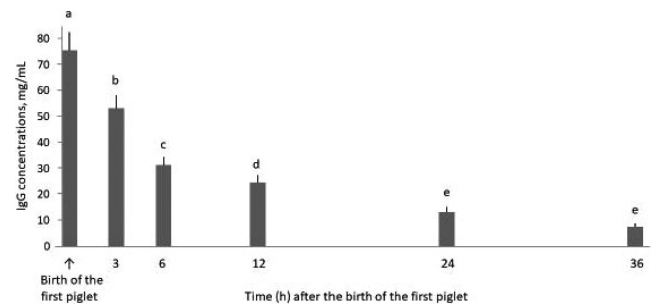


FIGURE 3 Pattern of average colostrum IgG concentrations (\pm SE) during 36 hr after the birth of the first piglet. Means with different superscripts differ significantly ($p < 0.05$) (from Le Dividich et al., 2017; Spanish Journal of Agricultural Research, INIA)

development of systemic and intestinal immunity by measuring immune cell populations, peripheral blood mononuclear cell (PBMC) functional properties and expression of genes involved in intestinal immune functions. Their results suggested that birthweight and milk intake affect the growth performances and the development of immunity by modulating the expression of genes associated with immunity and oxidative stress in piglets' intestinal tissue, and by affecting the leucocyte populations involved in innate and cell-mediated immunity in nursing piglets. Piglets with low birthweight had less intestinal antigen-presenting cells, and compared to high-birthweight piglets, the increase of B cells was impaired (Lessard et al., 2018).

Competition for colostrum and milk intake, crowding and re-grouping are common stress factors in large litters. Social stress may induce short- and long-term effects in pigs, for their immunity and for neuroendocrine regulation. Psychosocial stress may alternate changes in the reactions of both the innate and adaptive immunity, such as leucocyte distribution, cytokine secretion, lymphocyte proliferation, antibody production and immune responses to viral infection or vaccination (Gimsa, Tuchscherer, & Kanitz, 2018). In addition, social stress may induce or promote gastrointestinal (GI) diseases through dysregulation of inflammatory processes and glucocorticoid resistance of lymphocytes (Gimsa et al., 2018), cortisol being the main stress-induced glucocorticoid in pigs. The mechanisms governing susceptibility to stress-induced GI disease remain poorly understood.

Some studies found increased pre-weaning mortality in large litters (Baxter et al., 2013; Rutherford et al., 2013). An explanation to these findings can be found in prolonged farrowing and lower birthweight associated with large litter size. Results from a study conducted in four Norwegian herds found that piglet plasma IgG content, at 1 day after birth, decreased linearly by 0.4 g/L with each piglet born, indicating that delayed parturition within a large litter size can be detrimental to establishment of piglets' passive immunity (Kielland, Rootwelt, Reksen, & Framstad, 2015).

Many studies found a clear negative correlation between litter size and piglet birthweight (Beaulieu et al., 2010; Kapell, Ashworth, Knap, & Roehe, 2011; Quesnel et al., 2008; Quiniou, Dagorn, & Gaudré, 2002; Smit et al., 2013), as shown in Figure 2. Three

different studies consistently found a decline in litter average birthweight ranging from 35 to 43 g for each additional pig born across three different populations of litters recorded (respectively 35 g in Quiniou et al., 2002; 43 g in Beaulieu et al., 2010; and 39 g in Smit et al., 2013). A lower birthweight can affect negatively colostrum intake, increasing the risk of mortality (Declerck, Dewulf, Sarrazin, & Maes, 2016; Ferrari et al., 2014; Le Dividich, Charneca, & Thomas, 2017). Piglet serum IgG concentrations increased with increased piglet weight, while piglets from larger litters had lower serum IgG (Nguyen, Cassar, Friendship, & Hodgins, 2013). Similarly, greater amount of colostrum ingested at birth increases the IgG content in the serum of piglets at 24 hr after birth (Moreira et al., 2017). Another study found that piglet serum IgG concentration at 24 hr and 10 and 20 days of age was positively correlated with colostrum intake and with the serum IgG concentration of the mother, but was not correlated with birthweight (Ferrari et al., 2014). Prolonged farrowing associated with high litter competition may expose piglets not only to a decreased colostrum intake, but also to a retarded colostrum intake after the start of parturition. This condition is not favourable if we consider that colostrum immunoglobulin content declines rapidly after the start of farrowing (Figure 3); moreover, a retarded colostrum intake can also be responsible for a reduced development of the piglets' intestine. A delayed intake, from the time of birth, of a standardized colostrum portion was found to affect negatively the amount of immunoglobulin absorption and the development of the piglets' intestinal villi, the latter having possibly long-term impair on piglets' digestive physiology (Cabrera, Lin, Ashwell, Moeser, & Odle, 2013). There was a longer delay in detecting IgG in the serum of piglets offered a standardized colostrum portion only after 12 hr from their birth than in piglets allowed to get the same colostrum portion immediately after the birth. The latter piglets had 4.4% more IgG transported to their blood (21.5 vs. 17.1%), perhaps because of the greater development of their jejunal villi (Cabrera et al., 2013). In a study population of 600 piglets, Klobasa, Schroder, Stroot, and Henning (2004) found a significant effect of birth order on the amount of immunoglobulin absorbed by the piglets. They found a lower plasma IgG in the last piglets born in the litters, with the authors concluding that the difference was to be accounted to the rapid changes in colostrum composition between the start of farrowing and the last piglet born in the litter. Similarly, in another study, piglet birth order accounted for 4% of the variation observed in piglet serum IgG concentration (Figure 4), with the piglets having lower serum IgG concentration and lower birthweight showing the lowest survival rate when compared to their larger siblings (Cabrera, Lin, Campbell, Moeser, & Odle, 2012). Another recent study from Manjarin, Montano, Kirkwood, Bennet, and Petrovski (2018) supports the importance of the farrowing-to-suckling interval in the acquisition of adequate immunoglobulin level for piglets. They found that a 4-hr retarded colostrum intake, from the start of farrowing, decreased significantly the percentage of plasma protein in piglets at 24 hr and 12 days post-partum. These findings are important to consider also when planning successful strategies for increasing colostrum intake in large litters, such as split suckling.

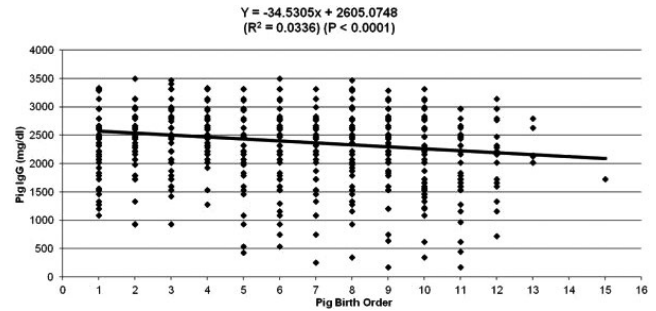


FIGURE 4 Effect of pig birth order on piglet serum IgG concentration (mg/dL) at 48–72 hr (from Cabrera et al., 2012; Journal of Animal Science and Biotechnology, BioMed Central)

7 | INTRAUTERINE GROWTH RESTRICTION (IUGR) PIGLETS

Large litters are often including more reduced-birthweight piglets with characteristics of IUGR (Matheson et al., 2018; Yuan et al., 2015) showing physiological dysfunctions including hypoglycaemia, temperature instability, and increased neonatal morbidity and mortality (Aucott, Donohue, & Northington, 2004). IUGR piglets are characterized by a low birthweight and a dolphin-like head conformation (Hales, Moustsen, Nielsen, & Hansen, 2013). During intrauterine restriction, foetuses react diverging more nutrients towards the growth of the brain (Amdi et al., 2013), trying to counterpart the insufficient placental transport (Roza et al., 2008). This adaptive reaction is intended to ensure proper development of the brain in adverse uterine conditions (Baschat, 2004). In IUGR piglets, the higher susceptibility to infection or environmental changes could be due to an ineffective immune system and subnormal size and histopathology of the thymus (Cromi et al., 2009; Zhong et al., 2012). In IUGR piglets, an overexpression of heat shock protein 70 (a cytoprotective protein produced in response to different cellular stressor factors) has been found in association with impaired cellular immunity at the intestine and liver levels (Li, Zhong, Zhang, Wang, & Wang, 2012; Zhong, Wang, Zhang, & Li, 2010), which suggests an impaired immune function (Yuan et al., 2015).

An impaired immune system in IUGR piglets could originate already from the uterine period. In mammals, the development and function of T cells are necessary for a successful growth, and the Notch signalling pathway, which includes Notch receptors and ligands, is fundamental to modulate T-lymphocyte development (Costa et al., 2005). Lin, Wang, Wang, Wu, and Lai (2013) found that normal foetuses had a greater proportion of T-cell subsets at earlier gestation periods than IUGR foetuses, and the Notch signalling pathway was likely partially responsible for these differences to some degree. Wang et al. (2008) found that the physiology of piglets right after birth was affected by IUGR status and their intermediary metabolism was altered (cellular signalling defects, redox imbalance, reduced protein synthesis and enhanced proteolysis). To balance this altered metabolism, it seems that IUGR piglets would need to acquire even more electrolytes and/or more colostrum, but this is challenged by being born in a large litter (Amdi et al., 2013). IUGR

piglets are sensibly smaller than other siblings in the litter, and this poses higher competition for colostrum intake to them (Amdi et al., 2013; Wang et al., 2008); therefore, the acquiring of their passive immunity is impaired.

8 | MEASURES TO IMPROVE SOW'S AND PIGLETS' IMMUNITY IN LARGE LITTERS AND FUTURE PERSPECTIVES

Large litters pose a serious challenge to the immunity of the sow and piglets. In these high-competitive conditions, underprivileged piglets, with low birthweight or with signs of IUGR, should have additional support in order to get access to adequate amount of high-quality colostrum. In order to minimize the sibling competition for colostrum intake, the litter is split into two groups. The heavier and stronger piglets are kept in the creep area or in a separate box, allowing the smaller piglets to suckle for 60–90 min; then, the groups are switched, and the procedure is repeated as many times within 12–16 hr from the beginning of farrowing.

In the case of small piglets and/or IUGR piglets, which are still not able to suckle successfully, assisted suckling should also be considered. Remembering that these smaller piglets have difficulties to suckle from big nipples, the smallest functioning nipples should be preferred when assisting suckling. In order to provide the best passive immunity, when possible, the procedure of split and assisted suckling should be effectively operated within the first 6 hr from the beginning of parturition, when the colostrum immunoglobulin content is at the maximum.

The IgG content of colostrum can be easily estimated at the farm level using a Brix refractometer and a drop of colostrum. A Brix value lower than 20% represents poor content of IgG, values ranging 20%–24% are considered borderline and not optimal (especially if towards the lower end of the range), and values over 24%

TABLE 1 The Brix value categories to estimate sow colostrum IgG content according to Hasan et al. (2016). This scale of interpretation is valid if the sample is taken within 0–3 hr from the start of farrowing, using a Brix refractometer with a scale range 0%–53% (adapted from Hasan et al., 2016)

Brix %	IgG estimation categories
<20	Poor
20–24	Borderline ^a
25–29	Adequate
≥30	Very good

^aThe category 'Borderline' should not always be considered to estimate a non-adequate IgG content, especially if the found Brix values are on the highest range of this category (23%–24%); on the contrary, levels falling at the lowest range of this category (20%–21%) can be considered not optimal. Taking another sample, after 1–2 hr, can allow better interpretation of the results, to see if the development of the estimated IgG content is stable, increasing or decreasing from the initial value (Hasan et al., 2016).

are considered of adequate IgG content (Hasan, Junnikkala, Valros, Peltoniemi, & Oliviero, 2016). Using the scale shown in Table 1, it is possible to assess rapidly the colostrum content of IgG and optimize the proper supportive colostrum intake strategies.

Easing the process of farrowing can reduce farrowing duration and therefore allow for more vital piglets. Less time interval gap from the start of farrowing to the intake colostrum, better colostrum yield and reduced pain/inflammation for the sow are considered to support the process of farrowing. Allowing the sow to farrow freely, providing a substrate (straw, sawdust, paper) 1–2 days before farrowing, can support nest building behaviour of the sow. This can reduce farrowing duration and stillbirth rate (Oliviero et al., 2008).

Prolonged farrowing increases the risks of piglets' asphyxia during parturition and the presence of less vital piglets at birth (Herpin, Hulin, Le Dividich, & Fillaut, 2001). Yun et al. (2014) demonstrated that providing space and abundant nest building material before farrowing increased sow plasma oxytocin concentration and tended to increase piglet serum IgG and IgM concentrations during early lactation.

With increasing occurrence of large litters, providing the sow with good basis to produce enough colostrum is fundamental. There are associations between changes in the energy reserves and colostrum yield, since the latter can be negatively associated with late gestation loss of back fat and consequently with sows arriving at farrowing with an inadequate body condition (Decaluwé et al., 2013). Therefore, it appears essential that sows improve gradually their body condition during the whole pregnancy, arriving to farrowing in good body condition to fulfil protein turnover and sufficient colostrum yield.

The composition of feeding along with timing of feeding during late pregnancy seems also to be of key importance to support the physiology of farrowing and colostrum quality. Many studies reported that specific essential fatty acids (conjugated linolenic, pinolenic and oleic acids) supplemented in gestating and lactating diets can improve sow colostrum immunoglobulins, piglet performance, average daily gain and weaning weight (Bontempo et al., 2004; Corino, Pastorelli, Rosi, Bontempo, & Rossi, 2009; Hasan et al., 2018; Yao et al., 2012). Although the exact mechanisms on how these dietary compounds can increase different immunoglobulin classes are not fully understood yet, their use in specific conditions of large litters and reduced colostrum quality could be beneficial.

The timing of feeding during pregnancy and especially in relation to parturition seems to be of relevance regarding the success of farrowing. Time lapse between the last feeding occasion prior to the onset of farrowing had no effect, if the time was short (<3 hr). However, if the time lapse exceeded 3 hr, a positive linear correlation for the time lapse and the duration of farrowing was reported (Feyera, Pedersen, Krogh, Foldager, & Theil, 2018). Glucose metabolism was considered to be of highest relevance behind this finding. Yet, other factors such as feeding fibre involving bacterial metabolism of the GI tract were thought to support farrowing to be more successful and less lasting, too (Feyera et al., 2018).

With the use of hyperprolific sows, there is a tendency to see piglets with more prolonged and complicated farrowings, more IUGR, lower birthweight and low-vitality, with increased competition for adequate colostrum intake. These aspects represent not only a production-related issue but also an ethical one. For some pig genetic lines, regarding the average piglet born per litter, it seems they have reached the maximum physiologically tolerable for the sows and the piglets. From now on, genetic selection should focus more on increased colostrum yield characteristics, udder conformation, number of udder nipples and maternal abilities in sows, and on robustness and higher vitality at birth for piglets.

AUTHOR CONTRIBUTIONS

All authors contributed to writing the review.

CONFLICT OF INTEREST

None of the authors have any conflict of interest to declare.

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