Excessive backfat of sows at 109 d of gestation induces lipotoxic placental environment and is associated with declining reproductive performance[1]

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ABSTRACT: This study investigated the influence of sow backfat thickness at 109 d of gestation on sow and piglet performance. Data from 846 farrowing multiparous Yorkshire sows with parity from 3 to 5 were collected from a pig breeding farm. Sows were divided into six groups based on backfat thickness (≤16, 17–18, 19–20, 21–22, 23–24, and ≥25 mm) at 109 d of gestation. The evaluation of reproductive performance included the litter size, litter weight at birth and at weaning of 21 d, weight of placenta at parturition, placental efficiency, and sow daily feed intake of lactation. Parameters related to plasma lipids and the placental-lipid concentration were measured. Data were analyzed to determine the relationships among backfat thickness, placental lipids, and piglet performance. No differences were observed in the number of piglets born, born alive, after cross-foster, and at weaning among groups ($P > 0.05$). The litter weight at birth and weaning, piglet birth weight, weaning weight, placental efficiency, and the number and percentage of piglets born with weight of <800 g showed a significantly quadratic effect of the backfat thickness ($P < 0.05$). During lactation, sow daily feed intake linearly decreased with increased backfat thickness at 109 d of gestation ($P < 0.05$). Although triglycerides and low-density lipoprotein cholesterol (**LDL-C**) showed no significant difference, cholesterol and high-density lipoprotein cholesterol (**HDL-C**) and free fatty acid (FFA) concentrations significantly increased ($P < 0.05$) in both maternal and umbilical cord blood with increased backfat thickness of sow. Placental-lipid concentrations also significantly increased ($P < 0.05$) with increased backfat thickness. Moreover, backfat thickness and placental-lipid concentration were positively correlated with the number of piglets weighing <800 g ($P < 0.01$) but negatively correlated with birth weight, litter birth weight, and piglet weaned weight ($P < 0.01$). In conclusion, backfat thickness of sow at end of gestation correlates with birth and weaning weight of piglets. Placental ectopic lipid accumulation-induced lipotoxicity is likely responsible for such correlation.

Key words: sow, backfat thickness, lipid accumulation, reproductive performance, placental tissue

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INTORDUCTION

In the swine industry, the optimal body condition of sows is an important issue considered to improve the effectiveness of their reproductive performance. Backfat thickness is an indicator of the body condition of sows (Kim et al., 2013). Maintaining backfat thickness throughout the reproductive cycle is more important than fixing this parameter at breeding alone (Houde et al., 2010). Studies have also shown that excessive loss of backfat during late gestation and lactation can lead to reproductive disorders, such as less litter size and litter growth (Clowes et al., 2003), as well as longer weaning-to-estrus intervals (Serenius et al., 2006). However, excess backfat during late gestation is associated with more serious farrowing difficulties and increasing number of stillborn piglets (Zaleski and Hacker, 1993), increased proportion of intrauterine growth restriction (**IUGR**), and had lower litter weight gain and litter size at weaning (Kim et al., 2015). Consequently, maintaining the backfat thickness of sows in a fitting range is essential to accomplish optimal reproductive performance.

The placental tissue is the only site for contact between the fetus and the mother during pregnancy; thus, such tissue is closely related to the health and development of the fetus (Leddy et al., 2008). Maternal conditions have been demonstrated to affect the placental morphology, blood flow, fetomaternal exchanges, and endocrine function (Tarrade et al., 2015). Studies have shown that obese pregnant women has increased lipid ectopic fat deposition in the placenta (Jarvie et al., 2010) and a more pronounced lipotoxic placental environment (Saben et al., 2014), which induces a proinflammatory response (Challier et al., 2008) and oxidative stress (Oliva et al., 2012). Maternal obesity markedly increases lipids concentrations in maternal blood and placenta and enhances inflammatory response signaling in the ewe (Ma et al., 2010; Zhu et al., 2010). Nevertheless, the effect of sow backfat thickness on the placental lipid accumulation and performance of sows and piglets have not been studied thoroughly. Therefore, the primary objective of this study was to evaluate the influence of backfat thickness to piglet performance. Furthermore, the data collected were used to establish the relationship between the backfat thickness and placental-lipid concentration of sows, as well as the piglet performance.

MATERIALS AND METHODS

The experimental protocol used in this study was reviewed and approved by the Animal Care and Use Committee of College of Animal Science and Technology, Huazhong Agricultural University (Committee of Science and Technology).

Animals and Management

The database used in this study was obtained from the research farm of Wuhan Golden Dragon Husbandry Co., Ltd, Hubei Province, China. A total of 846 farrowing records of multiparous Yorkshire sows and parity from 3 to 5 (parity 3, 396 sows; parity 4, 312 sows; and parity 5, 138 sows) were collected. Sows were divided into six groups on the basis of backfat thickness (≤16, 17–18, 19–20, 21–22, 23–24, and ≥25 mm) at 109 d of gestation. The parity distribution in each category of backfat thickness was shown in Supplementary Table S1. Sows were fed 2.5 to 3.0 kg of a common corn-soybean-based meal gestating diet (9.4 MJ NE/kg, 14% CP, and 0.6% lysine) per day, fed twice daily at 0700 and 1600 hours. During gestation, sows were housed individually in gestation stalls (2.2 × 0.7 × 1.1 m) that had 1.2 to 1.6 m of solid concrete in front and 0.6 to 1.0 m of slotted concrete in the back. Sows were moved to the farrowing rooms on day 109 of gestation after sows were washed and then housed individually in fully slatted farrowing crates, and their backfat recorded. Each crate was equipped with CallMatic 2 electronic sow feeding (Big Dutchman, Inc). During lactation, sows were fed a corn soybean diet (10.4 MJ NE/kg, 18.9% CP, and 1.1% lysine). The daily allowance was gradually increased from 0.5 kg on day 1 after farrowing to a maximum of 12 kg in later stages of lactation through electronic feeder. The lactation diet was supplied two times a day (0700 and 1600 hours) to ensure sows ad libitum access to feed. Feed refusals collected and weighed next morning before feeding. Water was freely available to sows and piglets throughout the experimental period. The farrowing room temperature was maintained at approximately 20 °C to 22 °C by a water cooling ventilation system (Big Dutchman, Inc). The lactation diet was supplied ad libitum with electronic feeders. Water was freely available to sows and piglets throughout the experimental period. After weaning, sows were returned to their respective gestation housing systems.

Data Collection and Measurements

Data collection and measurements were performed by the research team with the help of farm workers. Backfat thickness was measured at the last rib (P2; 6.5 cm from the midline over the last rib; Sulabo et al., 2010) by using ultrasound (PIGLOG105, SFAK-Technology, A Mode Scanner, SFK Technology A/S Helver, Denmark) and were taken by the same employee throughout the trial. The daily feed intake of sows during lactation was measured each morning by weighing the daily feed refusals. These feed refusals were weighed and summarized at weaning. The total number of piglets born, numbers of piglets born alive or dead, number of weaned piglets, and their individual birth weight and weaning weight were recorded, and the mummified fetuses were counted and included in the total number of born piglets. The number of IUGR (pigs born alive with birth weight <800 g) was recorded. Cross-fostering was complete within 24 h after farrowing. Expelled placentas were collected and weighed. The placental efficiency was calculated as the ratio between the birth weight (g) and placental weight (g) of born alive (van Rens et al., 2005).

Analysis of Blood Samples

Collection of 5 to 7 ml of blood samples from the ear vein from sows at farrowing. Umbilical cord blood samples were collected by the methods described previously (Dennis et al., 2014). Immediately after birth of a live born piglet, 1 to 2 ml of umbilical cord blood samples were collected from the umbilical cord. Umbilical cords were then clamped both at the placental end at the break and again at the piglet end approximately 7.5 cm from the piglet. The blood sample was collected from the two clamps. Three to five randomly selected live-born piglets per litter were used for the collection of data (a single blood sample from each piglet). Blood samples were transferred into chilled nonheparinized vacutainer tubes. Serum was collected and frozen at −80 °C for subsequent assay. Boehringer Mannheim/Hitachi 912 analyzer was used to quantitate the plasma cholesterol, high-density lipoprotein, low-density lipoprotein, very-low-density lipoprotein, and triglyceride (Roche Diagnostics, Indianapolis, IN) contents, as previously described (Zhu et al., 2010).

Placental Lipids

Placental lipids were extracted from 300 to 500 mg of placental villi with chloroform–methanol (2:1, vol/vol), allowed to dry to completion under nitrogen gas and then weighed (Saben et al., 2014).

Histological Analysis

Fresh placental tissues were collected and fixed in 4% neutral buffered formalin solution (HT501; Sigma). The tissues were sliced into 8 μm thick sections, stained with Oil-Red O (Ding et al., 2014), and then observed by optical microscopy and imaging (Olympus Polaroid DMC-IE camera, Polaroid Corp., Waltham, MA).

Statistical Analyses

Statistical analyses were conducted using the PROC MIXED procedure of SAS 9.2 (SAS Inst. Inc, Cary, NC). Backfat thickness at 109 d of gestation, parity, the interaction between parity and the categorized backfat thickness at 109 d of gestation were specified as fixed effects. Farrowing room was as a random effect. In the mixed model, the response variables were related measurements, including litter size, litter weight of born alive and weaning, placental weight, placental efficiency, sow daily feed intake during lactation, and plasma parameters. Regression analyses were performed to evaluate the linear and quadratic effects of backfat thickness on day 109 of gestation. Spearman correlations were used to determine the association between backfat thickness and placental lipid at 109 d of gestation, variations of birth weight, litter birth weight, number of piglets with weight of <800 g, and piglet weaned weight.

RESULTS

Effects of Backfat Thickness at 109 d of Gestation on Reproductive Performance, Placental Efficiency, and Feed Intake of Sows During Lactation

Descriptive statistics for backfat thickness and some production traits and reproductive performance, as well as feed intake of sows during lactation are summarized in Table 1. The total number of piglets born, born alive, after cross-foster, and weaning did not differ among the different levels of backfat thickness of sows ($P > 0.05$). The litter weight of born alive and at weaning showed a quadratic pattern ($P = 0.03$, $P = 0.05$, respectively), that is, increasing gradually and then decreasing as the backfat thickness at 109 d of gestation increased. Similarly, piglet weight of born alive and at weaning demonstrated a significant relationship in a quadratic effect ($P = 0.04$, $P < 0.01$, respectively) with increased backfat thickness at 109 d of gestation. The optimal level of backfat thickness ranged from 19 to 20 mm. The placental weight was not significantly associated with the backfat thickness ($P = 0.11$), but the placental efficiency exerted a quadratic effect ($P = 0.04$). Notably, the number and percentage of piglets born with weight of <800 g showed a quadratic effect (P = 0.02, P = 0.04, respectively). Moreover, the sow daily feed intake during lactation exhibited a linear decrease ($P < 0.05$) as the backfat thickness at 109 d of gestation increased. The effects of parity for litter performance, placental efficiency, and daily feed intake of lactating sows were not significantly different (Supplementary Table S2).

Effects of Backfat Thickness on Parameters Related to Lipids

The plasma lipid results are displayed in Table 2. Although the total triglyceride and low-density

Table 1. Effects of backfat thickness of sows at 109 d of gestation on litter performance, placental efficiency daily feed intake of lactating sows

	Backfat thickness (mm) of sows at 109 d of gestation							*P*-value	
Item	≤16	17–18	19–20	21–22	23–24	≥25	SEM	*L*	*Q*
Number of sows, *n*	85	107	122	143	134	255			
Litter size, *n*									
Total born	11.49	11.26	11.44	11.63	11.29	11.48	0.10	0.82	0.98
Born alive	10.51	10.63	10.91	11.01	10.90	10.85	0.11	0.10	0.22
After cross-foster	10.19	10.21	10.23	10.31	10.25	10.16	0.10	0.20	0.86
Weaning	9.23	9.27	9.95	9.92	9.61	9.51	0.10	0.41	0.62
Litter weight, kg									
Born alive	15.75	16.04	16.76	16.64	16.24	15.66	0.11	0.99	0.03
After cross-fostering	15.82	15.91	15.88	15.92	15.90	15.80	0.12	0.86	0.24
Weaning	52.79	56.00	61.51	59.41	56.42	53.89	0.58	0.89	0.05
Average pig weight, kg									
Born alive	1.51	1.56	1.60	1.57	1.55	1.52	0.03	0.96	0.04
After cross-foster	1.53	1.54	1.56	1.55	1.54	1.53	0.01	0.93	0.66
Weaning	5.62	6.04	6.19	6.13	5.91	5.63	0.05	0.87	<0.01
Placental weight, g	336.85	327.43	334.10	335.46	348.10	341.93	3.42	0.14	0.11
Placental efficiency	4.66	4.80	4.98	4.88	4.65	4.54	0.03	0.46	0.04
Piglets with weight < 800 g, *n*	0.48	0.33	0.35	0.47	0.52	0.68	0.01	0.11	0.02
Rate of piglets with weight <800 g, %[a]	4.20	2.77	2.74	4.27	4.36	5.85	0.04	0.15	0.04
Average daily feed intake during lactation, kg/d	5.65	5.70	5.51	5.38	5.25	5.08	0.05	<0.01	0.15

[a]For analyses, the square root arcsine transformation for proportions was used. Results shown are transformed back into percentages.

Table 2. Effects of backfat thickness of sows at 109 d of gestation on lipid levels in sow and umbilical cord plasma

	Backfat thickness (mm) of sows at 109 d of gestation							*P*-value	
Item	≤16	17–18	19–20	21–22	23–24	≥25	SEM	*L*	*Q*
Sows plasma									
Number of sows, *n*	30	35	40	45	40	55			
Triglyceride, mmol/L	0.26	0.29	0.29	0.31	0.29	0.28	0.04	0.42	0.68
Cholesterol, mmol/L	1.07	1.09	1.03	1.26	1.46	1.36	0.01	0.03	0.13
HDL-C, mmol/L	0.30	0.31	0.32	0.33	0.48	0.43	0.01	0.04	0.14
LDL-C, mmol/L	0.62	0.61	0.59	0.61	0.63	0.62	0.02	0.55	0.44
FFA, ng/mL	55.56	57.40	60.03	61.54	64.64	73.70	3.03	0.03	0.36
umbilical cord plasma									
Number of piglet, *n*	95	110	130	140	135	165			
Triglyceride, mmol/L	0.32	0.35	0.36	0.35	0.30	0.30	0.01	0.29	0.11
Cholesterol, mmol/L	0.89	0.91	0.90	0.97	1.25	1.21	0.04	0.02	0.30
HDL-C, mmol/L	0.29	0.33	0.32	0.33	0.35	0.34	0.02	0.04	0.13
LDL-C, mmol/L	0.24	0.26	0.27	0.24	0.40	0.48	0.02	0.08	0.24
FFA, ng/mL	52.33	56.61	57.64	52.84	61.69	76.51	3.58	0.03	0.47

HDL-C, low-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FFA, free fatty acid.

lipoprotein cholesterol (**LDL-C**) concentrations were not significantly different, the total cholesterol and high-density lipoprotein cholesterol (**HDL-C**) concentrations ($P < 0.05$) increased linearly at day 109 of gestation, when the backfat thickness increased in both maternal and umbilical cord blood. In maternal blood, FFA concentrations linearly increased ($P = 0.03$) as the backfat thickness at 109 d of gestation increased. There was no effect of parity for lipid levels of sow and umbilical cord plasma (Supplementary Table S3).

Effect of Backfat Thickness on Placental Lipid Accumulation

Lipid accumulation at different backfat levels was observed in the placenta of sows. A significant increase in the concentration of placental lipid was associated with increased backfat thickness (Figure 1). Oil Red O staining for lipids in the placental tissue is shown in Figure 2. Histological analysis demonstrated a significant increase in Oil Red O staining for lipids in the high-backfat group.

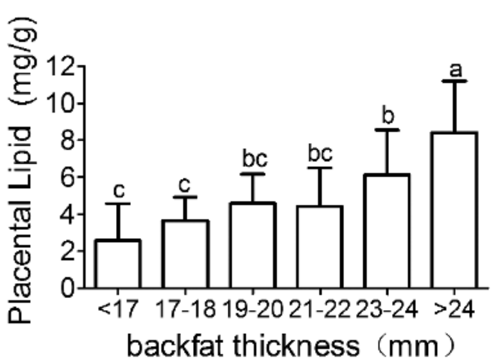

Figure 1. Effects of backfat thickness of sows at 109 d of gestation on placental lipid.

Effects of Backfat Thickness and Placental Lipids on Sow Reproductive Performance

Correlations among backfat thickness, placental lipid, birth weight, litter birth weight, number of piglets with weight of <800 g, and piglets weaned at a population level for sows are presented in Table 3. Significant positive correlations were observed among backfat thickness at day 109 of gestation, placental lipid, and number of piglets with weight of <800 g ($P < 0.01$). A significant positive correlation was also found between the placental lipid and number of piglets with weight of <800 g ($P < 0.01$). Significant negative correlations were found between the backfat thickness at day 109 of gestation, birth weight, litter birth weight, and piglet weaned weight ($P < 0.01$). Moreover, the placental lipid was negatively correlated with birth weight, litter birth weight, and piglet weaned weight ($P < 0.01$).

The relationships among placental lipid to birth weight, litter birth weight, and placental efficiency are presented in Figure 3. Statistical analyses revealed a highly significant ($P < 0.01$) effect of placental lipid on birth weight, litter birth weight, and placental efficiency by applying a second-order equation.

DISCUSSION

Maintaining an optimal body condition of sows will not only improve animal welfare but will also help achieve adequate reproductive efficiency and sow longevity during late gestation and lactation (Maes et al., 2004). During gestation, changes in body condition may influence piglet birth weight and litter uniformity (Campos et al., 2012). Charette et al. (1996) reported that backfat

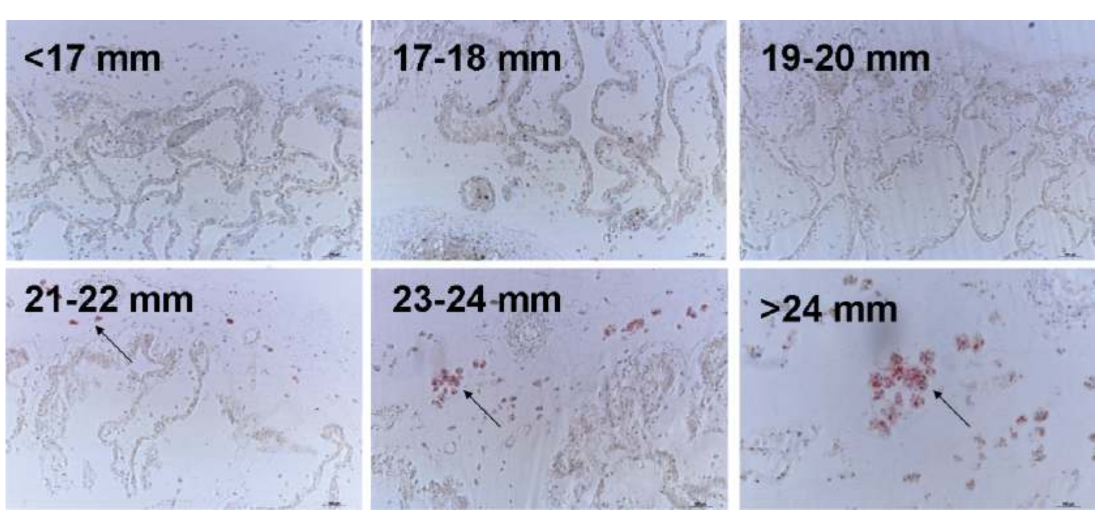

Figure 2. Lipid accumulation in placental tissues with Oil-Red O staining at parturition.

Table 3. Correlations between backfat thickness, placental lipid, and piglets performance

Source of variability	Placental lipid	Birth weight	Litter birth weight	Number of piglets with weight < 800 g	Piglets weaned weight
backfat thickness	0.6453**	−0.4432**	−0.4875**	0.5342**	−0.3586**
placental lipid		−0.4755**	−0.5143**	0.4489**	−0.4487**

**$P < 0.01$.

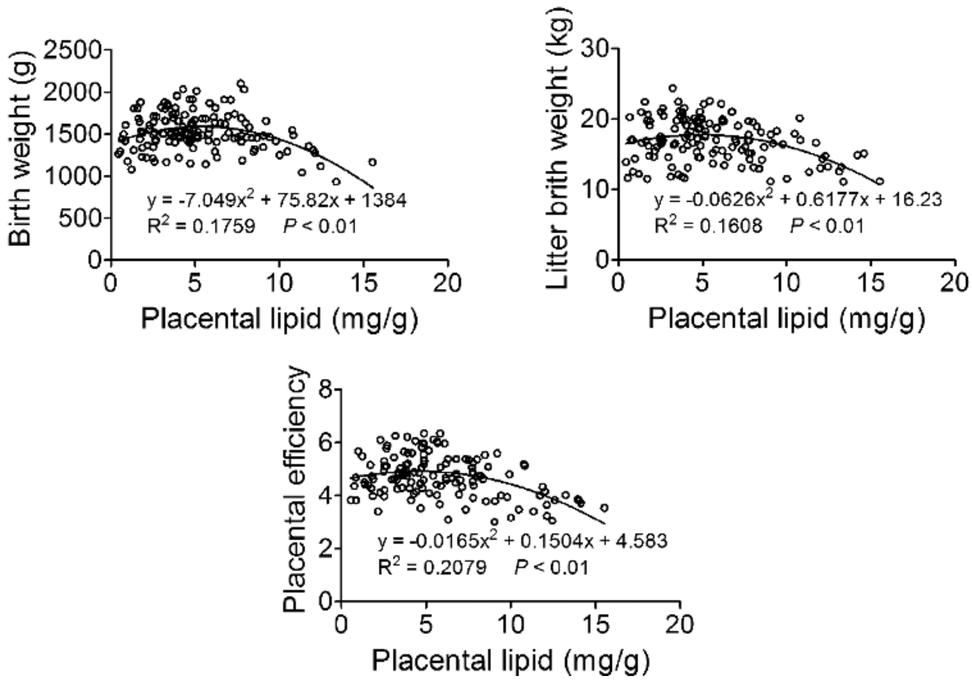

Figure 3. Relationships between placental lipid, birth weight, litter birth weight, and placental efficiency.

level was a more objective and precise parameter to assess the body condition of sows. Our results showed a quadratic effect between the backfat thickness at day 109 of gestation and litter weight, as well as the average weight of piglets born alive, litter weights, and average piglet weights of weaning. Kim et al. (2015) observed that increased sow backfat thickness at day 109 of gestation was associated with a concave down quadratic change in litter size and litter gain at weaning. By contrast, backfat thickness at farrowing was negatively associated with the total number of live born at over two parities (Houde et al., 2010). In addition, a significant difference was observed in third parity sows, with a higher number of live born in the low (backfat loss during lactation was <10%) compared with the high groups (backfat loss during lactation was >20%) of sows (Houde et al., 2010). Maintaining the optimal backfat thickness and body condition is very important for the reproductive performance, reproductive efficiency, and longevity of sows (Clowes et al., 2003; Houde et al., 2010; Kim et al., 2015). Kim et al. (2016) observed that sows with ≥20 mm backfat thickness had greater body weight of piglets at weaning, growth rate, and number of weaned piglets than that of sows with <20 mm backfat thickness at 107 d of gestation. In our study, sows with backfat thickness between 19 and 22 mm at day 109 of gestation had higher live weight of piglets at birth and weaning than sows with backfat thickness of over 22 mm and less then 19 mm. In a similar study, Vavrisinova et al. (2009) reported that backfat thickness was from 20 to 22 mm had more live weight of piglets at birth and at the age of 21 d that of sows with backfat was over 22 mm and less then 20 mm. Kim et al. (2015) showed that the backfat thickness of 17–21 mm is associated with higher litter size at weaning. Therefore, sow backfat thickness and body condition at the last phase of gestation should be maintained within an optimal range to ensure the best reproductive performance.

In domestic species such as pig, fetal growth restriction is associated with increased perinatal morbidity and mortality, negative effects on postnatal growth, body composition, and meat quality (Lekatz et al., 2010). In our data, increased levels of backfat thickness at 109 d of gestation increased the number and percentage of piglets born with weight of <800 g. Our results are consistent with those of Torres-Rovira et al. (2013), who reported that IUGR was found in 21.9% of the obese breed. Wu et al. (2006) showed that maternal overnutrition during gestation impaired the fetal development and postnatal survival, as well as increased number of IUGR. In the present study, the backfat thickness of 19–20 mm is associated with lowest number and percentage in IUGR newborn piglets.

During pregnancy, two principal changes occur in lipid metabolism: the accumulation of fat in maternal depots during the first two-thirds of gestation and the inhibition of accumulation of fat depots as result of increased lipolysis and mobilization during the last third of pregnancy (Herrera and Ortega-Senovilla, 2014). Maternal obesity during pregnancy results in reduced uptake and storage of fatty acids along with increases in lipolysis (Leddy et al., 2008; Jarvie et al., 2010), as well as promotes ectopic fat accumulation in placental tissues, which is associated with a lipotoxic placental environment (Saben et al., 2013; 2014). In the present study, increased levels of backfat thickness at 109 d of gestation resulted in increased concentration of placental lipids. Previous research indicated that the placenta from obese women contained 50% more lipids than the placenta from lean women (Saben et al., 2014). In a mouse model of maternal obesity induced by high-fat diet, the placental lipid was remarkably higher than that in the controls (Qiao et al., 2015). Our results showed a negative association among the placental lipid and birth weight, litter birth weight, and piglet weaned weight. By contrast, a positive relationship existed between the placental lipid and the number of piglets with weight of <800 g. Studies have shown that maternal obesity increased the lipotoxic in placental environment, which is associated with increased inflammation and oxidative stress (Oliva et al., 2012; Saben et al., 2014) that may consequently contribute to impaired placental vascular development and function, as well as blocked placental nutrient transport and altered fetal growth.

In conclusion, maintaining moderate (19–20 mm) backfat thickness at the end of gestation help improves piglet's weight at birth and weaning. Sows with higher (≥25 mm) backfat thickness at the end of gestation demonstrate reduced litter performance, thereby, exerting a positive effect on the number of IUGR associated with the lipotoxic placental environment. Therefore, the nutritional strategy and management can be employed to control the body condition during reproductive cycles.

SUPPLEMENTARY DATA

Supplementary data are available at *Journal of Animal Science* online.

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