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Original Research Article

Starch supplementation improves the reproductive performance of sows in different glucose tolerance status

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ABSTRACT

This study was to evaluate the effects of glucose tolerance status, maternal starch supplementation and soybean substitution in diets on the performance of dams and their offspring. Eighty-eight pregnant sows (Landrace × Large White) were selected from an initial total of 120 sows, based on blood glucose test values, and assigned to 4 experimental treatments in a 2 × 2 factorial design. The factors were glucose tolerance status (glucose intolerant [GIT] vs. normal glucose tolerant [NGT]) or dietary treatments (corn starch diet [CS] vs. soybean substitution diet [SS]). A higher area under the curve (AUC) for post-meal glucose was observed ($P < 0.05$) in the GIT group than in the NGT group on d 109 of gestation. The CS group had a lower value of homeostasis model assessment-insulin resistance than the SS group ($P < 0.05$) on d 109 of gestation. Corn starch supplementation for sows decreased the stillbirth rate ($P < 0.05$), regardless of the sows' glucose tolerance status. The villus height of the jejunum and the villus height to crypt depth ratio of the ileum were greater in normal birth weight piglets from the CS group than from the SS group ($P < 0.01$), and so was the activity of sucrase in the jejunum and ileum ($P < 0.01$). Compared with the SS group, the CS group showed a reduction in pre-weaning mortality rate, an increase in the number of high-birth-weight piglets, and a decrease in the number of low-birth-weight piglets ($P < 0.05$) under GIT status. In conclusion, sows fed CS decreased stillbirth rate and improved insulin resistance, as well as improving the intestinal morphology and digestive enzyme activities of their progeny, regardless of glucose tolerance status. Additionally, the CS group improved birth weight distribution and decreased pre-weaning mortality rate of piglets under GIT status.

1. Introduction

During the last third of gestation, fetal nutrient supply usually becomes limited. One of the main adaptive responses during late gestation to favor glucose availability to the pregnant uterus is the progressive insulin resistance of the mother, which corresponds to a decrease in the effectiveness of insulin in regulating blood glucose (Corson et al., 2008). Glucose tolerance of pregnant sows is closely linked to their reproductive performance. Poor glucose tolerance has been proposed as a potential contributor to the high (10% to 13%) pre-weaning mortality rate in piglets (Phillips et al., 1982).

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Additionally, studies have shown a positive correlation between pig mortality and glucose curve characteristics based on glucose tolerance tests, such as area under the curve (AUC), glucose clearance kinetics, and maximum increase in glucose (Kemp et al., 1996). Under the influence of glucose metabolic abnormality, the maternal fetus presents a low weight status. To date, little attention has been directed towards the glucose tolerance status of sows and its effect on the development of their offspring. Therefore, it is vital to recognize glucose tolerance status of late pregnant sows and develop related feed strategies to alleviate impaired glucose tolerance for improving the reproductive performance of sows.

Glucose tolerance in pregnant sows is influenced by diet composition in gestation (Bikker et al., 2007). Maternal diet appeared to influence the relationship between glucose tolerance and litter outcome (Huang et al., 2021a,b). Nevertheless, energy accounts for more than 70% of the diet composition, suggesting a necessity to develop appropriate energy sources in the diet during gestation and lactation to improve the reproductive performance of sows by regulating the balance of glycolipid metabolism. Starch and lipid are the main energy sources of sow diets, whereas legume animal feeds (in the form of soybean oil and extruded soybean) are good lipid sources for sows. Their concentration in the maternal diet has been shown to be related to glucose clearance time (Père and Etienne, 2019). Supplementing additional energy from starch sources to gestating sows has been demonstrated to improve glucose tolerance with no change for stillborn piglets (Van Der Peet-Schwering et al., 2004). High-fat diets have been reported to reduce the number of births and impair the insulin sensitivity of offspring (Taylor et al., 2005). It has also been reported that maternal fatty acid supplementation can alter the degree of insulin sensitivity (Corson et al., 2008), and maternal palm oil throughout gestation causes maternal glucose intolerance, which may be linked to the decreased number of stillborn piglets (Almond et al., 2015). Maternal diet compositions varied in their influences on maternal glucose tolerance (Gatlin et al., 2002). Currently, there is not a conclusive conclusion on the modulatory effects of maternal diet compositions on fetal consequences and insulin resistance.

A reduced activity of enterocyte brush border enzymes makes the enterocytes open to alimentary pathogens and xenobiotic substances for a longer period of time, which may increase the susceptibility to mortality of piglets (Ferenc et al., 2014). Neonatal piglets with intrauterine growth restriction showed continuous impairment of intestinal development and a decrease in both the expression of key enzymes related to glucose and energy metabolism and the thickness of mucosa and muscle layers in both the jejunum and ileum (Wang et al., 2010; Qi et al., 2020). Additionally, in the final stages of pregnancy and at birth, fetal gut morphology and function need to be finely modulated for the intrauterine environment (such as nutrition level) (Père and Etienne, 2007; Pinheiro et al., 2013). We hypothesized that the supplementation of starch and soybean substitution in the maternal diet of sows would influence the gut growth in piglets, thereby affecting the performance of offspring.

Maternal dietary treatment has been shown to affect maternal glucose metabolism in pregnant sows, but whether this effect is influenced by maternal glucose tolerance status remains to be elucidated (Père and Etienne, 2019). Additionally, it is still unknown whether maternal glucose intolerance can impair fetal intestinal function by intestinal morphology and enzyme activity, and result in poor growth of their offspring. Against this background, the aim of the present study was to determine the effects of glucose tolerance status, maternal starch supplementation and soybean substitution in diets during late gestation and lactation on the performance of sows and their offspring.

Table 1
The number of sows during the experimental period.

Item	No. of sows
All sows performed meal tests on d 75 of gestation	120
Sows were eliminated[1]	32
Subsample	88
GIT group[2]	44
NGT group[2]	44

GIT = glucose intolerant; NGT = normal glucose tolerant; AUC = area under curve.
[1] Sows with AUC values of blood glucose ranging from ($AUC_{Mean\_120\ sows}$ - $0.5SD_{\_120\ sows}$) to ($AUC_{Mean\_120\ sows}$ + $0.5SD_{\_120\ sows}$) were eliminated.
[2] To meet the needs of great difference of AUC for blood glucose after meal of subsamples, 44 sows with AUC values of blood glucose less than ($AUC_{Mean\_120\ sows}$ - $0.5SD_{\_120\ sows}$) were allotted to the GIT group, and 44 sows with AUC of blood glucose greater than ($AUC_{Mean\_120\ sows}$ + $0.5SD_{\_120\ sows}$) were allotted to the NGT group.

2. Materials and methods

All experimental procedures involving animals were approved by the Animal Care and Use Committee of the Institute of Subtropical Agriculture, Chinese Academy of Science (ISA-2019-025) and followed the Guidelines for the Care and Use of Laboratory Animals of South China Agricultural University (Guangzhou, China).

2.1. Meal tests

Meal tests were performed before the experiment (d 75 of gestation) and in late gestation (d 109). On d 75 of gestation, meal tests were performed on a total of 120 multiparous sows (Landrace × Large White). Specifically, sows were deprived of feed from 15:00 in the afternoon to 08:00 the following day. The sows had a meal of 1.5 kg, and blood samples were taken from the ear vein. Blood glucose concentrations were measured at 0, 30, 60, 90 and 120 min after the beginning of the meal using an automatic glucometer (Sinocare Inc., Changsha, China). For the meal test profiles concerning the tolerance tests, AUC for blood glucose was calculated by linear interpolation of glucose concentrations between the measurements, using the fasting glucose concentration as the base line (GraphPad Prism, GraphPad, San Diego, CA, USA).

2.2. Experimental design, animals, and housing

From the initial population of 120 sows, 32 sows were eliminated from the experiment based on blood glucose AUC values from ($AUC_{Mean\_120\ sows} - 0.5SD_{\_120\ sows}$) to ($AUC_{Mean\_120\ sows} + 0.5SD_{\_120\ sows}$) after their meal on d 75 of gestation (Table 1). To meet the needs of significant difference in blood glucose AUC values post a meal, we sampled the remaining 88 sows from the original AUC dataset in order to establish a subsample. Forty-four sows with blood glucose AUC values less than ($AUC_{Mean\_120\ sows}$ - $0.5SD_{\_120\ sows}$) were allotted to the glucose intolerant (GIT) group (Table 2). Forty-four sows with blood glucose AUC values greater than ($AUC_{Mean\_120\ sows} + 0.5SD_{\_120\ sows}$) were allotted to the normal glucose tolerant (NGT) group (Table 3). Eighty-eight sows (Landrace × Large White) with an average parity of 3.19 ± 0.15 and an average BW of 269.33 ± 4.1 kg were finally selected.

Forty-four sows from each group were assigned to 2 dietary treatments: corn starch diet (CS, $n = 22$) and soybean substitution diet (SS, $n = 22$) in the form of extruded soybean and soybean oil. The experimental diets were formulated to meet the nutrient requirements of sows (NRC 2012), and their composition and nutrient content are presented in Table 4. The experiment was performed from d 85 of gestation to the end of weaning (d 21 of lactation).

Table 2
The number of sows during the gestation and lactation period.

Item	NGT		GIT	
No. of sows	44		44	
Gestation diet	SS	CS	SS	CS
On d 75 of gestation	22	22	22	22
Excluded during gestation[1]	3	2	2	3
On d 109 of gestation	19	20	20	19
Excluded during gestation[1]	3	2	2	1
Farrowing	16	18	18	18
Excluded during lactation[2]	2	–	2	–
Weaning	14	18	16	18

NGT = normal glucose tolerant; GIT = glucose intolerant; SS = soybean substitution diet in the form of extruded soybean and soybean oil; CS = corn starch diet.
[1] Sows were culled when returning to oestrus, miscarried or non-pregnant or because of illness, death or serious lameness.
[2] Sows with piglets suffering from severe diarrhea.

Feed was offered twice a day at 08:00 and 15:00 during the experiment. Both gestation and lactation diets were in pellet form. Sows were fed 3.0 kg/d from d 85 of gestation to farrowing, and half of the daily feed was given in each meal. During lactation, all sows were allowed to consume 2 diets ad libitum (Table 4). Sows and piglets were given free access to drinking water. During the experimental period, sows with piglets that were suffering from severe diarrhea were excluded (Table 2). Furthermore, data from sows with illness, serious lameness, death and reproductive failure were also excluded from further analysis (Table 2). Feed samples were analyzed in terms of crude protein (CP) (ISO 5983-2), crude fiber (CF) (ISO 6865-2000), and ether extract (EE) (ISO 6492-1999).

2.3. Recording and sampling

The body weight (BW) of all sows was measured on d 85 and 109 of gestation, and at farrowing and weaning. On d 109 of gestation, 32 sows were chosen from 4 groups for meal tests. The numbers of total piglets born, born alive, cross-fostering, d 10 and 21 of lactation, and stillborn at farrowing were recorded. Cross-fostering was kept within diet treatments to adjust litter size within 48 h post parturition. Piglet weights were recorded separately at farrowing, cross-fostering, d 10 and 21 of lactation and weaning. The feed intake of sows was recorded every day in lactation. On d 109 of gestation, blood samples were collected from 32 sows (8 sows per dietary treatment with a similar parity and BW) after an overnight fast (12 h) using a 5-mL syringe and 5-mL vacuum blood collection tube containing an anticoagulant (EDTAK2) and then placed on ice immediately. Blood samples were centrifuged at 4 °C and 3,000 × *g* for 15 min to obtain the serum and plasma, followed by storage at −20 °C for further analysis. Four different groups were chosen from 24 litters (6 litters per group), with 2 piglets selected from each litter, including one with normal birth weight (NBW, 1.3 to

Table 4
Ingredients and nutrient composition of experimental gestation and lactation diets (as-fed basis, %).

Item	Gestation diet		Lactation diet	
	SS	CS	SS	CS
Ingredients				
Corn	51.55	19.35	52.90	9.10
Soybean meal (43% CP)	10.80	20.00	23.50	28.50
Corn starch	–	32.00	–	42.00
Wheat bran	19.70	19.70	9.75	10.55
Corn protein powder[1]	1.50	3.50	1.50	4.50
Extruded soybean	8.00	–	2.00	–
Soybean oil	3.00	–	5.00	–
Dicalcium phosphate	2.00	2.00	2.00	2.00
Limestone	1.35	1.35	1.35	1.35
Salt	0.30	0.30	0.30	0.30
Sodium sulfate	0.30	0.30	0.30	0.30
Choline chloride	0.20	0.20	0.10	0.10
Lysine sulfate (70%)	0.20	0.20	0.20	0.20
Premix[2]	1.00	1.00	1.00	1.00
Mildewcide	0.10	0.10	0.10	0.10
Calculated composition				
DE, Mcal/kg	3.21	3.19	3.38	3.36
NE, Mcal/kg	2.36	2.33	2.46	2.42
CP	15.59	15.59	17.58	17.57
EE	7.28	2.07	8.06	1.58
CF	3.55	3.27	3.19	2.80
Starch	37.58	49.25	36.46	51.05
NDF	14.32	12.18	11.52	8.89
Ca	1.07	1.07	1.09	1.09
NPP	0.50	0.46	0.49	0.45
Lys	0.87	0.90	1.06	1.09
Met	0.28	0.26	0.31	0.29
Thr	0.59	0.58	0.70	0.69
Trp	0.20	0.20	0.23	0.23
Analyzed composition				
CP	15.77	15.64	18.60	18.63
CF	3.42	3.21	3.59	3.22
EE	6.98	2.04	7.60	1.96

SS = soybean substitution diet in the form of extruded soybean and soybean oil; CS = corn starch diet; EE = ether extract; CF = crude fiber; NDF = neutral detergent fiber; NPP = non-phytin phosphorus.
[1] Calculated chemical concentrations using values for feed ingredients from (NRC, 2012), the nutritive values of corn protein powder referred to the Feed Composition and Nutritive Values in China from China Feed-database Information Network Centre (http://www.chinafeeddata.org.cn).
[2] Provided the following per kilogram of diet: Cu, 10.0 mg; Fe, 130 mg; Mn, 45 mg; Zn, 60 mg; I, 0.30 mg; Se, 0.27 mg; Co, 0.1 mg; Vitamin A, 6,760 IU; Vitamin D_3, 4,992 IU; Vitamin E, 209.8 mg; Vitamin K_3, 3.7 mg; Thiamin, 3.7 mg; Riboflavin, 12 mg; Vitamin B_6, 7.5 mg; Vitamin B_{12}, 0.050 mg; Niacin, 50 mg; Folic acid, 3.7 mg; D-pantothenic acid, 31.2 mg; D-biotin 0.624 mg; Vitamin C 200 mg.

Table 3
Blood glucose concentrations and area under the curve (AUC) of glucose after a meal in sows on d 75 of gestation.

Item	GIT[1]	NGT[2]	SEM	*P*-value
No. of sows	44	44		
Blood glucose, mmol/L				
Fasting (0 min) blood glucose	3.7	4.0	0.033	0.00
30 min postprandial glucose	4.5	4.3	0.059	0.07
60 min postprandial glucose	5.1	4.4	0.062	0.00
90 min postprandial glucose	4.4	4.1	0.038	0.00
120 min postprandial glucose	4.4	4.1	0.049	0.03
AUC, mmol/L per min				
0 to 60 min AUC	266.0	254.7	2.372	0.02
0 to 120 min AUC	537.9	506.5	4.185	0.00

GIT = glucose intolerant; NGT = normal glucose tolerant.
[1] Sows with AUC values of blood glucose less than ($AUC_{Mean\_120\ sows}$ - $0.5SD_{\_120\ sows}$) were allotted to the GIT group.
[2] Sows with AUC of blood glucose greater than ($AUC_{Mean\_120\ sows}$ + $0.5SD_{\_120\ sows}$) were allotted to the NGT group.

1.5 kg) and one with low birth weight (LBW, <1.1 kg). Piglets were slaughtered by an intra-arterial injection of pentobarbital (200 mg/kg) after general anaesthesia. Meanwhile, the duodenum, jejunum, ileum, stomach, heart, spleen, lung, kidney, livers, and pancreas of the piglets were removed. Finally, the mucosal samples of the jejunum and ileum were snap-frozen in liquid nitrogen and stored at −80 °C, and the samples of the jejunum and ileum were fixated in neutral buffered formaldehyde for further analysis.

2.4. Chemical analyses

Plasma glucose concentrations were determined using a glucose dehydrogenase activity colorimetric assay kit (Nanjing Jiancheng Bioengineering Institute, Nanjing, China) according to the manufacturer's instructions. The plasma insulin level was determined using an ultrasensitive pig insulin ELISA kit (Wuhan Mskbio Biotechnology Institute, Wuhan, China) according to the manufacturer's instructions. Insulin resistance and sensitivity were evaluated by the homeostasis model assessment (HOMA) values using the following indirect methods (Tan et al., 2018).

HOMA-insulin resistance (HOMA-IR) = [Fasting insulin (mIU/L) × Fasting glucose (mmol/L)]/22.5

HOMA-insulin sensitivity (HOMA-IS) = 1/[Fasting insulin (mIU/L) × Fasting glucose (mmol/L)]

2.5. Visceral organ indices

The visceral organ indices were obtained by weighing the duodenum, jejunum, ileum, stomach, heart, spleen, lung, kidney, liver, and pancreas immediately after animal sacrifice. The lengths of the small intestine were also measured. The specific visceral organ index was calculated as follows, and the intestinal weight per length was calculated as follows (Zhang et al., 2018).

The specific visceral organ index (g/kg) = The visceral organ weight (g)/Final BW before slaughtering (kg)

The intestinal weight per length = The intestine weight (g)/The intestine length (cm)

2.6. The small intestinal morphology

After embedding the samples of the small intestine tissues (approximately 3 cm from jejunum and ileum) in paraffin wax, 4 transverse sections (5 μm) were cut, installed on glass slides and stained with hematoxylin-eosin for analysis. Villus height, crypt depth and the villus height to crypt depth ratio were determined with a projecting microscope (Olympus CX41, Japan). The villus height was measured from the tip to the base, and the crypt depth was measured from the crypt—villus junction to the base. A total of 8 well-oriented villi and their associated crypts per section were selected and measured under a light microscope at 40 × magnification and analyzed using Image Pro-Plus 5.0 image analysis software (Media Cybernetics, Rockville, MD, USA).

2.7. Measurement of digestive enzyme activities

Frozen mucosal samples of jejunums and ileums (0.5 g each) were weighed and homogenized with 9 times the volume (wt/vol) of pre-cooled physiological saline. Next, the mixture was centrifuged at 4,000 × *g* for 10 min at 4 °C to collect the supernatant solution, followed by measuring the supernatant protein concentration as well as the activities of lactase, maltase, and sucrase in the supernatant solution using commercial kits according to the manufacturer's instruction (Nanjing Jiancheng Bioengineering Institute, Nanjing, China).

2.8. Statistical analyses

The data related to the reproductive performance of sows and glucose tolerance were analyzed as a 2 × 2 factorial treatment arrangement using the general linear model procedure of SAS (SAS Inst. Inc., Cary, NC, USA). The model utilized included the main factors of glucose tolerance status, diets (CS or SS) and their interaction. The data with significant effects of interactions were statistically analyzed using one-way ANOVA and Duncan's multiple-range tests. The piglet stillbirth rate, pre-weaning mortality rate, and birth weight range were analyzed using the Chi-square test. Differences between mean values were considered statistically significant at $P < 0.05$, and a trend toward significance was noted at $0.05 \leq P \leq 0.10$.

3. Results

3.1. Meal tests in sows

In Table 3, a higher AUC of glucose (GIT: 537.9 vs. NGT: 506.5, $P < 0.01$) from 0 to 120 min after the meal was seen in the GIT group than in the NGT group on d 75 of gestation, coupled with differences in 0 (fasting), 60-, 90-, and 120-min postprandial blood glucose concentration ($P < 0.05$), indicating a lower rate of glucose clearance in these sows. This result demonstrates the successful construction of the model of GIT and NGT for pregnant sows.

Fig. 1 shows the effects of maternal dietary CS and SS on glucose tolerance in NGT and GIT sows. A higher AUC of glucose from 0 to 120 min ($P < 0.05$; Fig. 1A and B) after the meal was seen in the GIT group than in the NGT group on d 109 of gestation, which accorded with the results on d 75 of gestation, indicating that the poor glucose tolerance of sows on d 75 of gestation remained unchanged on d 109 of gestation. The GIT group exhibited a higher insulin concentration than the NGT group, whereas the CS group decreased the blood glucose of sows ($P < 0.05$; Fig. 1C) compared with the SS group. Homeostasis model assessment values were affected by the glucose tolerance status and dietary treatments ($P < 0.05$; Fig. 1D). Additionally, the CS group had a lower HOMA-IR value and a greater HOMA-IS value than the SS group.

3.2. Sow performance

Table 5 shows the effects of diets and glucose tolerance status on BW and feed intake of sows during lactation. The BW was not affected by glucose tolerance status and diets ($P > 0.05$). From d 1 to 21 of lactation, ADFI exhibited an increase in the CS group vs. the SS group ($P < 0.05$). No interaction was observed between glucose tolerance and diets in their effects on BW and ADFI throughout lactation in this study.

3.3. Piglet performance

Table 6 shows the effects of diets and glucose tolerance status on the performance of sows and piglets. Specifically, both diets and glucose tolerance status showed no impact ($P > 0.05$) on the numbers of total piglets born, born alive and after cross-fostering, but the number of piglets on d 10 of lactation was greater in the CS group than in the SS group ($P < 0.05$). The BW of piglets on d 10 of lactation and ADG from d 1 to 10 of lactation showed a reduction ($P < 0.05$) in the GIT group compared with the NGT group. Furthermore, the GIT group tended to have a lower litter weight on d 10 of lactation than the NGT group ($P = 0.05$). However, glucose

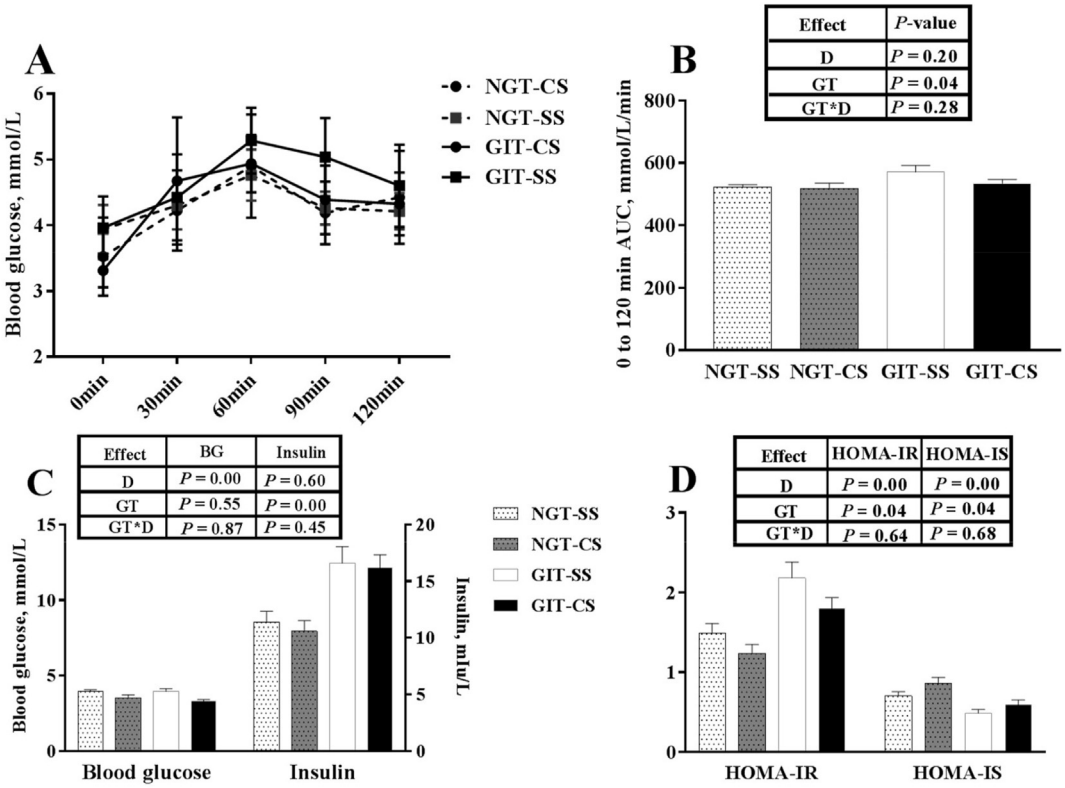

Fig. 1. Effects of maternal dietary treatment, glucose tolerance status and their interaction on (A) meal tests, (B) area under the curve (AUC) of glucose from 0 to 120 min after meal, (C) plasma glucose and insulin, and (D) HOMA-IR and HOMA-IS in sows on d 109 gestation. NGT-SS = normal glucose tolerant sows fed a soybean substitution diet; NGT-CS = normal glucose tolerant sows fed a corn starch diet; GIT-SS = glucose intolerant sows fed a soybean substitution diet; GIT-CS = glucose intolerant sows fed a corn starch diet; BG = blood glucose; HOMA-IR = homeostasis model assessment-insulin resistance; HOMA-IS = homeostasis model assessment-insulin sensitivity. GT = glucose tolerance effect of sows; D = diet effect of sows. Data are expressed as means ± SEM; $n = 8$.

Table 5
Effects of maternal dietary treatment, glucose tolerance status and their interaction on body weight (BW) and feed intake of sows during lactation.

Item	NGT		GIT		SEM	*P*-value		
	NGT-SS	NGT-CS	GIT-SS	GIT-CS		GT	D	GT × D
No. of sows	14	18	16	18				
BW of sows, kg								
Day 85 of gestation	257.5	266.6	262.7	270.6	3.781	0.55	0.27	0.93
Day 109 of gestation	272.8	281.2	277.1	287.1	3.840	0.52	0.24	0.91
Gain during gestation	15.4	14.5	14.4	16.6	1.038	0.79	0.72	0.46
Parturition	247.4	255.7	252.3	259.2	3.676	0.58	0.32	0.93
Weaning	225.3	228.6	235.2	240.9	3.439	0.12	0.52	0.86
Loss during lactation	22.1	27.1	17.1	18.3	1.591	0.07	0.21	0.81
Average daily feed intake, kg								
1st week of lactation	3.10	3.39	3.23	3.54	0.105	0.50	0.17	0.97
2 nd week of lactation	5.43	5.71	5.54	5.87	0.109	0.56	0.17	0.90
3rd week of lactation	5.46	5.98	5.51	5.98	0.123	0.92	0.05	0.91
Mean from 1st week to 3rd week	4.67	5.03	4.76	5.13	0.080	0.54	0.02	0.97

NGT = normal glucose tolerant; GIT = glucose intolerant; NGT-SS = NGT sows fed a soybean substitution diet; NGT-CS = NGT sows fed a corn starch diet; GIT-SS = GIT sows fed a soybean substitution diet; GIT-CS = GIT sows fed a corn starch diet; GT = glucose tolerance effect of sows; D = diet effect of sows.

tolerance status exhibited no effects ($P > 0.05$) on the weight of piglets and litter on d 21 of lactation or ADG from d 1 to 21 of lactation among the 4 treatments. The weight of piglets at birth and the litter weight on d 21 of lactation showed an increased tendency in the CS group compared with the SS group ($P = 0.08$ and 0.09).

3.4. Stillbirth rate and pre-weaning mortality rate

Starch supplementation decreased the stillbirth rate, regardless of the glucose tolerance status of sows ($P < 0.05$). Pre-weaning mortality rate was lower in the CS group than in the SS group only in GIT status ($P < 0.05$) (Fig. 2).

3.5. Birth weight range of neonates

Compared with the SS group, the CS group significantly reduced the proportion of piglets in the birth weight range from 0.8 to 1.0 kg ($P < 0.05$) and increased the proportion of piglets in the birth weight range above 1.8 kg ($P < 0.05$) for pregnant sows in GIT status (Fig. 3).

3.6. Relative weight of the internal organs and small intestine

Table 7 shows the relative weight of the internal organs and small intestine of piglets. No difference was observed among LBW

Table 6
Effects of maternal dietary treatment, glucose tolerance status and their interaction on the performance of sows and piglets.

Item	NGT		GIT		SEM	*P*-value		
	NGT-SS	NGT-CS	GIT-SS	GIT-CS		GT	D	GT × D
No. of sows	14	18	16	18				
No. of pigs per litter								
Total piglets born	14.6	12.3	12.1	13.3	0.445	0.38	0.53	0.05
Piglets born alive	12.1	11.7	10.6	12.7	0.454	0.81	0.37	0.18
After cross-foster	9.6	9.9	10.1	10.2	0.157	0.24	0.65	0.75
Piglets on d 10	9.00	9.61	8.56	9.61	0.200	0.58	0.04	0.58
Piglets on d 21	9.00	9.56	8.50	9.50	0.205	0.50	0.06	0.59
Piglet mean BW, kg								
At Birth	1.3	1.4	1.3	1.4	0.030	0.83	0.08	0.77
After cross-foster	1.6	1.6	1.5	1.5	0.047	0.35	0.88	0.76
On d 10	3.8	3.6	3.2	3.4	0.087	0.03	0.82	0.40
On d 21	6.3	6.3	5.8	5.9	0.127	0.26	0.87	0.87
Litter weight, kg								
At Birth	16.3	17.0	17.1	19.3	0.487	0.11	0.13	0.43
After cross-foster	15.2	15.9	14.9	15.5	0.522	0.74	0.56	0.99
On d 10	33.7	35.3	28.1	32.7	1.140	0.05	0.08	0.44
On d 21	56.3	60.1	50.0	56.9	1.760	0.16	0.09	0.64
Average daily gain, g/d								
1 to 10 d	216.7	206.3	174.6	186.0	6.299	0.03	0.91	0.43
11 to 21 d	256.4	262.8	261.6	255.9	8.020	0.91	0.96	0.69
1 to 21 d	473.1	469.1	436.2	441.9	10.907	0.27	0.92	0.90

NGT = normal glucose tolerant; GIT = glucose intolerant; NGT-SS = NGT sows fed a soybean substitution diet; NGT-CS = NGT sows fed a corn starch diet; GIT-SS = GIT sows fed a soybean substitution diet; GIT-CS = GIT sows fed a corn starch diet; GT = glucose tolerance effect of sows; D = diet effect of sows.

piglets in the weight of the duodenum, jejunum, stomach, heart, spleen, lung, and kidney ($P > 0.05$). However, the pancreas weight of LBW piglets was greater in the GIT group than in the NGT group ($P < 0.01$). An interaction was observed between diets and glucose tolerance status in their effect on the ileum weight per length ($P < 0.05$). NBW piglets showed no difference ($P > 0.05$) among the 4 treatments in the weight of the duodenum, jejunum, ileum, spleen, lung, kidney, and pancreas, except for greater stomach weight in the NGT group than in the GIT group ($P < 0.01$). The weight of the heart was positively affected in the LBW piglets of the CS group relative to those of the SS group ($P < 0.01$).

3.7. Small intestinal morphology

The intestinal morphologies of the jejunum and ileum of newborn piglets are shown in Table 8 and Fig. 4. Specifically, compared to the NGT group, the GIT group showed a decrease ($P < 0.01$) in the villus height to crypt depth ratio of the jejunum in NBW piglets. Compared to the NGT sows fed a soybean substitution diet (NGT-SS) group, the GIT group showed an increase ($P < 0.05$) in the crypt depth of the jejunum in NBW piglets. Meanwhile, the villus height of the ileum or jejunum was greater in LBW or NBW piglets from CS-fed sows than those from SS-fed sows (Fig. 4A and B), with an increase ($P < 0.01$) in NBW piglets from CS-fed sows over those from SS-fed sows in terms of the villus height to crypt depth ratio of ileum Table 8.

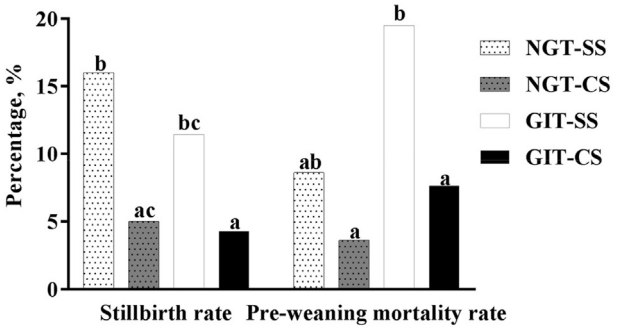

Fig. 2. The Chi-square test of maternal dietary treatment and glucose tolerance status on stillbirth rate and pre-weaning mortality rate of piglets. NGT-SS = normal glucose tolerant sows fed a soybean substitution diet; NGT-CS = normal glucose tolerant sows fed a corn starch diet; GIT-SS = glucose intolerant sows fed a soybean substitution diet; GIT-CS = glucose intolerant sows fed a corn starch diet. [a, b] Mean values with different small letters indicate significant difference ($P < 0.05$).

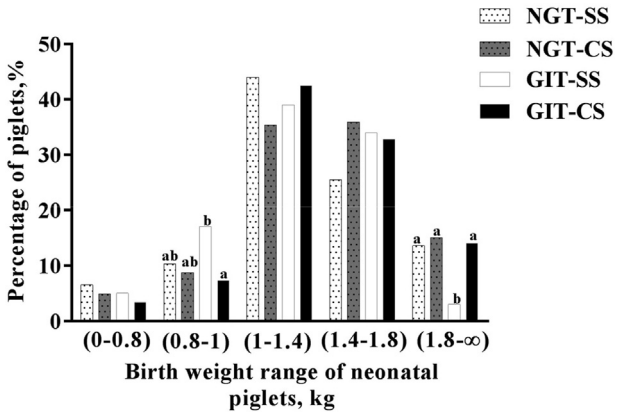

Fig. 3. The Chi-square test of maternal dietary treatment and glucose tolerance status on birth weight ranges of neonatal piglets. NGT-SS = normal glucose tolerant sows fed a soybean substitution diet; NGT-CS = normal glucose tolerant sows fed a corn starch diet; GIT-SS = glucose intolerant sows fed a soybean substitution diet; GIT-CS = glucose intolerant sows fed a corn starch diet. [a, b] Mean values with different small letters indicate significant difference ($P < 0.05$).

3.8. Small intestinal digestive enzyme activities

Table 8 shows the digestive enzyme activities of the jejunum and ileum in different groups. Compared with the NGT group, the GIT group showed a decrease ($P < 0.01$) in the amount of lactase in the ileum of LBW and NBW piglets. The activity of sucrase was greater ($P < 0.01$) in the ileum of LBW and NBW piglets from CS-fed sows than those from SS-fed sows. In the jejunum of NBW piglets,

Table 7
Effects of maternal dietary treatment, glucose tolerance status and their interaction on weight of internal organs and intestinal weight per length of newborn piglets.

Item	NGT		GIT		SEM	*P*-value		
	NGT-SS	NGT-CS	GIT-SS	GIT-CS		GT	D	GT × D
No. of piglets	6	6	6	6				
Piglets with LBW								
Duodenum[1], g/cm	0.09	0.08	0.10	0.09	0.007	0.48	0.68	0.99
Jejunum[1], g/cm	0.06	0.07	0.07	0.06	0.005	0.34	0.32	0.42
Ileum[1], g/cm	0.06	0.07	0.07	0.06	0.003	0.67	0.47	0.04
Stomach[2], g/kg BW	4.99	6.08	5.21	5.48	0.326	0.70	0.18	0.41
Heart[2], g/kg BW	6.92	7.55	9.06	6.90	0.226	0.48	0.51	0.27
Liver[2], g/kg BW	21.58	24.74	27.16	24.63	1.374	0.12	0.85	0.10
Spleen[2], g/kg BW	0.84	1.01	1.00	1.05	0.045	0.23	0.19	0.47
Lung[2], g/kg BW	19.09	18.02	17.51	15.12	0.725	0.24	0.36	0.72
Kidney[2], g/kg BW	7.64	8.00	8.34	8.74	0.392	0.25	0.53	0.98
Pancreas[2], g/kg BW	0.83	0.93	1.11	1.13	0.060	0.00	0.42	0.64
Piglets with NBW								
Duodenum[1], g/cm	0.12	0.14	0.10	0.12	0.008	0.42	0.29	0.71
Jejunum[1], g/cm	0.09	0.10	0.08	0.09	0.004	0.28	0.22	0.73
Ileum[1], g/cm	0.09	0.10	0.08	0.10	0.004	0.76	0.04	0.67
Stomach[2], g/kg BW	5.57	5.53	4.45	4.37	0.260	0.00	0.86	0.95
Heart[2], g/kg BW	6.34	6.70	5.82	7.09	0.281	0.49	0.00	0.33
Liver[2], g/kg BW	27.49	26.79	26.51	28.34	1.560	0.89	0.79	0.55
Spleen[2], g/kg BW	0.89	0.92	0.97	0.92	0.046	0.60	0.90	0.55
Lung[2], g/kg BW	15.69	16.54	17.32	16.78	1.007	0.51	0.92	0.63
Kidney[2], g/kg BW	6.62	7.34	6.76	7.42	0.288	0.78	0.09	0.93
Pancreas[2], g/kg BW	0.98	1.08	1.07	1.06	0.053	0.68	0.56	0.53

NGT = normal glucose tolerant; GIT = glucose intolerant; NGT-SS = NGT sows fed a soybean substitution diet; NGT-CS = NGT sows fed a corn starch diet; GIT-SS = GIT sows fed a soybean substitution diet; GIT-CS = GIT sows fed a corn starch diet; NBW = normal birth weight; LBW = low birth weight; GT = glucose tolerance effect of sows; D = diet effect of sows.
[1] Intestinal weight per length = Intestine weight (g)/Intestine length (cm).
[2] Weight of internal organ = Organ weight (g)/Piglet birth weight (kg).

Table 8
Effects of maternal dietary treatment, glucose tolerance status and their interaction on intestinal morphology and digestion and absorption-related enzyme activity in the small intestine of newborn piglets.

Item	NGT		GIT		SEM	*P*-value		
	NGT-SS	NGT-CS	GIT-SS	GIT-CS		GT	D	GT × D
No. of piglets	6	6	6	6				
Piglets with LBW								
Jejunum								
Villus height, μm	512.92	660.79	626.36	717.24	28.356	0.11	0.03	0.58
Crypt depth, μm	57.43	60.94	61.67	64.93	2.500	0.45	0.53	0.98
VH:CD ratio	9.54	11.09	10.49	11.74	0.345	0.23	0.04	0.81
Lactase, U/mg prot	64.31	85.19	83.47	77.24	4.701	0.56	0.44	0.16
Sucrase, U/mg prot	1.52[a]	1.58[a]	0.62[b]	1.51[a]	0.107	0.00	0.00	0.00
Maltase, U/mg prot	5.42	6.16	4.36	6.11	0.337	0.41	0.07	0.44
Ileum								
Villus height, μm	475.89	547.56	477.10	618.70	19.538	0.27	0.00	0.28
Crypt depth, μm	50.97	54.32	59.58	58.62	2.136	0.15	0.78	0.62
VH:CD ratio	9.98	10.42	9.37	10.98	0.335	0.97	0.14	0.39
Lactase, U/mg prot	22.76	26.01	19.72	21.83	0.667	0.00	0.02	0.58
Sucrase, U/mg prot	1.24	1.59	0.95	1.56	0.076	0.17	0.00	0.28
Maltase, U/mg prot	6.22	7.34	6.45	6.93	0.232	0.41	0.07	0.44
Piglets with NBW								
Jejunum								
Villus height, μm	593.84	772.87	641.08	752.37	25.031	0.74	0.00	0.41
Crypt depth, μm	53.23[a]	65.09[ab]	76.70[b]	68.12[b]	2.856	0.01	0.73	0.04
VH:CD ratio	11.62	12.59	8.92	11.36	0.429	0.00	0.02	0.27
Lactase, U/mg prot	78.75	98.73	59.93	83.17	4.686	0.04	0.01	0.84
Sucrase, U/mg prot	1.80	2.53	1.56	2.20	0.107	0.09	0.00	0.78
Maltase, U/mg prot	6.91	9.91	7.26	8.33	0.483	0.50	0.03	0.30
Ileum								
Villus height, μm	501.20	550.12	538.24	624.36	19.138	0.14	0.08	0.61
Crypt depth, μm	51.26	52.31	56.02	52.71	1.477	0.41	0.72	0.49
VH:CD ratio	10.36	10.94	9.79	12.10	0.291	0.55	0.00	0.10
Lactase, U/mg prot	26.20	37.61	23.51	31.06	1.294	0.00	0.00	0.18
Sucrase, U/mg prot	2.42[a]	2.18[a]	1.45[b]	2.52[a]	0.105	0.02	0.00	0.00
Maltase, U/mg prot	7.37	8.51	7.85	7.30	0.241	0.50	0.03	0.30

NGT = normal glucose tolerant; GIT = glucose intolerant; NGT-SS = NGT sows fed a soybean substitution diet; NGT-CS = NGT sows fed a corn starch diet; GIT-SS = GIT sows fed a soybean substitution diet; GIT-CS = GIT sows fed a corn starch diet; LBW = low birth weight; NBW = normal birth weight; GT = glucose tolerance effect of sows; D = diet effect of sows; VH:CD ratio = ratio of villus height to crypt depth; prot = protein.
[a, b] Mean values with different small letters indicate significant difference ($P < 0.05$).

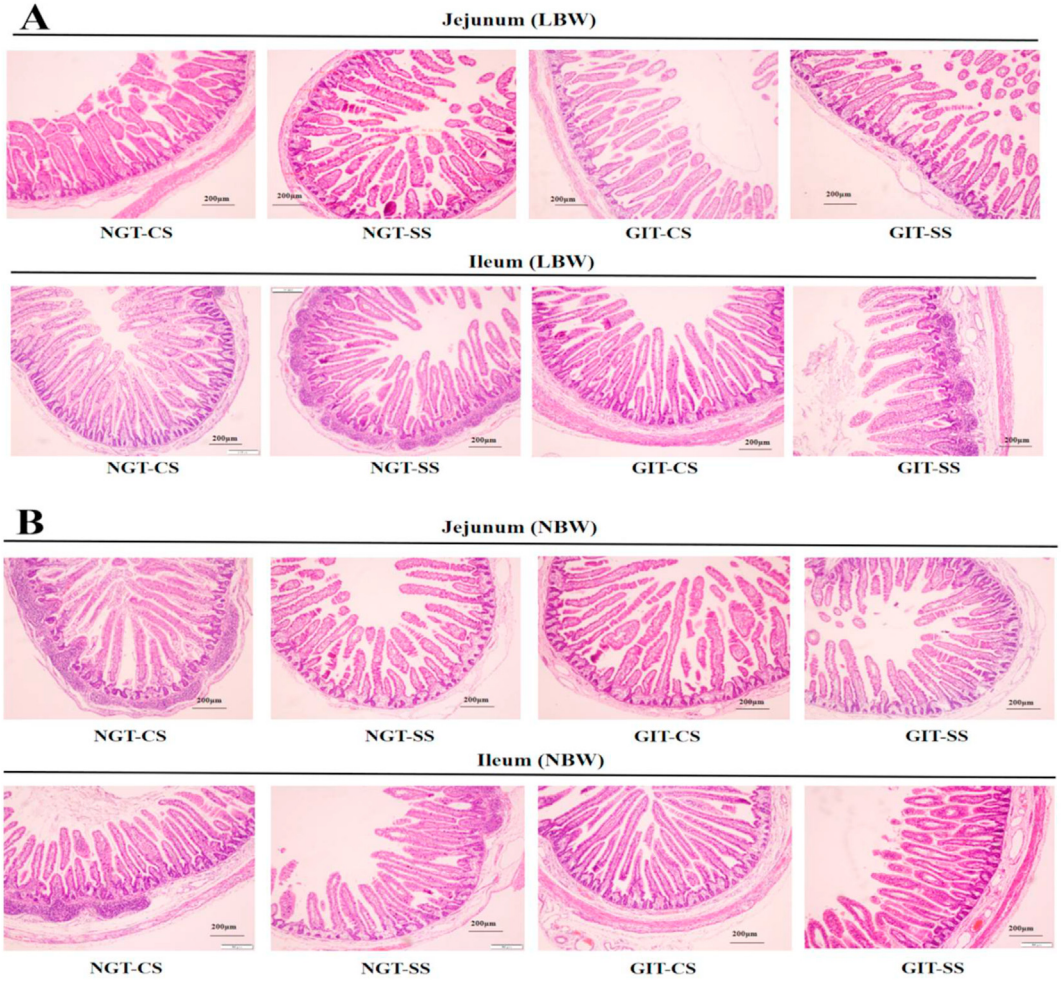

Fig. 4. Effects of maternal dietary treatment and glucose tolerance status on the histomorphological structures of the jejunum and ileum in (A) low birth weight (LBW) and (B) normal birth weight (NBW) of newborn piglets ($n = 6$). NGT-SS = normal glucose tolerant sows fed a soybean substitution diet; NGT-CS = normal glucose tolerant sows fed a corn starch diet; GIT-SS = glucose intolerant sows fed a soybean substitution diet; GIT-CS = glucose intolerant sows fed a corn starch diet. Magnification, 40 × ; scale bar, 200 μm.

the CS group had higher ($P < 0.01$) levels of sucrase than the SS group. Diets and glucose tolerance status showed an interaction ($P < 0.01$) in their effects on the sucrase activity of both the jejunum of LBW piglets and the ileum of NBW piglets. The jejunum of LBW piglets and the ileum of NBW piglets from the GIT sows fed a soybean substitution diet (GIT-SS) group showed lower sucrase activity ($P < 0.05$) than the others. Interestingly, GIT decreased ($P < 0.01$) the sucrase activity in the jejunum of LBW piglets and ileum of NBW piglets, whereas starch supplementation restored it to the NGT level ($P < 0.01$).

4. Discussion

The first aim of the present study was to evaluate the effects of glucose tolerance status on the reproductive performance of sows. We started with the glucose tolerance status of sows, which was classified as NGT or GIT based on AUC of blood glucose after the meals in late pregnancy. A higher AUC of glucose was seen in the GIT group than in the NGT group on d 75 of gestation, indicating the success in constructing the model of GIT and NGT pregnant sows.

During pregnancy and lactation, the sow undergoes many physiological and metabolic changes, such as progressive and reversible insulin resistance, to favor glucose availability to the pregnant uterus (Tan et al., 2016). Progressive insulin resistance at the end of pregnancy has been reported in pregnant sows, which continues during lactation and returns to normal sensitivity after weaning (Père and Etienne, 2007). Here, the GIT group had a high AUC of glucose on d 109 of gestation, which was consistent with the result on d 75 of gestation, indicating that the poor glucose tolerance of sows on d 75 of gestation remained unchanged on d 109 of gestation. Pregnant sows have been confirmed to be in poor glucose tolerance status near parturition (Père and Etienne, 2007). When compared to the NGT group, the GIT group showed an increase in the plasma insulin of sows on d 109 of gestation, which may well indicate the poor glucose tolerance in GIT sows. The insulin resistance has been reported to result from the insulin-desensitizing effects of hormonal products of the placenta, usually coupled with an increase of insulin secretion from pancreatic β-cells to compensate for the insulin resistance of pregnancy (Yaribeygi et al., 2020).

Glucose intolerance during pregnancy was considered as an adverse effect on fetal outcome (Buchanan et al., 2012; Amissah et al., 2020; Hu et al., 2021). In the present study, sows with GIT were shown to produce piglets with a lower litter weight (NGT: 34.5 kg vs. GIT: 30.4 kg) and BW (NGT: 3.7 kg vs. GIT: 3.3 kg) on d 10 of lactation, and a reduced ADG on d 1 to 10 of lactation (NGT: 211.5 g/d vs. GIT: 180.3 g/d). Intriguingly, those parameters (litter weight and BW) from sows fed with starch were restored to the

normal level on d 21 of lactation, regardless of glucose tolerance status. The potential relationship between the parameters and starch inclusion in the diet needs to be further elucidated.

Previous studies have reported the small intestine as an important component of glucose homeostasis (Mingrone and Castagneto-Gissey, 2014; Isah and Masola, 2017; Simon et al., 2020). Gut development could be expected to link with the fetal weight and correspondingly tissue growth and development (Ferenc et al., 2014). In this study, maternal GIT status was shown to have a negative influence on the villus height to crypt depth ratio and the amount of lactase as well as sucrase of the jejunum and ileum, with greater crypt depth of jejunum in the small intestine of piglets. This suggests that various degrees of maternal GIT might affect fetal gut morphology and function, leading to poor performance of piglets.

However, the GIT-induced increase in weight and length of its own small intestine has been observed in other studies (Mingrone and Castagneto-Gissey, 2014). Adachi et al. (2003) demonstrated that diabetes induced intestinal hyperplasia could contribute to postprandial hyperglycaemia by increasing the total activity of disaccharidases, such as sucrase and maltase in its own small intestine. This suggests that there is a more complicated connection between maternal glucose tolerance status and fetal gut development in the maternal and fetal circulation, but it needs further investigation.

Our results showed that when compared with SS, maternal dietary CS substantially increased the value of HOMA-IS and reduced the value of HOMA-IR on d 109 of gestation, regardless of glucose tolerance status, which is in agreement with the results of Brunzell et al. (1971), Van Der Peet-Schwering et al. (2004), and Almond et al. (2015). One possible explanation for this result is the lower blood glucose in the CS group on d 109 gestation, which was consistent with a previous study (Verdonk et al., 1981; Bonora et al., 2000), showing that high starch feeding could cause a decrease in plasma glucose levels, coupled with a numerical decline in fasting plasma insulin levels, suggesting an increase in tissue insulin sensitivity or a counter-regulatory response to the glucose level. Additionally, it can be inferred that dietary CS, which produces glucose by hydrolysis of glycosidic bonds, is more efficient than SS in blood glucose clearance.

Unfortunately, the decrease of insulin sensitivity in sows can result in a lower feed intake during lactation (Mosnier et al., 2010). However, when compared to the SS group, the CS group exhibited an increase in ADFI throughout lactation, regardless of sows' GIT status. These results further demonstrate that starch contributes to the improvement of insulin sensitivity. Furthermore, as a satiety factor and an initiation signal, the blood glucose level is dynamic in control of feed intake. Dietary starch might respond to the reduced blood glucose by decreasing the neuronal signaling for glucose metabolism, contributing to the feed intake of sows (Yang et al., 2019).

Maternal starch supplementation has a large impact on the performance of sows and piglets, whereas indexes vary with maternal glucose tolerance status to different degrees. Starch supplementation for sows tended to increase the weight of piglets at birth and weaning, and decrease the stillbirth rate, regardless of the glucose tolerance status of sows, which was in line with previous studies (Jones et al., 2002; Drozdowski et al., 2010). One possible explanation for the discrepancy of piglet weight is the difference in fetal gut growth and development. Due to the occurrence of most nutrient absorption in the small intestine of piglets, the gut typically undergoes a rapid development in the final weeks of pregnancy prior to delivery, which is a crucial stage for achieving the full intestinal length and maturation of digestive activities (Funston et al., 2010; Lalles, 2013; Qi et al., 2020). The influence of maternal nutrients on the maturation of fetal intestinal tract was reflected by the increased BW of fetal pigs (Wright and Irwin, 2010; Wang et al., 2018). When compared with the SS group, the CS group showed an increase in the villus height of the ileum or jejunum in LBW or NBW piglets and the villus height to crypt depth ratio of the ileum in NBW piglets, suggesting an increased intestinal surface area for piglets from CS-fed sows, endowing them with greater capacity to absorb available nutrients and contributing to the weaning weight of piglets.

Moreover, the digestive enzyme activity of the intestinal epithelial cells is fully developed in piglets for the absorption of nutrients after birth. One of the most important energy substances is carbohydrate, such as lactose, which is extremely important for the development of neonatal piglets (Kluess et al., 2010; Chen et al., 2017; Navis et al., 2020). A variety of carbohydrates have been found in the brush border of the small intestinal epithelium of pigs, such as the well-studied lactase, maltase and sucrase. The present study showed the activities of enzymes such as lactase, sucrase, and maltase were improved in the small intestine of piglets from CS-fed sows, hinting that starch supplementation can improve the digestibility of nutrients, especially carbohydrates, to some extent, and increase the weaning weight of piglets (Theil et al., 2014). Interestingly, GIT decreased the sucrase activity in the jejunum of LBW piglets and in the ileum of NBW piglets, which was restored to the normal level by starch supplementation. This is an important piece of evidence to support the assertion that starch can ameliorate the decline of the intestinal digestive ability induced by poor glucose tolerance.

In previous studies, poor glucose tolerance of pregnant sows was reported as a risk factor for the survival of piglets after birth (Kemp et al., 1996; Muns et al., 2016). In the present study, starch supplementation lowered the pre-weaning mortality rate only under poor glucose tolerance status rather than normal status. This implies that starch supplementation, owing to its ability to improve insulin resistance, may contribute to reduced postnatal mortality of piglets from sows under GIT status.

Another possible explanation for the discrepancy of pre-weaning mortality rate is the different ranges of birth weight after cross-fostering of piglets (GIT:1.5 kg vs. NGT:1.6 kg, despite no statistical difference). Many pieces of evidence have shown that birth weight is the most important determinant for piglet survival, with a direct impact on thermoregulatory capacity and growth (Herpin et al., 2002; Chris et al., 2012; Panzardi et al., 2013). Chris et al. (2012) have defined LBW piglets as piglets weighing between 0.8 and 1.0 kg, and high birth weight piglets as piglets weighing over 1.8 kg. The LBW piglets are weak and often die before weaning (Quiniou et al., 2002). Several studies have shown a survival rate of over 90% for high birth weight piglets (with an individual birth BW of 1.8 kg) (Chris et al., 2012). In the present study, only in the GIT status, when compared with the SS group, the CS group of pregnant sows significantly reduced the proportion of piglets weighing from 0.8 to 1.0 kg and increased the proportion of piglets weighing above 1.8 kg. These results may help to demonstrate that dietary starch supplementation can improve the pre-weaning mortality rate. However, it is unclear whether starch affects the survival of piglets directly or indirectly by improving glucose tolerance status, and the mechanism for the effects of starch on birth weight ranges of neonates needs to be further elucidated.

5. Conclusions

In the present study, regardless of glucose tolerance status, starch inclusion in maternal diet was demonstrated to improve the sows' insulin resistance during late gestation, increase the weight

of piglets at birth and weaning, and decrease the stillbirth rate by improving intestinal development. The improvement of litter performance in response to starch is affected by the glucose tolerance status of sows. Only under poor glucose tolerance status could dietary starch improve pre-weaning mortality rate, increase the number of high birth weight piglets and decrease the number of LBW piglets. These findings have shed light on the glucose tolerance of sows and its effect on the development of their offspring as well as facilitated the development of feed strategies to alleviate impaired glucose tolerance to enhance the reproductive performance of sows.

Author contributions

Wenliang He, **Xinggang Qiu** and **Yanzhen Xu** provided the study materials, reagents, laboratory samples, animals and instrumentation. **Yulong Yin** and **Chengquan Tan** designed the research and analysed the data. **Yunyu Yang**, **Jianzhao Chen**, **Xichen Zhao**, **Ming Deng** and **Kaili Xiao** conducted the research. **Yunyu Yang** and **Ming Deng** wrote the article. **Yulong Yin** and **Chengquan Tan** had primary responsibility for the final content.

Conflict of interest

We declare that we have no financial and personal relationships with other people or organizations that can inappropriately influence our work, and there is no professional or other personal interest of any nature or kind in any product, service and/or company that could be construed as influencing the content of this paper.

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References

Adachi T, Mori C, Sakurai K, Shihara N, Tsuda K, Yasuda K. Morphological changes and increased sucrase and isomaltase activity in small intestines of insulin-deficient and type 2 diabetic rats. Endocr J 2003;50:271–9.
Almond KL, Fainberg HP, Lomax MA, Bikker P, Symonds ME, Mostyn A. Substitution of starch for palm oil during gestation: impact on offspring survival and hepatic gene expression in the pig. Reprod Fertil Dev 2015;27:1057.
Amissah E, Brown J, Harding J. Carbohydrate supplementation of human milk to promote growth in preterm infants. Cochrane Database Syst Rev 2020;9: CD000280.
Bikker P, Fledderus J, Kluess J, Geelen M. Glucose tolerance in pregnant sows and liver glycogen in neonatal piglets is influenced by diet composition in gestation, vol. 124. Publication-European Association For Animal Production; 2007. p. 203.
Bonora E, Targher G, Alberiche M, Bonadonna RC, Saggiani F, Zenere MB, et al. Homeostasis model assessment closely mirrors the glucose clamp technique in the assessment of insulin sensitivity: studies in subjects with various degrees of glucose tolerance and insulin sensitivity. Diabetes Care 2000;23:57–63.
Brunzell JD, Lerner RL, Hazzard WR, Porte Jr D, Bierman EL. Improved glucose tolerance with high carbohydrate feeding in mild diabetes. N Engl J Med 1971;284:521–4.
Buchanan TA, Xiang AH, Page KA. Gestational diabetes mellitus: risks and management during and after pregnancy. Nat Rev Endocrinol 2012;8:639.
Chen Y, Mou D, Hu L, Zhen J, Che L, Fang Z, et al. Effects of maternal low-energy diet during gestation on intestinal morphology, disaccharidase activity, and immune response to lipopolysaccharide challenge in pig offspring. Nutrients 2017;9.
Chris T, Saskia B, Egbert F, Eveline W. The economic benefit of heavier piglets: relations between birth weight and piglet survival and finisher performance. In: Proceeding of the 22nd International Pig Veterinary Society Congress; 2012. p. 159.
Corson A, Laws J, Litten JC, Dodds P, Lean I, Clarke L. Effect of dietary supplementation of different oils during the first or second half of pregnancy on the glucose tolerance of the sow. Animal 2008;2:1045–54.
Drozdowski LA, Clandinin T, Thomson ABR, Drozdowski LA, Clandinin T, Thomson AB. Ontogeny, growth and development of the small intestine: understanding pediatric gastroenterology. World J Gastroenterol 2010;16:787–99. World J Gastroenterol 16: 787-799.
Ferenc K, Pietrzak P, Godlewski MM, Piwowarski J, Kilianczyk R, Guilloteau P, et al. Intrauterine growth retarded piglet as a model for humans–studies on the perinatal development of the gut structure and function. Reprod Biol 2014;14:51–60.
Funston RN, Larson DM, Vonnahme K. Effects of maternal nutrition on conceptus growth and offspring performance: implications for beef cattle production. J Anim Sci 2010;88:E205–15.
Gatlin LA, Odle J, Soede J, Hansent JA. Dietary medium- or long-chain triglycerides improve body condition of lean-genotype sows and increase suckling pig growth. J Anim Sci 2002;80:38–44.
Herpin P, Damon M, Le Dividich J. Development of thermoregulation and neonatal survival in pigs. Livest Prod Sci 2002;78:25–45.
Hu C, Wu Z, Huang Z, Hao X, Wang S, Deng J, et al. Nox 2 impairs VEGF-A-induced angiogenesis in placenta via mitochondrial ROS-STAT3 pathway. Redox Biol 2021;45:102051.
Huang S, Wu Z, Hao X, Huang Z, Tan C. Maternal supply of cysteamine during late gestation alleviates oxidative stress and enhances angiogenesis in porcine placenta. J Anim Sci Biotechnol 2021a;12:91.
Huang Z, Huang S, Song T, Yin Y, Tan C. Placental angiogenesis in mammals: a review of the regulatory effects of signaling pathways and functional nutrients. Adv Nutr 2021. Online ahead of print.
Isah MB, Masola B. Effect of oleanolic acid on small intestine morphology and enzymes of glutamine metabolism in diabetic rats. Int J Physiol Pathophysiol Pharmacol 2017;9:128.
Jones G, Edwards S, Sinclair A, Gebbie F, Rooke J, Jagger S, et al. The effect of maize starch or soya-bean oil as energy sources in lactation on sow and piglet performance in association with sow metabolic state around peak lactation. Anim Sci 2002;75:57–66.
Kemp B, Soede N, Vesseur P, Helmond F, Spoorenberg J, Frankena K. Glucose tolerance of pregnant sows is related to postnatal pig mortality. J Anim Sci 1996;74:879–85.
Kluess J, Schoenhusen U, Souffrant W, Jones P, Miller B. Impact of diet composition on ileal digestibility and small intestinal morphology in early-weaned pigs fitted with a T-cannula. Animal 2010;4:586–94.
Lalles JP. Long term effects of pre- and early postnatal nutrition and environment on the gut. J Anim Sci 2013;90:421–9.
Mingrone G, Castagneto-Gissey L. Type 2 diabetes mellitus in 2013: a central role of the gut in glucose homeostasis. Nat Rev Endocrinol 2014;10:73.
Mosnier E, Le Floc'h N, Etienne M, Ramaekers P, Sève B, Père M-C. Reduced feed intake of lactating primiparous sows is associated with increased insulin resistance during the peripartum period and is not modified through supplementation with dietary tryptophan. J Anim Sci 2010;88:612–25.
Muns R, Nuntapaitoon M, Tummaruk P. Non-infectious causes of pre-weaning mortality in piglets. Livest Sci 2016;184:46–57.
Navis M, Muncan V, Sangild P, Møller Willumsen L, Koelink P, Wildenberg M, et al. Beneficial effect of mildly pasteurized whey protein on intestinal integrity and innate defense in preterm and near-term piglets. Nutrients 2020;12.
NRC. Nutrient requirements of swine. 11th revised edn. Washington, DC: National Academy Press; 2012.
Père M-C, Etienne M. Insulin sensitivity during pregnancy, lactation, and postweaning in primiparous gilts. J Anim Sci 2007;85:101–10.
Père M, Etienne M. Influence of litter size on insulin sensitivity in multiparous sows. J Anim Sci 2019;97:874–84.
Panzardi A, Bernardi M, Mellagi A, Bierhals T, Bortolozzo F, Wentz I. Newborn piglet traits associated with survival and growth performance until weaning. Prev Vet Med 2013;110:206–13.
Phillips R, Panepinto L, Spangler R, Westmoreland N. Yucatan miniature swine as a model for the study of human diabetes mellitus. Diabetes 1982;31:30.
Pinheiro DF, Pinheiro PF, Buratini Jr J, Castilho AC, Lima PF, Trinca LA, et al. Maternal protein restriction during pregnancy affects gene expression and immunolocalization of intestinal nutrient transporters in rats. Clin Sci 2013;125:281–9.
Qi M, Wang J, Tan B, Liao S, Long C, Yin Y. Postnatal growth retardation is associated with intestinal mucosa mitochondrial dysfunction and aberrant energy status in piglets. J Cell Mol Med 2020;24:10100–11.
Quiniou N, Dagorn J, Gaudré D. Variation of piglets' birth weight and consequences on subsequent performance. Livest Prod Sci 2002;78:63–70.
Simon M-C, Reinbeck AL, Wessel C, Heindirk J, Jelenik T, Kaul K, et al. Distinct alterations of gut morphology and microbiota characterize accelerated diabetes onset in nonobese diabetic mice. J Biol Chem 2020;295:969–80.

Tan C, Sun H, Wei H, Tan J, Long G, Jiang S, et al. Effects of soluble fiber inclusion in gestation diets with varying fermentation characteristics on lactational feed intake of sows over two successive parities. Animal: An Int J Animal Biosci 2018;12:1388–95.
Tan C, Wei H, Ao J, Long G, Peng J. Inclusion of konjac flour in the gestation diet changes the gut microbiota, alleviates oxidative stress, and improves insulin sensitivity in sows. Appl Environ Microbiol 2016;82:5899–909.
Taylor PD, McConnell J, Khan IY, Holemans K, Lawrence KM, Asare-Anane H, et al. Impaired glucose homeostasis and mitochondrial abnormalities in offspring of rats fed a fat-rich diet in pregnancy. Am J Physiol Regul Integr Comp Physiol 2005;288:R134–9.
Theil PK, Lauridsen C, Quesnel H. Neonatal piglet survival: impact of sow nutrition around parturition on fetal glycogen deposition and production and composition of colostrum and transient milk. Animal 2014;8:1021–30.
Van Der Peet-Schwering C, Kemp B, Binnendijk G, Den Hartog L, Vereijken P, Verstegen M. Effects of additional starch or fat in late-gestating high nonstarch polysaccharide diets on litter performance and glucose tolerance in sows. J Anim Sci 2004;82:2964–71.
Verdonk CA, Rizza RA, Gerich JE. Effects of plasma glucose concentration on glucose utilization and glucose clearance in normal man. Diabetes 1981;30:535–7.
Wang X, Wu W, Lin G, Li D, Wu G, Wang J. Temporal proteomic analysis reveals continuous impairment of intestinal development in neonatal piglets with intrauterine growth restriction. J Proteome Res 2010;9:924–35.
Wang X, Zhu Y, Feng C, Lin G, Wu G, Li D, et al. Innate differences and colostrum-induced alterations of jejunal mucosal proteins in piglets with intra-uterine growth restriction. Br J Nutr 2018;119:734–47.
Wright NA, Irwin M. The kinetics of villus cell populations in the mouse small intestine : I. Normal villi: the steady state requirement. Cell Prolif 2010;15:595–609.
Yang Y, Hu CJ, Zhao X, Xiao K, Deng M, Zhang L, et al. Dietary energy sources during late gestation and lactation of sows: effects on performance, glucolipid metabolism, oxidative status of sows, and their offspring. J Anim Sci 2019;97:4608–18.
Yaribeygi H, Sathyapalan T, Atkin S, Sahebkar A. Molecular mechanisms linking oxidative stress and diabetes mellitus. Oxid Med Cell Longev 2020;2020:8609213.
Zhang S, Zhang X, Qiao H, Chen J, Fang C, Deng Z, et al. Effect of timing of post-weaning supplementation of soybean oil and exogenous lipase on growth performance, blood biochemical profiles, intestinal morphology and caecal microbial composition in weaning pigs. Ital J Anim Sci 2018;17:967–75.