DIFFERENCES IN BACKFAT THICKNESS AFTER WEANING AND REPRODUCTION TRAITS BETWEEN THE GENOTYPES OF OBESE GENE IN SOWS (WITH REPRODUCTION DISORDERS)

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Abstract. The aim of the present study was to identify polymorphism in the Obese (leptin) gene of crossbred sows with disordered reproduction and to investigate if there are differences between the genotypes of sow Obese (leptin) gene in backfat thickness after weaning, viability of piglets and preservation of piglets until weaning.

The polymorphism of the porcine leptin gene of sows of disordered reproduction and differences between the genotypes of Obese (leptin) gene in backfat thickness after weaning, born piglets' viability and preservation of piglets were analyzed in 85 crossbred sows. The backfat thickness was determined after the last weaning of piglets using a-mode ultrasonography in 3 points (P): P(1) - between 6-7 ribs; P(2) - 10th rib; P(3) - behind the last rib. The number of born alive, stillborn and weaned piglets was estimated from reproductive cards of sows.

DNA samples from the blood of sows for determining polymorphism were obtained by PCR and restricted fragment lengths with restriction enzyme *Hinf*I were: 152 bp (allele T) and 84 + 68 bp (allele C).

The frequencies of detected genotypes TT, TC and CC were 0.63, 0.31 and 0.06 respectively of sows with disordered reproduction population. The estimated frequencies of alleles were 0.79 for allele T and 0.21 for allele C.

Based on our research results we found that backfat thickness after weaning in sows of the CC genotype was highest compared to the sows of TT and TC genotypes at: P(1) - 4.6 and 3.1 mm ($P<0.05$), at P(2) - 5.0 and 4.5 mm ($P<0.05$) and at P(3) - 3.5 and 2.7 mm ($P<0.05$) respectively.

The biggest number (52.94 %) of sows with anoestrus after weaning was detected in TT genotype group.

There was no statistically significant difference among different genotypes and the number of born, stillborn piglets, but there was a tendency that sows with CC genotype with a higher backfat thickness had got more live born and less stillborn piglets compared with sows with TC and TT genotype.

We found that preservation of piglets till weaning was best in sows of TT genotype (90.63 %) compared with sows of TC and CC genotypes. The piglets preservation quality for sows with TC and CC genotype was by 0.78 % and 3.25 % lower ($P<0.05$) respectively.

Keywords: leptin gene, backfat thickness, reproduction disorders, sow.

LAŠINIŲ STORIO PO PARŠELIŲ ATJUNKYMO IR REPRODUKCINIŲ SAVYBIŲ SKIRTUMAI TARP SUTRIKUSIOS REPRODUKCIJOS PARŠAVEDŽIŲ LEPTINO GENO GENOTIPŲ

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Santrauka. Šio darbo tikslas buvo nustatyti mišrūnių paršavedžių su reprodukcijos sutrikimais leptino geno polimorfizmą ir galimus jų lašinių storio po atjunkymo, atvestų paršelių gyvybingumo bei išsaugotų paršelių skaičiaus iki atjunkymo skirtumus tarp genotipų.

Tyrimui atrinktos 85 sutrikusios reprodukcijos paršavedės, nustatytas jų leptino geno polimorfizmas bei įvertinti galimi lašinių storio po atjunkymo, atvestų paršelių gyvybingumo, išsaugotų paršelių skaičiaus iki atjunkymo skirtumai tarp Leptino geno genotipų. Lašinių storis po paskutinio atjunkymo echoskopu nustatytas trijuose taškuose (T): T(1) – tarp 6–7 šonkaulių, T(2) – ties 10 šonkauliu, T(3) – už paskutinio šonkaulio. Atvestų gyvų ir negyvų bei atjunkytų paršelių skaičius nustatytas iš paršavedžių reprodukcijos kortelių duomenų.

DNR išskirta iš kraujo. Leptino geno polimorfizmui identifikuoti taikytas PGR-RFIP metodas, PGR produktas karpytas *Hinf*I restrikciniu fermentu. Sukarpytas T alelis buvo 152 bp, o C alelis – 84 bp ir 68 bp dydžio.

Tirtoje sutrikusios reprodukcijos paršavedžių populiacijoje leptino geno TT genotipas nustatytas 0,63 dažniu, TC genotipas – 0,31, o CC genotipas pasireiškė 0,06 dažniu. T alelis pasireiškė 0,79 dažniu, o C – 0,21 dažniu.

Nustatyta, kad CC genotipo paršavedžių nugaros lašiniai po atjunkymo buvo storesni už TT ir TC genotipų paršavedžių P(1) taške 4,6 mm ir 3,1 mm ($p<0,05$), P(2) taške – 5,0 ir 4,5 mm ($p<0,05$), o P(3) taške – 3,5 ir 2,7 mm ($p<0,05$).

Daugiausia paršavedžių (52,94 proc.), kurioms atjunkius paršelius pasireiškė ilgalaikis *anoestrus* buvo TT genotipo grupėje.

Nors statistiškai patikimo skirtumo tarp atvestų gyvų/negyvų paršelių skaičiaus skirtingo genotipo paršavedžių grupėse nenustatyta, pastebėta tendencija: CC genotipo, turinčios daugiau lašinių paršavedės atveda daugiau gyvų ir mažiau negyvybingų paršelių palyginti su TC ir TT genotipo paršavedėmis.

Įvertinę skirtingo genotipo paršavedžių iki atjunkymo išsaugotų paršelių skaičių nustatėme, kad daugiausia (90,63 proc.) paršelių iki atjunkinimo išsaugojo mažiausiai riebalų atjunkymo metu turėjusios TT genotipo paršavedės. TC ir CC genotipo paršavedės paršelių išsaugojo atitinkamai 0,78 proc. ir 3,25 proc. ($p<0,05$) mažiau.

Raktažodžiai: leptino genas, lašinių storis, reprodukcijos sutrikimai, paršavedė.

Introduction. In pigs, the Obese gene (or leptin gene) is considered to be an eligible gene to follow characteristics of economic importance, such as feed intake, pig backfat thickness, growth, and reproduction (Lagonigro et al., 2003). The gene is located in the pig chromosome 18, consists of three exons and two introns in the structure observed homology with genes from human and mouse is in the 80 % (Орешин, 2010).

Leptin, the product of leptin gene, is a 16 kDa protein synthesized by adipose tissue, it is secreted into the blood by adipocytes (Ramsay et al., 1998) and respectively it is involved in regulation of feed intake, energy balance, fertility, reproductive and immune functions (Campfield et al., 1995; Barb et al., 1998; Houseknecht and Portocarrero, 1998; Feuhbeck et al., 1998; Cunnigham et al., 1999; Lagonigro et al., 2003). Leptin may act as a metabolic gate, which permits activation of the reproductive axis (Barb et al., 2000). Metabolic imbalance and related disturbances of neurohumoral regulation can cause reproductive disorders. Pig selection is carried out purposefully to get more fat-free pork when swine breeding is growing constantly. However productive features not always match with reproductive features. The reproductive age of sows has a tendency to decrease. The most common reasons for culling are repeat breeding, the long non-productive period (weaning to servis), pathological changes: anoestrus, follicular cysts, a high number of stillborn piglets in the litter, insufficient preservation of piglets, etc... Metabolic imbalance and related disturbances of neurohumoral regulation can be influenced of Obese (leptin) gene mutation when the function of its product leptin, as an endocrine messenger from the body to the brain, is changing (Compfield et al., 1995; Keisler et al., 1999). The Obese (leptin) gene product leptin is the key signal providing information linking energy balance to reproduction (Myers et al. 2009), and the fat, in turn, is a precursor of sex hormones.

Four polymorphisms – C/T at position 867, A/G at position 1112, C/T at position 3469 and G/T at position 3714, in the Obese (leptin) gene of four pig breeds (Duroc, Hampshire, Landrase and Large White) were related with fatness (Jiang and Gibson, 1999).

One of the most common mutations in the Obese (leptin) gene - ob C3469T is a point mutation in the third exon. It is noted that the pigs with the appropriate genotype point mutation (CC), are characterized by a rapid weight gain due to the accumulation of fat in the lumbosacral spine, while the TT genotype is associated with a lower backfat thickness. The use of genetic markers of quantitative trait loci of farm animals, and, in particular, pigs, opens up new perspectives in breeding. Selection by genotype has several advantages over traditional methods. It does not account for the variability of economically useful traits due to the external environment, making the selection at an early age regardless of the sex of the animals and, ultimately, increase of efficiency possible (Орешин, 2010).

It has not been analyzed in research papers which polymorphism of leptin gene is typical for sows with disordered reproduction. Although Obese (leptin) gene is analysed in various other aspects the data about the influence of Obese (leptin) gene genotypes on features of sows with disordered reproduction, as backfat thickness after weaning, vitality of born piglets and their preservation, are lacking.

The aim of the present study was to identify polymorphism in the Obese (leptin) gene of crossbred sows with disordered reproduction and investigate if there are differences between genotypes of sow Obese (leptin) gene in backfat thickness after weaning, viability of piglets and preservation of piglets until weaning.

Materials and methods. A group of 85 sows with reproduction disorders (repeated oestrus or consumption problems with long anoestrus after weaning) after weaning was selected from 1721 sows of one pig-breeding farm. Mean parity order of pluriparous sows was 2.18±0.66. All sows received the same complete feed according to the period of reproduction. Lactation time lasted for 24 days.

Blood samples were collected from the jugular vein of 85 crossbred sows with disordered reproduction. The blood was sampled from each individual to vacuum test-tube with EDTA anticoagulant (Venoject, Terumo Europe N. V., Leuven, Belgium).

DNA was extracted from blood by chloroform/ phenol method. Genotyping of Obese of gene was performed by polymerase chain reaction - restriction fragment length polymorphism (PCR/RFLP) method (Stratil et al., 1997), using a pair of primers with the following sequences: 5'TGCAGTCTGTCTCCTCCAAA3' (forward) and 5'CGATAATTGGATCACATTTCTG3' (reverse), which amplifies an amplicon of 152 bp. The PCR reaction was

carried out in GeneAmp PCR System After 2700 (AppliedBiosystem).

Preheating at 95°C for 2 min, amplification was done using 34 cycles at 95°C for 1 min, 55°C for 1 min, and 72°C for 1 min. For the PCR assays, 1 U Taq DNA polymerase, 10X PCR buffer, 3.0 mM $MgCl_2$, 200 µM of each dNTP, 10 pM of each primer and 200 ng genomic DNA in a final volume of 20 µL were used.

After amplification, 10 µL of the PCR amplicon was digested with 2 U *Hinf*I restriction enzyme; genotyping was performed on a 3 % agarose gel using pBR322 DNA/AluI molecular marker (MBI Fermentas) and coloured with ethidium bromide (10 mg/mL) and the results were visualized in UV light.

Measurements of the backfat thickness have been made after weaning. The backfat thickness was determined after the last weaning of piglets using a-mode ultrasonography (Lean-meater, Renco Corporation, Minneapolis, MN, 2005). Backfat level was measures in 3 points (P): P(1) - between 6-7 ribs; P(2) - 10^{th} rib; P(3) - behind the last rib.

The number of born alive, stillborn and preserved (weaned) piglets was estimated from reproductive cards of experimental sows.

Statistical analysis. Statistical analysis was performed using the SPSS statistical package *No 20* for Windows (SPSS for Windows 20.0, SPSS Inc., Chicago, IL, USA). The data included in the model were analyzed using descriptive statistics (means±SD) and one-way and multifactorial ANOVA analyses. The differences among investigated groups were analyzed by multiple comparisons LSD method. The data was considered to be statistically significant when: $P<0.05$.

Results. Genotyping at the Obese locus. In the studied sows population with impaired reproductive performance two allelic Obese (leptin) genes T and C were identified. There were three possible genotypes of emergence: TT, TC and CC.

Two alleles of Obese (leptin) gene were identified: T contained one 152 bp fragment, C had two fragments (84 and 68 bp), (Fig. 1).

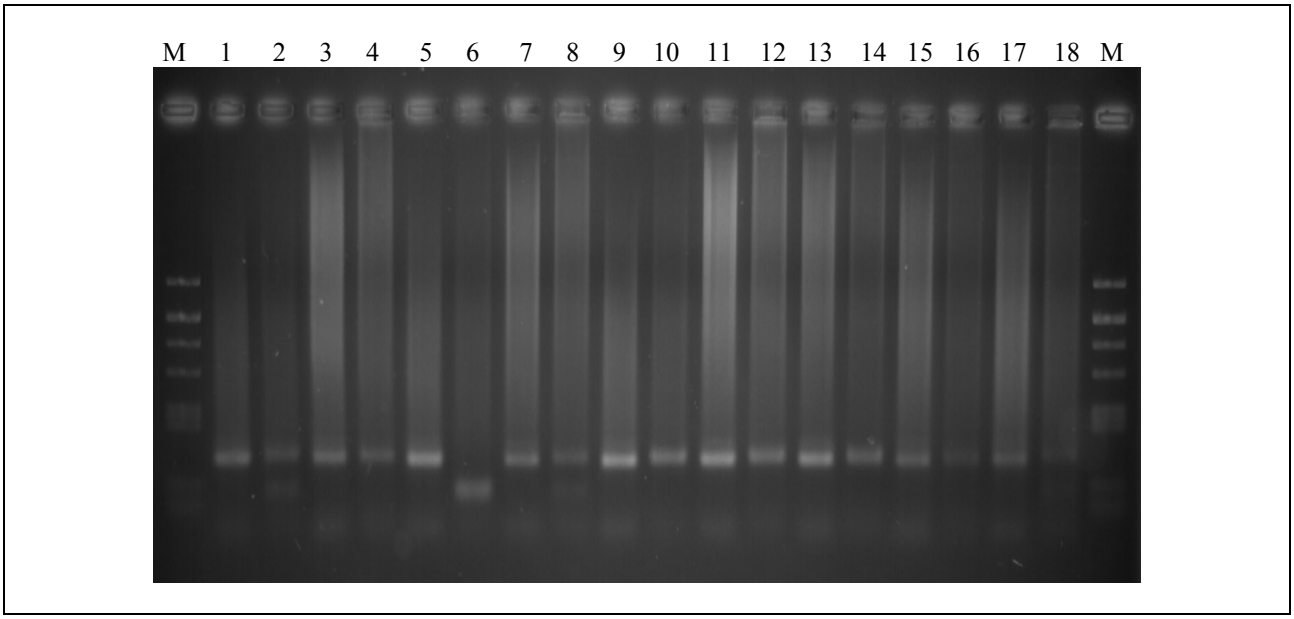

Fig. 1. ***Hinf*I polymorphisms in the Obese** (leptin) **gene detected by polymerase chain reaction-restriction fragment length polymorphism** (PCR-RFLP). **The PCR products were run on a 3.5% agarose gel. M = pBR322 DNA/AluI Marker, 20 (MBI Fermentas, Lithuania); lanes 1, 3, 4, 5, 7, 9-17 = samples of TT genotype; lanes 2, 8, 18 = samples of TC genotype; lane 6 = sample of CC genotype**

Table 1. **Frequencies of genotypes and alleles in the crossbred sows with disordered reproduction performance**

Occurrence	Genotypes LEP/*Hinf*I			Genotypes LEP/*Hinf*I	
	TT	TC	CC	T	C
Number	54	26	5	0.79	0.21
Frequency	0.63	0.31	0.06		

The observed genotype frequencies were 63.53 % for TT genotype, 30.59 % for TC genotype and 5.88 % sows had CC genotype. The frequency of C allele was 0.21 and T allele – 0.79 of the studied sows population with disordered reproduction performance (Table 1).

According to the obtained data, the most common reproductive disorder of sows was anoestrus 78.82 % (n=67), with the weaning to slaughter interval for

anoestrous sows averaging to 63.40±1.7 days; the rest 21.18 % (n=18) of the sows were with repeated oestrus and failure of conception for the second and the third insemination.

Evaluating the influence of genotype on the manifestation of reproductive disorders (Fig. 2) it was established that most sows (52.94 %) did not show oestrus (long-term anoestrus) in group of TT genotype. There were 21.18 % and 4.70 % anoestrus sows in groups of TC and CC genotypes respectively.

The highest percent (10.59%) of repeat breeding also was detected in the group of sows with TT genotype.

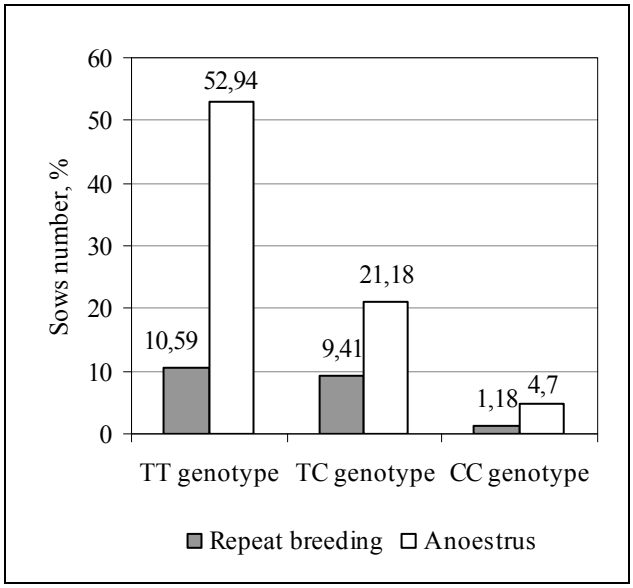

Fig. 2. **Differences in the occurrence of reproductive disorders between genotypes of sow Obese** (leptin) **gene**

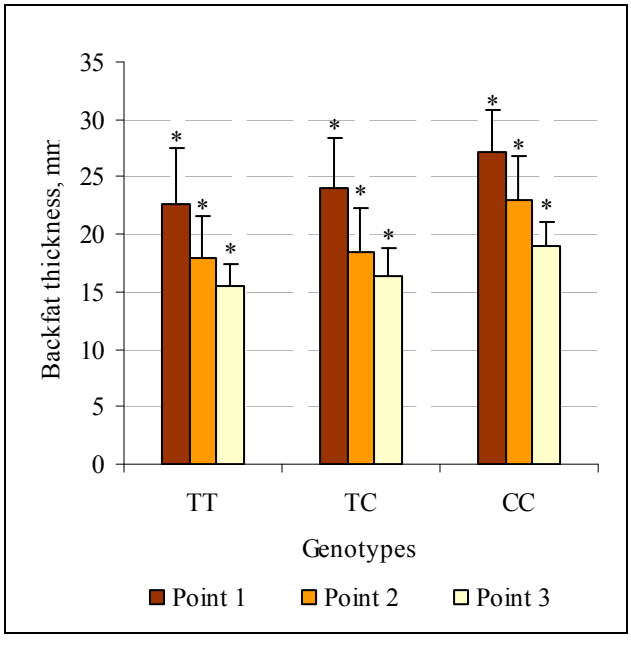

Fig. 3. **Differences in backfat thickness after weaning between genotypes of sow Obese** (leptin) **gene**

The same symbol means the difference is significant between the genotypes *P < 0.05

Based on the obtained results (Fig. 3), we found that in sows of the CC genotype the backfat thickness after weaning was biggest at all 3 points (P(1) – 27.2±1.92, P(2) – 23.0±2.52, P(3) – 19.0±2.03) compared to the TT and TC genotypes: at P(1), the backfat thickness was bigger by 4.6 mm and 3.1 mm (P<0.05), at P(2) by 5.0 and 4.5 mm (P<0.05) and at P(3) by 3.5 and 2.7 mm (P<0.05) respectively.

The study shows that backfat thickness in sows, with a mutated C allele in Obese (leptin) gene is bigger than in sows with T allele (P<0.05).

We found (Fig. 4) that sows with TT genotype had the smallest number - 8.75±2.57 (2.15 % less than TC genotype and 5.45 % less than CC genotype) of live born piglets, when sows of TC genotype had the bigger number (9.36±2.58) and sows with CC genotype had the biggest number (10.3±2.54) of alive born piglets.

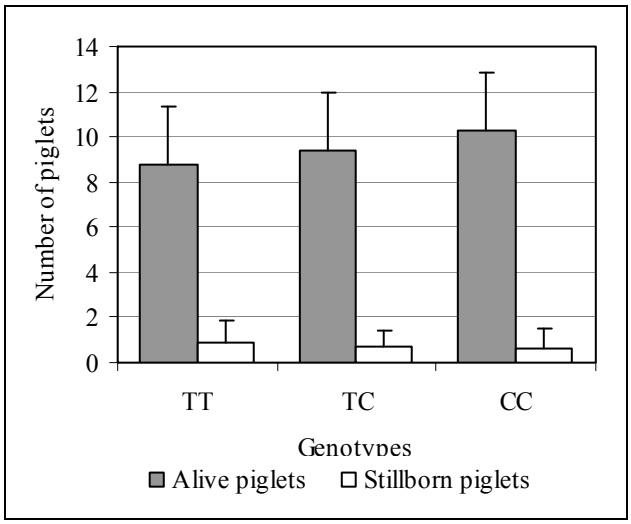

Fig. 4. **Number of born alive and stillborn piglets from sows of different genotypes**

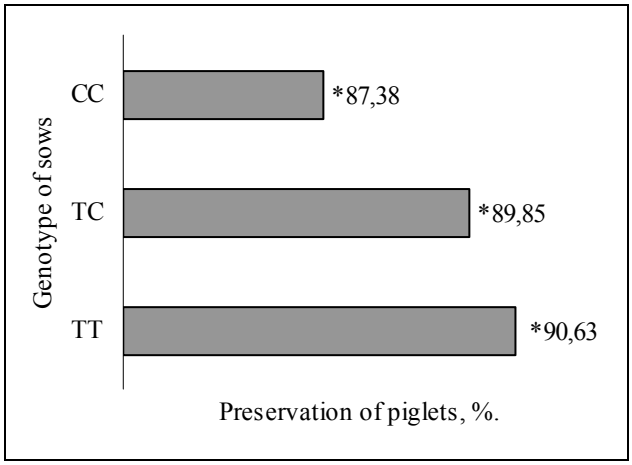

Fig. 5. **Differences in preservation of piglets between genotypes of sow Obese** (leptin) **gene** (%)

The same symbol means the difference is significant between the genotypes *P < 0.05

Evaluating the rate of stillborn piglets it was established that sows with CC genotype had by 2.07 % less stillborn piglets than sows with TC genotype and by 9.94 % stillborn piglets less than sows with TT genotype. There were no statistically significant differences detected between different genotypes and the number of born and stillborn piglets (Fig. 4).

The highest % of preserved piglets after weaning (Fig. 5) was detected in sow group with TT genotype (90.63 %), which had least backfat thickness at all points at weaning (P(1) – 22.63 ± 4.93, P(2) – 18.02 ± 4.31, P(3) – 15.52 ± 3.60) and % of preserved piglets in sow groups with TC and CC genotypes was respectively lower by 0.78 % and 3.25 % (P<0.05).

Discussion. The aim of the present study was to identify polymorphism in the Obese (leptin) gene of crossbred sows with disordered reproduction performance and investigate if there are differences between genotypes of Obese (leptin) gene in backfat thickness after weaning, born piglets viability and preservation of piglets.

Two alleles of Obese gene were identified for sows with reproductive disorders: T contained one 152 bp fragment, C had two fragments (84 and 68 bp) and a rise of three genotypes was detected: TT, TC and CC. The frequency of C allele was 0.21 and T allele 0.79 between sows with disordered reproduction. The same allele frequencies have been found by other researchers (Szydlowski et al., 2004; Silveira et al., 2008) but in normal (without reproduction disorders) pigs populations.

Only sows with normal reproduction performance were examined by other researchers and in many cases they did not find evidence for an association of the Obese (leptin) gene promoter genotype with the fatness traits in sows (Stachowiak et al., 2007). However Segantini et al., (2002) concluded that allele C may be associated with fat accumulation. Орешин, (2010) also detected that the pigs with the appropriate genotype point mutation (CC), are characterized by a rapid weight gain due to the accumulation of fat in the lumbosacral spine, while the TT genotype is associated with a lower backfat thickness. Changes in body weight or nutritional status are characterized by altered adipocyte function; reduction in adipose tissue leptin expression. Leptin expression may also be altered by fasting or obesity in swine (Houseknecht et al., 1998; Ramsay et al., 1998). Serum concentrations of leptin at farrowing and weaning are highest in sows exhibiting the greatest amount of backfat (Estienne et al., 2000).

The CC genotype is very rare (frequency ranging from 0 – 0,02 to 0,08) in most of the pig breeds (Kennes et al., 2001; Kuryl et al., 2003; Amillis et al., 2007). We also detected mutated CC genotype only in 5.88 % of sows with disordered reproduction. In our studies, the backfat thickness of sows of the CC genotype after weaning was highest (P<0.05) compared to the TT and TC genotypes. It is known that TT genotype may be more advantageous for decreasing fat deposition in the carcass than genotype TC (Kuryl et al., 2003). In the studies performed by Blicharski et al., (2004), the highest daily gain was detected in CC genotype sows too, but Kennes et al., (2001) obtained contrasting results, where the TT genotype individuals grew faster.

Leptin resistance has been identified with disruptions of signal transduction processes at the level of leptin receptors with effects on food behaviour and obesity (Lubis et al., 2008); thus, leptin resistant individuals are Obese (leptin) gene genotypes with elevated leptin levels but unable to suppress feeding when food is in excess (Martin et al., 2008; Myers et al., 2008).

Leptin is Obese (leptin) gene product and may act as the critical link between adipose tissue and the reproductive system, indicating whether adequate energy reserves are present for normal reproductive function. Gary et al., (2012) reported that leptin is a key metabolic signal synthesized and secreted by fat cells that communicates information about body energy reserves, nutritional state, and metabolic shifts to the reproductive axis. Leptin can act peripherally at the ovary or centrally at the hypothalamus to augment reproductive function of females. Scientists Barb and Krealing, (2004) hypothesized that estradiol modulates the hypothalamic-pituitary response to leptin. However, high fat sows also can be resistant to leptin, and this resistance contributes to the reduced reproductive function in these animals (Ramsay et al., 1998).

Although we did not find statistically significant differences between different Obese (leptin) gene genotypes and the number of born alive and stillborn piglets, but there is an evident tendency that sows with CC genotype, which have more fat, get more live and less stillborn piglets. Vanderhaeghe et al., (2010) in their study found that of all stillborn piglets, 10 % dies shortly before farrowing, 75 % during farrowing and the remaining 15 % immediately after farrowing. However the researchers have not found out how Obese (leptin) gene influences the viability of born piglets.

We detected statistically significant (P<0.05) difference of preservation of piglets between different Obese (leptin) gene genotypes. The sows with TT genotype, which had the least backfat thickness after weaning, preserved piglets better (P<0.05) compared to TC and CC genotypes. These results indicate that sows with TT genotype used energy intensively for milk production and feeding of piglets. The hypothesis, that lactation is a complex and unique physiological state characterized by behavioural and neuroendocrine adaptations, which shift the energy balance to milk components synthesis, is not new, however the milk production and composition are not affected by maternal leptinemia (Summer et al., 2009).

A variety of metabolic signals and other hormones modulates the body homeostasis by regulating the food intake and energy balance; however, sex hormone synthesis and estrus cycle are disturbed when energy resources are depleted (Gary et al., 2012). The highest number of sows (52.94 %) in our Obese (leptin) gene TT genotype group, which after weaning had long-term anoestrus, also confirmed these propositions.

Conclusions. 1. Sows with disordered reproduction had Obese (leptin) gene genotype frequencies: TT

genotype 63.53 %, TC genotype 30.59 % and CC genotype 5.88 %. The frequency of C allele was 0.21 and T allele 0.79.

2. Backfat thickness after weaning of sows with mutated C allele is bigger than that of sows which have T allele ($P<0.05$).

3. There was no statistically significant ($P>0.05$) difference between different genotypes and the number of piglets born alive and stillborn.

4. Sows with TT genotype preserved piglets till weaning best compared to TC and CC genotypes ($P<0.05$).

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