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## THE STUDY OF THE PREVALENCE AND IMPACT OF POLYMORPHISM OF THE C/T GENE ACTN3 (RS1815739) IN THE PHYSICAL DEVELOPMENT OF CHILDREN BORN WITH LOW BIRTH WEIGHT

**T. O. Levchuk-Vorontsova**

**Zaporizhzhia State Medical University, Zaporizhzhia, Ukraine**

Levchuk-Vorontsova T. O., MD, Assistant of the Department of Children Diseases, Zaporizhzhia State Medical University, Ukraine; 28A, Novgorodskaya street, Zaporizhzhia, 69076;  
Tel .: +380674352467, e-mail: [tatyana0702@gmail.com](mailto:tatyana0702@gmail.com); ID orcid 0000-0003-0557-6714

### **Abstract**

**The work aims at** studying the prevalence and influence of polymorphism of the C/T gene polymorphism of ACTN3 gene (rs1815739) on the physical development of children born with low body weight.

**Materials and methods of research.** To study the C/T polymorphism of the ACTN3 gene (rs1815739), 170 newborns were examined. Newborns were divided into 4 groups depending on birth weight: Group I - 50 premature babies weighing 1500-1999 grams ( $1776.26 \pm 20.06$  grams), Group II - 64 premature babies with birth weight 2000-2499 grams ( $2225.31 \pm 19.46$  grams), group III - 25 children with normal gestational age at birth, but with intrauterine growth retardation ( $2105.00 \pm 56.41$ ), group IV (control group) - 31 children with normal gestational age and birth weight more than 2500 grams ( $3009.03 \pm 73.04$  grams). Genotyping was performed by polymerase chain reaction according to the instructions

(Applied Biosystems, USA) using total DNA samples isolated from whole venous blood using a set of reagents "SNP-Screen" (manufactured by "Syntol") on the CFXte™ Real-Time PCR amplifier (Bio-Rad Laboratories, Inc., USA).

**Results.** In all studied children, the frequency of detection of C allele polymorphism of the C / T gene polymorphism of the ACTN3 gene (rs1815739) was 51.47%, T allele - 48.52%., The frequency of genotypes had the following distribution: CC-30.59%, TT-26.65%, CT-41.76%. In this case, in group I was the following distribution of alleles and genotypes: alleles C and T were detected in the ratio of 46.67% to 53.93%, genotypes SS-32.00%, TT-28.00%, ST-40, 00%, in group II alleles - C-51,56%, T - 48,44%, genotypes - CC 28,13%, TT-25,00%, CT - 46,88%, in group III - allele C was significantly more often registered than T (68.00% vs. 32.00%,  $p < 0.05$ ) and genotype TT - more often than CC and CT (52.00% vs. 16.00% and 32.00%). In IV (control) group there was the following distribution of the frequency of alleles and genotypes of gene polymorphism: allele C - 40.00%, allele T - 60.00%, genotype CC - 38.71%, genotype TT - 19.35%, genotype CT - 41.93%. The lowest monthly values of body weight and weight gain were associated with the TT genotype of the ACTN3 gene (rs1815739) in preterm infants and children with normal gestational age at birth, but with intrauterine growth retardation in the first half, and among children in the comparison group - in the second half, but the overall weight gain for 12 months had no genotypic dependence. Premature infants (observation groups I and II) with the TT genotype of the ACTN3 gene (rs1815739) had unevenly lower body lengths during the first year of life, while children with normal gestational age at birth, but with intrauterine growth retardation lagged behind in their growth in the first year, and children from the control group - in the second half. The total annual increase in body length for the first year of life in all children with the TT genotype was the lowest and amounted to in the first group -  $28.50 \pm 1.03$  cm, in the second -  $24.03 \pm 0.93$  cm, in the third -  $25.50 \pm 1.04$  cm, in IV -  $23.00 \pm 0.98$  cm. A probable positive correlation was found between the duration of breastfeeding and the monthly increase in body length in children with the TT genotype of the ACTN3 gene (rs1815739):  $\gamma = 0.58$ ,  $\gamma = 0.76$ ,  $\gamma = 0.61$  from the I, II and III observation groups, respectively.

**Conclusions.** It was found that the TT genotype of the ACTN3 gene (rs1815739) in children is associated with their uneven physical development in the first year of life and significantly lower rates of body length gain in 12 months, and long-term breastfeeding, especially premature babies and children with delayed fetal development, their normal growth.

**Key words:** children; physical development; body weight; length; polymorphism; genotype.

## **ВИВЧЕННЯ РОЗПОВСЮДЖЕНОСТІ ТА ВПЛИВУ ПОЛІМОРФІЗМУ С/Т ГЕНА АСТN3 (RS1815739) НА ФІЗИЧНИЙ РОЗВИТОК ДІТЕЙ, НАРОДЖЕНИХ З МАЛОЮ МАСОЮ ТІЛА**

**Т. О. Левчук-Воронцова**

**Запорізький державний медичний університет, Запоріжжя, Україна**

### **Резюме**

**Мета роботи:** Вивчити розповсюдженість та вплив поліморфізму гена АСТN3 (rs1815739) на фізичний розвиток дітей, народжених з малою масою тіла.

**Матеріали та методи дослідження.** Для вивчення поліморфізму С/Т гена АСТN3 (rs1815739) було обстежено 170 новонароджених дітей. Діти були розподілені на 4 групи в залежності від ваги при народженні: I група - 50 передчасно народжених дітей з вагою при народженні 1500-1999 грам ( $1776,26 \pm 20,06$  грам), II група - 64 передчасно народжених дітей з вагою при народженні 2000-2499 грам ( $2225,31 \pm 19,46$  грам), III група – 25 дітей з нормальним строком гестації при народженні, але з затримкою внутрьошноутробного розвитку ( $2105,00 \pm 56,41$ ), IV група (контрольна) – 31 дітей з нормальним строком гестації і вагою при народженні більше 2500 грам ( $3009,03 \pm 73,04$  грам). Генотипування проводилося методом полімеразної ланцюгової реакції згідно з інструкцією (Applied Biosystems, USA) з використанням зразків тотальної ДНК, виділеної з цільної венозної крові з використанням набору реагентів «SNP-Скрін» (виробник «Syntol») на ампліфікаторі CFX96TM Real-Time PCR Detection Systems («Bio-Rad laboratories, Inc.», USA).

**Результати.** У всіх досліджених дітей частота виявлення алеля С поліморфізму гена поліморфізму С/Т гена АСТN3 (rs1815739) склала 51,47%, алеля Т – 48,52 %, частота зустрічаємості генотипів мала наступний розподіл: СС-30,59%, ТТ- 26,65%, СТ-41,76%. При цьому, у I групі був наступний розподіл алелів та генотипів: алелі С та Т були виявлені в співвідношенні 46,67% до 53,93%, генотипи СС-32,00%, ТТ-28,00 %, СТ- 40,00%, у II групі алелі - С-51,56%, Т – 48,44%, генотипи - СС 28,13%, ТТ- 25,00%, СТ- 46,88%, у III групі - алель С достовірно частіше реєструвалась, ніж Т

(68,00% проти 32,00%,  $p < 0,05$ ) і генотип ТТ – частіше, ніж СС та СТ (52,00% проти 16,00% та 32,00%). В ІV (контрольній) групі був такий розподіл частоти алелів і генотипів поліморфізму гена: алель С- 40,00 %, алель Т- 60,00%, генотип СС- 38,71%, генотип ТТ – 19,35%, генотип СТ-41,93%. Найнижчі щомісячні показники маси тіла та її приросту асоціювались із генотипом ТТ гена АСТN3 (rs1815739) у передчасно народжених дітей та дітей зі ЗВУР у першому півріччі, а серед дітей групи порівняння – у другому півріччі, проте загальні показники приросту маси тіла за 12 місяців не мали генотипової залежності. Передчасно народжені діти (І та ІІ групи спостереження) з генотипом ТТ гена АСТN3 (rs1815739) мали нерівномірно менші показники довжини тіла впродовж першого року життя, в той час як діти зі ЗВУР відставали в своєму зростанні в першому, а діти з групи контролю – у другому півріччі. Загальний річний приріст довжини тіла за перший рік життя у всіх дітей з генотипом ТТ, був найнижчим та склав в І групі –  $28,50 \pm 1,03$  см, в ІІ –  $24,03 \pm 0,93$  см, в ІІІ –  $25,50 \pm 1,04$  см, в ІV –  $23,00 \pm 0,98$  см. Встановлена вірогідна позитивна кореляційна залежність між тривалістю природнього вигодовування та щомісячним приростом довжини тіла у дітей з генотипом ТТ гена АСТN3 (rs1815739):  $\gamma = 0,58$ ,  $\gamma = 0,76$ ,  $\gamma = 0,61$  з І, ІІ та ІІІ груп спостереження, відповідно.

**Висновок.** Встановлено, що генотип ТТ гена АСТN3 (rs1815739) у дітей асоціюється з їх нерівномірним фізичним розвитком на першому році життя та достовірно меншими показниками приросту довжини тіла за 12 місяців, а тривале природнє вигодовування, особливо передчасно народжених дітей та дітей із затримкою внутрішньоутробного розвитку, сприятиме їх нормальному зростанню.

**Ключові слова:** діти; фізичний розвиток; маса тіла; довжина; поліморфізм; генотип.

# ИЗУЧЕНИЕ РАСПРОСТРАНЕННОСТИ И ВЛИЯНИЯ ПОЛИМОРФИЗМА С/Т ГЕНА ACTN3 (RS1815739) НА ФИЗИЧЕСКОЕ РАЗВИТИЕ ДЕТЕЙ, РОДИВШИХСЯ С НИЗКОЙ МАССОЙ ТЕЛА

Т. О. Левчук-Воронцова

Запорожский государственный медицинский университет, Запорожье, Украина

## Резюме

**Цель работы:** Изучить распространенность и влияние полиморфизма гена ACTN3 (rs1815739) на физическое развитие детей, рожденных с низкой массой тела.

**Материалы и методы.** Для изучения полиморфизма С/Т гена ACTN3 (rs1815739) было обследовано 170 новорожденных детей. Дети были разделены на 4 группы в зависимости от веса при рождении: I группа - 50 недоношенных детей с весом при рождении 1500-1999 г ( $1776,26 \pm 20,06$  грамм), II группа - 64 недоношенных детей с весом при рождении 2000-2499 грамм ( $2225,31 \pm 19,46$  грамм), III группа - 25 детей с нормальным сроком гестации при рождении, но задержкой внутриутробного развития ( $2105,00 \pm 56,41$ ), IV группа (контрольная) - 31 детей с нормальным сроком гестации и весом при рождении более 2500 грамм ( $3009,03 \pm 73,04$  грамм). Генотипирование проводилось методом полимеразной цепной реакции согласно инструкции (Applied Biosystems, USA) с использованием образцов тотальной ДНК, выделенной из цельной венозной крови с использованием набора реагентов «SNP-Скрин» (производитель «Syntol») в амплификаторе CFX96TM Real-Time PCR Detection Systems («Bio-Rad laboratories, Inc.», USA).

**Результаты.** У всех исследованных детей частота встречаемости аллеля С полиморфизма гена полиморфизма С / Т гена ACTN3 (rs1815739) составила 51,47%, аллеля Т - 48,52%., частота встречаемости генотипов имела следующее распределение: СС-30,59%, ТТ- 26,65%, СТ-41,76%. При этом в первой группе был следующей распределение аллелей и генотипов: аллеля С и Т были обнаружены в соотношении 46,67% к 53,93%, генотипы СС-32,00%, ТТ-28,00%, СТ 40, 00%, во II группе аллели - С- 51,56%, Т - 48,44%, генотипы - СС 28,13%, ТТ-25,00%, СТ 46,88%, в III группе - аллель С достоверно чаще регистрировалась, чем Т (68,00% против 32,00%,  $p < 0,05$ ) и генотип ТТ - чаще, чем СС и СТ (52,00% против 16,00% и 32,00%). В IV (контрольной) группе был такой распределение частоты аллелей и генотипов полиморфизма гена: аллель С-

40,00%, аллель Т 60,00%, генотип СС 38,71%, генотип ТТ - 19,35%, генотип СТ - 41,93%. Самые низкие ежемесячные показатели массы тела и ее прироста ассоциировались с генотипом ТТ гена ACTN3 (rs1815739) у недоношенных детей и детей со ЗВУР в первом полугодии, а среди детей группы сравнения - во втором полугодии, однако общие показатели прироста массы тела за 12 месяцев генотиповой зависимости. Преждевременно рожденные дети (I и II группы наблюдения) с генотипом ТТ гена ACTN3 (rs1815739) имели неравномерно меньшие показатели длины тела в течение первого года жизни, в то время как дети со ЗВУР отставали в своем росте в первом, а дети из группы контроля - в втором полугодии. Общий годовой прирост длины тела за первый год жизни у всех детей с генотипом ТТ, был самым низким и составил в первой группе -  $28,50 \pm 1,03$  см, во II -  $24,03 \pm 0,93$  см, в III -  $25,50 \pm 1,04$  см, в IV -  $23,00 \pm 0,98$  см. Установлена достоверная положительная корреляционная зависимость между продолжительностью естественного вскармливания и ежемесячным приростом длины тела у детей с генотипом ТТ гена ACTN3 (rs1815739):  $\gamma = 0,58$ ,  $\gamma = 0,76$ ,  $\gamma = 0,61$  с I, II и III групп наблюдения соответственно.

**Выводы.** Установлено, что генотип ТТ гена ACTN3 (rs1815739) у детей ассоциируется с их неравномерным физическим развитием на первом году жизни и достоверно меньшими показателями прироста длины тела за 12 месяцев, а продолжительное естественное вскармливание, особенно недоношенных детей и детей с задержкой внутриутробного развития, будет способствовать их нормальному росту.

**Ключевые слова:** дети; физическое развитие; масса тела; длина; полиморфизм; генотип

**Introduction.** Impaired physical development of children born with low birth weight is an urgent problem around the world, because the optimal rate of increase in their weight, body length, head circumference ensure normal physical development during their life later on. If the child does not increase body length/height, does not gain weight in accordance with the established genetic program of development, then there is no adequate increase in brain mass, which can negatively affect intellectual development. Early child development is considered one of the most important stages of life, which determines health, well-being, ability to learn, and behavior throughout life [1]. Today, the World Health Organization (WHO) identifies physical development as one of the fundamental criteria in a comprehensive assessment of a child's health. Therefore, the factors influencing the rate of physical development of premature infants require further study [2].

According to the modern understanding of genetics, the peculiarities of physical development are due to DNA polymorphisms, of which there are more than 17 million. More than 214 genes are now known, the polymorphisms of which are associated with the development and manifestation of human physical qualities. ACTN3 is a gene that encodes  $\alpha$ -actinin-3, a protein expressed only in type II muscle fibers. It is well known that skeletal muscle is made up of individual muscle fibers, which are classified as slow-type fibers (type I fibers) and fast-type fibers (type II fibers). Type I fibers are more effective at using oxygen to produce ATP, which affects the ability to perform resilience and endurance exercises, such as marathons or cycling. The work of type II fibers requires a lot of energy, but the way to get it is under anaerobic conditions, which leads to low endurance of muscles, which in turn affects the quality of muscle tissue as a whole. A common polymorphism of this gene is R577X (rs1815739), where the replacement of C by T alleles results in the conversion of the arginine base (R) to a premature stop codon (X). According to the analysis, X-allelic homozygotes have a deficiency of the protein  $\alpha$ -actinin-3, which is associated with a lower percentage of rapid fiber contraction. In most studies, the ACTN3 genotype is associated with the phenotypes of speed and power, which affect the quality of muscle tissue. However, there are a small number of studies linking the effect of ACTN3 C / T gene polymorphism (rs1815739) on motor activity, density, and bone growth. [3, 4, 5]

**Materials and methods.** To study the C/T polymorphism of the ACTN3 gene (rs1815739), 170 newborns were examined. Newborns were divided into 4 groups depending on birth weight: Group I - 50 premature babies weighing 1500-1999 grams ( $1776.26 \pm 20.06$  grams), Group II - 64 premature babies with birth weight 2000-2499 grams ( $2225.31 \pm 19.46$  grams), group III - 25 children with normal gestational age at birth, but with intrauterine growth retardation ( $2105.00 \pm 56.41$ ), group IV (control group) - 31 children with normal gestational age and birth weight more than 2500 grams ( $3009.03 \pm 73.04$  grams). Genotyping was performed by polymerase chain reaction according to the instructions (Applied Biosystems, USA) using total DNA samples isolated from whole venous blood using a set of reagents "SNP-Screen" (manufactured by "Syntol") on the CFXte™ Real-Time PCR amplifier (Bio-Rad Laboratories, Inc., USA). This study was conducted in the Department of Molecular Genetic Research of the Training Medical and Laboratory Center at the Department of Microbiology, Zaporizhzhia State Medical University, Zaporizhzhia. The work was carried out within the framework of the research department of the Children Diseases Department of Zaporizhzhia State Medical University 114U001397.

The results of the distribution of allele frequencies and genotypes of the studied gene took into account the analysis of the genetic structure of the population according to Hardy-Weinberg's law. To compare the frequencies of alleles and genotypes in different groups a nonparametric statistical method "2 × 2 Table", the Chi-square (df = 1) was used. We also calculated the odds ratio (OR) using a four-point table with the calculation of the confidence interval (CI) by the Woolf method. The correlation between the indicators was performed by the Spearman method  $r_s$  or Gamma ( $\gamma$ ).

Non-parametric statistics methods of the licensed software package Statistica for Windows 13 were used to process the results of the study.

**The work aims at** studying the prevalence and influence of polymorphism of the C/T gene polymorphism of ACTN3 gene (rs1815739) on the physical development of children born with low body weight.

**Results.** Molecular genetic study of CT polymorphism of the ACTN3 gene (rs1815739) in all studied children showed that the frequency of detection of the C allele was 51.47%, the T allele - 48.52%, the frequency of occurrence of genotypes SS-30.59%, TT-26, 65%, CT-41.76%. In group I there was the following distribution of alleles and genotypes: alleles C and T were detected in the ratio of 46.67% to 53.93%, genotypes SS-32.00%, TT-28.00%, CT-40.00%, in group II alleles - C-51.56%, T – 48.44%, genotypes CC 28.13%, TT-25,00%, CT - 46,88%, in group III - allele C was significantly more often registered, than T (32.00% vs. 68.00%,  $p < 0.05$ ), genotypes - CC– 16.00%, TT-52.00%, CT-32.00%. The control group had the following distribution of the frequency of alleles and genotypes of gene polymorphism: allele C - 40.00%, allele T - 60.00%, genotype CC - 38.71%, genotype TT - 19.35%, genotype CT-41.93%. These data are clearly presented in fig. 1 and in table 1.

Analyzing the data in Table 1, we can conclude that the CC genotype is significantly less common in children of group III who had intrauterine growth retardation than among children of groups I, II, and IV ( $p < 0.05$ ). The TT genotype is significantly less common among children weighing more than 2500 g ( $p < 0.05$ ) than among children in other groups. Heterozygous type of CT was significantly more common among children of group II than among children of group I and children of group III - significantly less common than among children of groups I, II, and IV.

Further in our study, we decided to estimate body weight, body length, and weight gain and body length monthly in the first year of life, depending on the genotype of the polymorphism of the C/T polymorphism gene of the ACTN3 gene (rs1815739). These data are shown in tables 2-11.



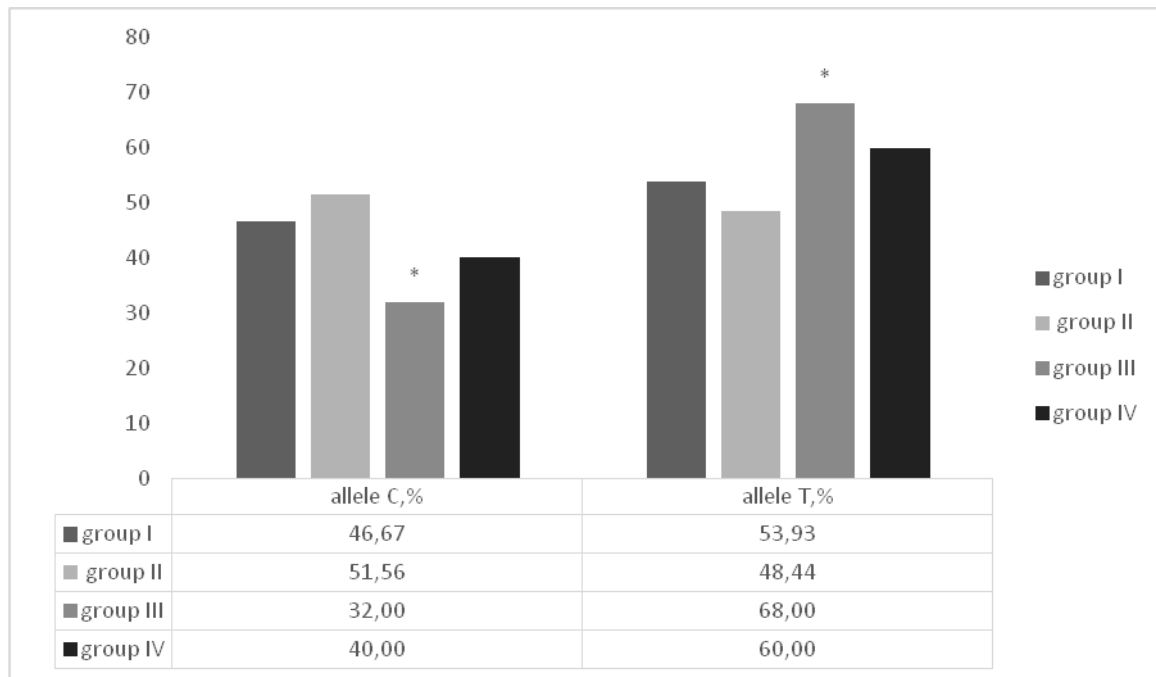


Fig.1. Frequency of alleles of polymorphism of the gene of polymorphism of C/T of the ACTN3 gene (rs1815739)

\*p<0.05

Table 1. Characterization of genotypes of the ACTN3 gene (rs1107946) polymorphism (abs./%)

Groups	n	Genotype abs/%		
		CC	TT	CT
Group I	50	16/32.00%	14/28.00%	20/40.00%
Group II	64	18/28.13%	16/25.00%	30/46.88%
p I-II		p<0.05	p<0.05	p<0.05
Group III	25	4/24.00%	13/44.00%	8/32.00%
p I-III		p>0.05	p<0.05	p>0.05
p II-III		p>0.05	p<0.05	p>0.05
Group IV	31	12/38.71%	6/19.35%	13/41.93%
p I- IV		p>0.05	p<0.05	p>0.05
p II- IV		p>0.05	p<0.05	p<0.05
p III- IV		p<0.05	p<0.05	p>0.05

Table 2. Dynamics of weight and weight gain in children of group I in the first year of life, depending on the genotype of the C/T polymorphism of the ACTN3 gene (rs1815739)

Age and increase per month	CC genotype	TT genotype	CT genotype
0 month (at birth)	1885.00±151.28	1740.00±130.89	1750.00±132.29
1st month	3033.33±199.56	2784.23±167.34	3135.24±206.78
Increase in 1 month	1225.08±168.61*	1065.02±206.37*,**	1356.43±156.23**
2nd month	4380.34±699.28	3678.45±622.42	4180.00±592.38
Increase in 2 month	950.45±367.25*	880.45±623.08*,**	896.45±53.91**
3rd month	5234.01±189.05*	4965.32±236.05*	5010.78±236.05
Increase in 3 month	1106.00±402.23*	756.91±356.12*,**	1045.23±345.45**
4th month	5620.40±602.01	5340.84±502.10	5735.34±467.23
Increase in 4 month	492.00±136.27	456.24±103.18	501.34±161.82
5th month	6360.67±737.11	5930.24±534.23	6245.91±430.26
Increase in 5 month	605.00±68.07	405.00±103.24	562.81±87.57
6th month	6530.00±389.87*	6235.83±289.34*,**	6635.50±367.20**
Increase in 6 month	570.00±87.47	378.23±102.34	510.30±99.23
7th month	6795.00±190.53	6500.67±184.94	6812.31±170.28
Increase in 7 month	222.00±76.94	150.32±90.43	231.08±69.34
8th month	7585.00±771.56	6925.12±345.12	7430.80±556.17
Increase in 8 month	430.00±28.28	217.20±78.12	405.34±61.38
9th month	7835.00±305.51	7325.12±207.18	7925.50±290.34
Increase in 9 month	362.50±53.03	324.45±62.87	330.12±63.81
10th month	8205.33±432.47	7785.91±322.71	8305.50±398.98
Increase in 10 month	350.00±45.64	205.35±96.91	300.01±51.98
11th month	8490.50±538.23	8230.50±431.81	8360.45±502.87
Increase in 11 month	162.50±47.87	150.54±76.23	195.50±59.94
12 month	8950.00±1184.62	8435.50±352.23	8755.98±962.35
Increase in 12 month	97.50±31.67	85.50±41.13	105.50±53.23
Weight gain overall 12 months	7435.00±165.87	6755.00±334.98	7356.50±198.56

\* P <0.05 significant difference between children of group I with genotype CC and TT

\*\* P <0.05 significant difference between children of group I with genotype CT and TT.

Children of group I with the TT genotype had a significantly lower weight at the age of 3.6 months compared with children with the SS genotype (p <0.05) and at the age of 6 months - with the CT genotype (p <0.05). Regarding the monthly weight gain, it was found that in this observation group, children with the TT genotype had a significantly lower weight gain at 1, 2, 3, 6 months than children with the CC and CT genotypes (p <0.05). But at 12 months of age, both mean body weight and total annual gain did not depend on the genotype of the ACTN3 gene polymorphism (rs1815739).

Among children of group II, significantly lower weight was found among children with TT genotype at the age of 1 and 2 months compared with children with CC genotype ( $p < 0.05$ ). No significant difference with heterozygotes was found (table 3).

Table 3. Dynamics of weight and weight gain in children of group II in the first year of life, depending on the C/T polymorphism of the ACTN3 gene (rs1815739)

Age and increase per month	CC genotype	TT genotype	CT genotype
0 month (at birth)	2210.40±181.59	2225.50±151.92	2230.60±146.06
1st month	3650.02±234.23*	3150.00±212.13*	3450.08±251.20
Increase in 1 month	1330.00±190.20	1130.00±160.76	1410.25±200.82
2nd month	4987.67±518.07*	4616.67±417.33*	4863.67±534.37
Increase in 2 month	1083.33±329.64	983.56±221.54	1057.23±345.44
3rd month	5432.06±465.43	5125.00±365.47	5253.43±474.33
Increase in 3 month	501.25±103.45	422.50±208.38	462.33±231.45
4th month	5956.11±523.08	5350.00±414.34	5750.23±516.73
Increase in 4 month	720.34±251.09	662.51±231.07	689.49±211.12
5th month	6275.39±245.92	5934.34±204.11	6175.59±265.16
Increase in 5 month	389.20±93.21	350.00±84.52	402.23±76.54
6th month	6553.00±267.31	6350.00±342.26	6710.30±300.18
Increase in 6 month	352.46±102.83	292.86±142.68	286.18±155.85
7th month	7123.49±242.14	6950.00±342.26	7215.01±290.61
Increase in 7 month	398.00±129.58	400.00±209.31	420.01±229.45
8th month	7532.10±143.85	7330.00±263.63	7623.82±143.27
Increase in 8 month	230.87±65.34	120.00±57.01	255.67±58.88
9th month	7765.00±273.86	7450.00±263.56	7672.02±232.13
Increase in 9 month	211.26±69.34	208.33±73.60	230.33±59.80
10th month	8156.73±234.52	7666.67±273.25	7866.67±205.31
Increase in 10 month	178.44±58.10	166.67±93.09	156.35±67.23
11th month	8542.39±306.17	8441.67±352.73	8601.70±302.22
Increase in 11 month	190.30±31.82	165.00±41.83	205.33±45.33
12 month	9134.45±298.45	9016.67±365.61	9221.34±321.11
Increase in 12 month	103±45.32	91.67±58.45	120±36.82
Weight gain overall 12 months	7345.00±152.12	6967.5±212.89	7348.00±356.67

\*  $P < 0.05$  significant difference between children of group II with genotype CC and TT

\*\*  $P < 0.05$  significant difference between children of group II with genotype CT and TT

Children from the third observation group, who were born with intrauterine growth retardation and genotype TT, had a significantly lower birth weight compared with children with genotype CC and CT ( $p < 0.05$ ). Also, children with the TT genotype had a significantly lower weight at the age of 1, 2, and 3 months compared with children with the dominant CC genotype ( $p < 0.05$ ). No significant difference with heterozygotes was found (table 4). At the same time, weight gain among children of group III depending on CT polymorphism of the

ACTN3 gene (rs1815739) was significantly lower in children with minor genotype compared to children with major genotype at 3, 5, and 8 months ( $p < 0.05$ ). A significant difference between children with the TT and CT genotype was found only at the age of 5 months ( $p < 0.05$ ).

Table 4. Dynamics of weight and body weight gain in children of group III in the first year of life, depending on the C/T polymorphism of the ACTN3 gene (rs1815739)

Age and increase per month	CC genotype	TT genotype	CT genotype
0 month (at birth)	2310.00±143.03*	1860.00±353.71**	2070.00±156.34**
1st month	3130.00 ±506.38*	2890.00±276.08*	3350.00±395.29
Increase in 1 month	890.00±433.73	525.00±151.71	1000.00±360.41
2nd month	4130.86±711.68*	3760.00 ±415.93*	4247.5±289.87
Increase in 2 month	1070.00±422.20	580.00±83.67	1202.50±468.40
3rd month	4970.00±223.50*	4300±380.79*	5242.86±430.53
Increase in 3 month	1000.00±223.50*	400.00±236.1*	915.00±247.45
4th month	5325.00±817.91	5750.00±516.85	6000.00±424.26
Increase in 4 month	600.00±339.75	550.00±178.89	966.67±202.07
5th month	6000.00±1378.22	6500.00±368.21	6470.00±1266.33
Increase in 5 month	670.00±167.09*	450.00±74.36*,**	682.50±170.49**
6th month	6650.00±1240.03	7000.00±377.52	7398.33±917.39
Increase in 6 month	550.00±154.97	430±127.95	650.00±150.00
7th month	7400.00±1343.50	7400.00±325.19	7604.00±766.05
Increase in 7 month	400.00±160.56	400±157.89	440.00±152.49
8th month	7850.00±1325.03	7850.00±724.22	8100.00±787.40
Increase in 8 month	500.00±72.23*	300±57.01*	460.00±69.797
9th month	8400.00±1398.03	8347.50± 406.10	8700.00±921.61
Increase in 9 month	420.00±124.50	340±58.99	512.00±103.68
10th month	8950.00±1501.77	8737.50±300.83	9300.00±1035.52
Increase in 10 month	300.00±65.19	250±111.22	380.00±88.531
11th month	9500.00±1123.56	9460.00±188.41	9800.00±1143.68
Increase in 11 month	250.00±86.41	200±108.39	230.00±79.34
12 month	10100.00±913.05	9160.00±173.26	10000.00±1171.75
Increase in 12 month	225.00±52.44	200±109.75	220.00± 35.09
Weight gain overall 12 months	7155.00±555.00	6943.33±365.49	7246.25±301.75

\*  $P < 0.05$  significant difference between children of group III with genotype CC and TT

\*\*  $P < 0.05$  significant difference between children of group III with genotype CT and TT

Among children of control group IV, the effect of C/T polymorphism of the ACTN3 gene (rs1815739) on weight and its monthly increase was detected in the second half of the year, namely, children with homozygous recessive TT genotype had significantly lower weight and weight gain compared to children with CC genotype and at the age of 10, 11 and

12 months ( $p < 0.05$ ). There was no significant difference between weight and monthly gain among children with CC and CT genotypes (Table 5).

Table 5. Dynamics of weight and body weight gain in children of group IV in the first year of life, depending on the C/T polymorphism of the ACTN3 gene (rs1815739)

Age and increase per month	CC genotype	TT genotype	CT genotype
0 month (at birth)	2945.00±417.75	3195.00±512.77	2790.00±334.47
1st month	3725.00±198.34	3565.06± 156.43	3680.54±205.12
Increase in 1 month	987.54±48.13	950.26±52.01	1001.03±56.50
2nd month	4650.06±134.56	4430.00±127.86	4675.93±131.05
Increase in 2 month	765.98±67.23	754.03±56.06	788.01±63.09
3rd month	5425.73±187.45	5260.98±204.12	5335.06±198.34
Increase in 3 month	664.83±70.01	634.72±65.23	652.01±91
4th month	6100.65±187.23	5985.12±186.45	6050.56±178.23
Increase in 4 month	599.34±56.23	584.98±34.09	607.98±57.12
5th month	6720.04±198.56	6550.34±178.56	6660.34±182.36
Increase in 5 month	510.11±45.78	487.12±51.12	513.05±43.12
6th month	7345.23±220.62	7125.78±189.34	7230.34±91.97
Increase in 6 month	420.16±71.23	398.12±54.98	412.34±81.01
7th month	8125.20±234.56	7890.65±256.10	8090.41±54
Increase in 7 month	390.12±67.23	325.67±39	376.24±28.65
8th month	8765.93±233.45	8345.24±212	8450.25±234.56
Increase in 8 month	467.24±63.29	367.91±78.34	478.29±39.23
9th month	9010.32±245.73	8765.12±203.34	8995.23±225.65
Increase in 9 month	427.23±88.09	350.73±76.22	456.23±83
10th month	9355.27±301.48*	9020.09±201.38*,**	9650.87±290.29**
Increase in 10 month	389.12±131.39*	290.13±102.34*,**	406.39±102.41**
11th month	10010.34±387.23*	9450.98±302.83*,**	9990.45±342.71**
Increase in 11 month	561.23±152.56*	351.03±87.34*,**	490.34±122.34**
12 month	10705.43±257.56*	9955.98±189.90*,**	10565.65±234.65**
Increase in 12 month	243.89±98.45*	150.98±34.43*,**	234.51±87.54**
Weight gain overall 12 months	7896.50±214.76	7345.00±256.89	7689.00±234.62

\*  $P < 0.05$  significant difference between children of group IV with genotype CC and TT

\*\*  $P < 0.05$  significant difference between children of group IV with genotype CT and TT

Based on the data in table 6, we can conclude that body length was significantly shorter in children with the TT genotype compared with the CC genotype at birth and 1 month of age. With further growth of the child, both the indicators of the dynamics of body length and its monthly growth were lower in children with the TT genotype, compared with the other two genotypes, at the age of 3, 4, 5, 6, 7, and 8 months ( $p < 0, 05$ ).

Table 6. Dynamics of body length and its monthly growth in children of group I in the first year of life, depending on the C/T polymorphism of the ACTN3 gene (rs1815739)

Age and increase per month	CC genotype	TT genotype	CT genotype
0 month (at birth)	42.90±1.02*	41.75±2.25*	41.10±1.75
1st month	45.50±1.22*	42.90±2.49*	43.40±1.52
Increase in 1 month	3.10±0.22	3.06±1.37	2.70±0.45
2nd month	49.40±17.63	50.67±3.72	46.60±1.95
Increase in 2 month	3.40±0.96	2.58±0.49	3.60±1.14
3rd month	53.60±3.77*	48.20±1.52*	49.60±1.52
Increase in 3 month	3.40±0.55	2.80±0.84	3.70±0.71
4th month	54.20±1.30*	50.40±2.70*,**	53.40±1.52**
Increase in 4 month	3.80±0.45*	1.60±0.89*,**	3.80±0.44**
5th month	57.60±0.89*	53.25±1.5*,**	56.80±1.48**
Increase in 5 month	3.00±0.71*	1.70±0.45*	2.80±0.84
6th month	59.83±1.83*	56.40±1.14*,**	58.83±1.73**
Increase in 6 month	2.83±0.75*	1.60±0.89*	2.50±1.05
7th month	65.17±1.17*	61.67±1.16*,**	62.60±1.95**
Increase in 7 month	3.00±0.71*	1.30±0.84*,**	3.33±0.71**
8th month	66.50±1.52*	62.50±2.38*,**	65.20±1.48**
Increase in 8 month	2.67±0.82	1.80±0.84	2.40±0.55
9th month	67.67±1.21	66.40±2.79	67.60±1.14
Increase in 9 month	2.67±0.52	2.00±0.71	2.60±0.55
10th month	69.67±0.81	70.50±0.71	69.40±0.55
Increase in 10 month	2.00±0.89	1.40±0.55	1.60±0.89
11th month	71.50±0.84	70.80±1.64	71.00±0.71
Increase in 11 month	2.00±0.63	1.20±0.84	1.80±0.45
12 month	73.00±1.26	72.75±2.36	72.80±1.30
Increase in 12 month	1.83±0.75	1.75±0.50	1.80±0.84
The average increase in body length over 12 months	31.25±0.96*	28.50±1.03*,**	30.50±0.89**

\* P <0.05 significant difference between children of group I with genotype CC and TT

\*\* P <0.05 significant difference between children of group I with genotype CT and TT

Regarding the characteristics of body length among children of group II, it was found that children with the TT genotype had significantly lower rates compared with children with the CC genotype at the age of 0, 1, 6, 9, and 12 months (p <0.05).

The effect of ACTN3 gene polymorphism (rs1815739) on body length and growth in children born with intrauterine growth retardation depending on genotype was detected mainly in the first half of the year. Thus, children with TT genotype had shorter body length than children with CC genotype at the age of 1, 2, and 3 months, CT and CT genotypes at 4.5 and 6 months (p <0.05), and shorter length gain body was detected at the age of 1, 2, 3 and 4 months in children with genotypes TT and CC, at the age of 5 months - with genotypes TT and CT and CC (p <0,05) (table 8).

Table 7. Dynamics of body length and its monthly growth in children of group II in the first year of life, depending on the C/T polymorphism of the ACTN3 gene (rs1815739)

Age and increase per month	CC genotype	TT genotype	CT genotype
0 month (at birth)	47.50±3.67*	43.75±1.71*	45.50±1.05
1st month	50.83±2.79*	48.75±1.71*	49.35±0.75
Increase in 1 month	5.00±1.41	4.25±1.26	3.33±0.82
2nd month	54.10±1.67	52.00±3.16	54.17±1.47
Increase in 2 month	5.00±1.45	3.00±0.89	3.33±1.21
3rd month	58.20±1.64	55.17±2.64	57.17±1.72
Increase in 3 month	7.00±5.66	2.67±0.82	2.83±0.75
4th month	59.80±1.30	57.33±2.50	59.17±2.23
Increase in 4 month	2.45±1.50	2.83±0.75	2.00±0.63
5th month	62.50±1.91	59.33±2.58	62.00±1.89
Increase in 5 month	3.00±0.75	2.25±0.61	2.83±0.75
6th month	65.67±1.53*	62.08±2.54*	63.50±2.26
Increase in 6 month	1.76±0.93	2.08±0.49	1.67±0.82
7th month	66.60±3.58	63.00±1.41	65.50±2.43
Increase in 7 month	2.00±0.76	2.17±0.52	2.00±0.89
8th month	68.83±2.57*	64.83±1.47*,**	67.83±2.26**
Increase in 8 month	2.00±0.68	2.00±1.26	2.33±0.41
9th month	69.42±1.96*	66.00±1.26*	67.75±1.89
Increase in 9 month	1.15±0.50	1.17±0.75	1.58±0.38
10th month	70.58±1.86*	68.00±1.79*	67.50±3.54
Increase in 10 month	2.35±0.45	2.00±0.89	1.17±0.26
11th month	73.00±1.96*	69.50±1.87*,**	71.83±1.72**
Increase in 11 month	1.76±0.48	1.33±0.52	1.53±0.32
12 month	75.50±2.89*	71.33±1.37*	73.17±1.60
Increase in 12 month	3.67±1.00*	1.63±0.89*	1.75±1.05
The average increase in body length over 12 months	27.75±0.95*	24.03±0.93*	26.50±0.89

\* P <0.05 significant difference between children of group II with genotype CC and TT

\*\* P <0.05 significant difference between children of group II with genotype CT and TT

Table 8. Dynamics of body length and its monthly growth in children of group III in the first year of life, depending on the C/T polymorphism of the ACTN3 gene (rs1815739)

Age and increase per month	CC genotype	TT genotype	CT genotype
0 month (at birth)	47.43±1.62	45.00±1.41	47.25±1.83
1st month	50.71±2.48*	45.33±2.52*	48.25±4.35
Increase in 1 month	3.38±2.40*	1.50±0.71*	2.7±0.67
2nd month	55.25±1.89*	48.00±3.61*	54.50±2.06
Increase in 2 month	5.70±1.92*	2.33±1.53*	4.80±1.30
3rd month	56.25±3.03*	50.33±4.16*	58.50±1.61
Increase in 3 month	2.75±0.50*	1.63±0.48*	3.60±2.22
4th month	59.25±1.47*	53.25±5.32*,**	60.4±2.07*,**
Increase in 4 month	3.5±1.95*	1.88±0.25*	2.60±0.82
5th month	62.17±3.66*	54.13±5.45*,**	64.50±1.29*,**
Increase in 5 month	2.92±1.90*	0.8±0.57*,**	3.75±0.96*,**
6th month	63.00±2.45*	55.75±5.74*,**	66.40±2.41*,**
Increase in 6 month	2.30±1.10	1.63±0.48	2.60±0.89
7th month	66.38±1.49	59.00±7.87	65.67±1.53
Increase in 7 month	2.13±1.65	1.25±0.65	2.00±1.00
8th month	68.00±1.83	63.00±6.56	68.00±0.71
Increase in 8 month	2.00±0.82	1.25±1.04	2.38±0.75
9th month	68.80±2.46	65.00±5.57	69.70±0.84
Increase in 9 month	2.20±1.35	1.63±1.11	1.63±0.45
10th month	70.38±1.70	65.5±5.07	71.33±2.52
Increase in 10 month	2.50±1.29	1.75±0.96	1.7±0.84
11th month	71.50±1.63	66.88±5.36	71.88±1.65
Increase in 11 month	2.60±1.14	1.33±0.75	1.63±0.48
12 month	72.75±2.22	69.75±4.57	73.75±0.30
Increase in 12 month	1.60±0.55	2.38±1.11	2.00±1.41
The average increase in body length over 12 months	27.88±0.64*	25.50±1.04*	26.57±1.13

\* P <0.05 significant difference between children of group III with genotype CC and TT

\*\* P <0.05 significant difference between children of group III with genotype CT and TT



Table 9. Dynamics of body length and its monthly growth in children of group IV in the first year of life, depending on the polymorphism of the C/T gene ACTN3 (rs1815739)

Age and increase per month	CC genotype	TT genotype	CT genotype
0 month (at birth)	53.45 ± 0.78	52.53 ± 0.68	52.07 ± 0.75
1st month	54.75 ± 1.75	53.05 ± 1.33	53.05 ± 1.66
Increase in 1 month	2.24 ± 0.92	2.04 ± 1.00	2.50 ± 1.05
2nd month	58.50 ± 1.50	55.50 ± 1.36	57.50 ± 0.98
Increase in 2 month	4.75 ± 1.07	4.35 ± 0.87	4.50 ± 1.05
3rd month	61.30 ± 0.76	60.07 ± 1.01	62.5 ± 1.33
Increase in 3 month	2.35 ± 0.85	1.85 ± 1.33	2.05 ± 0.68
4th month	63.60 ± 1.25	61.55 ± 1.50	62.63 ± 1.24
Increase in 4 month	2.5 ± 0.50	2.25 ± 0.67	2.01 ± 0.89
5th month	65.60 ± 1.45	64.55 ± 1.05	65.05 ± 1.11
Increase in 5 month	1.5 ± 0.51	1.5 ± 0.51	1.5 ± 0.51
6th month	67.00 ± 0.79	66.05 ± 1.25	64.31 ± 0.85
Increase in 6 month	2.50 ± 0.45	2.0 ± 0.65	2.0 ± 1.00
7th month	68.56 ± 0.67	67.50 ± 0.95	66.05 ± 1.01
Increase in 7 month	2.0 ± 0.5	2.05 ± 0.45	1.75 ± 0.45
8th month	69.05 ± 1.75	69.45 ± 1.45	68.65 ± 1.05
Increase in 8 month	1.35 ± 0.75	1.05 ± 0.56	1.75 ± 0.45
9th month	70.5 ± 0.97	70.1 ± 1.33	70.3 ± 0.95
Increase in 9 month	3.0 ± 1.0	2.50 ± 1.05	2.75 ± 1.33
10th month	73.45 ± 1.85*	71.42 ± 1.80*,**	74.02 ± 1.45**
Increase in 10 month	3.0 ± 0.88*	2.0 ± 0.45*,**	2.33 ± 0.75**
11th month	74.5 ± 2.65*	72.05 ± 1.45*,**	75.03 ± 2.55**
Increase in 11 month	1.75 ± 0.95*	1.05 ± 0.45*,**	1.50 ± 0.53**
12 month	76.0 ± 0.95*	72.50 ± 0.56*,**	75.00 ± 0.85**
Increase in 12 month	3.05 ± 1.05*	1.5 ± 1.04*,**	2.75 ± 0.98**
The average increase in body length over 12 months	25.67±0.79*	23.00±0.98*,**	26.5±0.87**

\* P <0.05 significant difference between children of group VI with genotype CC and TT

\*\* P <0.05 significant difference between children of group VI with genotype CT and TT

Based on the data in table 10, the indicators of body length and growth in children with control group IV were significantly lower among children with the TT genotype than with other genotypes, at the age of 10, 11, 12 months and overall indicators of body length and growth in the first year of life.

Table 10. The state of feeding in the first 6 months

Groups	Natural feeding	Artificial feeding	Mixed feeding
Group I	13.95%	69.77%	16.27%
p I-II	p>0.05	p>0.05	p<0.05
Group II	33.87%	53.22%	12.90%
Group III	23.53%	58.82%	17.65%
p I-III	p>0.05	p>0.05	p<0.05
p II-III	p>0.05	p>0.05	p<0.05
Group IV	54.83%	35.48%	22.58%
p I- IV	p<0.05	p<0.05	p<0.05
p II- IV	p>0.05	p>0.05	p<0.05
p III- IV	p>0.05	p>0.05	p<0.05

Further analysis of the type of breastfeeding in the first year of life showed that in the first group of observations, 13.95% of children were on natural feeding, 69.77% - on mixed, 16.27% - on artificial. In group II - 33.87% of children were on natural feeding, 53.22% - on mixed, 12.90% - on artificial. In group III - 23.53% of children were breastfed, 58.82% - on mixed, 17.65% - on artificial, in group IV - 54.83% of children were on natural feeding, 35.48% - on mixed, 22.58% - on artificial.

However, a correlation between the type of feeding and the increase in body weight and length, or their monthly growth rates, taking into account the genotypes of the ACTN3 gene (rs1815739) was not registered. However, a probable positive correlation was found between the duration of breastfeeding and the monthly increase in body length in children with the TT genotype of the ACTN3 gene (rs1815739):  $\gamma = 0.58$ ,  $\gamma = 0.76$ ,  $\gamma = 0.61$  with I, II, and III observation groups, respectively.

**Discussion.** At the beginning of the discussion, we note that in foreign sources, to show that the polymorphism of the ACTN3 gene replaces arginine (R) at position 577 in the stop-codon (X), alleles are also denoted as R and X, while in our study as C and T. The homozygous genotype SS or RR is called major, and the homozygous genotype TT or XX - minor.

We also compared the results of our study with global population studies. The frequency of detection of recessive T allele and homozygous TT genotype in children from the study is much higher than in the world population. The frequency of the C allele is lower than the world data, and the genotypes of ST and CC, compared with world data, have slightly lower values. The frequency of occurrence of C and T alleles in our study is close to the data of the United States of America (USA) and South Asia. The frequency of CC

genotype of children in our study is close to European data, TT genotype - to US data, CT genotype - to South Asian data (Fig. 3) [6].

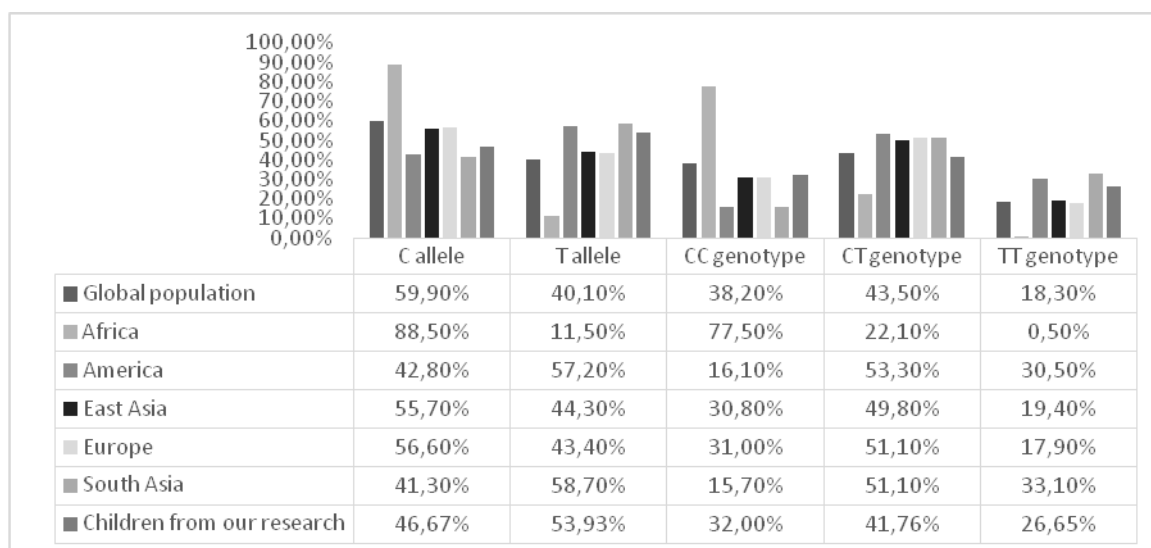


Fig. 3. Comparison of the frequency of alleles and genotypes of polymorphism of the ACTN3 gene (rs1815739) with world data

Zaccagni L. and co-authors studied the relationship between anthropometric parameters and genetic factors in Croatian sprinters. The study involved 104 Croatian sprinters: 36 women (mean age  $37.0 \pm 14.8$  years) and 68 men (mean age  $33.2 \pm 12.8$  years). As for the ACTN3 polymorphism, the most common genotype was RX (53 subjects, 51%), followed by RR (32 subjects, 31%) and XX (19 subjects, 18%). The frequency of the R allele was 56% and X was 44%, with no significant difference by sex. Anthropometric data included determination of the length of the lower limb and lower leg, the length of the foot. The most significant predictors of higher running speed were foot size and leg length. However, this study did not examine the relationship between anthropometric data and genotypes [7].

In a study by Ana Paula Renno Sierra and co-authors, the C / T polymorphism of the ACTN3 gene (rs1815739) was studied among amateur runners. It was found that athletes with genotype XX had less body weight ( $70.1 \pm 8.5$ ) than athletes with genotype RR and RX ( $71.6 \pm 8.8$  and  $77.4 \pm 10.0$ ), with the latter had less training experience than runners with genotype XX ( $7.15 \pm 5.1$  years vs.  $6.14 \pm 4.3$  and  $5.6 \pm 4.7$ ) [8].

Güereca-Arvizuo and colleagues found that both male and female athletes with the RR genotype had a mesomorphic somatotype, whereas men with the XX genotype had an

ectomorphic somatotype. Mesomorphic type or normothermic type is characterized by moderately rapid muscle gain, ectomorphic or asthenic type of body structure, characterized by underdeveloped muscles, slim physique [9].

Natalia Potocka and colleagues in her study did not find such a pattern. Analyzing the relationship between genotypes and somatotypes, the authors observed differences between men and women. Most women with RR and RX genotypes had endomorphic body type, while genotype XX was most often represented by women with ectomorphic body type. In contrast, in the male group, all genotypes were most represented in individuals with mesomorphic body type. Comparison of male endomorphs with ectomorphs revealed more individuals with the RR genotype (containing  $\alpha$ -actinin-3 in muscle) in the ectomorph group [10].

We did not determine the somatotype in our study, but we observed this trend, children with the TT (XX) genotype had less weight and weight gain than children with the CC (RR) genotype.

There are also scientific studies that determine the association of ACTN3 gene polymorphism with the risk of sports injuries. Qi et al. and Massidda et al. studied the relationship between exercise intensity and non-contact muscle damage. From these studies, it became known about the protective effect of the R allele and/or RR genotype from damage, and in the XX genotype athletes had almost three times more injuries than carriers of the R allele [11,12]. Based on these data, we can assume that the RR genotype affects human physical activity during life, ie children with the RR genotype will be more active, which in turn leads to better muscle mass gain, and children with the XX genotype will be less active, which in turn affects muscle mass gain and body weight in general.

In addition, it has been established that the ACTN3 XX genotype is associated with less muscle volume, reduced strength, strength, and endurance [13]. Besides, Arthur Cunha and co-authors studied genetic variants of ACTN3 and their effect on craniofacial skeletal bone growth and malocclusion. Thus, it was found that in the examined subjects, the presence of malocclusion class II and impaired bone growth of the facial skeleton was associated with a statistically significant higher incidence of minor homozygous genotype XX (or TT) of the ACTN3 gene (rs1815739) [5].

### **Conclusions**

1. Molecular genetic study of CT polymorphism of the ACTN3 gene (rs1815739) in all examined children showed that the frequency of occurrence of allele C was 51.47%, allele T - 48.52%, the frequency of genotypes SS-30.59%, TT- 26.65%, ST-41.76%, but only in children with intrauterine growth retardation significantly more often the T allele (68.00%)

than the C allele (32.00%) and the TT genotype (52.00%) than genotypes CC (16.00%) and CT (32.00%),  $p < 0.05$ .

2. The lowest monthly values of body weight and weight gain were associated with the TT genotype of the ACTN3 gene (rs1815739) in premature infants and children with intrauterine growth retardation in the first half of life, and among children in the comparison group - in the second half, but the overall rates of body weight gain 12 months had no genotypic dependence.

3. Premature infants (groups I and II of observation) with the TT genotype of the ACTN3 gene (rs1815739) had unevenly lower body length during the first year of life, while children with intrauterine growth retardation were behind in their growth in the first half of the year, and children from the control group - in the second half of the year. The total annual increase in body length for the first year of life in all children with the TT genotype was the lowest and amounted to in the first group -  $28.50 \pm 1.03$  cm, in the second -  $24.03 \pm 0.93$  cm, in the third -  $25.50 \pm 1.04$  cm, in IV -  $23.00 \pm 0.98$  cm.

4. A positive correlation was found between the duration of breastfeeding and monthly increase in body length in premature infants and children with intrauterine growth retardation with the TT genotype of the ACTN3 gene (rs1815739):  $\gamma = 0.58$ ,  $\gamma = 0.76$ ,  $\gamma = 0.61$ , therefore, for their normal growth, long-term natural feeding should be recommended, especially for this contingent of subjects.

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**Conflict of interests:** none.

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