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BOROZENETS V.V.[1]✉, BABALIAN V.O.[2], FEDOTAO.M.[1]
[1] *V.N. Karazin Kharkiv National University,*
Ukraine, 61058, Kharkiv, Svoboda sq., 6, e-mail: amsfedota@gmail.com
[2] *Kharkiv Medical Academy of Postgraduate Education,*
Ukraine, 61176, Kharkiv, Amosova str., 58, e-mail: babalyanvladimir@gmail.com
✉ *Vikaborozenets1984@gmail.com, (097) 629-52-37*

GENETIC ASPECTS OF LACTASE PERSISTENCE IN DIFFERENT ETHNIC GROUPS

Aim. The aim of this study was evaluation of the genetic aspects of lactase persistence (LP) in persons from different ethnic groups. ***Methods***. Genealogical and medical information was collected about Ukrainian, Indian, Nigerian, Israel, Egypt, Palestine, Turkey, Jordan students (n=361) and their first degree relatives (n=413). Statistical analysis was carried out by Shapiro-Wilk test, χ^2, Spearman correlation. ***Results***. The phenotype of LP was found in 69.9 % of Ukrainians, lactose intolerance - in 7.2 %. The highest LP is observed in 95.2 % of Nigerians, the lowest - Palestinians, 51.9 %. Analysis in all ethnic groups showed that the number of LP people is less among parents than among students ($r = - 0.529$, $p < 0.05$). The LP score is 72.7 - 95.2 % among Nigerian, Israeli, Egyptian, Turkish, Indian students, and 60 - 76.5 % among their parents. The LP phenotype is 50 – 68.8 % and 53.9 – 70.9 % among Ukrainian, Palestinian Jordanian students and their parents. It is likely that adult-type hypolactasia may appear after 20 years and older, indicating a high degree of heterozygosity. The highest number of persons with first exogamy degree is 82.6-85.5 % among Turks, Palestinians, Egyptians and the lowest value of LP phenotype is observed in these groups - 51.9 - 72.3 %, ($r = – 0.786$, $p<0.05$). A positive correlation is determined between the traits of hypolactasia and first degree of parents exogamy ($r = 0.905$, $p<0.05$). The changes in metabolic status with age could be a predictor for multifactorial pathology. ***Conclusions***. Adult hypolactasia is an age-dependent trait. Relations between the parameters of LP and the origin were established.

Keywords: lactase persistence, lactose intolerance, exogamy, genotypes.

Continued production of lactase throughout adult life - lactase persistence(LP) is found at moderate to high frequencies in Europeans and some African, Middle Eastern and Southern Asian populations [1,2].Many intolerant individuals could tolerate low levels of lactose in their daily diet [3].According to the National Library of Medicine data, lactose intolerance in adulthood is most prevalent in people of East Asian descent, affecting more than 90 percent of adults in some of these communities[4].Lactose intolerance is also very common in people of West African, Arab, Jewish, Greek, and Italian descent.

Currently, it is believed that in different ethnic groups the trait of LP is associated with at least five independent single nucleotide variants in a regulatory region about 14 kb upstream of the lactase gene [-13910*T (rs4988235), -13907*G (rs41525747), -13915*G (rs41380347), -14009*G (rs869051967) and -14010*C (rs145946881)] [5].

The aim of this study was evaluation of the genetic aspects of lactase tolerance in persons from different ethnic groups.

Materials and methods

Genealogical and medical information was collected about Ukrainian, Indian, Nigeria, Middle East Countries (Israel, Egypt, Palestine, Turkey, Jordan) students. The number of people participating in the study was 774, male – 370, female – 404, ages from 14 to 69 years. The data were divided into two groups: about students aged 17 to 30 years old and their parents aged 38 to 67 years old. The students average age was 22.2 ± 1.09 years, parents - 49.2 ± 2.74 years. Each group was classified according to ethnicity, age, gender, degree of parents exogamy. The survey on the consumption and assimilation of cow's milk and dairy products was conducted on a scale: from the 1st-always consumed to the 3rd - never consumed. The method of exogamy degree estimation was described previously [6].Statistical analysis had been carried out using Shapiro-Wilk test for normality, Chi-square test, Spearman correlation.

Results and discussion

The analysis of the results obtained in the Ukrainians study indicated that lactose persistence phenotype is found in 69.9 % of persons and lactase intolerance – in approximately 7.2 %.The highest LP phenotype is observed in Nigerians - 95.2 % and none of them has lactose intolerance. It is detected that only 51.9 % of Palestine subjects were consuming milk. The proportion of people with lactose persistence among students and parents in most countries is not comparable($\chi 2 = 23.56$, $p= 0.0014$).Analysis in all ethnic groups showed that the frequency of lactose tolerance is less among parents than among students. A significant negative correlation between percentage of persons with lactose persistence and age have been revealed, $r = – 0.529$ ($p <0.05$).Our results are in world data trends .It is known that the genotype associated adult-type hypolactasia, especially associated with genotype C/C−13910, begins at an early age with a further decrease to complete loss. Age varies among ethnic groups, ranging from 1 to 20 years. Whereas in the literature there are no exact data on the onset age of a decrease in lactase activity. For example, a study by Rasinperä H. and employees showed differences in African and Finnish children and revealed that the decline of lactase activity was somewhat earlier in African compared with Finnish children[7].

In our investigation the LP score is 72.7 - 95.2 % among Nigerian, Israeli, Egyptian, Turkish, Indian students, and 60 - 76.5 % among their parents. In accordance with the data obtained, it could be assumed that students from India, Nigeria, Israel, Egypt, Turkey maintain the absorption of lactose longer at a young age, and not lose ability in early childhood. Really, according Seppo L. although primary hypolactasia normally appears before the age of 20 years, the decline in lactase activity may on occasions continue after that age [8]. In investigation by Bulhões A. et al. [9]demonstrated that one of the 10 subjects with the CCGG genotype (lactase non-persistence) had negative hydrogen breath test, without symptoms. This could be explained by a slow decrease of lactase levels, with hypolactasia developing later in life [9].It is likely that adult-type hypolactasia may appear after 20 years and older, and could indicating a high degree of heterozygosity.

The analysis of Ukraine, Palestine and Jordan groups showed that lactose tolerance phenotype in students and parents are comparable. The LP phenotype is 50 – 68.8 % and 53.9 – 70.9 % among Ukrainian, Palestinian Jordanian students and parents. We concluded that students from these ethnic groups at the age of 20 years have achieved a trait of lactose tolerance. The results of studies are shown in Table 1.

An analysis of individuals distribution according to the parents exogamy degree (Table. 2) showed that the highest number of persons with first exogamy degree is 82.6-85.5 % among Turks, Palestinians, Egyptians and the lowest value of LP phenotype is observed in these groups - 51.9 - 72.3 %.

A statistically significant negative correlation between the parameters of first degree of parents exogamy and lactose persistence phenotype was found, $r = – 0.786$ ($p<0.05$).

In all ethnic groups a statistically significant positive correlation between the trait of adult-type hypolactasia and number of persons with the first degree of parents exogamy is determined, $r = 0.905$ ($p<0.05$).

The results obtained about the influence of the individuals origin on the trait under study may be related to the effect of the exogamy degree on the frequency of genetic recombination [10-12].

The tendency for associative marriages has the effect of increasing the inbreeding level. It leads to a decrease in genetic diversity, an increase in the number of similar loci in chromosomes during conjugation, and thus to an increase in the recombination processes associated with chromosome rearrangements, and consequently to a decrease the number of homozygotes [13].The results of our previous studies have shown that people who consumed milk and dairy products in childhood and decreased this ability with age had heterozygous genotypes: CTGA of SNPs- 13910C-T (rs4988235) and 22018G-A (rs182549) of *MCM6*gene [6]. Therefore, the results of this study are consistent with previous findings.

We also proposed that LI should not be regarded as an isolated trait but considered as a possible trigger for further diseases. The change in metabolic status with age could be a predictor for multifactorial pathology.

Lactose intolerance is the risk factor for fractures and osteoporosis but is also could associated with gastrointestinal pathologies. Our results obtained previously indicate that patients with CTGA genotype had osteoporosis and disorders of the gastrointestinal tract, such as gastritis (43 %), peptic ulcer (29 %), stomach cancer (12.5 %) and others [6].

Table 1. Distribution of milk consumption trait in different ethnic groups

Inhabitants of the countries	Age range, min – max, years old	N	Consumption of cow's milk, %		
			Life-long	Lose with age	Never
Nigeria	17-25 20.8 ± 0.56	21	95.2	4.8	0.0
	38-61 48.0 ± 0.28	17	76.5	23.5	0.0
Average	34.4	38	85.9	14.1	0.0
Israel	19-27 24.0 ±0.51	19	78.9	15.8	5.3
	38-63 49.4 ± 1.18	21	66.8	28.8	4.8
Average	36.7	40	72.8	22.2	5.0
Palestine	19-27 22.5 ± 1.03	8	50.0	50.0	0.0
	39-67 50.8 ± 1.31	26	53.9	23.1	11.5
Average	36.7	34	51.9	36.5	5.8
Egypt	19-24 21.5 ± 0.65	11	72.7	27.3	0.0
	40-61 51.7 ± 1.99	9	55.6	44.4	0.0
Average	36.6	20	64.1	35.9	0.0
Turkey	17-27 22.5 ± 0.76	13	84.6	15.4	0.0
	40-69 49.1 ± 2.77	10	60	40	0.0
Average	35.8	23	72.3	27.7	0.0
Jordan	22-25 23.6 ± 0.22	16	62.5	25.0	12.5
	40-67 51.9 ± 1.67	18	66.7	22.2	11.1
Average	37.8	34	64.6	23.6	11.8
India	18-28 22.0 ± 2.30	103	81.2	15.3	3.5
	40-62 46.9 ± 6.95	61	73.3	20.0	6.7
Average	34.5	164	77.3	17.7	5.1
Ukraine	17-30 20.9 ± 2.66	170	68.8	25.3	5.9
	38-66 45.9 ± 5.76	251	70.9	20.8	8.4
Average	33.4	421	69.9	23.1	7.2

Note. N – the number of persons interviewer.

Table 2. Distribution of persons by degrees of parents exogamy, %

Inhabitants	Degree of parents exogamy			
	Ist	IInd	IIIrd	IVth
Nigeria	18.4	73.7	7.9	0.0
Ukraine	25.5	37.3	29.4	7.8
India	37.3	62.7	0.0	0.0
Israel	75.0	22.5	2.5	0.0
Jordan	76.5	17.7	5.9	0.0
Turkey	82.6	8.7	4.4	4.4
Palestine	84.9	12.1	3.0	0.0
Egypt	85.5	5.0	0.0	0.0

Conclusions

The lactase persistence indices have a negative correlation with age. Analysis in all ethnic groups showed that the number of lactose tolerance people is less among parents than among students. The parameters of first degree of parents exogamy have a negative correlation with the lactase persistence and a positive correlation with trait of adult-type hypolactasia. The obtain results could be the basis for future researches.

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БОРОЗЕНЕЦЬ В.В.[1], БАБАЛЯН В.О.[2], ФЕДОТА О.М.[1]
[1] Харківський національний університет імені В.Н. Каразіна,
Україна, 61058, м. Харків, майдан Свободи, 4, e-mail: amsfedota@gmail.com
[2] Харківська медична академія післядипломної освіти,
Україна, 61176, м. Харків, вул. Амосова, 58, e-mail: babalyanvladimir@gmail.com

ГЕНЕТИЧНІ АСПЕКТИ ПЕРСИСТЕНЦІЇ ЛАКТАЗИ У ЛЮДЕЙ З РІЗНИХ ЕТНІЧНИХ ГРУП

Мета. Оцінка генетичних аспектів лактозної толерантності (ЛТ) у людей з різних етнічних груп. ***Методи.*** У дослідженні зібрано та проаналізовано генеалогічну та медичну інформацію щодо українських, індійських, нігерійських, ізраїльських, єгипетських, палестинських, турецьких, йорданських студентів (n=361) та їх родичів першого ступеня споріднення (n=413). Статистичний аналіз проведено з використанням критерію нормальності Шапіро-Уілка, U критерію Манна-Уітні, χ^2 та кореляційного аналізу за Спірменом. ***Результати.*** Фенотип ЛТ зустрічається у 69,9 % українців, лактозної непереносимості – у 7,2 %. Найбільша частка осіб з ЛТ спостерігалася у вибірці нігерійців – 95,2 %, найменша – у палестинців, 51,9 %. Частка батьків з ЛТ менша, ніж частка студентів ($r = - 0,529$, $p<0,05$). Показник ЛТ склав 72,7–95,2 % для нігерійських, ізраїльських, єгипетських, турецьких, індійських студентів та 60–76,5 % для їх батьків. Фенотип ЛТ серед українських, палестинських йорданських студентів та їх батьків – 50–68, 8 % та 53,9–70,9 %. Ймовірно, гіполактазія дорослого типу розвивається після 20 років і старше, що може свідчити про високий ступінь гетерозиготності. Серед студентів з Туреччини, Палестини, Єгипту виявлено найбільшу частку осіб з першої ступенем екзогамії батьків (82,6-85,5 %), та найменший показник ЛТ – 51,9–72,3 %, ($r = - 0,786$, $p<0,05$). Встановлено позитивний зв'язок між ознаками гіполактазії та часткою осіб з першим ступенем екзогамії батьків ($r = 0,905$, $p<0,05$). Зміни метаболічного статусу з віком можуть бути передумовою розвитку мультифакторіальної патології. ***Висновки***. Гіполактазія дорослого типу залежна від віку ознака. Встановлено зв'язки між показниками ЛТ та походженням.
Ключові слова: лактазна персистенція, лактозна непереносимість, екзогамія, генотипи.