The Primary Hypolactasia Frequency in 7-12-Year-old Albanian Pupils in F.Y.R.O. Macedonia

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Abstracts - Through this research, the frequency of the primary hypolactasia phenotype has been determined and it includes the Albanian pupils in Macedonia from 7 to 12 years of age, as a result of the existence of the LacR allele. The correlation between the lactose maldigestion prevalence and the age advancement changes has also been analyzed. The research included 115 primary school children in Macedonia at the age of 7 to 12 years of Albanian nationality. The glucose level in them was measured before and 40 minutes after the input of 200 – 220 ml of milk on an empty stomach, or 2 grams of lactose per one kilogram body weight. The emergence of clinical signs, such as glucose level increases with less than 1.1 mmol/L, stomachaches, belly bulge, diarrhea, etc., have been considered as determining parameters of the existence of primary hypolactasia and LacR allele in the persons in question. The result is that the average of the primary hypolactasia phenotype in the Albanian population sample in Macedonia which underwent the analysis has been represented in 71.22% of the cases.

Keywords: Primary; hypolactasia; LacR; phenotype; frequency; intolerance; lactase; pupil; MTT; lactose; glucoses.
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I. INTRODUCTION

Lactose intolerance is the inability to metabolize lactose, because of a lack of the required enzyme lactase in the digestive system.[8] All healthy children from three to five years of age possess a considerable amount of the lactase ferment in their digestive tract. Lactase hydrolyzes the glycosidic linkages β1, 4 that exist between the glucose and lactose with in the composition of lactose as disaccharide. With the growth of the person, there are changes occurring in terms of the activity of this enzyme. This phenomenon is known as primary hypolactasia and is present in different ethnic communities with a varying frequencies. These persons are considered to be intolerant towards lactose – IL. It is estimated that 75% of adults worldwide show some decrease in lactase activity during adulthood.[8] The frequency of decreased lactase activity ranges from as little as 5% in northern Europe, up to 71% for Sicily, to more than 90% in some African and Asian countries.[8]

II. OBJECTIVE

The main objective of this research was to find the dispersion frequency of the primary hypolactasia phenotype in Albanian pupils in Macedonia of an age from 7 to 12 years old. This would provide a clear picture about the allele LacR frequency within the same population. The correlation between the phenotype dispersion and the age of the individuals has also been analyzed.

III. METHOD

115 pupils of Albanian nationality took place in this research. Their age ranged from 7 to 12 years old. The utilized test for the determination of the primary hypolactasia as a phenotype of the LacR allele is the one that measures the level of glucose in blood and is known as MTT (milk tolerance test). The glucose measurement has been carried out with a glucose-meter before and 40 minutes after the provision of 200-220 ml of highly adopted cow’s milk or 2 grams of lactose per each kilogram of body’s weight. The increase in the level of glucose of 1.1 mmol/l is considered as a sign that the person in question suffers from primary hypolactasia. Other symptoms, such as stomachaches, belly bulge, diarrhea, etc. helped us identify those with hypolactasia.

Pupils with general poor health or gastrointestinal illnesses as well as those with family histories of illnesses of gastrointestinal or genetic character were excluded from the research.

The data were processed and grouped in that way to determine the primary hypolactasia dispersion frequency along with the LacR allele. The correlation coefficient between the primary hypolactasia phenotype...
dispersion and the age of the individuals has also been reckoned.

**IV. RESULTS**

115 pupils were divided into 5 classes according to their age, with one year interval difference. **Initial sample data:** interval mean $x_{mi}(vj)$ of the respective age-group, number of pupils in class-$N_i$, numeric frequency of pupils with IL $y_{oi}(num.)$, and the observed relative frequency in % $y_{oi}$(%), for $y_{oi}$(%) referring to values of $x_{mi}$(years) as well as for the increasing linear function have been given in Table 1 also.

Table 1. Initial sample data according to the tendency of the increase of relative frequency of pupils with IL from class to class. The flow of the observed relative frequency of pupils with IL from class to class has been illustrated in the picture below.

<table>
<thead>
<tr>
<th>$x_{mi} (vj)$</th>
<th>$N_i$</th>
<th>$y_{oi} (num.)$</th>
<th>$y_{oi}$ (%)</th>
<th>Class 1-5 (Ladas)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interval mean of the class members’ age</td>
<td>Number of pupils in class</td>
<td>Numberic frequency of pupils with IL</td>
<td>Observed relative frequency of pupils with IL in class</td>
<td>Linear line reg. equation</td>
</tr>
<tr>
<td>7.5</td>
<td>23</td>
<td>13</td>
<td>56.5</td>
<td>$y=6.39x+10.50$</td>
</tr>
<tr>
<td>8.5</td>
<td>23</td>
<td>15</td>
<td>65.2</td>
<td></td>
</tr>
<tr>
<td>9.5</td>
<td>23</td>
<td>16</td>
<td>69.6</td>
<td></td>
</tr>
<tr>
<td>10.5</td>
<td>24</td>
<td>21</td>
<td>87.5</td>
<td></td>
</tr>
<tr>
<td>11.5</td>
<td>22</td>
<td>17</td>
<td>77.3</td>
<td>$0.025&lt;p&lt;0.050$</td>
</tr>
<tr>
<td>Total</td>
<td>115</td>
<td>82</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Fig. 1.** The polygonal line of the observed relative frequency of pupils with primary hypolactasia in the initial sample.

*a) The variation of frequency in pupils with IL according to their age, in the interval from 7 to 12.

In Table 1 we can see the data for $y_{oi}$(%) referring to values of $x_{mi}$(years), of the group-age interval means within the respective grades, from 1 to 5, that have been included in the work sample, with a tendency of frequency increase of the IL, as well as the acquired results according to an increasing linear function. By using the method of least squares, the equation of the linear regression line for the age interval 7-12 has been determined and it is as follows:

$Y_e = 6.39x + 10.50$  \hspace{1cm} (1)

$Y_e = 6.49x - 7.30$  \hspace{1cm} (2)
along with the correlation coefficient between the variables \( r = 0.86 \). The level of significance \( 0.05 > p > 0.025 \) has been determined from the formulas and respective statistical charts of critical values for the correlation coefficients, mentioned in the references. \([4, 6, 10]\)

As a reference point the values given by Ladas \([8]\) have also been given for the analog equation:

\[ y = 6.39x + 10.50 \]

\[ y = 6.49x - 7.30 \]

![Polygonal line of frequencies; linear regression lines: according to our sample and according to Ladas.](image)

We can see that within the 7-12 years of age interval, the data expected from our model (1) are approximately 17% higher from those in equation (2).

V. DISCUSSION

From the data in Table 1 and Figure 1 we can conclude that the observed relative frequency of pupils with primary hypolactasia \(-y_o-(\%)\) in classes from 1 to 5 has an increasing tendency.

Having previously processed the data from the initial sample, we can see that the average of the primary hypolactasia phenotype and the Lac, allele in the Albanian population sample in Macedonia that underwent the analysis is 71.22%. Having into consideration the fact people coming from the same ethnic background, regardless of their distance of residence, are characterized by the same primary hypolactasia prevalence, we can assume that the Albanians living in Albania or Kosovo will most probably have an approximate frequency. However, it has to be verified with further studies.

The quite broad variation of the intolerance prevalence against lactose has led into the assumption that the lactose deficiency is a normal or natural state, whereas the persistence of the significant activity of the lactase in Northern European populations represents an “abnormal” mutation, which, as it seems, has created an advantage to those that use milk and other dairy products. It is not clear even today whether the usage of milk and dairy products has led to the maintenance of the lactasic activity or the persistence of the lactasic activity itself has helped in the inclusion of dairy products in people’s everyday diet.\([1]\)

Today, the allele that determines the intolerance towards lactose and is original and restrictive is Lac\(_R\) - (a), whereas the persistence allele is considered to be a dominant mutation –Lac\(_P\)-(A). By considering the population in equilibrium (a characteristic of civilized populations) and by using the Hardy – Wainberg equation, we have calculated the allele frequencies as shown below:

\[ p^2Lac_p = \frac{82}{115} = 0.713; qLac_R = 0.844 \]

whereas \( pLac_p = 0.156 \).

We have gained the assumed values of the presence of the allele Lac\(_R\) from the values of the presence of the primary hypolactasia phenotype, and we can conclude in advance that the Albanian population in Macedonia can be put in the group of those populations where the lactose intolerance prevails: Lac\(_R\) > 0.84, which means it belongs in the
same group with population from Central Africa, Australia, Malaysia, and Southwestern Asia, based on the classification provided by Danil L. Swagerty. [6]

VI. CONCLUSION

After the procession and analysis of the data from the research on IL that included 115 pupils aged between 7 and 12 from the Albanian population living in Macedonia, characterized as a zone with increasing frequencies, we have come to the conclusion that among the interest variables (the relative frequency of pupils with IL – y_o% and pupils’ age – x-years), there is a positive correlation of \( r = 0.86 \), with a level of significance \( 0.0025 < p < 0.05 \).

The model of best approximation of sample points with a tendency to increase, which expresses the relative frequency dependency \( y_o \) (%) expected in pupils with IL, from the age of \( x \) (years), and within the interval of 7 – 12 years of age, is given with the equation of the linear regression line:

\[ y_o = 6.4x + 10.50. \]

We can conclude that the relative frequency of primary hypolactasia in children aged between 7 and 12 in the Albanian population in Macedonia is 71.22% which means it belongs in the same group with population from Central Africa, Australia, Malaysia, and Southwestern Asia, based on the classification provided by Danil L. Swagerty [6] and has an increasing tendency with the ageing process itself.

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