RESEARCH ARTICLE

Modern Possibilities of the Use of Non-Invasive Serological Biomarkers Severe in Population Studies

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ABSTRACT:
The ethnic and gender factors materially affect the prevalence of gastric atrophy. All the patients were divided into five ethnic groups: Russians, Karachays, Abazins, Circassians, Nogais. The decrease in serum gastrin-17 less than 10 pmol/l is a sensitive and specific biomarker for antral mucosal atrophy, pepsinogen-I less than 25 µg/l is a corpus mucosal atrophy biomarker (Se – 89% and 92%, Sp – 97% and 96%). Gastrin-17 and pepsinogen-I are also sensitive and specific biomarkers for mild, moderate, severe atrophy of the antrum and corpus (for severe antral mucosal atrophy Se – 96%, Sp – 92%, for severe corpus mucosal atrophy Se – 88%, Sp – 97%). A total of 75 patients with multifocal atrophic gastritis were examined histologically. 67 patients had gastrin-17 <10 pmol/l and pepsinogen-I <25 µg/l at the same time. 7 patients had gastrin-17 from 10 to 11.5 pmol/l, 1 patient had gastrin-17 = 19 pmol/l (Se – 89%). Therefore, the level of gastrin-17 and pepsinogen-I simultaneously decreases among patients with multifocal atrophic gastritis. The prevalence of atrophic gastritis is significantly different among some ethnic populations living in the same territory under the same environmental and living conditions. These differences prove the presence of genetic polymorphism in different ethnic groups of the population.

KEYWORDS: Atrophic Gastritis, Serological Screening, Gastrin-17, Pepsinogen-I, Population.

INTRODUCTION:
Background:
The ethnic factors materially affect the prevalence of gastric atrophy. As an example, it is significantly different between Caucasians and Mongoloids. The differences were also found among Caucasians and ethnic Japanese; with a higher atrophy prevalence among the Japanese1. Atrophy prevailed in Caucasians when compared to Khakas and Evenks. Tuvans were as much affected by this pathology as non-native residents. The prevalence of malignant diseases of the stomach also differed between different ethnic groups.

They were more frequent among Europeans compared to Evenks and Khakas, while their prevalence was record high among Tuvans2. The incidence was higher among urban residents of Siberia compared to European countries and the United States. Among Yakuts, being representatives of a Mongoloid ethnic group, the prevalence of atrophy is higher than among residents of Eastern and Asian countries3. This pattern (with the prevalence of atrophic lesions among residents of Japan, Singapore, and China being higher than that among Europeans) is very typical. It is influenced by their lifestyle and nutrition. Villagers in Yakutia lack fresh vegetables and fruits4,5,6,7, while fast food and refined products prevail in the diet of urban dwellers8. The prevalence of gastric atrophy makes 16.7% among Yakutsk residents and reaches 25.6% among the rural population3. The rate of atrophic changes of the stomach
among residents of Novosibirsk is 2.5 times the rate among rural residents. PGI above 130 ng/ml is more typical of Caucasians (29.9–32.1% of the population) compared to Mongoloids (4.4–16.7%). Some studies did not reveal any difference in the pepsinogen level between Europeans and Asians.

**The normal values of serum pepsinogen:**

The normal values of serum pepsinogen were calculated for the population of West Siberia who did not have any pathological stomach changes as follows: PGI – 30–130 µg/l, PGII – 4–22 µg/l. Normally, the PGI/PGII ratio should be more than three. Pepsinogen-I reduction below 25 µg/l is an evidence of atrophy, while the ratio reduction below three confirms this fact. In the Arkhangelsk Krai, PGI equaled to 100.2±5.3 ng/ml among surveyed patients aged 25–64. The scatter of results is: 0.25–314.10 ng/ml.

Dependences between stomach atrophy and family relationship:

Among randomly selected persons within the population studies, severe stomach atrophy was observed in 10.9% of cases, while this value equaled to 27.6% among people who had a family relationship. In case of stomach atrophy localized in the body of the stomach, the prevalence was accordingly 12.6% and 48.3%. The prevalence of atrophic gastritis within a population group can be affected by genetic polymorphism. Gastric cancer risk correlates with the severity and extent of atrophic gastritis. Besides, Kyoto Global Consensus Report on Helicobacter Pylori Gastritis acknowledged as proven the statement that serum biomarkers of stomach atrophy are useful for the risk stratification. Thus, the diagnostics of atrophic gastritis as a precursory syndrome of gastric cancer with serum markers is a modern non-invasive and patient-friendly method.

**MATERIALS AND METHODS:**

Classification of examined persons into ethnic groups:

We examined 2713 persons for markers of antrum and stomach body mucosa atrophy within the framework of the targeted republican program for early detection of patients with atrophic gastritis during 2012 and 2013 in Cherkessk, the capital of the Karachayevo-Cherkessian Republic. 2031 of them were also examined for antibodies to Helicobacter pylori. The urban population was selected with the purpose of excluding as much as possible the impact of environmental and living conditions factors in various ethnic cohorts. Thus, we managed to form ethnic cohorts with a high quality of randomization. The people were subjected to a non-invasive diagnostic examination after a previous clinical examination according to the following selection criteria: aged 40 or older, signed informed consent for clinical intervention. All the examined patients were divided into 5 ethnic groups: Russians, Karachays, Abazins, Circassians, and Nogais. The enzyme immunodetection of markers in all 2713 patients was conducted by antibody screening with a GastroPanel® line diagnostic set (Finland Biohit Plc, Helsinki) and included the detection of postprandial gastrin-17, fasting pepsinogen-I, and anti-HP IgG. The mild, moderate, and severe atrophy of the antrum and stomach body mucosa were detected using the criteria developed by S.M. Kotelevets and S.A. Chekh.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Atrophy severity</th>
<th>Postprandial gastrin-17</th>
<th>pepsinogen-I</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No atrophy</td>
<td>&gt;10 pmol/l</td>
<td>&gt;25 µg/l</td>
</tr>
<tr>
<td>2</td>
<td>Mild</td>
<td>7-10 pmol/l</td>
<td>15-25 µg/l</td>
</tr>
<tr>
<td>3</td>
<td>Moderate</td>
<td>4-7 pmol/l</td>
<td>9-15 µg/l</td>
</tr>
<tr>
<td>4</td>
<td>Severe</td>
<td>0-4 pmol/l</td>
<td>0-9 µg/l</td>
</tr>
</tbody>
</table>

The atrophic gastritis stages were determined using the OLGA classification (Table 2).

**Table 2: Atrophic gastritis stages according to the OLGA classification**

<table>
<thead>
<tr>
<th>Stomach body</th>
<th>Antrum Atrophy</th>
<th>0 none</th>
<th>1 weak</th>
<th>2 moderate</th>
<th>3 severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 none</td>
<td>Stage I</td>
<td>Stage I</td>
<td>Stage II</td>
<td>Stage III</td>
<td>Stage IV</td>
</tr>
<tr>
<td>1 weak</td>
<td>Stage I</td>
<td>Stage I</td>
<td>Stage II</td>
<td>Stage III</td>
<td>Stage IV</td>
</tr>
<tr>
<td>2 moderate</td>
<td>Stage II</td>
<td>Stage II</td>
<td>Stage III</td>
<td>Stage IV</td>
<td></td>
</tr>
<tr>
<td>3 severe</td>
<td>Stage III</td>
<td>Stage III</td>
<td>Stage IV</td>
<td>Stage IV</td>
<td></td>
</tr>
</tbody>
</table>

Gastric cancer was detected by the method of P. Sipponen according to Table 3.

**Table 3: Stomach risk calculation based on the severity of atrophy depending on its location in the antrum or body of the stomach. Sipponen et al. Int J Cancer. 1985.**

<table>
<thead>
<tr>
<th>Stomach part</th>
<th>Normal stomach body</th>
<th>Non-atrophic gastritis</th>
<th>Mild atrophy</th>
<th>Moderate atrophy</th>
<th>Severe atrophy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal antrum</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Non-atrophic antrum gastritis</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Mild atrophic antrum gastritis</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Moderate atrophic antrum gastritis</td>
<td>2</td>
<td>4</td>
<td>5</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Severe atrophic antrum gastritis</td>
<td>18</td>
<td>36</td>
<td>36</td>
<td>90</td>
<td></td>
</tr>
</tbody>
</table>
RESULTS:
Prevalence of atrophic gastritis with mild, moderate, and severe atrophy in both parts of the stomach among different ethnic groups:
We defined the shares of AG patients with correspondent atrophy in persons of both sexes among the main ethnic groups residing in Cherkessk of the Karachayevo-Cherkessian Republic of the Russian Federation. The patients were defined by serum indicators: the criterion of mild, moderate, or severe antrum atrophy was gastrin-17 whose level in such subjects was below 10 pmol/l and/or pepsinogen-I reflecting mild, moderate, or severe stomach body atrophy was below 25 μg/l. The prevalence was as follows: Russians – 54% (1541 patients; 836 of them have AG), Karachays – 53% (297/564 patient have AG), Abazins – 59% (123/208 patients have AG), Circassians – 54% (182/338 patients have AG), and Nogais – 55% (34/62 patients have AG). We detected slight differences between different ethnic groups, but they were statistically insignificant when all the groups were compared (p>0.05). The total number of AG patients 1472 was (54%).

In each ethnic group, we studied the gender differences with respect to the prevalence of this diseases in case of mild, moderate, or severe antrum and stomach body atrophy. The prevalence of AG with mild, moderate, or severe atrophy in both parts of the stomach in each ethnic group was as follows (in men and women, accordingly): Abazins – 71% and 55%; Circassians – 66% and 49%; Karachays – 63% and 48%; and Russians – 60% and 52%. The difference in prevalence between the male and female groups was statistically significant for Abazins – p<0.05, Circassians – p<0.05, Karachays – p<0.001 and, accordingly, Russians – p<0.01. Among Nogais, the prevalence was also higher among men (60%), while the prevalence among women was 53%. The difference of the prevalence between the gender groups of the Nogais was statistically insignificant (p>0.05).

Prevalence of Helicobacter pylori infection among different ethnic groups:
In order to figure out the effect of the population-based differences on the prevalence of Helicobacter pylori (HP) infection, we defined the share of Helicobacter pylori-positive patients among the men and women of all the groups. The prevalence of HP infection among different ethnic groups was as follows: Russians – 79% (944 of 1199 patients were HP-positive), Karachays – 76% (250/330 HP-positive patients), Abazins – 81% (143/176 HP-positive patients), Circassians – 76% (216/283 HP-positive patients), and Nogais – 67% (29/43 HP-positive patients). No statistically significant difference was revealed between the groups. HP infection prevalence between different groups is equal. This fact confirms the equal everyday life conditions for all groups. Total number of patients was 2031, and 1582 of them were HP-positive (78%).

The prevalence of Helicobacter pylori infection among men and women, accordingly, is as follows: Abazins – 84% and 80%; Circassians – 74% and 77%; Karachays 76% of both men and women; Russians — 79% each. No statistically significant difference was defined between these groups (p>0.05). As a result, it may be stated that there was no difference in the prevalence of Helicobacter pylori infection between the male and female groups of the Abazin, Circassian, Karachay, and Russian ethnic groups. At the same time, a statistically significant difference was observed between the Nogai men and women – 91% and 59% (p<0.01).

Prevalence of severe atrophic antrum gastritis in Helicobacter pylori-negative patients:
We determined the share of atrophic antrum gastritis patients with severe atrophy among men and women. We studied the prevalence of atrophic antrum gastritis with mild, moderate, and severe atrophy. We identified HP-negative patients with severe antrum atrophy by the serum parameters: in such patients, gastrin-17 was below 4 pmol/l, pepsinogen was above 25 μg/l, which indicated no atrophy in the body of the stomach; the mass concentration of antibodies to Helicobacter pylori (anti-HPlgG) was less than 35 EIU.

Differences among Helicobacter pylori-negative patients:
The prevalence of atrophic antrum gastritis with severe atrophy of HP-negative patients among different ethnic groups was as follows: Russians – 6% (74 of 1199 patients HP-negative), Karachays – 6% (21/330 HP-negative patients), Abazins – 8% (14/176 HP-negative patients), Circassians – 10% (27/283 HP-negative patients), and Nogais – 19% (8/43 HP-negative patients). We calculated the chi square criterion. As a result, it was found that the differences in the prevalence of atrophic antrum gastritis with severe atrophy in HP-negative patients among all the ethnic groups were statistically significant. The chi square criterion equaled to 13.233, with the number of degrees of freedom equal to 4 (p=0.01). Total number of patients surveyed in all groups was 2031, and 144 of them were HP-negative with severe antrum atrophy (7%).

The prevalence of atrophic antrum gastritis with severe atrophy in HP-negative Abazin patients, both male and female, equaled to 8%. Among the Circassians, the share of the male patients (12%) was higher than that of the female (9%). Karachays: male (9%) and female patients share (5%). Nogais: female (22%) male share (9%).
Among the Russians, the prevalence was higher among men (11%) and lower among women (5%).

Prevalence of mild, moderate, and severe atrophic antrum gastritis regardless of the Helicobacter pylori status:
In order to find out how the population-specific differences impact the prevalence of atrophic antrum gastritis with mild, moderate, and severe atrophy regardless of the Helicobacter pylori status of the patients involved in the thesis research, we found the shares of the examined patients with atrophic antrum gastritis who had mild, moderate, and severe atrophy regardless of the Helicobacter pylori status among the males and females of all the ethnic groups (2713 examined persons totally; 593 of them (22%) were AG patients). The patients with severe antrum atrophy were detected regardless of the HP status by serum parameters: in patients, gastrin-17 was below 4 pmol/l, pepsinogen-I was above 25 µg/l, which meant no atrophy in the stomach body. The mass concentration of anti-HP IgG was disregarded. The prevalence of atrophic antrum gastritis among different groups was as follows: Russians – 21% (1541 patients; 327 of them have AG), Karachays – 20% (115/564 patients AG), Abazins – 24% (49/208 patients have AG), Circassians – 26% (87/338 patients have AG), and Nogais – 24% (15/62 patients have AG). There were also the patients from other ethnic groups; the total number of them was 152, and 37 of them were AG patients (24%). An exception was the difference in the prevalence of atrophic antrum gastritis with severe atrophy regardless of the HP status between the Karachays and Circassians.

For the Abazins, the prevalence of atrophic antrum gastritis with severe atrophy regardless of the Helicobacter pylori status was higher among males (34%) compared to females (19%). For the Circassians, the prevalence of this disease was also higher among males (34%) compared to females (22%). For the Karachays, the share of severe antrum atrophy was higher among males (27%) compare to females (17%).

For the Nogai, the prevalence of atrophic antrum gastritis with severe atrophy regardless of the Helicobacter pylori status was higher among females (28%) compared to males (13%). For the Russians, the prevalence of this disease among male patients (29%) was higher than that among females (18%).

The mass concentration of antibodies to Helicobacter pylori (anti-HP IgG):
Patients with mild antrum atrophy regardless of the HP status were detected by serum parameters: in such patients, gastrin-17 was below 10 pmol/l and above 7 pmol/l, pepsinogen-I was above 25 µg/l, which meant that the stomach body had no atrophy. The total was 2713 patients; 375 of them had AG (14%). The prevalence of atrophic gastritis localized in the antrum with moderate atrophy regardless of the Helicobacter pylori status among different ethnic groups was as follows: the Russians – 14% (1541 patients; 220 of them have AG), Karachays – 14% (78/564 patients have AG), Abazins – 16% (34/208 patients have AG), Circassians – 10% (34/338 patients have AG), and Nogais – 15% (9/62 patients have AG). The difference between the Russians and Circassians (p<0.05), the Circassians and Abazins (p<0.05) was statistically significant.

The gender aspect of the differences in the prevalence of atrophic antrum gastritis with moderate mucosa atrophy was characterized by the correspondent marker represented by the level of gastrin-17 above 4 pmol/l and below 7 pmol/l. For the Abazins, the prevalence was higher among females (17%) compared to males (16%). For the Circassians the prevalence among male patients (12%) was higher than among females (9%). For the Nogais, the share of male patients (20%) was higher than that of females (13%). For the Russians the prevalence was higher among males (16%) compared to females (14%). The difference between the male and female groups of the Abazin, Circassian, Nogai, and Russian groups was statistically insignificant (p>0.05). For the Karachays, the prevalence of atrophic antrum gastritis with moderate atrophy regardless of the Helicobacter pylori status was higher among males (19%) compared to females (11%).
to females (15%). For the Circassians, the prevalence of males (13%) was higher than among females (12%). The prevalence of this disease among Karachays was higher among females (15%) compared to males (10%). For the Nogais, the prevalence was higher among males (20%) compared to females (6%). For the Russians, the prevalence was higher among males (11%) compared to females (12%). The differences between these cohorts were small.

**Prevalence of severe atrophic gastritis in both parts of the stomach among Helicobacter pylori-positive patients:**
To find out the impact of ethnic differences on the prevalence of atrophic gastritis localized in the antrum or the stomach body with severe atrophy in infected persons of both sexes, we found the shares of Helicobacter pylori-positive patients with atrophic gastritis localized in the antrum or body of the stomach with severe atrophy among the ethnic groups. We also studied the prevalence of atrophic gastritis in the antrum or body of the stomach with mild or moderate atrophy in HP-positive patients.

**The prevalence of atrophic gastritis with severe atrophy in Helicobacter pylori-positive patients among different ethnic groups:**
The prevalence of atrophic gastritis localized in the antrum or body of the stomach with severe atrophy in Helicobacter pylori-positive patients among different ethnic groups was as follows: the Russians − 17% (1199 patients; 206 of them have AG), Karachays − 16% (53/330 patients have AG), Abazins − 18% (32/176 patients have AG), Circassians − 20% (56/283 patients have AG), and Nogais − 12% (5/43 patients have AG). Certain statistically insignificant differences were found between some of the groups (p>0.05). Therefore, it may be stated that there is no difference between the prevalence of atrophic gastritis localized in the antrum or body of the stomach with severe atrophy, as well as mild and moderate atrophy, among HP-positive patients belonging to different ethnic groups. The sample included 2031 persons, and 352 of them were AG patients (17%).

For the Abazin Helicobacter pylori-positive patients, the prevalence of atrophic gastritis localized in the antrum or body of the stomach with severe atrophy was higher among males (28%) compared to females (14%). For the Circassians, the prevalence among male patients (25%) was higher than females (18%). For the Karachay HP-positive patients, the prevalence of atrophic gastritis localized in the antrum or body of the stomach with severe atrophy was higher among males (21%) compared to females (14%). Among the Russians, the pathology shares of male patients (22%) was higher than females (16%). Significant differences were found between these groups (p<0.05). The prevalence among the Nogais was as follows: males − 9%, females − 13%.

**Peculiar features of the prevalence of various atrophic gastritis stages depending on the ethnic group:**
Patients with the first-stage AG were identified by serum markers according to the OLGA classification. The first-stage AG prevalence among different ethnic groups was as follows: the Russians − 12% (1541 patients; 179 of them were gastritis patients with first-stage atrophy), Karachays − 13% (75/564 patients have first-stage atrophy), Abazins − 17% (35/208 have first-stage atrophy), Circassians − 13% (43/338 have first-stage atrophy), and Nogais − 8% (5/62 have first-stage atrophy). The difference between the Abazin and Nogai groups was statistically significant with the share of each of them being 17% and 8%, accordingly. The p-test of significance of the difference between the Abazin and Nogai groups (16% and 8%, accordingly) was less than 0.05. The number of patients was 2713, and 337 of them were gastritis patients with first-stage atrophy (12%).

**Second-stage AG prevalence in different ethnic groups:**
Patients with the second-stage AG were identified by serum markers: gastrin-17 for the antrum and pepsinogen-I for the body of the stomach, according to the OLGA classification. The second-stage AG prevalence among different ethnic groups was as follows: the Russians − 16% (1541 patients; 247 of them have second-stage atrophy), Karachays − 15% (86/564 patients have second-stage atrophy), Abazins − 16% (34/208 patients have second-stage atrophy), Circassians − 11% (38/338 patients have second-stage atrophy), and Nogais − 16% (10/62 patients have second-stage atrophy). The difference between the Russian and Circassian groups was significant with the share of each of them being 16% and 11%, accordingly. Besides, an exception was the difference between the other ethnic groups and Circassians. The p-test of significance of the difference between the other ethnic groups and Circassians (19% and 11%, accordingly) was less than 0.05. The total number of patients was 2713, and 415 of them have AG with second-stage atrophy (16%).

**Third-stage AG prevalence in different ethnic groups:**
Patients with the third-stage AG were identified by serum markers: gastrin-17 for the antrum and pepsinogen-I for the stomach body, according to the OLGA classification. In this case, the serum markers of atrophy characterizing the stomach mucosa acted as the “serological biopsy” which was correspondent to the
histological biopsy with high sensitivity and specificity. The third-stage AG prevalence was as follows: Russians – 25% (1541; 387 of them have AG with third-stage atrophy), Karachays – 23% (129/564 patients have AG with third-stage atrophy), Abazins – 25% (53/208 have AG with third-stage atrophy), Circassians – 28% (96/338 have AG with third-stage atrophy), and Nogais – 26% (16/62 have AG with third-stage atrophy). The total number of patients was 2713, and 681 of them were gastritis patients with third-stage atrophy (25%).

Ethnic differences in the prevalence of various risks of malignant changes in the stomach:
In order to find out the impact of ethnic differences on the prevalence of the low, moderate, and high risk of malignant changes in the stomach, we identified the shares of patients who had a low risk of malignant changes in the stomach among all the groups. The results were as follows: Russians – 75% (1541 patients, 1150 of them were patients of low risk), Karachays – 77% (435/564 were patients of low risk), Abazins – 75% (155/208 were patients of low risk), Circassians – 71% (241/338 were patients of low risk), Nogais – 73% (45/62 were patients of low risk). The total number of patients was 2713; 2026 of them were patients of low risk (75%).

Connections of male and female patients with a particular risk of gastric cancer formation:
In addition, we identified the shares of male and female patients with a particular risk of gastric cancer formation among the Abazin, Circassian, Karachay, Nogai, and Russian ethnic groups. The probability of risk development was calculated by P. Sipponen’s method32. The results are provided in Table 4.

Table 4: Gender differences in the prevalence of various probabilities of gastric cancer risk development among different ethnic groups

<table>
<thead>
<tr>
<th>Share of the identified risk (%)</th>
<th>Abazins</th>
<th>Circassians</th>
<th>Karachays</th>
<th>Nogais</th>
<th>Russians</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>66%</td>
<td>63%</td>
<td>71%</td>
<td>87%</td>
<td>67%</td>
</tr>
<tr>
<td>Women</td>
<td>78%</td>
<td>75%</td>
<td>80%</td>
<td>68%</td>
<td>78%</td>
</tr>
<tr>
<td>Total in the entire group</td>
<td>75%</td>
<td>71%</td>
<td>77%</td>
<td>73%</td>
<td>75%</td>
</tr>
<tr>
<td>Significance of differences</td>
<td>p&gt;0.05</td>
<td>p&lt;0.05</td>
<td>p&lt;0.05</td>
<td>p&gt;0.05</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Moderate risk</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>0%</td>
<td>3%</td>
<td>2%</td>
<td>0%</td>
<td>3%</td>
</tr>
<tr>
<td>Women</td>
<td>3%</td>
<td>3%</td>
<td>3%</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Total in the entire group</td>
<td>2%</td>
<td>3%</td>
<td>3%</td>
<td>3%</td>
<td>4%</td>
</tr>
<tr>
<td>Significance of differences</td>
<td>p&gt;0.05</td>
<td>p&lt;0.05</td>
<td>p&gt;0.05</td>
<td>p&gt;0.05</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>High risk</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>34%</td>
<td>34%</td>
<td>27%</td>
<td>13%</td>
<td>30%</td>
</tr>
<tr>
<td>Women</td>
<td>21%</td>
<td>22%</td>
<td>17%</td>
<td>28%</td>
<td>18%</td>
</tr>
<tr>
<td>Total in the entire group</td>
<td>24%</td>
<td>24%</td>
<td>20%</td>
<td>24%</td>
<td>20%</td>
</tr>
<tr>
<td>Significance of differences</td>
<td>p&lt;0.05</td>
<td>p&gt;0.05</td>
<td>p&lt;0.01</td>
<td>p&gt;0.05</td>
<td>p&lt;0.001</td>
</tr>
</tbody>
</table>

Patients with a low risk of malignant changes in the stomach were detected by P. Sipponen's method shown in Table 332. The score of the low risk of malignant changes in the stomach shown in the table was equal to 2. The prevalence of the low risk of malignant changes in the stomach among different ethnic groups was as follows: the Russians – 75%, Karachays – 77%, Abazins – 75%, Circassians – 71%, and Nogais – 73%. Certain statistically insignificant difference was found between some of the groups (p>0.05). The difference between the Karachays and Circassians was significant with the share of each of them being 77% and 71%, accordingly. The low risk according to P. Sipponen’s method was studied in the gender groups. It was as follows: 63% in men, 75% in women (the Circassians), 71% in men, 80% in women (the Karachays), and 67% in men and 77% in women (the Russians). In Abazins and Nogais groups, there were the following results: 66% in men, 78% in woman (the Abazins), and 87% in men, 68% in woman (the Nogais).

Prevalence of moderate risk of malignant changes:
Patients with a moderate risk of malignant changes in the stomach, scored 5, were detected by P. Sipponen’s method. The prevalence was as follows: the Russians – 4% (1541 patients, 55 of them were patients of moderate risk), Karachays – 2% (11/564 were patients of moderate risk), Abazins – 2% (4/208 were patients of moderate risk), Circassians – 3% (10/338 were patients of moderate risk), and Nogais – 3% (2/62 were patients of moderate risk). The statistical significance of the difference between the Russians and Karachays was verified by calculation (p<0.05). The number of patients was 2713, and 82 of them were patients of moderate risk (3%).

In order to define the impact of gender differences in different ethnic groups on the prevalence of the moderate gastric cancer risk, we determined the shares of male and female patients with a moderate risk of gastric cancer among the investigated ethnic groups. We failed to discover any statistically significant differences in the prevalence of the moderate risk of malignant changes in the stomach between the males and females of different ethnic groups. There were no males in the Abazin and Nogai ethnic groups at all (Figure 1).
High risk of malignant changes among different ethnic groups:
The prevalence of the high risk of malignant changes in the stomach among different ethnic groups was as follows: the Russians – 20% (1541 patients, 315 of them were patients of high risk), Karachays – 20% (112/564 were patients of high risk), Abazins – 24% (49/208 were patients of high risk), Circassians – 24% (82/338 were patients of high risk), and Nogais – 24% (15/62 were patients of high risk). The prevalence of the high risk of malignant changes in the stomach among different ethnic groups does not differ. The total number of patients was 2713, and 525 of them were patients of high risk (21%).

The prevalence of high risk was statistically higher in the males of the Abazin, Karachay, and Russian group. It was 34% in men and 19% in women (the Abazins), 27% in men and 17% in women (the Karachays), and 28% in men and 18% in women (the Russians). The high risk of malignant tumor development in the stomach, determined by P. Sipponen's method, was characterized by the absence of statistically significant differences between the ethnic groups under study, while the gender differences among the Abazins, Karachays, and Russians were statistically significant. In Circassians and Nogais groups, there were the following results: 31% in men, 21% in woman (the Circassians), and 13% in men, 28% in woman (the Nogais).

DISCUSSION:
Most authors rate highly the non-invasive serum screening used to measure gastrin-17 and pepsinogen-I and -II when diagnosing atrophic gastritis and patients with a high risk of gastric cancer
20,21,22,23. These serum markers of atrophic gastritis are recognized as sensitive and specific
24,25,26,27,28. The high sensitivity and specificity of the markers of pre-malignant changes in the stomach makes them an important factor of gastric cancer prediction for the nearest future. These markers should be used when forming high-risk patient groups and subjecting them to a yearly gastroscopic study for early gastric cancer detection
29,30,31,32,33. A number of authors from Asociación Española de Gastroenterología (AEG), Iran, Peru, and Latvia came to a conclusion that serum biomarkers of the GastroPanel® test panel are not useful for atrophic gastritis screening due to their low sensitivity
34,35,36,37. These authors’ conclusions cannot be correct as the studied cohorts of patients are not representative. The studies covered a small number of AG patients. McNicholl A. G. et al. assessed the morphofunctional comparison of six patients with antrum atrophy who were subjected to histology and at the same time measurement of gastrin-17; Hosseini M. et al. analyzed 48 patients with antrum atrophy, stomach body atrophy, and multifocal panatrophy of the stomach; Colarossi A. et al. came to certain conclusions based on a survey of 22 AG patients; Leja M. et al. assessed the morphofunctional comparison of 19 AG patients. Belkovets A. V. et al. analyzed the results of the survey of 1050 persons for serum biomarkers of gastric atrophy; therefore, their results are opposite to the results of the former authors
38. Belkovets A.V. et al. believe it is reasonable to widely implement serum screening with GastroPanel® for gastric diseases. Daugule I. et al. find useful to use serum biomarkers of atrophic gastritis in the OLGA (Operative Link for Gastritis Assessment) classification by analogy with the OLGA histopathological assessment
39. However, the assessment of atrophic gastritis by OLGA based on serum biomarkers of gastric atrophy requires biomarkers that enable the detection of mild, moderate, and severe atrophy in the antrum and body of the stomach
40,41. Nowadays, S. M. Kotelevets and S. A. Chekh have developed a detection methodology for mild, moderate, and severe atrophy in the antrum and
body of the stomach. Using the representative sample of 360 AG patients, they developed criteria for assessing mild, moderate, and severe atrophy in the antrum and body of the stomach by serum biomarkers of atrophy, gastrin-17 and pepsinogen-I, with the GastroPanel® test panel. It seems important to note that S.M. Kotelevets and S.A. Chekh propose other serological criteria for antral mucosa atrophy detection, different from those proposed by the GastroPanel® manufacturer, the Finnish company Biohit. The GastroPanel® manufacturer considers postprandial gastrin-17 <5 pmol/l to be the serological criterion of antrum atrophy, while S. M. Kotelevets and S. A. Chekh consider postprandial gastrin-17 <10 pmol/l to be the one. In this case, the method has the sensitivity of 89% and specificity of 97%. The high value of the method consists in the fact that using postprandial gastrin-17 <4 pmol/l as the serological criterion of severe antrum atrophy, one can detect patients with a high risk of gastric cancer with sensitivity of 96% and specificity of 92%, and ROC-analyses of serological criteria (gastrin-17) for severe antral atrophy – AUC=0.984. The authors believe it is wrong to use basal gastrin-17 as its product, G-cell, is functionally dependent on the amount of glucose, lipids, thyroid hormones, and kidney function. Therefore, the only correct way is to use postprandial gastrin-17 for antrum atrophy detection. It makes no sense to use the biomarkers of pre-malignant changes in the stomach, gastrin-17 and pepsinogen-I, for the assessment of inflammatory changes in the stomach mucosa and the activity of non-atrophic gastritis, as the latter is not a precancerous condition. This is what the Chinese authors tried to do for a large number of patients. The results of the study of atrophic gastritis prevalence among all the groups residing in the same living environment in Cherkessk have confirmed the differences between different ethnic groups.

CONCLUSIONS:
There are statistically significant differences between the prevalence of severe, moderate, and mild atrophic gastritis among the main ethnic groups residing in Cherkessk of the Karachayevo-Cherkessian Republic (the Karachays, Russians, Circassians, Abazins, and Nogais). The Helicobacter pylori-positive status among the ethnic groups did not show any significant differences, so the impact of the infection on atrophic gastritis development and its consequences should be treated as equal. We detected a certain difference in the prevalence of atrophic gastritis with the atrophy of various severity between males and females of the population groups in Cherkessk. There is a close correlation between the prevalence of severe atrophic gastritis and the risk of malignant stomach tumor development in different ethnic groups of the patients. The Abazin, Karachay, and Russian males are exposed to a higher risk of gastric cancer.

CONFLICT OF INTEREST:
The authors declare no conflict of interest.

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