ORIGINAL RESEARCH

The risk of type 2 diabetes in the native population of highlands Aksay of Kyrgyzstan

Marina S. Moldobaeva, Anastasiya V. Vinogradova, Cholpon A. Muratova

Department of Propaedeutic Therapy with Course on Endocrinology, Kyrgyz State Medical Academy named after I.K. Akhunbaev, Bishkek, Kyrgyzstan

Abstract

Objective: Highlands Aksay of Naryn region of Kyrgyzstan has specific natural and climatic conditions and located at altitude of 3000 m above sea level. We aimed to study 10-years risk of type 2 diabetes (T2DM) in the native population of highlands Aksay of Naryn Region of Kyrgyzstan.

Methods: Overall, 152 indigenous people (50 men and 102 women) of highlands Aksay of Naryn region (3260-3680 m) were studied using one-step sampling. The study was random, subjected to the conditions of singleness and territoriality. FINDRISC questionnaire was used to calculate the risk of T2DM.

Results: Women of highlands Aksay had a significantly higher prevalence of waist circumference (WC) >80 cm, body mass index (BMI) >25 kg/m^2 and irregular intake of fruits and vegetables, whereas men showed irregular intake of fruits and vegetables, BMI>25 kg/m^2, and WC> 94 cm.

Conclusion: The features of the 10-year-old risk of developing T2DM in the indigenous people of the highlands of Kyrgyzstan include the predominance of abdominal obesity and the irregular intake of fruits and vegetables. When stratifying the risks of developing T2DM, low risk predominates, and a very high risk does not occur. The prognosis of the indigenous people of the highlands of Kyrgyzstan regarding the risk of developing T2DM depends on phenotypic factors and living conditions in the highlands, with hypoxia playing the leading role. Among the mountain people of Kyrgyzstan, metabolic factors are dominated by abdominal obesity and, probably, to reduce the risks of developing diabetes, along with the fight against other negative factors, regular intake of vegetables and fruits is effective.

Key words: high-altitude, risk of diabetes type 2, native population, low risk

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Introduction

Three quarters of Kyrgyzstan territory are mountains, where a human is exposed to a full complex of hazardous conditions, of which hypoxia is the leading and most important one (1, 2). Highlands Aksay of Naryn region have specific natural and climatic conditions and located at altitude of 3000 m above sea level, with a population of 500 inhabitants. Low-altitude Chui valley of Chui Region is located at altitude of 500-1300 m above sea level, and in 2015 its total population was 870300.

Kyrgyzstan is a developing country (3-6). When analyzing selected studies, we found that in South Asian population type 2 diabetes mellitus (T2DM) develops in lower body mass index (BMI) range, compared to European Caucasians (7-16). In the age range of 20-79 years, national prevalence in the country was 5.2%, comparative prevalence 6.3%, number of adults with undiagnosed T2DM was 97.4 per 1000, and mortality from T2DM was 2560.3 (4). Because every other T2DM case remains undiagnosed in the world (4), timely

T2DM risk detection will entail cardiovascular (CV) risk drop in future (17, 18).

Such CV mortality indicators as increased cholesterol, systolic blood pressure (BP) and smoking were 3 times more prevalent in T2DM patients compared to healthy adults, sinceT2DM is a risk factor for CV diseases (19-21).Therefore, the overall CV risk (CVR) stratification in T2DM patients is germane, especially considering that in 20-30% of T2DM patients their CV complications are diagnosed already when diabetes is detected for the first time(19-27).

Studies haves shown that in high-altitude dwellers, blood sugar level is lower compared to low-altitude residents, and there was no single diabetes patient found above 3000 m. In all age groups of high-altitude residents, obesity is 3 times less prevalent compared to low-altitude dwellers, 5(1)% and 18(1)% accordingly (p<0.01).Other risk factors of T2DM are also less prevalent (1, 28, 29).

Woolcott et al. (30-32) also demonstrated an inverse relationship between height and obesity and better glucose control at high altitudes. Conversely, a study conducted in the high and low mountains of Peru suggests a higher incidence of T2DM at high altitude compared to low altitude. It is important to note that T2DM there is largely due to obesity (33). The relationship between obesity and T2DM is well known even in children (34). Recently, Hirschler et al. (35) reported a higher risk of T2DM in Argentinean indigenous children living at 3750 meters compared to children living at 1400 meters. The relationship between saturation of oxyhemoglobin at altitude and the development of metabolic syndrome and T2DM is also known (36).

Despite higher detectability in high-altitude Naryn region and middle-altitude Issyk-Kul region compared to admission levels, detectability of T2DM is still lower compared to middle-altitude Issyk-Kul region (by 2.7 and 3.0 times accordingly) (37).Therefore, studying risk factors of T2DM in the indigenous population of high-altitude regions of Kyrgyzstan in order to produce evidence-based recommendations taking in account mountainous climate to prevent T2DM is pertinent.

Objective: to study 10-years risk of diabetes type 2 in the indigenous residents of highlands Aksay of Naryn Region of Kyrgyzstan.

Methods

Population and design

Using a single-stage territorial sampling, 152 indigenous people of the highlands Aksay of the Naryn region (3260-3680 m) were examined. Indigenous people are people who have been living permanently in this territory since birth. Of these, men - 50, women – 102. Overall, 177 residents of low-altitude Chui valley of Chui region were studied as controls, of whom 56 were men and 121 women. The study was cross-sectional

and random, subjected to the conditions of singleness and territoriality and we randomized subjects in regions and sex. Inclusion criteria were age 18 - 70 years, indigenous people. Exclusion criteria were patients with an established diagnosis of T2DM, non-indigenous residents with severe conditions, children under 18 years of age. Study period: May 1 - August 30, 2017.

This study was approved by KSMA bioethics committee. Each subject in this study provided informed consent to participate.

Characteristics of altitudes

In the highlands Aksay, our study was conducted because it is the only high-altitude region in Kyrgyzstan in which the indigenous population lives and works. In comparison with the low-altitude region, the duration of winter is longer, and dwelling and nutrition are associated with a more severe climate in high-altitudes; therefore, we studied the highlands Aksay and compared it with the lowlands Chui. Other regions have low and medium altitudes. Therefore, a comparison of the 10-year risk of developing T2DM was carried out by us in the Aksay high-altitude and Chui low-altitude regions.

FINDRISC questionnaire to determine T2DM risk

We used FINDRISC questionnaire to determine T2DM risk, which considers age, BMI, waist circumference (WC), physical activity, regular intake of fruits and vegetables, regular use of antihypertensive medications and family history of the disease. Obesity was diagnosed using the formula: body mass (kg)/height (m)2 (WHO,1995). Subjects with BMI exceeding 25 kg/m2 were considered overweight. WC was measured on a midpoint of the distance between the costal arch and the iliac crest. Abdominal obesity (AO) was diagnosed when WC exceeded 94 cm in men and 80 cm in women (FINDRISC). The FINDRISC questionnaire was developed by the Finnish Diabetes Association - FINnish Diabetes Risk SCore (FINDRISC) to assess the 10-year risk of T2DM in adults (38).

A one-time, individual, full-time questionnaire survey was used. No walking or physical activity for less than 30 min a day was treated as low physical activity. The risk was classified using the following grading approach: less than 7 – low risk; 7-11 –moderate risk; 12-14 medium risk; 15-20 – high risk; more than 20 – very high risk (27, 39-41).

Statistical analysis

We used online calculator for statistical analysis (42). In this cross-sectional study, we used descriptive statistics and calculated prevalence rate (PR) of risk factors for T2DM and 95% confidence interval (CI).

Results

Risk factors of T2DM in female population

In the group of women, the frequency of the BMI risk factor above 25 kg/m2 is lower in the highlands Aksay (55.9%)

(p<0.05, PR 0.56, CI 0.46-0.66) than in the lowlands Chui (62%) (p<0.05, PR 0.62, CI 0.53-0.71), regardless of age. In the same group, the frequency of the risk factor WC>80 cm is lower in the high altitudes (80.38%) (p<0.05, PR 0.80, CI 0.72-0.88) than in the low altitudes (81.4%) (p<0.05, PR 0.81, CI 0.74-0.88), mainly under the age of 55 years in both groups (26.58% and 42.7%, respectively). An active lifestyle is also lower in the highlands Aksay (74.6%) (p <0.05, PR 0.74, CI 0.66-0.82) than in the lowlands Chui (84.5%) (p<0.05 , PR 0.84, CI 0.78-0.9), mainly under the age of 45 years in both groups (25.4% and 46.9%, respectively), with increasing age, activity decreases.

The frequency of the risk factor as the irregular consumption of fruits and vegetables was also lower in the high-altitudes (40.2%) (p<0.05, PR 0.40, CI 0.31-0.49) than in the low-altitudes (56.3%) (p<0.05, CI 0.47-0.65), regardless of age.

The regular intake of antihypertensive drugs was lower in the highlands Aksay (5.5%) (p<0.05, PR 0.56, CI 0.02-0.10) than in the lowlands Chui (7.8%) (p<0.05, CI 0.03-0.13) and increases with age.

In the highlands, high blood glucose in history (e.g. determined during a health examination, during an illness, during pregnancy) had 4 people (2.6%), of which 3 were women (2.9% among all women) (PR 0.03, CI 0-0.06), 1 male (2% among all men) (PR 0.02, CI-0.02-0.06). In the lowlands Chui, there are 6 people (3.4%) with history of high blood glucose level, of which: women - 4 (3.3% among all women) (PR 0.03, CI 0-0.06), men - 2 (3.6% among all men) (PR 0.03, CI-0.01-0.07). The indicators are not quite high both in the main groups and in the groups by gender, but with risk stratification, we considered them in conjunction with other risk factors. The frequency of the risk factor as a family history of T2DM is higher in the highlands Aksay (15.7%) than in the Chui region (11.4%) (p>0.05).

Thus, of all T2DM risk factors in women, WC>80 cm was significantly most prevalent, both in highlands Aksay (80.38%) and lowlands Chui (81.4%), followed by BMI>25 kg/m2 (55.9% and 62% accordingly), and irregular intake of fruits and vegetables (40.2% and 56.3% accordingly) and intake of antihypertensive medications (5.5% and 7.8%, respectively) (Fig.1).
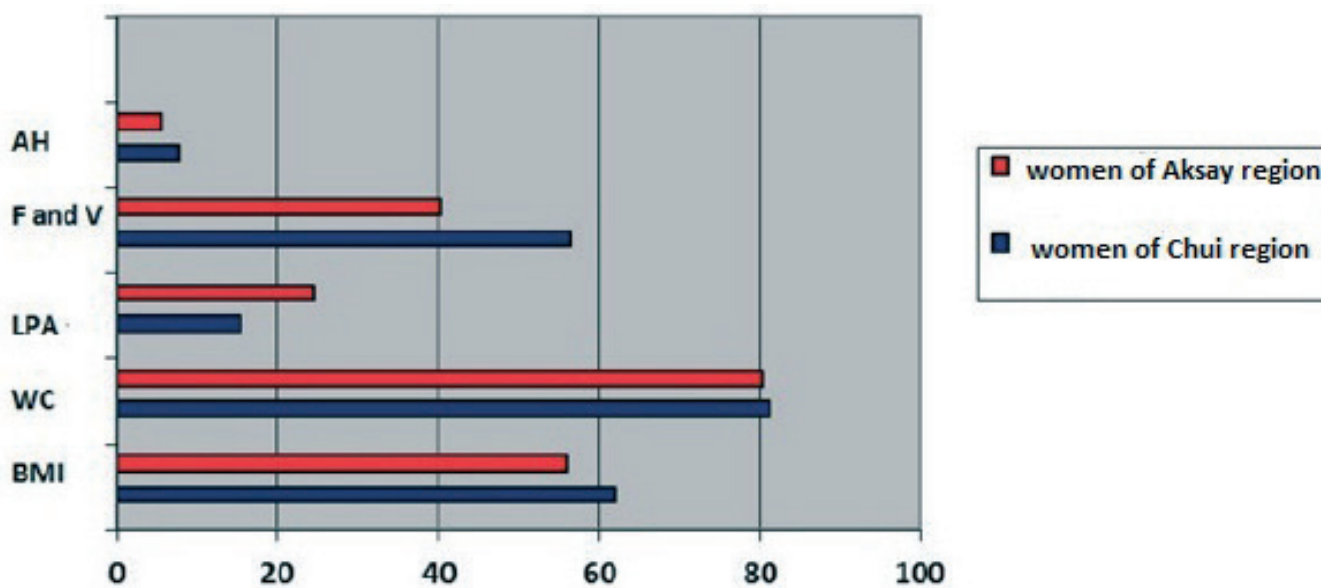

Figure 1. Comparative prevalence of risk factors in indigenous female residents of highlands Aksay and lowlands Chui

AH – regular use of antihypertensive medications, BMI – body mass index, F and V – irregular intake of fruits and vegetables, LPA – low physical activity, WC – waist circumference

Women have a predominantly low risk of developing diabetes, both in the high altitudes (82.3%) (PR 0.82, CI 0.75-0.89) and in the low altitudes (45.6%) (PR 0.45, CI 0.36 -0.54) (Fig. 2). Very high risk was not detected.

Risk factors of T2DM in male population

In the group of men, the frequency of the BMI risk factor above 25 kg/m2 is lower in the high-altitude residents (26%) (p<0.05,

PR 0.26, CI 0.14-0.38) than in the residents of low altitudes (46.2%) (p<0.05, PR 0.46, CI 0.33-0.59), mainly under the age of 55 years (22% and 23.3%, respectively).

The risk factor frequency WC>94 cm is lower in the highlands Aksay (22.4%) (p<0.05, PR 0.22, CI 0.11-0.33) than in the Chui region (45.3%) (p<0.05, PR 0.45, CI 0.32-0.58), mainly at the age of less than 55 years (20.3% and 14.9%, respectively), decreases with age.
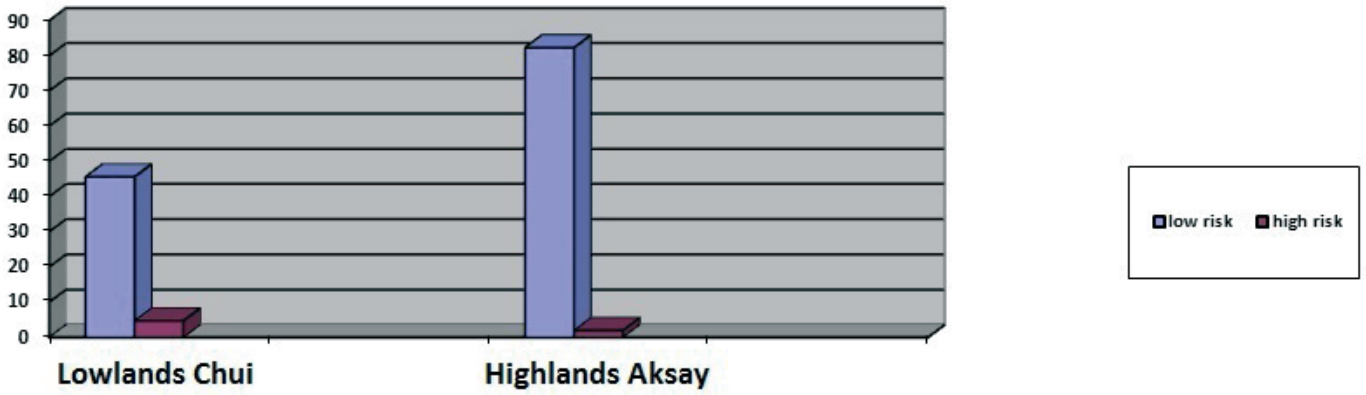
Figure 2. Comparative prevalence of diabetes risk factors in indigenous female residents of highlands Aksay and lowlands Chui

An active lifestyle is higher in the high altitudes (94%) (PR 0.94, CI 0.88-1.0) than in the low altitudes (88.3%) (p<0.05, PR 0.83, CI 0.78-0, 96), mainly at the age of less than 55 years (87% and 71.3% respectively), decreases with age. In our opinion, this is due to the fact that in the highlands men are engaged in cattle breeding all year round.

Irregular consumption of fruits and vegetables is lower in the highlands Aksay (48.8%) (p <0.05, PR 0.48, CI 0.35-0.61) than in the Chui region (100%) (p <0.05, PR 1, CI 1), decreases with age.

The regular intake of antihypertensive drugs in the group of men is lower in the highlands (6%) (p <0.05, PR 0.06, CI 0-0.12) than in the low mountains (10.7%) (p <0.05, PR 0.11, CI 0.03-

0.19), regardless of age.

In the same group, the frequency of the risk factor family history of T2DM is relatively higher in the high altitudes (8%) than in the low altitudes (7%), more at the age of 55 years, which decreases with age.

Thus, T2DM risk factors in men living in highlands Aksay were grouped as follows: irregular fruits and vegetables intake (48.8%), BMI>25 kg/m2 (26%), followed by WC> 94 cm (22.4%). In lowlands Chui, irregular intake of fruits and vegetables was also a leading risk factor (100%), followed by BMI>25 kg/m^2 (46.2%) and WC>94 cm (45.3%). All these risk factors prevailed in the age group below 55 and lessened in both regions with age (Fig.3).
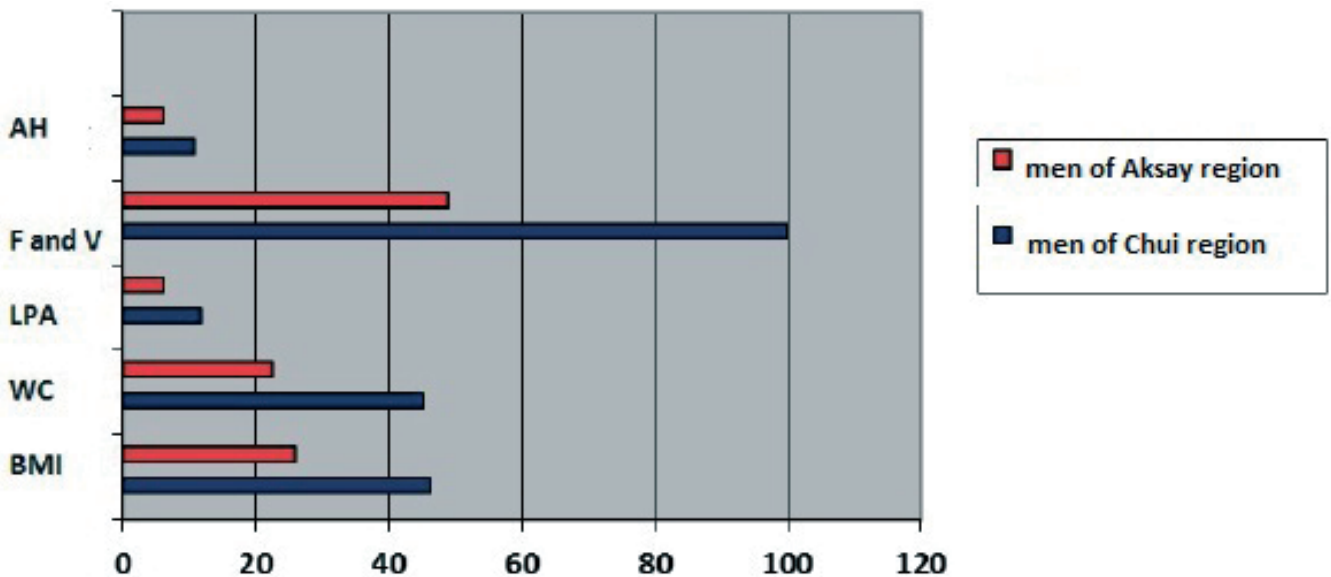

Figure 3. Comparative prevalence of risk factors in indigenous male residents of highlands Aksay and lowlands Chui

AH – regular use of antihypertensive medications, BMI – body mass index, F and V – irregular intake of fruits and vegetables, LPA – low physical activity, WC – waist circumference

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In men living in highlands Aksay as well as in lowlands Chui, the leading risk level was low- 64% (PR 0.64, CI 0.51-0.77) and 69% (PR 0.7, CI 0.58-0.82) accordingly. There was no very high risk (Fig. 4).
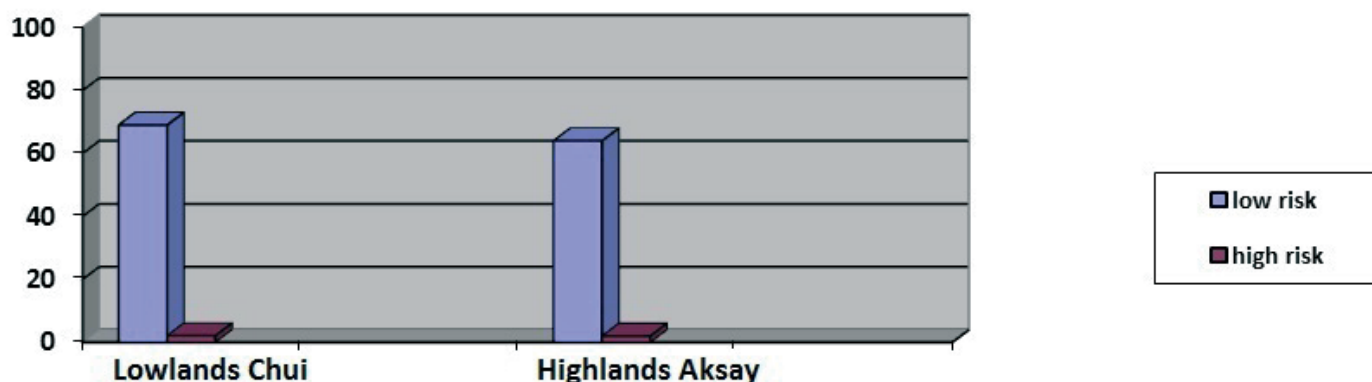

Figure 4. Comparative prevalence of diabetes risk factors in indigenous male residents of highlands Aksay and lowlands Chui

Discussion

The question of whether growth and / or residence in high mountain regions are risk factors for the development of T2DM remains a matter of discussion (43). Earlier, we in the Kyrgyz population studied the 10-year risk of developing T2DM higher among residents of low altitudes compared to high altitudes (44). We did not identify any high-risk groups among residents with a low or high incidence of disease. The leading FINDRISC composites are elevated levels of WC and BMI, possibly due to irregular consumption of fruits and vegetables, which depend on altitude of residence and age (44).

Among the highlands Aksay and lowlands Chui populations surveyed by us, the factors of the 10-year risk of developing T2DM, depending on the place of residence and gender, have their own characteristics. Of the metabolic phenotypes of the 10-year risk of developing T2DM in the indigenous population of the high-altitudes and low-altitudes of Kyrgyzstan, there are 3 main risk factors. Of these, according to the frequency of occurrence, the following were identified: in the first place, WC> 80 cm, then BMI> 25 kg/m^2 and irregular intake of vegetables and fruits in women; in men, irregular consumption of fruits and vegetables comes first, followed by BMI> 25 kg/ m^2 and WC> 94 cm.

Risk factor arterial hypertension was much less common. It is definitely difficult to answer. Despite the fact that arterial hypertension is closely associated with salt intake and obesity, prolonged exposure to low atmospheric pressure and hypoxia in indigenous highlanders leads to a decrease in the incidence of arterial hypertension . The highlanders' organism has high risks of a reflex effect of the pulmonary circulation on systemic circulation and the development of pulmonary

arterial hypertension and other adaptive mechanisms for living in the mountains (1). There are conclusions on arterial hypertension in high altitudes, which contradict this. Systemic blood pressure, cholesterol (total and low-density lipoprotein) and glucose levels were higher in high-altitude children, but at least based on mean (SD) values, these levels were normal: mean systolic blood pressure was 87 (14) mmHg (35) compared with 100 mmHg as the 50th percentile of systolic blood pressure in the same age group of the control group (46). Higher blood pressure values are associated with lower temperature at high altitude (a decrease of 6.5° C per 1000 m) due to cutaneous vasoconstriction (46).

In low-altitude and high-altitude, women reliably had high prevalence of WC >80 cm (81.4% and 80.38% respectively), then BMI>25 kg /m2 (62% and 55.9% respectively), then irregular intake of vegetables and fruits (56.3% and 40.2% respectively). Risk factors are expressed at the age of 55 years and older in the highlands Aksay (p>0.05), in the lowlands Chui - under the age of 55 years (p<0.05).

Risk factors among men are distributed in a slightly different way: in low altitudes and high altitudes, irregular consumption of fruits and vegetables (100% and 48.8%) comes first, followed by BMI>25 kg/m^2 (46.2% and 26%) and WC>94 cm (45.3% and 22.4% respectively). Risk factors are expressed at the age of less than 55 years in both regions (p<0.05). Although we did not set the goal of our study to study the dependence of risk factor on age, we suggest the high incidence of increased BMI and abdominal obesity in men of working age under 55 years of age in low altitudes and high altitudes.

Compared with other studies, our data on the prevalence of increased BMI in low altitudes in men (28% and 19.1% vs 46.2% and 26%, respectively), in women (41% and 30.5% vs

62% and 55.9% respectively); the prevalence of abdominal obesity in the low-altitudes among men (33.5% and 21.6% vs 45.3% and 22.4%, respectively) and among women (73.7% and 57% vs 81.4% and 80.38%, respectively); the prevalence of hypertension: in men it is low both in low altitudes (4.6%) and in high altitudes (10.7%), in women also there is a low hypertension rate 7.8% and 5.5%, respectively, confirm data of previous study (22). Frequency of hypertension in low-altitude and high-altitude among men and women is not marked, increased with increasing age in women in both regions.

The main risk factor in the high-altitudes for men is the irregular consumption of fruits and vegetables, and for women – abdominal obesity. When comparing the incidence rate of increased BMI and abdominal obesity in men and women, these risk factors were higher in low altitudes under 55 years of age. This once again confirms that insulin resistance plays a major role in the development of T2DM. In high-altitude conditions, the development of insulin resistance is apparently reduced due to environmental factors, of which due to hypoxia among other metabolic risk factors. Changes in insulin resistance are adaptive in nature and this issue has not been fully studied (47-50). Hirschler et al. presented interesting clinical and metabolic characteristics for a relatively large sample of schoolchildren - residents of varying altitudes. In addition to metabolic risk factors, the HOMA-IR value turned out to be less than the threshold level of 3.16 for children living at high and low altitudes, i.e., the risk of developing diabetes in children in low altitudes and high altitudes is reduced (35, 51).

The peculiarity was that these risk factors were identified at working age in our populations, which is possibly associated with the characteristics of housekeeping and the nature of labor, nutrition in low and high altitudes, the distribution of fat in deep subcutaneous layers in Asians and the influence of the mountain climate.

The risk factor as a history of high blood glucose in the high altitudes (2.6%) is lower than in the low altitudes (3.4%).

The frequency of occurrence of 2 or more risk factors is very low (7%), stratification revealed a predominance of low risk regardless of the region of residence and gender, a very high risk does not occur.

Study limitations

The main study limitation is that risk factors were determined only using a questionnaire. Larger epidemiological studies are needed to confirm these findings.

Conclusion

The features of the 10-year-old risk of developing T2DM in the indigenous people of the high-altitudes of Kyrgyzstan include the predominance of abdominal obesity and the irregular intake of fruits and vegetables. When stratifying the risks of developing T2DM, low risk predominates, and a very high risk does not occur. The prognosis of the indigenous people of the high-altitudes of Kyrgyzstan regarding the risk of developing T2DM depends on phenotypic factors and living conditions in the high altitudes, with hypoxia playing the leading role. Among the highlanders of Kyrgyzstan, metabolic factors are dominated by abdominal obesity, and it is likely that regular intake of fruits and vegetables is effective to reduce the risks of developing diabetes, along with the fight against other negative factors.

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