

ANNOTATION

of dissertation work of Akhmetova Kamshat Musakhanovna on the topic:
"Improving preventive measures and predicting the metabolic syndrome in people
of reproductive age" submitted for the degree of Doctor of Philosophy (PhD) in the
specialty 6D110100 "Medicine"

The relevance of research:

Chronic non-communicable diseases have now become one of the main problems of world health. According to the World Health Organization (WHO) data on chronic diseases, two-thirds of the world's deaths are caused by non-communicable diseases such as cardiovascular disease (CVD), diabetes and obesity [Riley, L., et al., 2016]. The reason is that the prevalence of metabolic syndrome (MS) components, especially obesity and diabetes, has increased worldwide [Pucci, G., et al., 2017].

The prevalence of MS worldwide is about 20-25%, which is three times higher than the prevalence of type 2 DIABETES [Saklayen, M.G., 2018]. The prevalence of MS has different values in different countries, for example, the frequency of MS spread in the United States is 33.4% [Moore, J.X., et al., 2017], and in China -14.4% [Lan, Y., et al., 2018].

The prevalence of MS varies depending on the age, nationality and gender of the subjects [Kaur, J., 2014], and the severity and number of components of MS increase with the age of a person [Gündogan, K., et al., 2009]. Therefore, the identification and prediction of the prevalence of MS in young people, the implementation of preventive measures contribute to the prevention of CVD diseases in old age.

According to the results of the WHO assessment of the incidence rate in the world, Kazakhstan occupies a leading position in mortality from non-communicable diseases in comparison with European countries. In Kazakhstan, mortality between the ages of 30 and 69 is 82%, in other countries this indicator is 71% [WHO, 2018]. Four main categories of non-communicable diseases - CVD, cancer, obstructive pulmonary disease and DM2, make up the majority of national-scale diseases leading to premature mortality, the probability of death from one of them is 19.28% [Statistical Handbook of the Ministry of Health of the Republic of Kazakhstan. Nur-Sultan, 2020].

Based on this, the multi-year state programs for the development of healthcare in the Republic of Kazakhstan are taking consistent steps on systemic policy measures aimed at the prevention of chronic non-communicable diseases. In accordance with this policy of our country, prevention of non-communicable diseases is an important direction.

Justification of forecasting and preventive measures of MS, which became the main epidemic of the XXI century in the conditions of the city of Astana, is an actual scientific direction of practical importance.

The purpose of the study: Improve the prediction of metabolic syndrome and related preventive measures in people of reproductive age (Astana)

Research objectives:

1. To study the prevalence of metabolic syndrome components in people of reproductive age;
2. Identify risk factors for metabolic syndrome;
3. To assess the state of health and nutrition in people with metabolic syndrome;
4. To scientifically substantiate the prognosis and preventive measures for metabolic syndrome.

Research methods:

The study was carried out within the framework of the project «Study of the features of the genetic risk of diseases associated with metabolic syndrome in the Kazakh population».

The study involved residents of the city of Astana of reproductive age (18-49 years).

Study design: observational, one-step, comparative study

I. Survey:

- Passport data (age, gender);
- Education (secondary, higher, special);
- Marital status (single, married, divorced, widower);
- Lifestyle (smoking, alcohol consumption);
- Data on 24-hour meals (chemical composition of food products).

II. General clinical research methods:

- Survey, inspection;
- Anthropometric data (height, weight, waist circumference, hip circumference, BMI, biological age, visceral fat index);
- DAD, SAD, heart rate;

III. Laboratory research methods:

- General blood test;
- Biochemical blood test;
- Genetic analysis .

IV. According to the IDF criterion, respondents should determine MS and assess the prevalence of MS and MS components.

V. Statistical research methods:

- Mann-Whitney U Test;
- Welch's t-test;
- Chi-squared test;
- odds ratio;
- Hardy-Weinberg equation;
- 5 different inheritance models;
- max and 3 max statistic;
- Spearman's correlation.

VI. Justification of the prognosis and preventive measures of MS based on the results obtained

Number of respondents who took part in the study

№	Name	total	men		women		Respondents with MS
			MS-	MS+	MS-	MS+	
1	Determining the prevalence of MS	1340	486	115	612	127	242
2	Respondents taken from MS within the framework of the project		-	219	-	110	329
3	Total number of respondents with MS		334		237		571

The main provisions submitted for protection:

In persons of reproductive age:

1. Changes in the body associated with metabolic syndrome occur in men more often than in women: indicators of waist volume, body weight, triglycerides, atherogenicity coefficient and non-HDL cholesterol are higher, HDL is lower.

2. According to the results of the analysis, the occurrence of metabolic syndrome is influenced by five polymorphisms (rs 7903146, rs 157582, rs 4506565, rs 7578597, rs 4072037).

3. The development of metabolic syndrome is influenced by factors such as overweight, marital status, calendar age, physical inactivity and smoking.

4. The decision tree, developed on the basis of genetic, clinical, anthropometric indicators, allows you to predict the risk of developing a metabolic syndrome

Conclusions:

1. The prevalence of metabolic syndrome among people of reproductive age was 18.1%; among men-19.1%, among women-17.1%. Components of the metabolic syndrome abdominal obesity was 42.9%, obesity - 31.3%, hypoalphacholesterolemia - 29.8%, hypertriglyceridemia - 9.5%, hyperglycemia - 5.7%, arterial hypertension - 40.3%. Among the components of the metabolic syndrome, it was found that hypertriglyceridemia ($p=0.024$) and arterial hypertension ($p<0.001$) are more common among men than in women.

2. The following risk factors for metabolic syndrome were identified: overweight formed before the age of 12, unmarried/unmarried status, physical inactivity, smoking, calendar age. Overweight formed before the age of 12 increases the chances of developing metabolic syndrome by 14.86 times (men 27.2, women 18.9) ($p<0.001$), unmarried/unmarried status by 2.92 times (men 3.69, women 2.54) ($p<0.01$), physical inactivity by 2.04 times (men 2.06, women women 3.3) ($p<0.05$), smoking in men 1.7 times ($p=0.021$), calendar age 1.07 times (men 1.08, women 1.1) ($p<0.001$), and having a family, drinking alcohol in small quantities, playing sports, not eating fatty and sweet foods ($p<0.05$) showed a reduction in the risk of developing metabolic syndrome.

3. 5 single-nucleotide polymorphisms affecting the development of metabolic syndrome were identified: rs 7903146, rs 157582, rs 4506565, rs 7578597, rs 072037. It has been proved that polymorphisms rs 7903146, rs 157582, rs 4506565, rs 7578597 (T alleles) increase the risk of developing metabolic syndrome by 1.5

times in the additive model and rs 4072037 (C alleles) increase the risk of developing metabolic syndrome in the recessive model by 1.99 times ($p < 0.05$).

4. It has been established that patients with metabolic syndrome suffer from: obesity, accompanied by excessive accumulation of visceral fat, an increase in waist circumference and body mass index; impaired functional activity of the liver, kidneys and heart; changes in indicators of general blood analysis, biochemical analysis and lipid profile; increase in biological age and acceleration of the aging process ($p < 0.001$).

It was found that the actual nutrition of these patients contains micronutrients of calcium, magnesium, potassium and iodine, vitamins A, D, E, C and group B and dietary fiber in insufficient quantities, and calories and sodium coming from carbohydrates and fats ($p < 0.05$) exceed the norm.

5. Based on the data revealed as a result of the study, the presence of atherosclerosis and type 2 diabetes mellitus, high levels of glucose (more than 5.67 mmol/L), visceral fat index (more than 2.3), triglyceride (more than 1.57 mmol/L) and low levels of high-density lipoprotein (less than 1.23 mmol/L) a model for predicting metabolic syndrome has been created. Based on the prediction model and primary, secondary and tertiary preventive measures, the concept of metabolic syndrome management, conducted online, is proposed.

Scientific novelty: Within the framework of the study in people of reproductive age living in the city of Nursultan for the first time:

1. the prevalence of metabolic syndrome was studied (metabolic syndrome – 18.1%, components of metabolic syndrome: abdominal obesity – 42.9%, obesity – 31.3%, hypoalphacholesterolemia – 29.8%, hypertriglyceridemia – 9.5%, hyperglycemia – 5.7%, arterial hypertension – 40.3%).

2. risk factors of metabolic syndrome (overweight, formed before the age of 12, genetics, family status, physical inactivity, smoking, calendar age, poor nutrition);

3. 5 single-nucleotide polymorphisms affecting the development of metabolic syndrome were identified (rs7903146, rs 157582, rs 4506565, rs 7578597, rs 072037).

4. the state of health and nutrition in persons suffering from metabolic syndrome was assessed;

5. the measures of prediction and prevention of metabolic syndrome (prediction model, the concept of management of metabolic syndrome) are justified.

Theoretical and practical significance of scientific work:

1. Methodological recommendations developed based on the results of the work can be used by doctors in the clinic when working with patients.

2. Preventive measures recommended for the prevention of metabolic syndrome in people of reproductive age help prevent the spread of non-communicable diseases.

3. The implementation of the results obtained in the educational process of the Department of Preventive Medicine and Nutrition, Internal Diseases - will allow to prepare specialists for bachelor's degree, internship and postgraduate education.

4. Based on the results obtained, it is possible to predict genetic predisposition to metabolic syndrome based on genotypes rs 7903146, rs 157582, rs 4506565, rs 7578597, rs 4072037.

Implementation of research results:

- 2 utility model patents;
- 5 certificate of state registration of rights to the copyright object;
- 2 methodological recommendations for doctors of the Hospital of the Medical Center of the Office of the President of the Republic of Kazakhstan;
- 1 act of introduction into the educational process of the Department of Preventive Medicine and Nutrition of the NAO "Astana Medical University";
- 1 act of introduction into practice of the Hospital of the Medical Center of the Office of the President of the Republic of Kazakhstan.

Personal contribution of a doctoral student:

The dissertation student independently collected the material, conducted analysis and statistical processing. All the results presented in the dissertation work and having scientific novelty were obtained by the author personally.

Publications on the topic of the dissertation

12 publications have been published on the topic of the dissertation, including 5 works in publications recommended by the Committee for Control in the Field of Education and Science of the Ministry of Education and Science of the Republic of Kazakhstan; 5 articles in the journal of the international citation database Scopus; 2 publications in collections of scientific materials of conferences.