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CROSS - SECTIONAL STUDY ON A POPULATION OF DIABETES MELLITUS NEWLY DIAGNOSED PATIENTS. RELATIVE RISK OF CORONARY HEART DISEASE (CHD) MORBIDITY USING UKPDS RISK ENGINE

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Abstract

Patients recently diagnosed with diabetes mellitus need to go to a complex evaluation regarding not only glycaemia and HbA1C, but also blood pressure values, lipid metabolism, kidney function, medical history and lifestyle choices. Cardiovascular risk assessment can reveal which patients fall into moderate and high categories of risk, where regular follow-up and intensive therapy addressing all the risk factors must be strictly performed. We selected a group made of 385 diabetes mellitus type II patients, a representative for the whole population of newly diagnosed diabetic patients from our county in 2017. We determined their anthropometric indicators, their biochemical parameters, their lifestyle choices and we assessed their coronary heart disease risk at 10 years using UKPDS risk engine.

Keywords*: diabetes type II, coronary heart disease prediction in diabetic patients*

Rezumat

Pacienții nou-diagnosticați cu diabet zaharat trebuie să fie supuși unei evaluări complexe în ceea ce privește nu numai glicemia și procentul hemoglobinei glicozilate, dar și valorile tensiunii arteriale, metabolismul lipidic, funcția renală, istoricul medical și stilul de viață. Determinarea riscului cardiovascular ne poate arăta care dintre pacienți intră în categoriile de risc moderat și înalt, la care monitorizarea clinică și tratamentul medicamentos intensiv trebuie să fie strict respectate. Am selectat un grup de 385 de pacienți cu diabet zaharat tip 2, alcătuind un eșantion reprezentativ pentru întreaga populație de diabetici nou-diagnosticați în județul nostru în anul 2017. Pentru acești pacienți am determinat indicatorii antropometrici, parametrii biochimici, stilul lor de viață și riscul de boală coronariană la 10 ani utilizând motorul de risc UKPDS.

Cuvinte cheie*: diabetul zaharat tip II, predicția riscului de boală coronariană la diabetici*

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Introduction

The diabetic patient has a two times to four times higher risk of developing coronary heart disease than the general population[1]. Diabetes mellitus is a risk factor for coronary artery disease but at the same time it is considered an equivalent for coronary artery disease[2], patients with diabetes without a history of myocardial infarction have the same risk of coronary artery disease death as nondiabetic patients with history of myocardial infarction. Type II diabetes, the most common type of diabetes, is defined by insulin resistance that appears as a consequence of obesity. Obesity represents an independent cardiovascular risk factor[3], appearing as a consequence of sedentary lifestyle and high caloric intake. Therefore at the moment of diagnosis, the diabetic patient has already, at first sight, at least four cardiovascular risk factors: sedentary lifestyle, obesity, insulin resistance and hyperglycemia. Pathological consequences of insulin resistance and obesity lead to atherogenic dyslipidemia[4], sympathetic hypertonia, increased inflammation[5], endothelial dysfunction[6], platelet function anomalies, hypercoagulability, and high blood pressure. All these factors are a component of metabolic syndrome. We conclude that the newly diagnosed diabetic patient has a large number of traditional and non-traditional risk factors which explains the association between diabetes mellitus and coronary artery disease.

In this paper we discuss the differences between some clinical and biochemical parameters of newly diagnosed diabetes mellitus patients and we calculate the coronary heart disease morbidity risk using UKPDS risk engine[7], a special score conceived for the diabetic patients that includes in its equation the glycated hemoglobin and the diabetes duration.

Material and methods

In the study were included 385 patients newly diagnosed with diabetes mellitus type 2, 185 men (48.05%) and 200 women (51.94%). From all the patients diagnosed with diabetes mellitus in 2017, a total of 2705 patients, we selected each 7th patient, making this way a representative group for the whole population of patients. For every patient we determined the BMI, glycated haemoglobin (HbA1C), waist circumference (WC), systolic blood pressure (SBP), diastolic blood pressure (DPB), total cholesterol, LDL-cholesterol, triglycerides, HDL-cholesterol, glomerular filtration rate (GFR) and liver enzymes. We also determined the patients' medical history and asked the patients about their lifestyle like physical effort, diet, salt intake, and smoking. We divided the population into different groups

Indicators of lifestyle	Urban	Rural	Total	p
Smoking	28.36%(59)	26.55%(47)	27.52%	0.693
Sedentarism	60.09%(125)	35.59%(63)	48.82%	<0.001
High sugars intake	78.88%(162)	54.23%(96)	67.54%	<0.001
High lipidic intake	49.51%(103)	90.96%(161)	68.56%	<0.001
Soda consumption	60.57%(126)	28 .24%(50)	45.70%	<0.001
Excess salt	55.76%(116)	77.96%(138)	65.96%	<0.001
Alcoohol consumption	52.88%(110)	71.18%(126)	61.29%	0.002

Table nr. 1. *Distribution of indicators concerning lifestyle according to urban or rural environment*

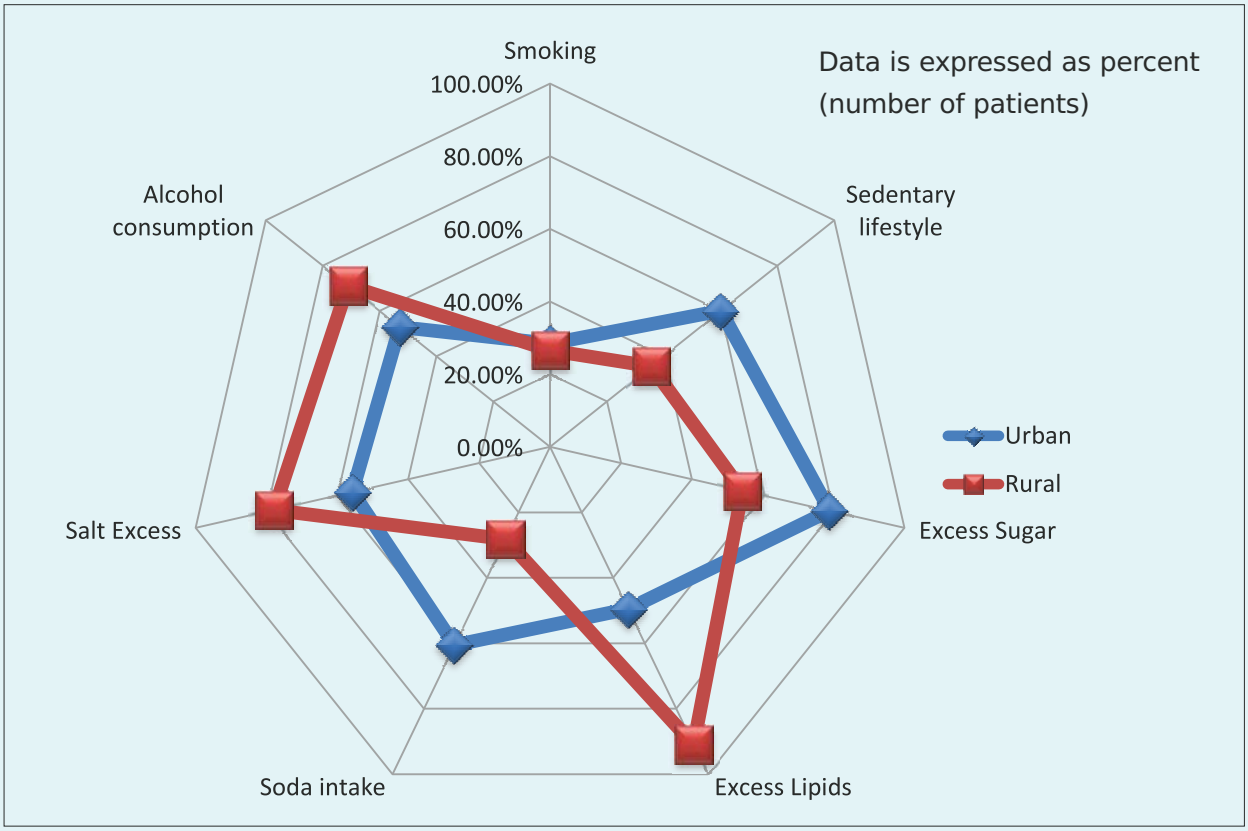

Figure. nr. 1 *Lifestyle in urban and rural environment*

using different criteria like sex, environment, HbA1C percent, and systolic blood pressure and calculated the UKPDS risk of coronary heart disease. We determined the relative risk of a cardiovascular event compared to the simulated risk for persons with the same age as the mean age of group, without diabetes, hypertension, non-smokers, with normal cholesterol and HDL-cholesterol.

Results and discussion

The mean age of newly diagnosed type 2 diabetes patients was 57.47 years. Women had at diagnosis a more advanced age then men (58.2 years vs 56.7 years). Age difference at diagnosis between the two sexes is statistically significant, $p<0.05$.

Concerning urban or rural origin, in the analyzed population, urban environment predominated (45.97% vs. 54.03%), the difference being statistically significant ($p<0.05$). Out of 185 male patients, 50.27% came from rural environment while 49.27% came from urban environment, the difference not being statistically significant. Out of 200 female patients, 42% came from rural environment while 58% came from urban environment, the difference being statistically significant ($p<0.05$).

Of the included patients 15.58% had an universitary degree, the others 84.42% graduated only middle school or high school, the difference being statisically significant ($p<0.001$). 20.5% of men had a university degree, while 11% of female had a university degree. Diabetes mellitus family history was positive in 27.01% of patients. 21.08% of men had a familial positive history of diabetes, while 32.5% of women had a positive history of diabetes mellitus, the difference being statistically significant.

Lifestyle analysis in urban and rural environment shows the presence of some important differences. Patients with urban residence compared with those with rural residence are more frequently sedentary (60.09% vs. 35.59%, $p<0.001$), have a diet rich in sugars, usually refined, with a high glycemic index (78.88% vs. 54.23%, $p<0.001$), consume sodas more frequently (60.57% vs. 28.24%, $p<0.001$). Patients with rural residence compared with those with urban residence have more frequently a diet high lipids (90.96% vs. 49.51%, $p<0.001$), consume excess salt (77.96% vs. 55.76%, $p<0.001$), consume more frequently alcohol (71.18% vs. 52.88%, $p<0.001$). Smoking status did not differ significantly between the two sexes.

Clinical and biochemical profile according to sex

Clinical and biochemical parameters of men and women are illustrated in figure nr. 2. Body mass index was significantly higher in women

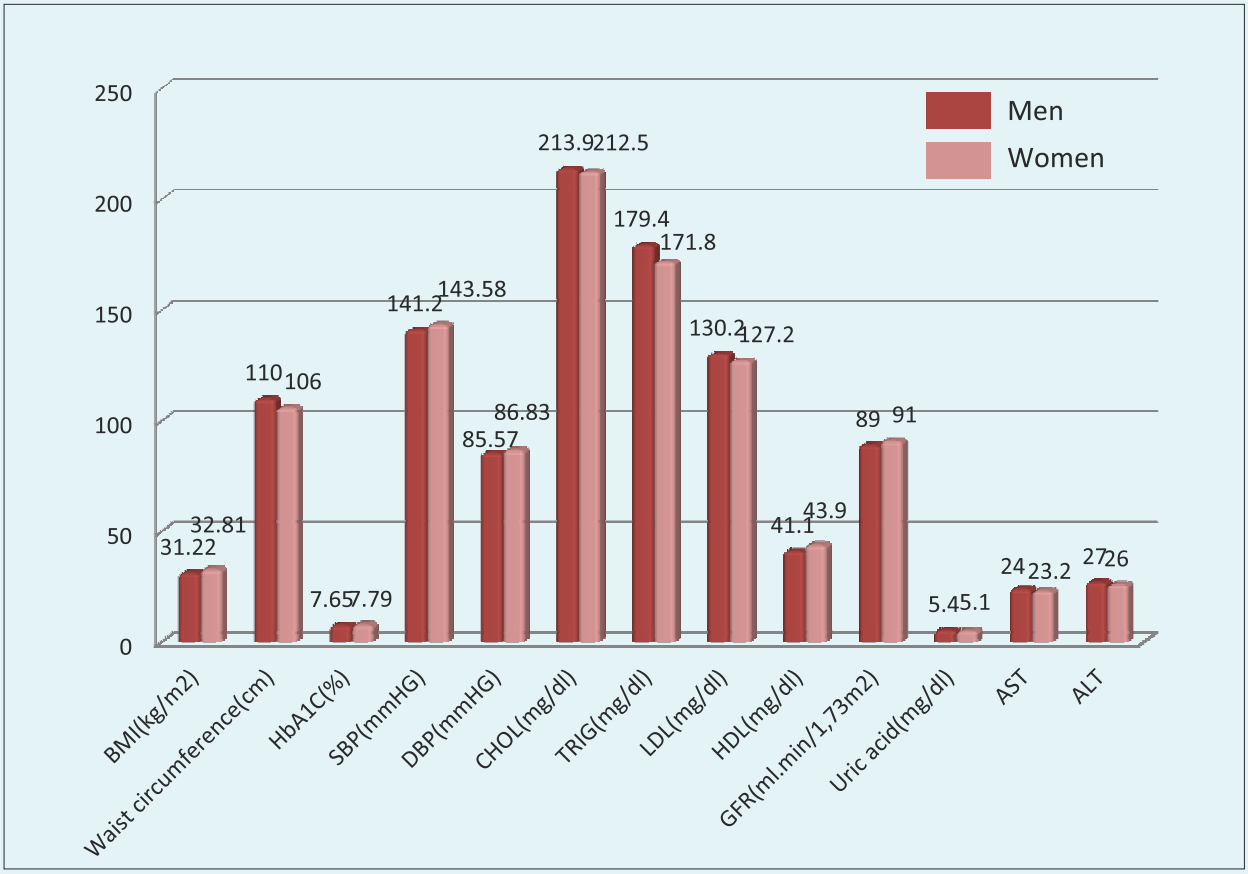

Figure nr. 2. *Characteristics of group according to sex*

than in men (32.81 kg/m^2 vs. 31.22 kg/m^2, p<0.05). We observe that the newly diagnosed diabetes patients are mostly obese, a fact demonstrated by the mean BMI of the patients included in the study, BMI= 32.04 kg/m^2. Mean waist circumference of men was 110 cm and of women was 106 cm, the difference being statistically significant, p<0.001. These values, both in men and women, overcome the waist circumference dimensions considered to represent a high cardiovascular risk (102 cm for men and 88 cm for women). Mean glycated haemoglobin was 7.72%. Patients with high percent of glycated haemoglobin had more frequently symptoms of hyperglycaemia, polyuria, polydipsia, and polyphagia (8.5% vs. 7.5%, p<0.001). Blood pressure values were high, we can say that the analysed population is a group of stage I hypertensive patients, the mean value of systolic blood pressure being 142.43 mmHG. Men had a mean systolic blood pressure of 141.20mmHG and women 143.58mmHG, the difference not being statistically significant (p=0.15).

Lipid parameters of the analysed groups were modified, exceeded the values considered normal for healthy population, without cardiovascular risk factors, and being a lot higher than the target values for diabetic patients, mean values of cholesterol being 213.17 mg/dL, for triglycerides being 175.45 mg/dL, for LDL-cholesterol 128.64 mg/dL, for HDL 42.5 mg/dL. The disparity between the two sexes are not statistically significant concerning total cholesterol and LDL-cholesterol, in contrast men had higher levels of triglycerides than women (179.4 mg/dL vs. 171.8 mg/dL, p<0.03) and lower levels of HDL cholesterol than women (41.1 mg/dL vs. 43.9mg/dL, p<0.05).

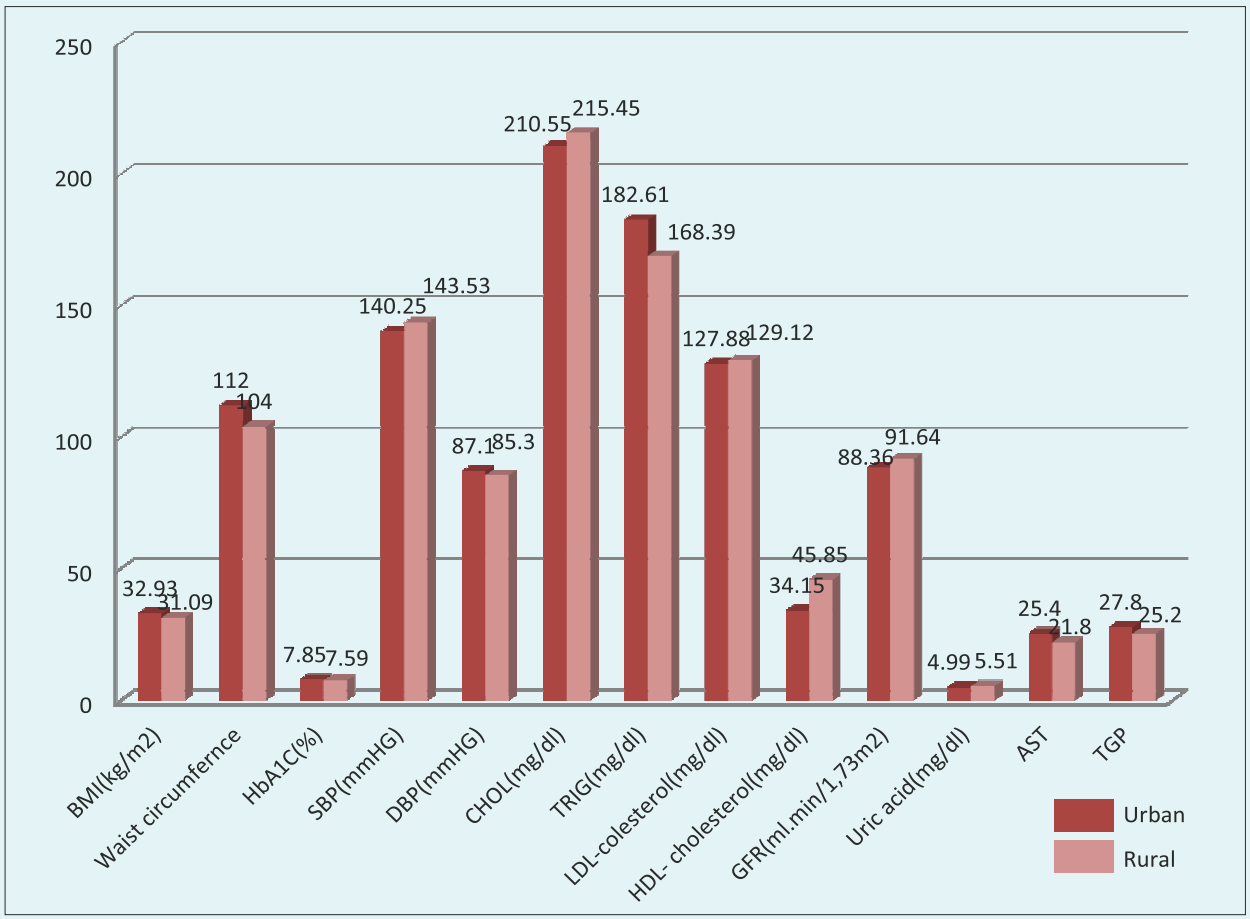

Figure nr. 3.*Characteristics of group according to residence*

Clinical and biochemical profile according to living environment

Patients from urban environment had a mean BMI greater than those from rural environment (32.93 kg/m^2 vs. 31.09kg/m^2, p=0.0041). Waist circumference of the patients from urban environment was greater than of those from rural environment (112 cm vs. 104 cm, p<0.05). We observe that in urban environment, where obesity level is greater and waist circumference is greater, glycated hemoglobin percent is higher (7.85% vs. 7.59%, p=0.21), which reflects the impact of obesity, especially of the abdominal obesity on the glycemic control. Mean total cholesterol of patients from urban environment has higher values than of patients from rural environment

Category of patients	Relative risk of CHD at 10 years	UKPDS Risk Engine	Category of risk
Men	**2.15**	**18.10%**	**MODERATE**
Women	**2.80**	**10.70%**	**LOW**
Total	**2.34**	**14.25%**	**LOW**
Urban	**2.67**	**17.20%**	**MODERATE**
Rural	**1.95**	**12.60%**	**LOW**
Normal weight	**1.85**	**11.95%**	**LOW**
Overweight	**2.13**	**13.75%**	**LOW**
Obese	**2.71**	**17.45%**	**MODERATE**
Whithout metabolic syndrome	**2.15**	**13. 85%**	**LOW**
With metabolic syndrome	**3.01**	**19.40%**	**MODERATE**
HbA1C<7%	**1.89**	**12.20%**	**LOW**
HbA1C 7 -8%	**2.19**	**14.15%**	**LOW**
HbA1C8 -9%	**2.56**	**16.50%**	**MODERATE**
HbA1C 9 -10%	**2.98**	**19.20%**	**MODERATE**
HbA1C>10%	**3.46**	**22.30%**	**HIGH**
Normotensive	**1.78**	**11.50%**	**LOW**
HT stage I	**2.26**	**14.55%**	**LOW**
HT stage II	**2.64**	**17%**	**MODERATE**
HT stage III	**3.05**	**19.70%**	**MODERATE**
Without dyslipidemia	**1.86**	**12.00%**	**LOW**
Hypercholesterolemia	**2.25**	**14.50%**	**LOW**
Low HDL	**2.47**	**15.95%**	**MODERATE**
Hypercholesterolemia+ low HDL	**2.76**	**17.80%**	**MODERATE**

Table nr. 2. *Relative risk of a coronary heart disease morbidity using UKPDS risk engine*

(215.45 mg/dL vs. 210.55mg/dL, p<0.05), also triglycerides had higher levels in urban environment (182.61 mg/dL vs. 168.39 mg/dL, p<0.001), LDL cholesterol was higher in rural population, without statistical significance, and HDL was lower in urban environment than in urban environment, the disparity being statistically significant (34.15 mg/dL vs. 45.85mg/dL, p<0.001).

Using UKPDS risk engine we calculated the CHD morbidity by dividing the population in different groups. We defined very low risk as CHD between 5% and 10%, low risk as CHD between 10% and 15%, moderate risk as 15% to 20%, and high risk above 20%. After that we compared the risk ratio between normal healthy population, in the same age group with a mean age of 57 years, and the population of newly diagnosed diabetic patients.

Data obtained proved that a level of HbA1C>10% has the highest risk of 10 years CHD morbidity, of 22.30%, this result is very interesting because it shows us that high values of glycaemia at the diagnosis of diabetes mellitus is more dangerous even that high blood pressure stage III or dyslipidemia. Values of HbA1C>10%, correspond without doubt, to a duration of diabetes of at least 2 to 5 five years. These patients are extremely insulin resistant, meaning that they have altered lipid metabolism and a high level of oxidative stress. Their relative risk of CHD is 3.46 higher than the risk of healthy population. Actually they are patients with undiagnosed diabetes, which proves the need for public health measures for early diagnosis of diabetes. The correlation between HbA1C % and UKPDS risk was statistically significant (p<0.001). Also importance of UKPDS risk engine is accentuated once more, scores like Framingham and SCORE cannot discern accurate risk in diabetic population because lack of inclusion of glycemic variables in their equation.

Newly diagnosed diabetic patients with stage III hypertension have a risk of CHD events of 19.70%, close to the cut-off value of 20%. Another category of diabetics close to high risk are the newly diagnosed patients with metabolic syndrome. Patients with high cholesterol and low HDL had a risk of 17.80%.

Conclusions

There are important differences between newly diagnosed diabetic men and women, and between urban and rural residence. Women had greater BMI, HbA1C, SPB, and HDL-cholesterol, while men had higher greater waist circumference, cholesterol and triglycerides. Patients living in urban environment have a sedentary lifestyle, consume refined sugars in excess, and drink a large quantity of sugar-sweetened beverages while patients from rural environment consume more lipids, use excess salt and consume more alcohol.

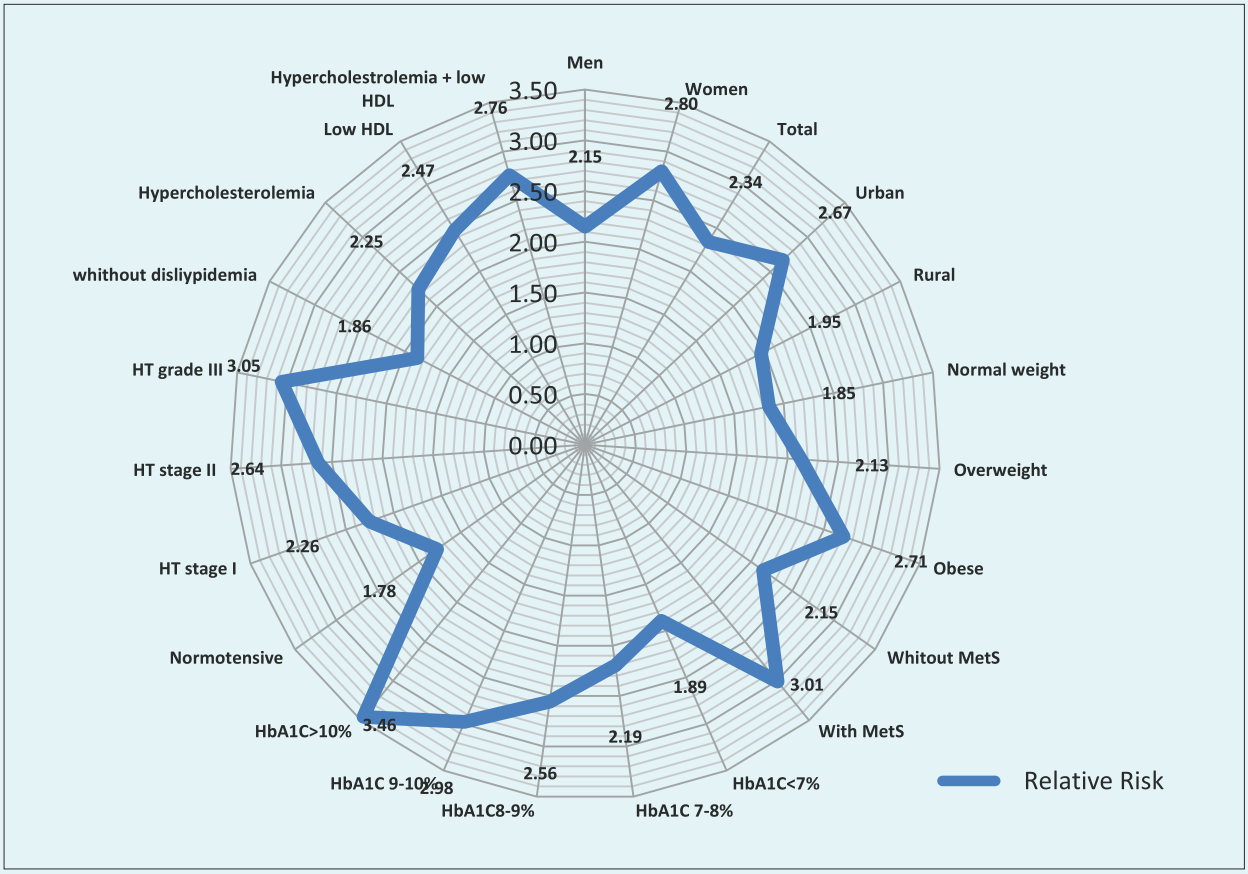

Figure nr. 4. *Relative risk of different categories of patients compared to general population*

Urban inhabitants had a higher BMI, HbA1C, waist circumference, higher triglycerides and lower HDL-cholesterol than rural inhabitants, while rural inhabitants had higher SBP, total cholesterol and LDL-cholesterol.

The category of patients with the highest 10 years coronary heart disease is the patients with a level of HbA1c>10% confirming the tight connection between diabetes mellitus and heart disease. Other categories with risk close to 20% at 10 years are: men, obese patients, stage III hypertensive patients, diabetics with metabolic syndrome and patients with high levels of cholesterol and low level of HDL-cholesterol.

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