

Study of carotid artery changes in patients with ischemic stroke and metabolic syndrome

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Abstract

Background: The metabolic syndrome is a major and escalating public-health problem and a clinical challenge worldwide. The increasing prevalence of metabolic syndrome is associated with heart and cerebrovascular diseases.

Material and methods: A "case-control" study was performed on 125 subjects that were examined in the Cerebrovascular Diseases Neurology Department of the Emergency Medicine Institute, in the period of March 2015–July 2015. All subjects underwent a complete clinical examination and ultrasound examination of the extracranial carotids.

Results: The present study shows that the patients with metabolic syndrome (MS) have values of the intima-media thickness and the internal diameter of the common carotid artery significantly higher than the subjects without the metabolic syndrome ($p < 0.05$). Regarding the relationship between the number of risk factors and the markers of atherosclerotic carotid damage, a strong dependence between the two parameters was observed. Thus, it can be stated that 74% of the IMT variation and 77% of the luminal diameter variation is explained by the variation of the number of risk factors constituting MS.

Conclusions: The obtained results, suggest that the cluster of risk factors, the MS constituents are connected with the alteration of the carotid arteries, these changes explain the relationship between the MS and the high risk of heart and cerebrovascular pathologies. In MS the risk of cerebrovascular diseases is multifactorial and its early detection and its treatment can prevent vascular events.

Key words: metabolic syndrome, stroke, risk factor, atherosclerosis.

Introduction

The metabolic syndrome (MS) is a major and escalating public-health problem and a clinical challenge worldwide. The increasing prevalence of MS is associated with heart and cerebrovascular diseases. A recent meta-analysis of 37 longitudinal studies revealed a 78% risk increase for vascular events and death in people suffering from MS [1]. The literature data shows that 25-35% of the world population meets the MS criteria and it is estimated that the number will double by 2025 [2]. According to some data collected from specialty literature, over 50% of patients with acute vascular events meet the MS criteria [3, 4, 5], and the presence of MS constituent disorders influences the unfavorable development of vascular diseases and the cognitive status of the individuals with this syndrome [6].

The association of metabolic syndrome increases the thickness of the intima-media, proving that the summation of metabolic risk factors is due to the appearance of anatomic changes of the vessel wall [7, 8]. In MS the risk of cerebrovascular disease is multifactorial and its early detection and treatment can prevent vascular events.

The aim of the study. To evaluate the ultrasound markers of atherogenesis (intima-media thickness (IMT) in the common carotid artery, luminal diameter of the common carotid artery and the presence of atheromatous plaques) in a group of subjects with ischemic stroke and MS compared to a control group of subjects with ischemic stroke, but without MS, and to identify the possible associations between these ultrasound parameters, anthropometric and clinical characteristics and other metabolic risk factors.

Material and methods

A "case-control" study was performed on 125 subjects that were examined in the Cerebrovascular Diseases Neurology Department of the Emergency Medicine Institute, in the period of March 2015–July 2015. The patients were selected according to the MS diagnostic criteria of the American Cardiology Association, the National Heart, Lung and Blood Institute and the International Diabetes Federation (2009). After the patients or their relatives signed an informed written consent, according to the declaration of Helsinki, the baseline data was collected by questionnaire. All subjects underwent a complete clinical examination and ultrasound examination of the extracranial carotids. Ischemic stroke diagnostic was made by a neurologist and confirmed by a brain CT scan.

Statistical analysis

Data were analysed by Microsoft Excel, GraphPad and SPSS 17 for Windows application, processing adapted medical statistics. We calculated average parameters, standard deviations; t-student was used for comparisons between two groups. A value of $p < 0.05$ was considered statistically significant. The graphs were done in Microsoft Excel and GraphPad. Patients were divided into two groups according to the presence / absence of the metabolic syndrome: Group I consisting of 68 patients with MS, respectively Group II consisting of 57 patients without MS, but who could also have one / two / no component of MS.

Results

Table 1

Analysis variables in group 1 (68 subjects):

- There were 37 females (54.41%) and 31 (45.59%) males
- Mean age of patients was 67 ± 1.37 years (minimum 37 years, maximum 97 years), mean age of females was 71.3 ± 1.58 years and 61.8 ± 2.04 years for men, it was established a maximum incidence of stroke in the age group of 65-75 years: 9 (29.03%) men and 19 (51.35%) women.
- All subjects have suffered an ischemic stroke, 17 of them have suffered a repeated stroke (25%);
- The most common location was the basins of the middle cerebral artery – 50%, other locations were the carotid artery (carotid occlusion) – 3%, the vertebra-basilar territory – 29.4% and lacunar stroke – 17.6%.
- Most participants had 3 of the 5 criteria for defining SM (38 people, 56%, fig. 1).

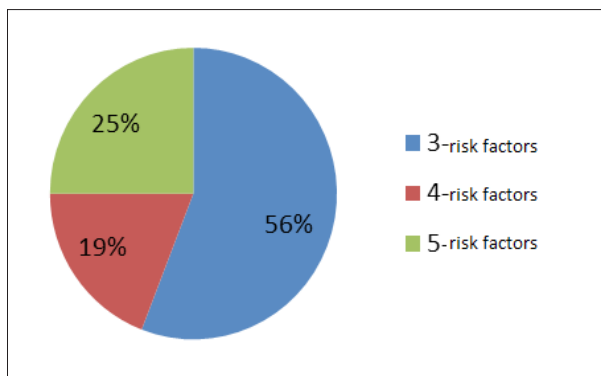


Fig. 1. The distribution of patients with ischemic stroke and MS according to the number of risk factors.

The prevalence of cardiovascular risk factors in the studied group (1st group) was (table 1):

- 36 patients (52.94%) were diagnosed with type 2 diabetes mellitus (DM), the majority were treated with oral antidiabetic 24 (66.7%), 13.89% were in dietary treatment and 19.44% in insulin treatment, the mean duration of diabetes until the stroke occurred, was 7.36 ± 2.03 years,
- Hypertension was a preexisting risk factor to 98.53% of the subjects with stroke and MS, 22% had ischemic heart disease, 3 subjects had atrial fibrillation (AF),
- two smokers (2.9%) and 12 ex-smokers (17.65%) had been indentified, the average duration of the smoking cessation was 14 ± 3.36 years,
- 27 subjects from the main group were overweight (39.7%), 34 obese (50%) and 100% of all participants had high waist circumference (WC) according to IDF-2005 criteria (≥ 80 cm in women and ≥ 94 cm men),
- 56.94% suffered from dyslipidemia.

The analysis variables in the group of study

Variables	Normal value	No / %	Mean \pm DS
Basal plasma glucose (mmol/l)	<5,6	9 (13.23%)	8,57 \pm 4,05
	\geq 5,6	59 (86.77%)	
Total Cholesterol (mmol/l)	<6,2	48 (70.6%)	5,7 \pm 1,12
	\geq 6,2	20 (29.4%)	
Triglycerides (mmol/l)	<1,7	36 (52.94%)	1,74 \pm 0,85
	\geq 1,7	32 (47.06%)	
Beta-lipoproteine (units)	<55	49 (72.1%)	46 \pm 13,6
	\geq 55	19 (27.9%)	
Fibrinogen (g/l)	<4,0	53 (78%)	3,36 \pm 1,00
	\geq 4,0	15 (22%)	
Systolic blood pressure (mm Hg)	<135	2 (2.9%)	144 \pm 10,2
	\geq 135	66 (87.1%)	
Diastolic blood pressure (mm Hg)	<85	26 (38.23%)	87 \pm 7,3
	\geq 85	42 (61.77%)	
BMI (kg/m ²)	<25	7 (10.3%)	31,1 \pm 6,2
	25-30	27 (39.7%)	
	30-35	17 (25%)	
	35-40	10 (14.7%)	
	>40	7 (10.3%)	
WC(cm)	Women		102,05 \pm 12,98
	<80	0 (0%)	
	\geq 80	37 (100%)	
	Men		
<94	0 (0%)	107 \pm 10,38	
\geq 94	31 (100%)		

Analysis variables in group 2 showed the following distribution (table 2):

- There were 20 women (35.08%) with the mean age 67.4 ± 2.03 years and 37 men (64.92%) with the mean age 65.38 ± 1.48 years, the average age being $66,09 \pm 1.18$ years,
- All subjects suffered an ischemic stroke, 13 of them had a repeated stroke (22.8%),
- 46 (80.7%) persons were suffering from hypertension, 15 (26.32%) had ischemic heart disease and 9 participants (15.79%) were diagnosed with AF,
- 14 smokers (24.56%) were identified, 13 of which were men (representing 35.13% of men), 16 were ex-smokers (mean duration of the non-smoking period was 17.2 ± 3.7 years), 2 were females (10% of women) and the remaining males (37.84% of men),
- 2 people in the control group had type 2 diabetes (3.5%), both were on dietary treatment,
- 24 (42.11%) persons were overweight, and 16 (28.07%) obese,
- 34 (59.6%) individuals had a high waist circumference, according to IDF-2005 criteria,
- 15 (26.31%) subjects suffered from dyslipidemia.

Table 2

Analysis variables in the control group

Variables	Normal value	Nr./%	Mean ±DS
Basal plasma glucose (mmol/l)	<5,6 ≥5,6	45 (78.95%) 12 (21.05%)	5,07±1,13
Total Cholesterol (mmol/l)	<6,2 ≥6,2	45 (78.95%) 12 (21.05%)	5,13±1,34
Triglycerides (mmol/l)	<1,7 ≥1,7	54 (94.74%) 3 (5.26%)	1,11±0,78
Beta-lipoproteine (units)	<55 ≥55	55 (96.5%) 2 (3.5%)	38,9±9,77
Fibrinogen (g/l)	<4,0 ≥4,0	55 (96.5%) 2 (3.5%)	3,05±0,55
Systolic blood pressure (mm Hg)	<135 ≥135	11 (19.3%) 46 (80.7%)	146±11,4
Diastolic blood pressure (mm Hg)	<85 ≥85	14 (24.56%) 43 (75.44%)	82±5,6
BMI (kg/m ²)	<25 25-30 30-35 35-40 >40	17 (29.82%) 24 (42.11%) 13 (22.8%) 3 (5.27%) 0 (0%)	27,4 ±4,54
WC (cm)	Women <80 ≥80 Men <94 ≥94	5 (25%) 15 (75%) 18 (48.65%) 19 (51.35%)	88,7±12,17 93,43±9,18

The descriptive analysis of the arterial parameters throughout the main group highlights their average values to limits that are considered pathological. Thus, the average value of CIM in subjects with MS was 0.99 ± 0.037 mm (95% CI 0.91 ÷ 1.07) and luminal CCA diameter was 6.94 ± 0.08 mm (95% CI, 6.78 ÷ 7.1 mm).

Atherosclerotic plaques were found in 59 (86.76%) participants. 9 participants were found without atherosclerotic plaques in extra-cranial carotid segment: 3 had AF, 2 had suffered from a lacunar stroke and 4 could not determine the cause of stroke. 36 patients (53%) with MS suf-

Table 3

Anthropometric characteristics of the group of study, compared with the control group

Parameter	1st group	2nd group	p
Sex Male / Female	31/37	37/20	
Age (Years)	67 ± 1,37	66,09±1,18	0,63
BMI (kg/m ²)	31,1±0,0,76	27,4 ±0,6	<0,001
WC (cm)	104±1,47	91,77±1,4	<0,001
Systolic blood pressure (mm Hg)	144±1,25	146±1,39	0,52
Diastolic blood pressure (mm Hg)	87±0,97	82±0,75	0,27

Comparing the two groups

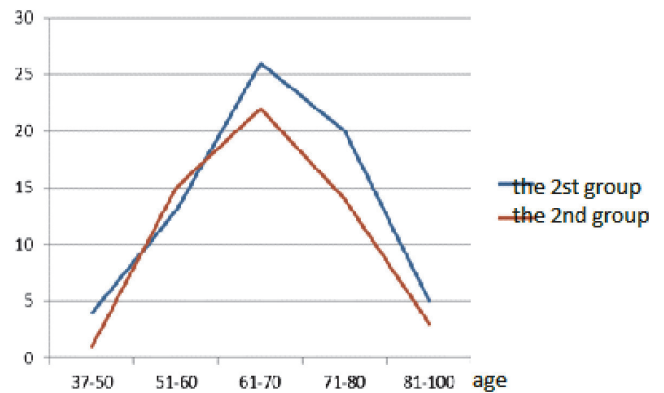


Fig. 2. Distribution on age.

fered from ischemic stroke and type 2 diabetes, the average values of IMT was 1.01 ± 0.05 mm and of internal diameter of the common carotid artery was 6.79 ± 0.09 mm (95% CI, 6.61 ÷ 6.97 mm).

The average values of IMT in patients hospitalized with ischemic stroke, but that did not meet the MS criteria (control group), was 0.84±0.037 mm (95% CI, 0.77÷0.91 mm), and the internal diameter of ACC was 6.5±0.09 mm (95% CI, 6.32÷6.68 mm). Atherosclerotic plaques were found in 24 (42.1%) participants from group 2.

There was no significant difference in age between the two study groups (p=0.63) (fig. 2).

It was found that the level of uric acid, beta-lipoprotein, triglycerides, fibrinogen in patients with ischemic stroke and MS is significantly higher than those without MS (p <0.05) (table 4).

It is necessary to point out that the number of constituent risk factors of the MS affects the IMT values, the internal diameter of carotid arteries and the development of carotid atheroma (fig. 3, 5, 7), so summing all the metabolic risk factors is reflected by the appearance of anatomical changes of the vessel wall [7, 8]. It has been noted that there is a significant difference between the IMT values and the diameter of common carotid artery (CCA) in these two groups (p <0.05, p <0.001) (table 5, fig. 4, fig. 6). The average luminal diameter of CCA in patients with five risk factors is lower than in those with 4 risk factors (fig. 7), the explanation of this phenomenon was found in specialty literature, all participants in this case study were suffering from type 2 diabetes mellitus (17 subjects, 25% of group 1), the mean duration of diabetes was 9 ± 2.1 years, and the research of this category of patients proved the internal carotid vessels remodeling, consequently an increase in IMT values and a decrease in the CCA internal diameter [10, 11, 14].

After searching the link between the values of intima-media and the metabolic profile, a weak relationship between IMT and total cholesterol (r = 0.13), IMT and glucose (r = 0.2) was detected. It did not reveal any correlation

Table 4

Biochemical characteristics of the various parameters in the study and control groups

Parameter	1st group	2nd group	p
Basal plasma Glucose (mmol/l)	8,56±0,49	5,07±0,15	<0,001
Total Cholesterol (mmol/l)	5,7±0,14	5,31±0,18	0,09
Triglycerides (mmol/l)	1,74±0,1	1,11±0,1	<0.001
Beta-lipoproteine (units)	45,8±1,67	34,9±1,3	<0.001
Fibrinogen (g/l)	3,36±1,12	3,05±0,07	0,045 (<0,05)
Uric Acid (mkmol/l)	405±19,31	331±10,63	0,007

Table 5

Ultrasound parameters

Parameter	Case group	Control group	p
IMT (mm)	0,99±0,037	0,84±0,037	0,0037
The CCA diameter (mm)	6,94±0,08	6,5±0,09	0,0005

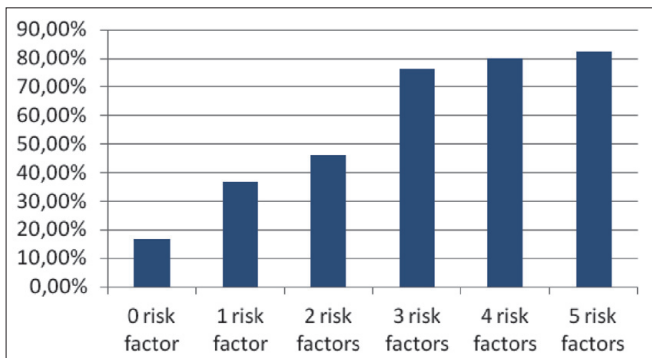


Fig. 3. Frequency of atheroma plates according to the number of the MS constituent risk factors in the general study group.

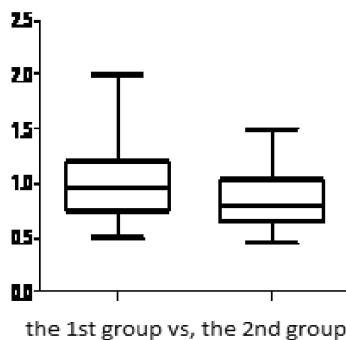


Fig. 4. The thickness of the intima - media at the level of the common carotid arteries, in the 2 groups.

between the beta-lipoprotein ($r = 0.001$) or triglycerides ($r = 0.02$) levels and the IMT values. There has been established the correlation between the anthropometric parameters and the values of intima-media complex: no connection detected between the systolic BP values ($r = 0.04$) and

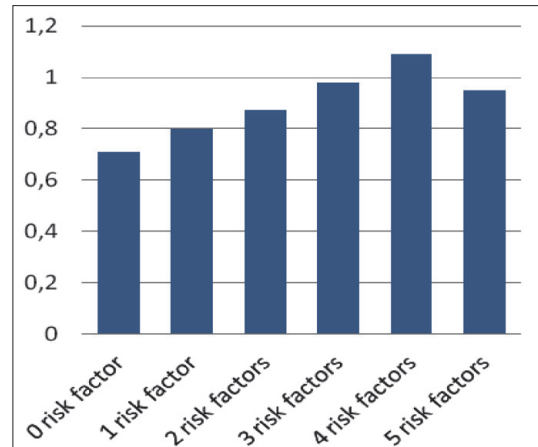


Fig. 5. The components of the metabolic syndrome in relation to IMT.

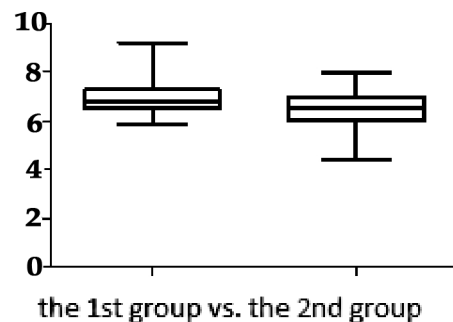


Fig. 6. The values of the luminal diameter at the level of the common carotid arteries, in the 2 groups.

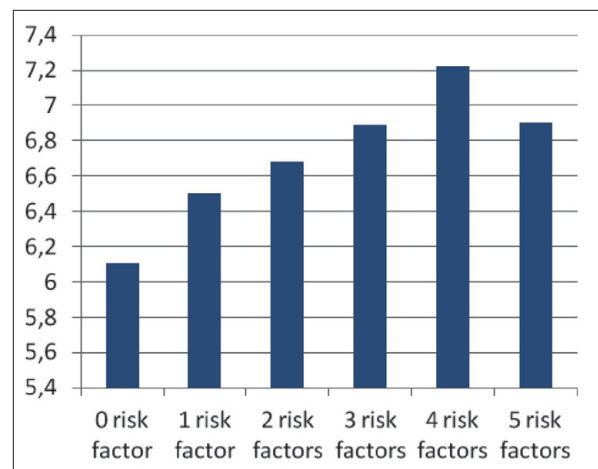


Fig. 7. The components of the metabolic syndrome in relation to internal diameter of the CCA.

diastolic ($r = 0.09$), a weak relationship with age was noted ($r = 0.17$), or BMI values ($r = 0.35$) (fig. 8), it can be stated that the most powerful relationship was with WC values ($r = 0.54$). It has been established a perfect correlation between the number of MS constituent risk factors and the markers of the atherosclerotic carotid damage, such as IMT ($r = 0.86$) and internal carotid diameter ($r = 0.87$).

The average values of IMT for the population with and

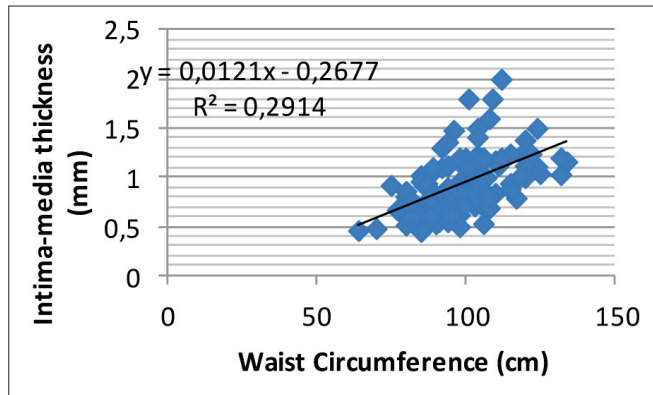


Fig. 8. The variation in the thickness of the intima-media common carotids according to the values of WC in the general group.

without atherosclerotic plaques have been compared (IMT = $1,01 \pm 0,035$ mm, 95% CI, $0,94 \div 1,08$ mm vs. IMT = $0,82 \pm 0,037$ mm, 95% CI, $0,75 \div 0,89$ mm), the IMT values were higher and statistically significant for the population with IMT carotid atheromatosis ($p < 0,001$). A statistically significant difference was found between the values of the CCA diameter in patients with atherosclerotic plaques (average value $6,93 \pm 1,0$ mm) and in patients without plaques ($0,13$ mm \pm $6,14$) ($p = 0,0028$). Thus, the arterial diameter values and IMT can be each connected to the process of atherosclerosis. Their separate or combined expansion may indicate different arterial phenotypes with different atherosclerotic risk [12]. It has been proved that the IMT of ex-smokers and smokers ($0,94 \pm 0,034$ mm, 95% CI, $0,87 \div 1,00$ mm) is not statistically significant and it's higher than that of non-smokers ($0,88 \pm 0,04$ mm, 95% CI, $0,8 \div 0,96$ mm) ($p = 0,18$).

Discussion

In both groups, the arterial hypertension was present in most cases ($> 80\%$), being the most frequent risk factor of a stroke, a fact confirmed by other research studies [9].

Dyslipidemia, when the total cholesterol and triglycerides levels increase, represents a risk factor according to some studies, it had a different distribution in the two groups as follows: in group 1, the predominant hypertriglyceridemia (47.06% vs. 5.26%) and hypercholesterolemia (29.4% vs. 21.05%) compared to the control group. Type 2 diabetes was more prevalent in MS patients (52.94%) than in those without MS (3.5%). It was discovered that the levels of uric acid, beta-lipoproteins, triglycerides, fibrinogen and glucose of patients with ischemic stroke and MS are significantly higher than of those without MS ($p < 0,05$).

The obesity of varying degrees was present in over 27% of subjects without MS and in 50% of patients with MS.

The present study shows that the patients with metabolic syndrome have values of the IMT and the internal diameter of the common carotid artery significantly higher than the subjects without the metabolic syndrome ($p < 0,05$), which is consistent with the specialty literature [8,

13]. Regarding the relationship between the number of risk factors and the markers of atherosclerotic carotid damage, a strong dependence between the two parameters was observed. Thus, it can be stated that 74% of the IMT variation and 77% of the luminal diameter variation is explained by the variation of the number of risk factors constituting MS ($r^2 = 0,74$, $r^2 = 0,77$ respectively).

Atherosclerotic plaques at the level of the extracranial carotid section were found in 86.76% of the participants from the basic group compared to 42.1% from the control group.

Since most risk factors are part of the modifiable category, it is likely that stroke can be prevented by keeping them under control. Diagnosis and proper MS management can be an important part of stroke prevention.

Conclusions

The obtained results, suggest that the cluster of risk factors, the MS constituents are connected with the alteration of the carotid arteries, these changes explain the relationship between the MS and the high risk of heart and cerebrovascular pathologies. In MS the risk of cerebrovascular diseases is multifactorial and its early detection and its treatment can prevent vascular events.

The current study outlines four directions for further research: 1. An extension of the study group that would increase the statistical power, 2. An evaluation of other parameters and / or improvement of those already used, 3. To examine the participants of the study in certain periods of time, 4. To promote the research conclusions as an evaluation algorithm for primary care and as advice to the population.

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Impact of active tobacco smoking and other associated determinants on tuberculosis evolution and treatment outcome

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Abstract

Background: Tuberculosis and smoking represent a major global health problem that is well recognized in the Republic of Moldova and worldwide. There is strong relationship between social vulnerability and psychotropic substance abuse: tobacco smoking, alcohol abuse and illicit drug use. The aim of the study was the impact assessment of active tobacco smoking and associated determinants on evolution of pulmonary tuberculosis and treatment outcome.

Material and methods: pulmonary TB patients diagnosed in the period 1.1.2014-31.12.2014 in Chisinau city were distributed in two groups: study group constituted 209 patients with pulmonary TB and active smoking and control group (CG) – 79 patients with pulmonary TB never-smokers.

Results: Risk factors for development of active TB at smokers are poverty-related conditions, male sex, single matrimonial status, medico-biological conditions and alcohol addiction, low educational status, urban residence. Case-management of smokers with pulmonary TB was worsened by the lack of health insurance (two thirds), late detection and epidemiological danger due to positive bacillary smear status. Co-morbidities and TB-related radio-morphological features (bilateral localization, lung destructions, dissemination, and positive bacillary status) adjusted to risk factors contribute to low treatment outcome.

Conclusions: Targeted interventions for smoking quitting in the frame of risk subgroups will diminish the rate of severe and complicated forms of TB and will increase success rate, strengthening TB control at the community level.

Key words: tuberculosis, tobacco smoking, risk groups.

Introduction

Tuberculosis (TB) represents a major global health problem that is well recognized in the Republic of Moldova (MDA) [3]. Annually are registered almost 10 million new TB cases that in association with human immunodeficiency virus represent a leading cause of death. In 2014 were registered 5,4 million new cases among men, 3,2 million cases among women and 1.0 million sick children worldwide. In addition to this in 2014 were registered 1,5 million deaths due to tuberculosis, among them – 1,1 million were HIV negative and 0,4 million were HIV-positive [15]. The Republic of Moldova shows a slow decreasing of disease prevalence during the period 2013-2015 with 3904 TB patients in 2013, 3450 patients in 2014 and 3073 patients in 2015 [3]. The social determinants of TB are well recognised in MDA as well as worldwide. The continuous

socio-economical, as well as, political crisis through which passes MDA determine the continuously increasing rate of socially vulnerable individuals [3]. It was defined a strong relationship between social vulnerability and psychotropic substance abuse: tobacco smoking, alcohol abuse and illicit drug use. Tobacco smoking is probably the most widespread with the major socio-economic impact. Smoking is defined as an addictive disease of persons who reported smoking at least 100 cigarettes during their lifetime and who, at the time when they participated in the survey, reported smoking every day or some days. About 1.1 billion people, that means one in every three adults, are smokers according to the World Health Organization [16]. Worldwide, tobacco smoking causes nearly 6 million deaths per year, and more than 8 million deaths annually are predicted by 2030 [6]. More than 160 million Americans are