THE ASSESSMENT OF THE RISK FACTORS FOR ATHEROSCLEROSIS AMONG POPULATION FROM THE NORTH-EASTERN REGION OF ROMANIA

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THE ASSESSMENT OF THE RISK FACTORS FOR ATHEROSCLEROSIS AMONG POPULATION FROM THE NORTH-EASTERN REGION OF ROMANIA (Abstract): Aim: This study investigates the factors that influence the risk of atherosclerosis for the population included in the research and to assess the relationship between these factors and atherosclerosis. Material and methods: A case-control study was conducted on cardiovascular risk factors that contribute to the occurrence of atherosclerosis which included a number of 207 patients of both sexes, selected from urban and rural areas, with permanent residence in the county of Iasi, aged between 20 and 80 years, during the period April-June 2014. Results: Analyzing the risk factors there was found a statistical significance for the values of the total cholesterol and triglycerides, as well as for other risk factors such as obesity (assessed by body mass index), blood pressure, smoking and physical inactivity. For other risk factors involved in the occurrence of atherosclerosis, such as: ischemic personal history, family history of coronary heart disease, diabetes, type of diet, history of infection with Chlamydia pneumoniae, Cytomegalovirus, Helicobacter pylori there were obtained insignificant statistical values. Conclusions: The results of this study provide information with practical implications that can be used by clinicians when they faced people with cardiovascular risk factors. Keywords: CARDIOVASCULAR DISEASES, ATHEROSCLEROSIS, RISK FACTORS, ROMANIA, PREVALENCE.

Atherosclerotic cardiovascular diseases are the leading cause of death worldwide (1). Atherosclerosis (ATS) is considered a chronic inflammatory disease related to age, with a long and slow asymptomatic phase. Recent data shows that it begins to develop early in life and presents clinical manifestation in many patients in a relatively advanced stage. The consequences of ATS responsible for the occurrence of cardiovascular diseases are among the leading causes of morbidity and mortality worldwide. It should also be noted that the coronary heart disease due to ATS is increasing. The diag-
nosis and treatment are a priority partly because the sudden death is a consequence of primary coronary artery disease in 50% of men and 64% of women (2).

Increased susceptibility to atherosclerosis is conditioned by the accumulation of the risk factors (RF): hypercholesterolemia, hypertension smoking (3).

The risk factors for atherosclerotic cardiovascular diseases includes (4, 5): individual characteristics (unchangeable = non-modifiable RF): age, sex, family history of atherosclerosis at a young age (for women < 65 years, for men < 55 years), previous personal history of atherosclerosis; the biochemical/physiological factors: hyper-LDL-cholesterol, hypo-HDL-cholesterol, hyper-triglycerides, high blood pressure (HBP), diabetes mellitus (DM) or impaired glucose tolerance, obesity, thrombogenic factors; lifestyle characteristics: diet rich in saturated fats, smoking, alcohol, physical inactivity (6).

The aim of this study was to investigate the factors that influence the risk of atherosclerosis for the population included in the research and to assess the relationship between these factors and atherosclerosis.

MATERIAL AND METHODS

A case-control study was developed to assess the risk of various factors among the study population. The case-control study on cardiovascular risk factors that contribute to the occurrence of ATS included a number of 207 patients of both sexes, selected from urban and rural areas, with permanent residence in the county of Iasi, aged between 20 and 80 years, during the period April – June 2014. Patients were divided into two groups, the group of cases which included 78 patients with ATS, recruited from people who visited the family doctor office, and the control group, which included a total of 129 persons selected from the subjects who were present in the Ambulatory of the “Dr. I. Czihac" Emergency Army Hospital from Iasi. The inclusion criteria were: age over 20 years, and the diagnosis of ATS confirmed by angiography or computed tomography. During the visit to the family doctor for each patient enrolled in the study was filled up a questionnaire with the following data: date of birth, age, gender, ethnicity, residence, education level, economic situation perceived by the patient, personal history, lipid profile (the total cholesterol value, the amount of LDL and HDL cholesterol and the amount of triglycerides), body weight, height, blood pressure value, the presence of diabetes, smoking, physical activity, type of food, the inflammatory markers C-Reactive Protein (CRP), evidences of the medical history of infections with Chlamydia pneumonia, Cytomegalovirus, and Helicobacter pylori.

A pilot study was conducted to validate the questionnaire used for the assessment of the risk factors for ATS. A number of 40 subjects were included in the study: 20 cases, recruited from people who visited the family doctor office and 20 controls, chosen from the subjects who were present in the Ambulatory of the “Dr. I. Czihac" Emergency Army Hospital from Iasi, during a period of 3 months, between January and March 2014.

In both studies, the information was collected using a questionnaire specially designed for this purpose, and then were included in an Excel database that has been further processed using Excel and Epi Info 7 programs. The variables under the study were analyzed and the values within the statistical confidence interval (CI) 95% (p <0.05) were considered values with statistical significance.
RESULTS
Characteristics of the subjects under the study. The study included a number of 207 participants of which 78 cases (37.68%) were cases with ATS and 129 (62.31%) were controls without a disease with clinical confirmation. Regarding the gender distribution, was found a preponderant presence of the disease in males (51.28%), because they have a higher risk of getting the disease.

The most affected patients were within the age group of 70-79 years (41.02%), followed by those aged 60-69 years (28.21%) (fig. 1).

Most of the cases were from urban areas (55.13%) compared with 44.97% from rural areas. A possible explanation could be that people in rural areas have a higher addressability to the doctor and an easier access to specialized medical services.

If we refer to the level of training, the cases with secondary education have been recorded in more than a half of the cases (51.28%), followed by those with higher level of training (28.21%) and those with primary education (20.51%).

![Fig. 1. The prevalence of atherosclerosis, according to different age groups](image)

The assessment of the relationship between different risk factors and ATS. The following risk factors were studied: personal history of ischemic heart disease, family history of coronary heart disease, the amount of LDL cholesterol, HDL cholesterol, triglycerides, body mass index, blood pressure, diabetes, smoking, sedentary lifestyle, type of diet, C Reactive Protein (CRP), history of infections with Chlamydia pneumoniae, Cytomegalovirus, Helicobacter pylori.

Analyzing the risk factors there was found a statistical significance for the values of the total cholesterol (TC) and triglycerides, as well as for other risk factors such as obesity (assessed by body mass index), blood pressure, smoking and physical inactivity. For other risk factors involved in the occurrence of ATS, such as: ischemic personal history, family history of coronary heart disease, diabetes, type of diet, history of infection with Chlamydia pneumoniae, Cytomegalovirus, Helicobacter pylori there were obtained insignificant statistical values (tab. I).
TABLE I

The relation between the risk factors and the atherosclerosis among the population under the study

<table>
<thead>
<tr>
<th>The studied factor</th>
<th>Cases</th>
<th>Controls</th>
<th>OR</th>
<th>X²</th>
<th>p</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td>67</td>
<td>85.9</td>
<td>54</td>
<td>41.9</td>
<td>2.8</td>
<td>13.5</td>
</tr>
<tr>
<td>High cholesterol</td>
<td>60</td>
<td>76.9</td>
<td>49</td>
<td>37.9</td>
<td>5.5</td>
<td>31.1</td>
</tr>
<tr>
<td>High LDL-cholesterol</td>
<td>57</td>
<td>72.2</td>
<td>42</td>
<td>32.6</td>
<td>5.2</td>
<td>30.5</td>
</tr>
<tr>
<td>Smoking</td>
<td>57</td>
<td>67.1</td>
<td>58</td>
<td>44.9</td>
<td>0.6</td>
<td>3.0</td>
</tr>
<tr>
<td>High triglycerides</td>
<td>50</td>
<td>64.1</td>
<td>29</td>
<td>22.5</td>
<td>6.3</td>
<td>35.9</td>
</tr>
<tr>
<td>High Blood Pressure</td>
<td>48</td>
<td>61.5</td>
<td>41</td>
<td>31.8</td>
<td>3.5</td>
<td>18.0</td>
</tr>
<tr>
<td>Sedentarism</td>
<td>43</td>
<td>55.7</td>
<td>52</td>
<td>40.3</td>
<td>1.8</td>
<td>4.5</td>
</tr>
<tr>
<td>Low HDL-cholesterol</td>
<td>34</td>
<td>43.6</td>
<td>103</td>
<td>79.8</td>
<td>0.2</td>
<td>28.9</td>
</tr>
<tr>
<td>Poor economic situation</td>
<td>34</td>
<td>43.6</td>
<td>30</td>
<td>23.2</td>
<td>2.6</td>
<td>9.6</td>
</tr>
<tr>
<td>Type of food</td>
<td>42</td>
<td>53.9</td>
<td>59</td>
<td>45.7</td>
<td>1.4</td>
<td>1.6</td>
</tr>
<tr>
<td>Infections with Ch. Pneumoniae, Cytomegalovirus, H. pylori</td>
<td>29</td>
<td>36.7</td>
<td>43</td>
<td>33.3</td>
<td>1.2</td>
<td>0.4</td>
</tr>
<tr>
<td>Family history of ischemic heart disease</td>
<td>23</td>
<td>29.5</td>
<td>33</td>
<td>25.6</td>
<td>1.2</td>
<td>0.4</td>
</tr>
<tr>
<td>Personal history of ischemic heart disease</td>
<td>17</td>
<td>21.8</td>
<td>26</td>
<td>20.2</td>
<td>1.1</td>
<td>1.1</td>
</tr>
<tr>
<td>Diabetes</td>
<td>14</td>
<td>17.9</td>
<td>29</td>
<td>22.4</td>
<td>0.7</td>
<td>0.5</td>
</tr>
<tr>
<td>CRP</td>
<td>4</td>
<td>5.1</td>
<td>4</td>
<td>3.1</td>
<td>1.7</td>
<td>0.5</td>
</tr>
</tbody>
</table>

For the subjects included in the study, it was observed an average of the cholesterol value above the normal value, as well as for the other biochemical indicators (LDL-cholesterol and triglycerides).

Regarding the variation coefficient, which shows us the scatter of the value series, the lower the value (as is the case with cholesterol) the closer it is to the average (tab. II).

TABLE II

Biochemical investigations among subjects included in the study

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Variation coefficient (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol</td>
<td>211.19</td>
<td>42.15</td>
<td>10.96</td>
</tr>
<tr>
<td>LDL-cholesterol</td>
<td>126.68</td>
<td>50.07</td>
<td>39.52</td>
</tr>
<tr>
<td>HDL-cholesterol</td>
<td>61.06</td>
<td>15.44</td>
<td>25.28</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>137.34</td>
<td>69.47</td>
<td>50.58</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>26.71</td>
<td>5.4</td>
<td>20.21</td>
</tr>
</tbody>
</table>

Retrospective and prospective epidemiological research regarding the risk factors among the studied subjects. Of the total number of ATS cases included in our study, it was observed that the most patients had high total cholesterol levels (76.92%), followed by increased LDL-cholesterol values (72.15%) and low HDL-cholesterol levels (56.41%). The most affected age group by the increased values of the cholesterol, triglycerides and LDL-cholesterol was 70-79 years of age, and the
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least affected was 20-29 years (fig. 2).

Another risk factor involved in the occurrence of ATS is the high triglyceride levels (normal values being between 50-150mg/dL). Laboratory investigations found that the most patients diagnosed with ATS had elevated triglycerides levels (>150mg/dL) (64.11%).

![Graph showing the distribution of atherosclerosis cases with high values for the total cholesterol, LDL-cholesterol and triglycerides according to age groups.](image)

**Fig. 2** The distribution of atherosclerosis cases with high values for the total cholesterol, LDL-cholesterol and triglycerides according to age groups

To assess the obesity as a risk factor for ATS, we calculated the Body Mass Index (BMI) for all patients included in the study. The most common classes of obesity were II degree, corresponding to a BMI values between 35.00 and 39.99 Kg/m² (37.44%) and I degree (BMI between 30.00 and 34.99) (22.82%). Following the analysis of ATS cases, the obesity has been found to affect most the age groups 70-79 years and 60-69 years, and then decreases with age (fig. 3).

![Graph showing the distribution of atherosclerosis cases among overweight and obese according to the age groups.](image)

**Fig. 3** The distribution of atherosclerosis cases among overweight and obese according to the age groups
Assessing another risk factor for ATS, namely high blood pressure (HBP), it was found to be present in most of the cases (61.54%). The most affected by hypertension among the atherosclerosis cases included in the study were those in the 70-79 age group (39.58%), followed by the age group 60-69 years (31.25%) (fig. 4).

Smoking, another risk factor for ATS, was present in 67.09% of the investigated cases, the most frequently affecting the age group of 40-49 years (40.35%) and the age group of 50-59 years (35.09%) (fig. 5).

Another risk factor involved in the occurrence of ATS is the sedentarism. In the current study, it was observed that more than a half of the patients (55.7%) were sedentary (walking <30 min/day), more frequently within the 70-79 age group (30.23%) (fig. 6).
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**DISCUSSION**

It has been noted that infectious factors play an important role in the development and progression of ATS, leading to chronic infections and persistent inflammatory process. Both the acute and chronic inflammation causes endothelial dysfunction. The main microorganisms that have been studied were *Chlamydia pneumoniae*, *Cytomegalovirus* and *Helicobacter pylori* (7). Also, some studies have reported that seropositive to *Chlamydia pneumoniae*, *Cytomegalovirus* and *Helicobacter pylori* is associated with coronary artery disease (8, 9). Infectious agents are considered risk factors or enhancers of other factors contributing to the occurrence of ATS (10).

In a study of the rural Chinese population, it was found that the most common risk factors involved in the occurrence of peripheral cardiovascular disease, more precisely in atherosclerosis, were high blood pressure and increased LDL-cholesterol / HDL-cholesterol ratio (11). Our data were similar to those found by Liang et al, the high blood pressure and high cholesterol levels being identified as risk factors with statistical significance.

There are several cohort studies that support a strong correlation between HDL-cholesterol and coronary risk. Some US epidemiologic studies involving many subjects (like the Framingham Heart Study, the Lipid Research Clinics Primary Prevention Trial) showed that low HDL-cholesterol levels increase the risk of coronary heart disease and argue that every 1 mg/dL increase in HDL-cholesterol level reduces the risk of coronary heart disease by 2% in men and 3% in women. The Framingham Heart Study supported the role of HDL-cholesterol as an independent factor for the coronary artery disease. The main mechanism by which HDL-cholesterol is considered to reduce the cardiovascular risk consists in the reverse transport of cholesterol, a way to remove the free cholesterol from macrophages into the arterial wall and to return to the liver for bile excretion (12). Our study did not found an increased risk for atherosclerosis when low values of HDL-cholesterol were registered (OR = 0.2, p < 0.01×10^{-4}).

Various epidemiological studies have shown that around 25% of US adults are estimated to have high levels of triglycerides (> 150mg/dL), leading to an increased risk of cardiovascular disease. It is well known that lowering the high level of low-density lipoprotein (LDL-cholesterol) remains the primary target of treatment to reduce the
risk of cardiovascular diseases. Also, a series of epidemiological studies including many subjects have shown that increased levels of triglycerides are associated independently with an increased incidence of cardiovascular events, even in patients treated with appropriate statins (13, 14). This fact was observed in the current study, which found that subjects diagnosed with ATS had elevated levels of both triglycerides and LDL-cholesterol. The same aspect was identified by Fukuda N et al. during an experimental trial conducted in 2013 involving 15 rabbits. The postprandial hypertriglyceridemia was found to be a risk factor in promoting the ATS (15).

The early measurements of BMI, cholesterol, triglycerides and the blood pressure were found to be more strongly associated with the presence and severity of coronary calcifications (16). In the current research obesity has been shown to be a risk factor in the development of atherosclerosis. Also, there are researchers shown that obesity induces a pro-inflammatory state due to the secretion of adipokines that are an essential event in the occurrence of cardiovascular disease (17). The risk factors for ATS and diabetes are based on inflammatory and genetic backgrounds that can be accounted for by the excess of fat. Longevity has increased in last past years and is related to a pro-inflammatory response with cardiovascular consequences. If lifestyle would include an increase in physical activity as well as a calories restricted diet, the low degree of obesity would have a limited effect on chronic inflammation, and the risk of atherosclerosis and diabetes mellitus could be reduced (17).

In a study of the prevalence of risk factors for atherosclerosis among the adults from the Philippines, which was conducted in 2008, the following results were obtained analyzing the 7,700 eligible subjects who participated in the study: the prevalence of dyslipidemia - 72%, high blood pressure - 24.6%, diabetes mellitus - 3.9%, obesity - 4.9%, smoking - 31%, and a history of coronary, cerebrovascular and peripheral disease - 1.1%, 0.9% and 1.0%, respectively. Following this comparative study, it was found that the prevalence of the risk factors for ATS was higher in 2008 than in 2003, indicating a need for active collaboration intervention with all government agencies and medical societies in the Philippines in order to prevent or control the action of these factors (18). A similar situation was found in our study, which showed that the economic situation of patients, high level of cholesterol, triglycerides, blood pressure, smoking, and sedentarism can influence the development of ATS.

Smoking is another risk factor with a major contribution in the development of cardiovascular and atherosclerotic diseases, but our study did not identified smoking as a risk factor for ATS (OR = 0.06, p = 0.04). Another research involving 299 subjects, from which 34 (11%) smokers, 73 (24%) former smokers and 192 (4%) who never smoked showed that smoking was associated with subclinical atherosclerosis in diabetic persons and was influenced by the duration of diabetes to promote the progression of ATS (19).

**CONCLUSIONS**

The actual research identified as risk factors with statistical significance for ATS the following conditions: obesity, high cholesterol, high LDL cholesterol, high triglycerides levels, high blood pressure, sedentarism, and poor economic situation. The findings of this study provide information with practical implications that can be used by clinicians when they faced with people with risk factors.

Most of the cases come from urban are-
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as. One possible explanation might be that the urban population has a greater addressability to the doctor and easier access to the specialist medical services. So, the future cardiovascular preventive strategies should address this issue.

This study showed that patients with high blood pressure have an increased risk of developing ATS due to hyperreactivity to risk factors. Although sometimes it is difficult to manage the systolic blood pressure in the elderly, the total cardiovascular risk can be reduced by action on other risk factors such as smoking, obesity, sedentarism, and high cholesterol levels. If the lifestyle would include an increase in physical activity as well as a calorie restricted diet and a diet rich in fruits, vegetables and fish, the low degree of obesity could have a limited effect on chronic inflammation and the risk of ATS and consequently the risk of cardiovascular disease may be reduced.

The measures used to prevent cardiovascular events in patients with coronary artery disease involve a multifactorial approach including the management of all the modifiable risk factors (especially high cholesterol, high LDL-cholesterol, high triglycerides levels, obesity, and high blood pressure). Prevention of cardiovascular disease should be a priority not only in research but also in clinical practice, especially in preventive medicine.

ACKNOWLEDGEMENTS

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REFERENCES


**NEWS**

**RISK OF ACUTE MYOCARDIAL INFARCTION WITH NSAIDS IN REAL WORLD USE: BAYESIAN META-ANALYSIS OF INDIVIDUAL PATIENT DATA**

Michèle Bally (epidemiologist in the Department of Pharmacy and Research Center, Centre hospitalier de l'Université de Montréal, Quebec, Canada) and her research team conducted a systematic review followed by a one stage bayesian individual patient data meta-analysis which shows that the use of nonsteroidal anti-inflammatory drugs (NSAIDs) is associated with a significantly increased risk for myocardial infarction (MI). A cohort of 446,763 individuals (61,460 with acute myocardial infarction) was included in the study. The results highlighted that taking any dose of NSAIDs for one week, one month, or more than a month was associated with an increased risk of MI. If the subject used the NSAIDs for one to seven days the probability of increased MI risk was 92% for celecoxib, 97% for ibuprofen, and 99% for diclofenac, naproxen, and rofecoxib. The corresponding odds ratios (95% confidence intervals) were 1.24 (0.91 - 1.82) for celecoxib, 1.48 (1.00 - 2.26) for ibuprofen, 1.50 (1.06 - 2.04) for diclofenac, 1.53 (1.07 - 2.33) for naproxen, and 1.58 (1.07 - 2.17) for rofecoxib. A greater risk of MI was reported for higher dose of NSAIDs, but the use for longer than one month, did not appear to exceed the risks associated with shorter durations. The study concluded that all NSAIDs, including naproxen, considered by some as one of the safest drugs in this class, were found to be associated with an increased risk of acute MI. The risk of MI with celecoxib was comparable to that of traditional NSAIDs and was lower than for rofecoxib. Also, the risk was greatest during the first month of NSAIDs use and with higher doses. (Bally M, Dendukuri N, Rich B, Nadeau L, Helin-Salmivaara A, Garbe E et al. Risk of acute myocardial infarction with NSAIDs in real world use: bayesian meta-analysis of individual patient data. *BMJ* 2017; 357 : j1909. doi.org/10.1136/bmj.j1909).