EPIDEMIOLOGIC CHARACTERISTICS OF HYPERTENSION IN THE CIVILIANS OF KOSOVO AFTER THE WAR

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SUMMARY

34th Greek regimen, which was part of the NATO forces, provided medical services to the civilians of Kosovo. We studied epidemiologic data in the population of Kosovo regarding hypertension in order to determine the prevalence and characteristics of hypertension. 830 patients (281 – 33.86% male, 62±26 yrs and 549 – 66.14% female, 49±28 yrs) were examined for different diseases. We identified 254 (30.6%) patients with hypertension (188 female and 66 male). According to the international criteria used for the classification of the severity of hypertension, more than half of the patients (51.2%) had severe hypertension, 31.5% modest and 17.3% mild. Statistically significant relation between the severity of hypertension and age or sex was not found out. Increased BMI as well as the presence of proteinuria and rheumatic diseases were significantly related to the severity of the hypertension while the coexistent heart disease, diabetes mellitus and chronic obstructive pulmonary disease (COPD) wasn't. The use of non--steroid anti-inflammatory agents (NSAIDs) was related to the severity of hypertension with a borderline significance. 31.4% of the patients were on treatment with NSAIDs and/or cortisone because of rheumatic disease or obstructive pulmonary disease. Overfunction of the sympathetic system was present in 62.99%. The mean heart rate was greater in women (84/min) than in men (72/min). 28.35% of the patients had secondary hypertension, including the patients on a drug that can elevate the blood pressure and patients with increased activity of the sympathetic nervous system. So, 8.6% of the patients had usual causes of secondary hypertension and 19.6% hypertension secondary related to the use of NSAIDs or cortisone, or due to the increased activity of the sympathetic nervous system. Antihypertensive treatment was started in 248 patients, i.e. in all of them except the ones already on treatment having their blood pressure well controlled. For antihypertensive treatment β-blockers or central adrenergic inhibitors either as monotherapy or in combination with other agents were used most frequently combined with diuretics and Ca antagonists and ACE inhibitors. In conclusion the diagnosis and treatment of hypertension in the population of Kosovo during the post war period had certain particularities.

Key words: epidemiology, Kosovo, hypertension, sympathetic nervous system, non-steroid anti-inflammatory drugs, steroids

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INTRODUCTION

War in Yugoslavia started after the Rabuaye agreement, which was signed in February 1999, was violated. Kosovo is an area of former Yugoslavia, where fighting between Serbs and Albanians has been on for almost a decade because of the fight of the Albanians for legal and political rights. The aim of Rabuaye convention was to achieve peace and obtain these rights for the Albanians. Its violation led to the attack of the NATO airforces, which resulted in further wounding of hundreds of civilians. Apart from the woundings during the fightings, there was also an increase in infectious and cardiovascular diseases. Incidence of certain diseases like hypertension, coronary heart disease and stroke increased due to the stressful conditions of the war (1–4). The importance of the stress and its relation to the pathogenesis, manifestation and deterioration of hypertension is well known (5, 6). Furthermore, the lack of health care and medication had a negative effect in the management of patients with hypertension (2).

MATERIAL AND METHODS

The medical group of the 34th Greek regimen, which was part of the NATO forces, provided medical services to the civilians of Kosovo, both Serbs and Albanians. Having Pristina as our base, we studied epidemiologic data in the population of Kosovo regarding hypertension.

In 20 villages in Cosovo six months after the war (from January to July 2000) and for a period of 6 months 830 patients were examined for different medical reasons. 281 (33.86%) of the individuals who were examined were male (mean age 62±26) and 549 (66.14%) women (mean age 49±28). For every individual general demographic data and specific details of their disease were recorded in a health card. In patients with hypertension we recorded their history, physical examination, concomitant diseases, laboratory tests, medication, and the follow up monthly visits.

Statistical analysis was performed using the SPSS 8.0 package. We explored the relationship between the severity of hypertension and age, gender, BMI, the use of NSAIDs, the presence of diabetes mellitus, COPD, proteinuria, heart disease and rheumatic diseases. The χ^2 statistical significance was defined as $p<0.05$.

Table 1. *Distribution of patients according to blood pressure stage, sex, age, BMI and co-existing diseases*

	Mild BP	Moderate BP	Severe BP	Total	P
	N (%)				
Sex					
Male	8 (8.7)	22 (8.7)	36 (14.2)	66 (26)	0.421
Female	36 (14.2)	60 (23.6)	92 (36.2)	188 (74)	
Age					
>65	18 (7.1)	28 (11)	54 (21.3)	100 (39.4)	0.133
50-64	16 (6.3)	46 (18.1)	56 (22)	118 (46.5)	
<50	10 (3.9)	8 (3.1)	18 (7.1)	36 (14.2)	
BMI					
Normal	26 (10.2)	34 (13.4)	28 (11)	88 (34.6)	0.001
Elevated	18 (7.1)	48 (18.9)	100 (39.4)	166 (65.4)	
Proteinuria					
Positive	2 (8)	22 (8.7)	54 (21.3)	78 (30.7)	0.001
Negative	42 (16.5)	60 (23.6)	74 (29.1)	176 (69.3)	
NSAIDs					
Yes	20 (7.9)	24 (9.4)	34 (13.4)	78 (30.7)	0.06
No	24 (9.4)	58 (22.8)	94 (37)	176 (69.3)	
Rheumatic diseases					
Yes	19 (7.5)	22 (8.7)	25 (9.8)	66 (26)	0.008
No	25 (9.8)	60 (23.6)	103 (40.6)	188 (74)	
Heart diseases					
Yes	5 (2)	8 (3.1)	14 (5.5)	27 (10.6)	0.95
No	39 (15.4)	74 (29.1)	114 (44.9)	227 (89.4)	
Diabetes mellitus					
Yes	4 (1.6)	5 (2)	7 (2.8)	16 (6.3)	0.692
No	40 (15.7)	77 (30.3)	121 (47.6)	238(93.7)	
COPD					
Yes	4 (1.6)	9 (3.5)	11 (4.3)	24 (9.4)	0.844
No	40 (15.7)	73 (28.7)	117 (46.1)	230 (90.6)	

BP = blood pressure; BMI = body mass index; NSAiDs = non-steroid anti-inflammatory drugs; COPD = chronic obstructive pulmonary disease

RESULTS

Out of the 830 patients that we examined, 254 were found to be hypertensives (30.6%). 188 of them were women (74%) and 66 men (26%). The prevalence of hypertension was higher in women (34.24%) compared to men (23.49%). Body mass index (BMI) was also more frequently increased in women (>24 kg/m^2 – 79.78%) than in men (> 25kg/m^2 – 27.27%).

According to the international criteria used for the classification of the severity of hypertension, more than half of the patients (51.2%) had severe (women 47.87%, men 54.55%), 31.5% modest (women 30.85%, men 33.33%) and 17.3% mild hypertension (women 19.15%, men 12.12%). Table 1 shows the distribution of hypertensive patients in relation to the severity of hypertension, gender, age, BMI, proteinuria, the use of NSAIDs, rheumatic diseases, heart diseases, diabetes mellitus, and chronic obstructive pulmonary disease (COPD). There was not statistically significant relation between the severity of hypertension and age or sex (p=0.133 and 0.421 respectively). Increased BMI was significantly related (p=0.001) to the severity of the hypertension (Fig. 1). Also the presence of proteinuria and rheumatic diseases was significantly related (p=0.001 and p=0.008 respectively) to the severity of the hypertension while the co-existence of heart disease, diabetes mellitus and COPD was not (p=0.95, p=0.692 and p=0.844 respectively). Finally, the use of NSAIDs was related to the severity of hypertension with a borderline significance.

Approximately half of the hypertensives had positive family history for hypertension (11.64% of the 830 totally examined individuals). The vast majority (76%) ignored their disease more frequently women (54.41% versus 45.59%), and 18.5% were not treated at all for several reasons, main one being the lack of health education and care. Only 5.5% of the patients were on regular antihypertensive treatment (9.09% men and 4.24% women), and out of those 42.9% had their blood pres-

Table 2. *Concomitant diseases in the hypertensive population*

	Male (%)	Female (%)	Total (%)
Rheumatic diseases	10 (15.2)	56 (29.8)	66 (26)
Heart diseases	20 (30.3)	7 (3.7)	27 (10.6)
COPD	20 (30.3)	4 (2.1)	24 (9.4)
Diabetes mellitus	8 (12.1)	8 (4.3)	16 (6.3)

Table 3. *Dysfunction of the autonomic nervous system: clinical features-symptoms in population of Kosovo with sex differences including statistical tests*

(N)	Male	Female	p
Palpitations	10	35	<0.05
Dizziness	5	68	<0.05
Headache	22	102	<0.05
Sweatiness	2	34	<0.05
Dyspepsia	2	10	<0.05
Atypical abdominal pains	3	12	<0.05
Anorexia	5	49	<0.05
Bulimia	21	98	<0.05
Insomnia	9	23	<0.05
Overfunction of sympathetic system (elevated mean heart rate)	20	110	<0.05

Table 4. *Sex differences in the failure rates in antihypertensive therapy*

(N)	Male	Female	Total	P
Failure in therapy	43	79	125	0.004

Table 5. *The most frequent categories of medicines used as antihypertensive treatment in population of Kosovo*

	Male (%)	Female (%)
β-blockers or central adrenergic inhibitors (as monotherapy or in combination with other agents)	59.20	67.03
Diuretics	42,57	54,80
Calcium antagonists	21,25	14,90
ACE inhibitors	19,80	8,52

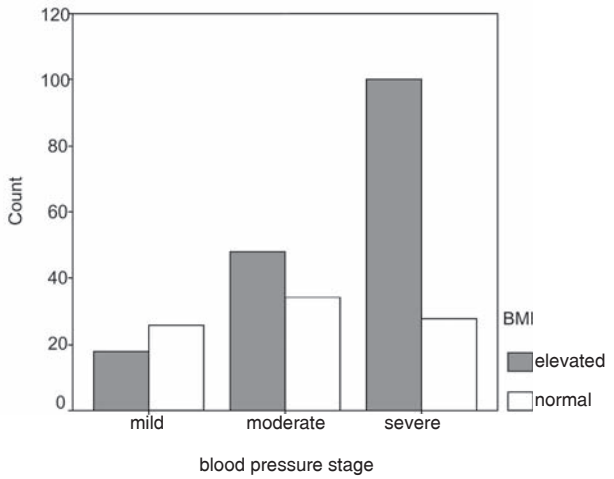

Fig. 1. *Correlation of BMI and blood pressure stage*

sure well controlled, i.e. only a small part of the total hypertensive population (3.03% men, 2.13% women).

In the hypertensive population 62.2% of the patients had concomitant diseases, like cardiovascular disease, diabetes, dyslipidemia and mainly rheumatic disease (Table 2). The most frequent concomitant disease in women was rheumatic disease (vs. men, p=0.02), whereas in men cardiovascular disease (vs. women, p=0.001) and COPD (p=0.001). 31.5% of the patients were on treatment with non-steroid anti-inflammatory agents (NSAIDs) and/or cortisone because of rheumatic disease or COPD.

135 (71.8%) of the hypertensive women and 25 (38%) of the men (p=0.001) complained of one or more of the following symptoms showing dysfunction of the autonomous nervous system: palpitations, dizziness, headache, sweatiness, dyspepsia, atypical abdominal pains, anorexia, bulimia and insomnia. Overfunction of the sympathetic system was present in 62.99% of the patients. Table 3 presents the sex differences in these symptoms of the dysfunction of the autonomous nervous system including statistical tests. The mean heart rate was also greater in women (84/min) than in men (72/min).

Patients were also examined with regard to any systemic complications of hypertension (target organ damage). Regarding kidneys, proteinuria was present in 88 (30.71%) patients in random urine analysis and in 38.5% of the patients with severe hypertension. 56.82% of the hypertensives with proteinuria had severe hypertension and in 32 (40%) of the patients treated with NSAIDs proteinuria was significantly related to severity of hypertension (0.8% patients with mild, 8.7% with moderate and 21.3% with severe hypertension, p=0.001).

118 patients (46.46%) had normal findings in fundoscopy, 66 (25.98%) stage I, 64 (25.2%) stage II, and 7 (2.76%) stage III findings. The majority of the patients (172 – 67.72%) had normal ECG, 74 (29.14%) had ischemic findings and 26 (10.24%) left ventricular hypertrophy (LVH).

Arrythmias and more specifically atrial fibrillation were present only in 8 (3.15%) patients. Antihypertensive treatment was started in 248 patients, i.e. in all of them except the ones already on treatment having their blood pressure well controlled. After the treatment was started 126 (50.8%) of the patients had their blood pressure (BP) controlled within 2 months (28/64 – 43.75% in men, 98/184 – 53.26% in women) according to the criteria we used (systolic BP < 140 mmHg, diastolic < 90 mmHg, heart rate < 70/min). Table 4 shows the rate of failure in therapy in the whole and according to the sex. 13.6% of the patients that did not respond to their initial treatment, had their BP controlled within 2 months after discontinuing treatment with NSAIDs.

34.6% of the patients were on a combined treatment, which included combination of 2 or 3 drugs like ACE inhibitors, diuretics, β-blockers, Ca antagonists and central adrenergic inhibitors (clonidine, methyl dopa, or moxonidin). The most frequently used antihypertensive treatment was β-blockers or central adrenergic inhibitors (59.2% in men, 67.03% in women) either as monotherapy or in combination with other agents, then diuretics (42.57% in men, 54.8% in women), then Ca antagonists (21.25% in men, 14.9% in women), and then ACE inhibitors (19.8% in men, 8.52% in women) (Table 5). The most frequently used combinations of 2 drugs were

β-blockers or central adrenergic inhibitors and ACE inhibitors, β-blockers and Ca antagonists, and β-blockers and diuretics. The most frequently used combinations of 3 drugs were ACE inhibitors and diuretics and β-blockers or β-blockers and diuretics and Ca^{2+} antagonists.

It is interesting that 28.35% of the patients had secondary hypertension, including the patients on a drug that can elevate the blood pressure and patients with increased activity of the sympathetic nervous system. So, 8.66% of the patients had usual causes of secondary hypertension (renovascular, renoparenchymal disease, adrenal disease) and 19.69% hypertension secondary to the use of NSAIDs or cortisone, or due to the increased activity of the sympathetic nervous system (50 patients, 40/188 – 21.28% women, 10/66 – 15.15% men). More specifically hypertension due to increased sympathetic activity was present in 35 patients, (13.78%, 32 – 17.02% women and 3 – 4.55% men, $p<0.05$), and hypertension secondary to the use of NSAIDs or cortisone in 15 patients (5.91%, 8 women – 4.26% and 7 men – 10.6%, $p>0.1$). Hypertension secondary to the increased sympathetic activity was defined as hypertension in which the continuous medical follow up and psychological support led to its control, control of the heart rate and remission of the symptoms of the sympathetic system. In these patients the use of centrally acting adrenergic blockers was very useful for the control of the blood pressure initially, but these drugs were discontinued within 3 months of follow up. Furthermore patients with hypertension secondary to the use of NSAIDs or cortisone were defined as the individuals who after the discontinuation or more appropriate use of these drugs had their blood pressure controlled within 3 months and their antihypertensive treatment stopped in the same period.

DISCUSSION

Overall mortality and morbidity in Kosovo increased during the war between 1998 and 1999, according to the findings of another study (1).

Stress, poor living conditions, lack of medicine and health care after the war resulted in a higher incidence of certain diseases like hypertension, which are not directly related to the fighting, but are a consequence of the stress and social implications of the war. A retrospective study has shown a higher incidence of left ventricular hypertrophy and diffuse atherosclerotic disease during the Second World War in Leningrad and also an increase in the number of admissions due to hypertensive crisis or hypertensive encephalopathy (1).

Most of hypertensives in our study were women (74%). This finding was probably related to the increased BMI and higher average age of women in comparison to men both during the war and peace. Another explanation for this could be the social conditions, i.e. women in Kosovo do not have access to medical care as easily as men do. Similarly in Paraguay, another country with low average level of living, more hypertensives were women (2).

In our study women with hypertension had higher mean heart rate comparing to men (84/min). This is probably due to the increased activity of the sympathetic nervous system, as more women in our study had autonomic system disorders than men, complaining for palpitations, sweatiness, diziness, headache, atypical abdominal pain, dyspepsia, bulimia, anorexia, perspiration and symptoms of irritable bowel syndrome. Another explanation for the increased heart rate in women could be hyperleptinemia, as women were more often overweight than men. It is well known that in women sympathetic nervous system activity can be increased during periods of stress (post menopause) and this results in the elevation of blood pressure (8). In Sweden, in a similar study, hypertensive women had increased sympathetic nervous activity more than men (3). Another finding which shows that increased sympathetic nervous system activity was more usual in women is the fact that women with secondary hypertension due to the increased sympathetic system activity were detected significantly more often than men.

The most frequent treatment used in our study was administration of central adrenergic inhibitors and β-blockers. This resulted in better control of the heart rate and the blood pressure in women than in men, fact showing that increased activity of the sympathetic nervous system played an important role in the pathogenesis of hypertension in our patients.

The relation between stress caused by war, increased activity of the sympathetic nervous system and hypertension was also observed in another study conducted in Croatian soldiers, in which 5% of the soldiers were found to have hypertension, percentage which is high taking into account their young age. In these patients the elevated levels of catecholamines due to war stress were the main reason for hypertension, and blood pressure was controlled with β-blockers (100 mg atenolol OD) (4).

The vast majority of our patients with hypertension (76%) ignored their disease, and only 5.5% were on treatment. These numbers when compared to numbers from studies in developed countries (9–11), where the rate of ignorance of the disease is between 32 and 60%, and the rate of patients being on treatment is 26 to 54.5% show the disability of the system to provide health care in Kosovo after the war. In Greece, the neighbour Kosovo, the numbers are 39.2% and 54.5% respectively.

Concomitant diseases in our patients were in descending order by incidence rheumatic, cardiovascular and COPD disorders. Therefore our hypertensive patients received also NSAIDs or cortisone often without any guidance and follow up from doctors, and as consequence their blood pressure remained uncontrolled (12, 13). This is the reason why in 19.69% of the patients hypertension was attributed secondary to the overuse of NSAIDs or cortisone.

50.8% of our patients had their blood pressure controlled according to the guidelines within 2 months of treatment, percentage that is similar to international data (14, 9–11, 15). 49.2% of the patients did not respond well to our treatment. This is probably because the follow up period was short, patients did not comply with their medication and diet, as the conditions of living during war were poor. Other possible reasons are drug interactions, white coat hypertension, or inadequate antihypertensive treatment for which we used combination of drugs that resulted to better blood pressure control (16–20).

It is well known that NSAIDs and cortisone inhibit the secretion of prostaglandins in the kidneys which leads to renal ischemia and elevation of the blood pressure because of the renin angiotensin system activation (21). This reversible complication of the use of NSAIDs is different from the direct toxic kidney effect of the NSAIDs which is known as nephropathy due to analgesics and occurs after chronic use of these drugs (22–24). It is also known

that NSAIDs and cortisone cause sodium retention and lead to volume dependent hypertension, which is well controlled with diuretics (25). For patients on NSAIDs, we used Ca antagonists as monotherapy or in combination with other agents, because Ca antagonists have renal vasodilating effect and decrease serum rennin levels (21, 25), and diuretics because they increase natriuresis and reduce the volume of blood.

The high rate of patients with systemic complications and target organ damage from hypertension is probably due to late diagnosis and treatment, which is a result of the insufficiency of the health care system (26, 27).

It is interesting that proteinuria was related to a high degree to the severity of hypertension but also to the use of NSAIDs. The relation between micro and macro albuminuria and hypertension has been confirmed in several studies (28–30). These show that proteinuria is more frequently present in severe hypertension, which is often combined with renal failure, retinopathy and heart damage (LVH). NSAIDs used for the treatment of rheumatic disease, which was frequent in our population due to poor living conditions, deteriorate proteinuria (31). ACE inhibitors and angiotensin II receptor blockers reduce albuminuria, directly by decreasing the glomerular pressure and indirectly by controlling the blood pressure (32, 33). This is the reason we used ACE inhibitors as a third choice agent, and as a first choice in patients with albuminuria.

In conclusion the diagnosis and treatment of hypertension in the population of Kosovo during the post war period had certain particularities. The incidence of hypertension was significantly greater in women than in men. Increased sympathetic system activity especially in women due to war stress and poor living conditions was the main reason for secondary hypertension, and this can possibly explain the better control of hypertension with adrenergic inhibitors, like β-blockers and central adrenergic inhibitors. Overuse of analgesics without any medical guidance was another reason of secondary hypertension. It is obvious, that instability in an area does not only have political and economical consequences, but also consequences to the population's health. War apart from the direct losses that causes during the fights, and the increased morbidity due to the poor health care, leads also to higher incidence of diseases which are related to war stress, like hypertension.

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