IRINA ANDRONIKASHVILI, GAIANE SIMONIA, DIANA LABARTKAVA, NATO PANTSULAIA

GENDER DIFFERENCES IN THE PREVALENCE OF METABOLIC SYNDROME AND SALT-SENSITIVE HYPERTENSION AMONG GEORGIAN PERSONS WITHOUT DIABETES

Vl. Bakhutashvili Institute of Medical Biotechnology, Department of Geriatrics, Tbilisi State Medical University, Georgia

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ირინა ანდრონიკაშვილი, გაიანე სიმონია, დიანა ლაბარტყავა, ნატო ფანცულაია

გენდერული განსხვავებები მეტაბოლური სინდრომისა და მარილმგრძნობიარე ჰიპერტენზიის გავრცელებაში შაქრიანი დიაბეტის არმქონე ქართველთა შორის

ვლ. ბახუტაშვილის სახ. სამედიცინო ბიოტექნოლოგიის ინსტიტუტი; გერიატრიის დეპარტამენტი; თბილისის სახელმწიფო სამედიცინო უნივერსიტეტი, საქართველო

რეზიუმე

ცნობილია, რომ მეტაბოლური სინდრომი არის გულ-სისხლძარღვთა დაავადებების მნიშვნელოვანი პრედიქტორი. მონაცემები დაავადების სიხშირის კავშირისა სქესთან შედარებით მწირია. არ არის ბოლომდე გასაგები მეტაბოლური სინდრომის დროს მარილმგრნობელობის გაზრდის მექანიზმი. არსებობს კვლევები, რომლებიც ადასტურებს, რომ მდედრობითი სქესი მარილმგრძნობიარე ჰიპერტენზიის განვითარების მნიშვნელოვანი რისკ ფაქტორია. ჩვენი კვლევა მიზნად ისახავდა მარილმგრძნობიარე ჰიპერტენზიასა და მეტაბოლურ სინდრომს შორის ურთიერთკავშირის დადგენას და სქესის პოტენციური როლის განსაზღვრას ამ პათოლოგიის დროს. ჩვენი კვლევის შედეგებმა აჩვენა, რომ არტერიული ჰიპერტენზიის მქონე ქართველები მოიხმარენ სუფრის მარილის ჭარბ რაოდენობას. საშუალო ასაკის ქართველ ჰიპერტენზიულ პირებში მარილმგრძნობიარობის სიხშირე აღემატება საშუალო საერთაშორისო მონაცემებს და უფრო ხშირია ქალებში. კვლევამ გამოავლინა მეტაბოლური სინდრომის პრევალირება და სარწმუნო დადებითი კორელაციური კავშირი ამ სინდრომს, მარილმგრძნობიარე ჰიპერტენზიას და მდედრობით სქესს შორის. მეტაბოლური სინდრომის და მარილმგრძნობიარობის სქესთან ასოცირების ცოდნამ და ამ მდგომარეობის ადრეულმა გამოვლენამ შესაძლოა მნიშვნელოვანი როლი შეასრულოს სქესთან დაკავშირებული სპეციფიური პრევენციული და სამკურნალო სტრატეგიის შემუშავებაში, რაც დადებით ზეგავლენას მოახდენს მთელი მოსახლეობის ჯანმრთელობაზე.

Introduction. The metabolic syndrome (MS), namely the clustering of disturbances in glucose metabolism, dyslipidemia, central obesity and essential hypertension, is a powerful predictor of cardiovascular disease [8,15]. However, there is considerable variation in the prevalence based on geography, age, sex and, definition used for diagnosis. Data on gender related differences in MS is relatively scarce [17]. Sex differences in the clinical expression and physiology of MS may be important in refining predictions of cardiovascular risk [16]. There are studies according to which MS contributes considerably to cardiovascular mortality, particularly among women [10].

Knowledge of gender differences in MS can help design gender specific preventative and therapeutic strategies that will have a positive impact on overall population health.

On the other hand, hypertension is a major public health problem worldwide because of its high prevalence and consequent increase in risk of vascular disease and premature death [13].

Although there are several different definitions of the metabolic syndrome, hypertension is included in all. The mechanisms of the increased blood pressure in patients with the MS are poorly understood [11].

Epidemiologic studies and clinical trials have demonstrated that a reduced intake of dietary sodium lowers blood pressure (BP) in both hypertensive and normotensive persons [3,14,15]. Salt sensitivity of blood pressure is a phenotype characterized by changes of BP that parallel changes in dietary salt intake. Salt sensitivity affects more than half of all hypertensive subjects as well as a quarter of

normotensive individuals in the United States and is a cardiovascular risk factor for both normotensive and hypertensive humans [19,20].

The underlying mechanism of increased salt-sensitivity among individuals with the metabolic syndrome is not fully understood. Insulin resistance and obesity are the most important underlying risk factors for MS [4]. Some studies suggested that insulin resistance is associated with salt-sensitivity [3,5]. Insulin resistance and concomitant compensatory hyperinsulinemia may lead to sodium retention and extracellular fluid volume expansion, thereby increasing BP responses to sodium intake [11]. There are some studies that proves that female sex is a major risk factor for salt-sensitive hypertension [7].

Based on aforementioned, the study aimed to assess an association between salt-sensitive hypertension and MS, to investigate potential role of gender in these disorders.

Methods. The study enrolled a total of 178 ethnically Georgian middle-aged (38–62-year-old) non diabetic patients of stage I essential hypertension (JNC VIII). 93 of them were females and 85 males. Anthropometry, blood pressure monitoring, and 24 hr. urinary sodium excretion were performed. All subjects were volunteers (signed informed consent form) and non-smokers. They were tested for salt-sensitivity: during the first week subjects were on high sodium diet (200 mmol/d per 70 kg) both by adding 100 mmol directly to the food and by administering 100 mmol in capsules ingested 3 times daily with meals. Next week subjects were placed on a low-salt diet aimed at a maximum intake of 40 mmol sodium per day. Compliance with the diet was confirmed by measurement of 24-hour urinary sodium excretion during the last 2 days of both weeks. The latter was assessed by the difference of mean arterial pressure (MAP) on high (200 mmol/day) vs. low (40 mmol/day) salt diet. Salt-sensitivity was considered when difference between MAP exceeded 3 mm Hg.

MS was classified as recommended by the International Diabetes Federation - IDF9, characterized by abdominal waist circumference ≥ 90 cm in men and ≥ 80 cm in women (at least two of the following criteria was considered for MS: triglycerides ≥150 mg/dl, HDL-cholesterol <40 for men <50 for women, systolic blood pressure ≥130 mm Hg and/or diastolic blood pressure ≥ 85 mm Hg, and fasting glucose ≥ 100mg/dl). The presence of diabetes mellitus did not exclude the diagnosis of MS. The association of three or more abnormal factors confirmed the diagnosis of MS.

Data obtained are presented as mean ± SEM. The effect of dietary Na intake on measured variables was determined by Student's *t* test and ANOVA. Correlation coefficient was calculated using Pearson method. $P<0.05$ was considered significant.

Results and discussion. Our results have shown that virtually all subjects consumed very high amount of sodium chloride in excess of 300 mmol sodium (Fig.1). Therefore, we skipped high-salt diet and placed hypertensive subjects on one-week low-salt diet to determine the salt sensitivity.

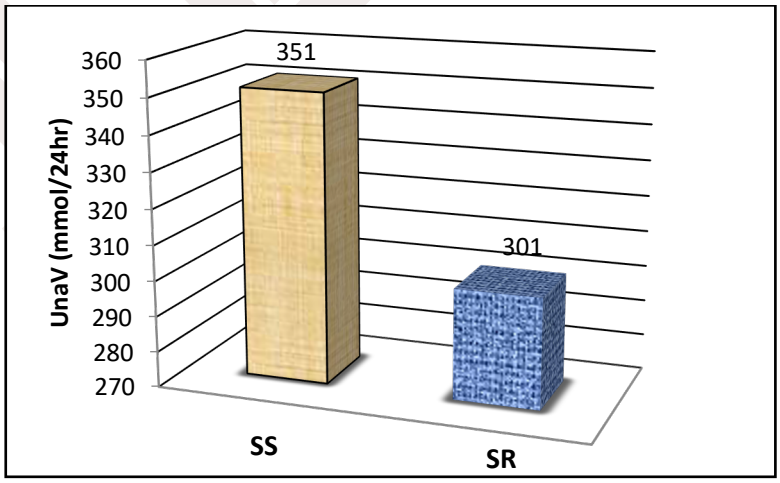

Fig.1. Urinary sodium excretion (UNaV) in salt-sensitive (SS) and salt-resistant (SR) patients with essential hypertension.

Salt sensitivity (when difference between MAP exceeded 3 mm Hg) was detected in 108 (61%) of hypertensive patients (64 i.e., 59% of them were females). From salt-resistant patients only 29 (41.4%) were females (fig.2).

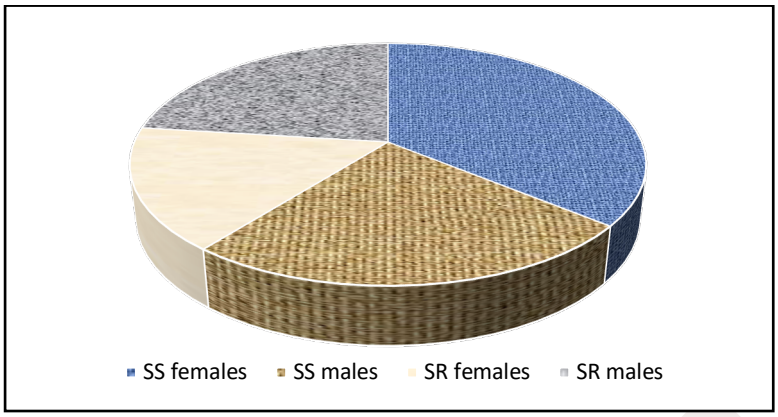

Fig. 2. Gender differences of salt-sensitivity in hypertensive patients.

According to our study a high prevalence of salt-sensitive hypertension was revealed in women ($p<0.05$). MS was detected in 81(45.5%) of all hypertensive patients. 62 (76.5%) of them was salt-sensitive (44 (70.97%) females and 18 (29%) males) and only 19 (23.5%) was salt-resistant (10 (52.6%) females and 9 (47.37%) males).

Our results revealed significantly higher incidence of MS in salt-sensitive hypertensives (predominantly in women) compared to salt-resistant hypertensive subjects ($p<0,001$).

Results of our preliminary study showed that in Georgia all hypertensive subjects consume high amount of sodium (app. 20 grams per day vs. recommended 1.5 grams for hypertensive patients). Our findings are quite alarming considering that Georgia is among the leading five countries worldwide with the highest incidence of hypertension. Based on our results we would suggest that high incidence of hypertension in Georgia might be related to prevalence of salt-sensitivity in hypertensives. Numerous studies confirmed that dietary sodium leads to elevation of blood pressure in certain part of population responding to dietary salt changes i.e., in salt-sensitive humans [2]. The results of this study indicate that in Georgian middle-aged individuals prevalence of salt-sensitivity exceeds average values and is more common in females. Therefore, our findings confirm results of numerous studies that demonstrate a higher risk of salt-sensitive hypertension in women [7,9].

As a main finding, this study showed high prevalence of MS and a positive significant association of this syndrome with female gender and salt-sensitive hypertension. So, our findings confirm results of some studies that demonstrate association of MS with gender and salt-sensitivity [18].

Our results suggest that metabolic syndrome enhances blood pressure response to sodium intake. Reduction in sodium intake could be an especially important component in reducing blood pressure in patients with multiple risk factors for metabolic syndrome. Sex differences in the clinical expression and physiology of metabolic syndrome may be important in refining predictions of cardiovascular risk.

The proposed relationship between the metabolic syndrome, salt-sensitive hypertension and gender needs to be confirmed in other studies.

Conclusions

1. Prevalence of salt-sensitive hypertension associated with high sodium intake has been detected in Georgian hypertensive subjects.
2. Our findings showed high incidence of salt-sensitive hypertension among females.
3. Our study suggests that the metabolic syndrome is significantly related to salt-sensitivity of BP and female gender, reduced intake of sodium may be particularly beneficial in individuals with the metabolic syndrome.

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Vl. Bakhutashvili Institute of Medical Biotechnology, Department of Geriatrics, Tbilisi State Medical University, Georgia

SUMMARY

It has been known that metabolic syndrome (MS) is a powerful predictor of cardiovascular disease. Data on gender related differences in MS is relatively scarce. The underlying mechanism of increased salt-sensitivity among individuals with the metabolic syndrome is not fully understood. There are some studies that prove that female sex is a major risk factor for salt-sensitive hypertension. The study aimed to assess an association between salt-sensitive hypertension and MS, to investigate potential role of gender in these disorders. Results of our study showed that in Georgia hypertensive subjects consume high amount of sodium. Prevalence of salt-sensitivity in Georgian middle-aged individuals exceeds average values and is more common in females. As a main finding, this study showed high prevalence of MS and a positive significant association of this syndrome with female gender and salt-sensitive hypertension. Early detection and knowledge of gender differences in MS and salt-sensitivity can help design gender specific preventative and therapeutic strategies that will have a positive impact on overall population health.

Keywords: metabolic syndrome, salt-sensitive hypertension, gender