Gender Differences in Biochemical and Electroneurographic Parameters of Median and Ulnar Nerve

Merita Tiric-Campara[1], Emir Tupkovic[2], Miro Denislic[3], Mirza Biscevic[4], Amira Skopljak[5], Lejla Zunic[6], Jasminka Djelilovic-Vranic[1], Azra Alajbegovic[1]

[1]Clinic for Neurology, Clinical Center, University of Sarajevo, Bosnia and Herzegovina
[2]Department for Neuropsychiatry, Primary Health Centre Tuzla, Bosnia and Herzegovina
[3]Medical Faculty of Ljubljana, Ljubljana, Slovenia
[4]Clinic for Orthopedics and Traumatology, Clinical Center, University of Sarajevo, Bosnia and Herzegovina
[5]Medical Faculty of Sarajevo University, Bosnia and Herzegovina
[6]Faculty for Health Sciences, University of Zenica, Zenica, Bosnia and Herzegovina

Corresponding author: Merita Tric Campara, MD, PhD. Department of neurology, Clinical centre Univeristy of Sarajevo, Bolnicka 25, 71000 Sarajevo, Bosnia and Herzegovina Tel: ++ 387 61 190 490. E-mail:merita.tiric@gmail.com

doi: 10.5455/aim.2015.23.360-363
ACTA INFORM MED. 2015 DEC; 23(6): 360-363
Received: 25 August 2015 • Accepted: 15 October 2015

ABSTRACT

Introduction: In this article are demonstrated differences in the aspects of the metabolic syndrome (MSy) between genders, as well as the association of MSy and neuropathy. **The aim:** The aim of our study was that in patients with newly discovered metabolic syndrome of both sexes make comparison of fasting blood glucose levels and after oral glucose tolerance test, as well as neurophysiological parameters of n.medianus and n.ulnaris. **Patients and methods:** All participants were examined dermatologically. The analysis included the 36 male and 36 female respondents with a newly discovered MSy. **Results:** The average age of men was 52.75±7.5 (40-65) years and women 52.1±7.7 (38-67) years. The average value of fasting blood glucose in women was 5.86±0.87 (4.5-8) mmol/L, and non significantly higher in men (p=0.0969) as 6.19±0.8 (4.7-8) mmol/L. Average values of blood sugar 120 minutes after oral glucose tolerance test were not significantly different (p=0.7052), and was 5.41±1.63 (3.3-9.7) mmol/L in women and 5.27±1.52 (2.7-9.8) mmol/L in men. Median motor velocity were significantly higher in women for n.medianus on the left (p=0.0024), n.ulnaris on the left (p=0.0081) and n.ulnaris on the right side (p=0.0293), and the median motor terminal latency were significantly longer in n.ulnaris on the left (p=0.0349) and n.ulnaris on the right side (p=0.011). There was no significant difference in the sensory conductivity velocity in n.medianus and n.ulnaris between the groups, but the amplitude with the highest peak of the sensory response was significantly higher in n.medianus on the left (p=0.0269) and n.ulnaris on the left side (p=0.0009) in female patients. **Conclusion:** The results indicate that there are differences in neurophysiological parameters of the investigated nerves between the genders, and that tested nerve structures in the course of MSy are affected slightly more in men. There were no significant differences in skin changes between genders.

Key words: metabolic syndrome, median nerve, ulnar nerve, motor velocity, sensory velocity.

1. INTRODUCTION

The first component of the metabolic syndrome (MSy) is central obesity defined by waist circumference, associated with at least two of the four following parameters: elevated triglycerides (TGL) decreased HDL cholesterol, elevated blood pressure and elevated fasting glycemia.

There are evidences that the incidence of MSy and distribution of its components in men and women differ. Studies of the working population in Spain indicate prevalence of MSy 11.5% among men and 4.1% among women with an increase in old age, and it actually varies in the different professions (1). Among persons in adulthood in Turkey MSy was present in 26.9% of respondents, from which 31.3% of women and 21.7% of men (2). About the possible consequences of this syndrome speaks the fact that in patients with acute ischemic syndromes MS was found even at 70.2% women and 52.6% of men (3).

Even in adolescence age, accumulation of intra-abdominal adipose tissue may start the development of MSy, involving metabolic and inflammatory component, which has a serious impact on blood pressure in men, which can be added to increased sympathetic activity also seen only in men (4). Overweight and obesity are strongly associated with MSy, and obesity has a stronger association with the insulin resistance risk in women (5).

There is an inverse association of adiponectin levels and insulin resistance. Subclinical inflammation is present in MSy with evidence of a difference in

the level and expression of various inflammation-sensitive biomarkers between genders. For example, in non-diabetic population, smoking combined with decreased levels of adiponectin, increased levels of high sensitive C-reactive protein (hs-CRP) and higher levels of receptor antagonists of interleukin-1 (IL-1Ra) in women (6, 7, 8).

In persons with acute ischemic syndromes and MSy men had more frequently increase in the concentration of TGL, and women decrease in the concentration of cholesterol–high density lipoprotein (HDL-C) (3). As a confirmation of a genetic predisposition in women according to the increase risk for low HDL-C, dyslipidemia and MSy alleles are associated with the apolipoprotein A5 gene (APOA5), namely APOA5 SNPs (9). According to a study performed in Sweden, women with MSy had higher Body Mass Index (BMI) and levels of C-reactive protein, and have a better chance to meet criteria for waist-hips ratio, and among them was more prevalent the syndrome characterized by obesity and low grade inflammation (10) .

There is a great interest in the role of free radicals and oxidative stress in the pathogenesis of MSy. Studies in Japan have shown that cellular antioxidant enzymes as glutathione peroxidase 1 (GPX1) play a central role in controlling an oxygen reactive species and GPX1 polymorphism (Pro198Leu) is associated with MSy in men but not in women (11).

Metabolic syndrome is, in fact, often present in patients with neuropathy, and with impaired glucose tolerance (IGT–impaired glucose tolerance) and normal glucose tolerance (NGT–normal glucose tolerance) compared with the prevalence in the general population (12). It is known that polyneuropathy of longer nerves is frequent complication of diabetes mellitus. However, intermittent hyperglycemia or insulin resistance associated with prediabetes may be sufficient to damage the distal parts of the nerves. Preferred small non myelinated nerve damage suggests the existence of prominent neuropathy pain, predominantly sensory impairment and early autonomic dysfunction (13).

Studies, therefore, confirm some differences in the gender aspects of MSy, as well as the association of MSy and neuropathy, but relatively few of them deals with this syndrome and electroneurography parameters in differences between genders. Therefore, the aim of our research is, to at least partially, to attempt to explain this problem.

The research goal is to examine in patients with newly discovered metabolic syndrome of both sexes comparable levels of fasting blood glucose levels and after the glucose tolerance test, as well as neurophysiological parameters of median and ulnar nerves.

2. PATIENTS AND METHODS

The analysis included 36 respondents of both sexes with a newly discovered MSy. The average age of men was 52.75 ± 7.5 (40-65) years and women 52.1 ± 7.7 (38-67) years. Eleven female and 9 male respondents had symptoms of sensory neuropathy in the hand. For all patients with MSy was determined the fasting level of glucose in the blood and oral glucose tolerance test (OGTT).

Neurophysiological tests were performed at room temperature, and the "physiological" temperature of the skin of the respondents lying on the back. For the measurement of parameters is used neurography EMNG machine Medelec Synergy (EMG and EP Systems OXFORD INSTRUMENTS 2004). Used was the superficial stimulating and registration bipolar (also called large touch proof) electrodes. Sensory conduction velocity in median and ulnar nerve was measured by stimulating the wrist and registration on the index and little finger, at the first interphalangeal joint (Figure 1). Terminal motor latency was measured by stimulating the wrist and registering on thenar and hypotehnar, precisely at 6 cm proximal from the registration electrodes on the stomach *abductor pollicis brevis* muscle for median nerve and *m. adductor digiti minnimi* for ulnar nerve. Proximal measurement for both nerves was done in the area just above the elbow. In electroneurography (ENG) processing were analyzed the sensory nerve conducting velocity (from stimulus artifact to the primary deflection on isoelectric line) with an amplitude of sensory nerve action potential (SNAP), terminal motor latency of median and ulnar nerve on both sides with the highest amplitude of a complex motor action potential (CMAP) measured from the center of the primary divergence at isoelectric line after stimulus artifact to the final return to the isoelectric line. Stimulation in the determination of motor and sensory responses was performed until stop of the CMAP and SNAP amplitudes increase.

Levels of blood glucose and glucose tolerance after 120 min. are presented by the mean value with standard deviation, and in statistical analysis of differences of these parameters between genders we were using the Student's T test and chi square test. In the statistical analysis of neurophysiological parameters were assessed median values by the nonparametric Mann-Whitney U test, and differences at level of $p<0,05$ were considered as statistically significant.

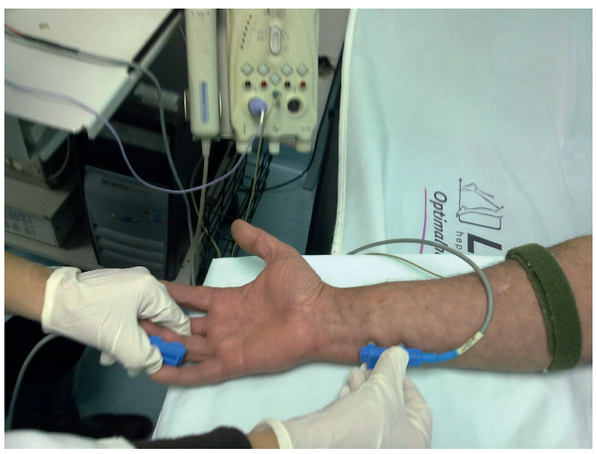

Figure 1. Part of EMNG procedure

3. RESULTS

The mean value of blood glucose in women was 5.86±0.87 (4.5 to 8) mmol/L, and not significantly higher in men ($p=0.0969$) with 6.19±0.8 (4 0.7 to 8) mmol/L. Most of the 27 female and 20 male subjects had glucose levels within the standard range (3.9 to 6.1 mmol/L), while values above this range had 9 women and 16 men, which was significantly different distribution by gender ($p=0.0189$).

Mean values of blood sugar after 120 minutes at the oral glucose tolerance test were not significantly different ($p=0.7052$), and was 5.41±1.63 (3.3 to 9.7) mmol/L in women

and 5.27±1.52 (2.7-9.8) mmol/L in male. By 23 persons of both sexes had a blood glucose within a standard, 8 women and 9 men above, and 5 women and 4 men below the standard range, so there were no significant differences in the distribution of these values among groups (p=0.8348).

Parameters of motor and sensory electroneurography analysis in n. medianus and n. ulnaris of males and females with metabolic syndrome are shown in Tables 1-4. Median velocity of motor conductivity tends to have higher values in women, while the terminal motor latency was lower.

Statistical analysis showed that the medians of the motor velocity n. medianus on the left, n. ulnaris on the left and n. ulnaris on the right side were significantly higher in women,

Motor velocity (m/s)	Median	Percentile (25-75)	Min.	Max.
Lt.n.medianus	57.95	55.60-61.35	51.6	66.8
Rt n.medianus	57.20	53.75-59.70	49.0	65.3
Lt. n.ulnaris	53.20	51.00-55.10	46.6	63.2
Rt. n.ulnaris	55.85	53.65-58.025	50.0	63.4
Motor latency (msec)	Median	Percentile (25-75)	Min.	Max.
Lt.n.medianus	3.4	3.15-3.67	2.6	4.9
Rt. n.medianus	3.27	2.85-3.66	2.6	5.8
Lt.n.ulnaris	2.75	2.4875-3.0125	2.1	3.7
Rt.n.ulnaris	2.65	2.3875-3.1	1.9	3.75
CMAP I (mV)	Median	Percentile (25-75)	Min.	Max.
Lt.n.medianus	20.7	14.925-24.825	8.0	40.2
Rt. n.medianus	19.5	16.5-32.325	6.9	40.8
Lt. n.ulnaris	14.2	10.95-19.65	5.2	37.1
Rt. n.ulnaris	14.9	10.55-18.8	4.1	25.8
CMAP II (mV)	Median	Percentile (25-75)	Min.	Max.
Lt.n.medianus	18.9	15.05-23.2	6.3	38.6
Rt.n.medianus	18.0	14-28.525	5.8	42.9
Lt.n.ulnaris	13.45	10.175-16.025	3.7	35.7
Rt. n.ulnaris.	14.5	10.9-16.45	3.1	24.6

Table 1. Parameters of motor neurography analysis of n.medianus and n.ulnaris of 36 female respondents with metabolic syndrome. CMAP: complex motor action potential I: CMAP after distal stimulation; II: CMAP after proximal stimulation

Motor velocity (m/s)	Median	Percentile (25-75)	Min.	Max.
Lt.n.medianus	54.6	51.325-58.825	44.0	62.9
Rt. n.medianus	55.6	52.05-58.0	34.0	62.4
Lt.n.ulnaris	50.9	48.05-53.975	32.4	61.3
Rt. n.ulnaris	52.8	50.7-56.7	46.8	61.5
Motor latency (msec)	Median	Percentile (25-75)	Min.	Max.
Lt. n.medianus	3.55	3.35-3.912	2.85	4.9
Rt. n.medianus	3.525	3.2375-3.825	2.6	5.2
Lt.n.ulnaris	2.925	2.8-3.05	2.3	3.65
Rt. n.ulnaris	3.05	2.7-3.25	2.05	4.1
CMAP I (mV)	Median	Percentile (25-75)	Min.	Max.
Lt.n.medianus	21.5	17.3-28.475	6.0	43.9
Rt.n.medianus	23.1	16.475-30.9	6.6	47.6
Lt.n.ulnaris	18.15	12.675-21.475	5.1	39.3
Rt. n.ulnaris	16.95	12-20.925	4.7	37.9
CMAPII (mV)	Median	Percentile (25-75)	Min.	Max.
Lt.n.medianus	19.9	16.15-27.675	6.5	38.4
Rt. n.medianus	21.15	14.5-28.075	3.7	46.8
Lt.n.ulnaris	15.0	11.425-19.725	3.8	35.9
Rt. n.ulnaris	15.1	10.35-19	4.0	28.8

Table 2. Parameters of motor neurography analysis of n.medianus and n.ulnaris of 36 male respondents with metabolic syndrome. CMAP: complex motor action potential I: CMAP after distal stimulation; II: CMAP after proximal stimulation.

Sensory velocity (m/s)	Median	Percentile (25-75)	Min.	Max.
Lt.n.medianus	49.45	45.975-53.8	0	57.7
Rt. n.medianus	49.1	43.675-52.225	0	58.9
Lt. n.ulnaris	48.9	45.2-51.45	39.7	54.9
Rt. n.ulnaris	49.05	46.475-51.025	41.5	56.2
SNAP amplitude (μV)	Median	Percentile (25-75)	Min.	Max.
Lt. n.medianus	16.9	11.55-23.4	0	35.0
Rt. n.medianus	14.65	10.675-20.05	0	49.7
Lt. n.ulnaris sin.	19.05	15.3-28.075	8.8	41.0
Rt. n.ulnaris dex.	18.35	11.25-26.2	2.25	46.1

Table 3. Parameters of sensory neurography analysis of n. medianus and n. ulnaris of 36 female respondents with metabolic syndrome. SD: standard deviation; Min.: minimum; Max.: maximum; SNAP: sensory nerve action potential.

Sensory velocity (m/s)	Median	Percentile (25-75)	Min.	Max.
Lt. n.medianus	49.55	45.525-52.975	37.1	62.2
Rt.n.medianus	49.0	44.35-52.325	29.5	60.0
Lt.n.ulnaris	48.1	44.625-50.35	19.8	55.0
Rt. n.ulnaris	47.2	45.15-50	40.7	59.5
SNAP amplitude (μV)	Median	Percentile (25-75)	Min.	Max.
Lt.n.medianus	12.05	9.2-16.85	2.7	28.9
Rt. n.medianus	11.65	8.15-17.15	4.7	30.0
Lt. n.ulnaris	13.4	8.075-21.2	4.3	33.9
Rt. n.ulnaris	16.1	10.9-18.65	4.2	30.5

Table 4. Parameters of sensory neurography analysis of n. medianus and n. ulnaris of 36 male respondents with metabolic syndrome. SD: standard deviation; Min.: minimum; Max.: maximum; SNAP: sensory nerve action potential.

MOTOR NERVE	PARAMETER	p
Lt.n.medianus	Velocity	0.0024
	TML	0.0545
Rt. n. medianus	Velocity	0.0733
	TML	0.0673
Lt. n.ulnaris	Velocity	0.0081
	TML	0.0349
Rt. n.ulnaris	Velocity	0.0293
	TML	0.011

Table 5. Significance of differences in motor conduction velocity of n. medianus and n. ulnaris of the male and female respondents with metabolic syndrome. TML: terminal motor latency

while the median motor terminal latency of n.ulnaris on both sides significantly longer in women (Table 5). Areas of CMAP obtained after proximal and distal stimulation showed no significant differences between genders (Table 6).

There was no significant difference in the velocity of sensory conductivity of n. medianus and n. ulnaris and between groups. However, the amplitude of the highest peak of the sensory response was significantly higher in n. medianus on the left and n. ulnaris on the left in women (Table 7). In one female patient we did not received a sensory response of n. medianus on the left side, and in one female patient of the n. medianus on the right side.

4. DISCUSSION

From our results it is clear that there are no significant differences in age of occurrence and diagnosis of metabolic syndrome between the male and female respondents. According to a study by Zaliūnas and associates (2008) on patients with acute ischemic syndrome, women with metabolic syndrome

MOTOR NERVE	CMAP	p
Lt.n.medianus	I	0.2437
	II	0.3384
Rt.n. medianus	I	0.7018
	II	0.4305
Lt.n.ulnaris	I	0.0989
	II	0.1712
Rt. n.ulnaris	I	0.2648
	II	0.4404

Table 6. Significance of differences in surface cmap of n.medianus and n.ulnaris of the male and female respondents with metabolic syndrome. I: CMAP after distal stimulation; II: CMAP after proximal stimulation

SENSORY NERVE	PARAMETER	p
Lt. n.medianus	Velocity	0.9865
	SNAP amplitude	0.0269
Rt. n. medianus	Velocity	0.8614
	SNAP amplitude	0.1122
Lt. n.ulnaris	Velocity	0.3412
	SNAP amplitude	0.0009
Rt. n.ulnaris	Velocity	0.1414
	SNAP amplitude	0.1161

Table 7. Significance of differences in sensory conduction velocities and snap amplitude of n.medianus and n.ulnaris of the male and female respondents with metabolic syndrome. SNAP: sensory nerve action potential.

were significantly older than men (68.1 compared to 60.2 year of age) (3).

Although in our study, we have a higher percentage of men with glucose levels above the reference values, however, there are no differences in blood glucose levels between the sexes 120 minutes after oral glucose tolerance test. There are interesting researches that, for example, a low level of total testosterone and sex hormone binding globulin (SHBG) are independent risk factor for developing metabolic syndrome and diabetes mellitus in middle-aged men. So hyperandrogenism is an early marker for insulin disorders and glucose metabolism, which can progress to metabolic syndrome or the risk of diabetes and may contribute to pathogenesis. However, in a study of individuals in late adolescence and early adult age, it was noted that among male respondents there is more obesity, have higher rates of hypertension and hypertriglyceridemia than women, but all cases of glucose intolerance were registered among women (15).

Men and women showed differences in neurophysiological parameters of n. medianus and n. ulnaris. Median values of motor conductivity velocity in our study were generally lower and terminal motor latency generally higher in males. On the other hand, the amplitude of sensory nerve response test on the left was significantly lower in men. These observations suggest that the neural structures examined in the course of metabolic syndrome are slightly more affected in men.

5. CONCLUSION

Motor velocity of n. medianus on the left, n. ulnaris on the left. and n. ulnaris on the right side are significantly higher, terminal motor latency of n. ulnaris on both sides are significantly longer and the amplitude of the highest tip of the sensory responses were significantly higher in n. medianus on the left and n.ulnaris left among women, suggesting that the tested neural structure during the metabolic syndrome are slightly more pronounced in men.

CONFLICT OF INTEREST: NONE DECLARED.

REFERENCES

1. Sánchez-Chaparro MA, Calvo-Bonacho E, González-Quintela A, Fernández-Labandera C, Cabrera M, Sáinz JC, Fernández-Meseguer A, Banegas JR, Ruilope LM, Valdivielso P, Román-García J. Occupation-related differences in the prevalence of metabolic syndrome. Diabetes Care. 2008;31(9):1884-1885.
2. Erem C, Hacihasanoglu A, Deger O, Topbaş M, Hosver I, Ersoz HO, Can G. Prevalence of metabolic syndrome and associated risk factors among Turkish adults: Trabzon MetS study. Endocrine. 2008; 33(1): 9-20.
3. Zaliūnas R, Slapikas R, Babarskiene R, Slapikiene B, Luksiene D, Milvidaite I, Laukaitiene J. The prevalence of the metabolic syndrome components and their combinations in men and women with acute ischemic syndromes. Medicina (Kaunas). 2008; 44(7): 521-528.
4. Syme C, Abrahamowicz M, Leonard GT, Perron M, Pitiot A, Qiu X, Richer L, Totman J, Veillette S, Xiao Y, Gaudet D, Paus T, Pausova Z. Intra-abdominal adiposity and individual components of the metabolic syndrome in adolescence: sex differences and underlying mechanisms. Arch Pediatr Adolesc Med. 2008; 162(5): 453-461.
5. Cordero A, León M, Andrés E, Ordoñez B, Laclaustra M, Grima A, Pascual I, Luengo E, Civeira F, Pocoví M, Alegría E, Casasnovas JA. On behalf of the MESYAS Registry investigators Gender differences in obesity related cardiovascular risk factors in Spain. Prev Med. 2008 Nov 7[In press].
6. Ahonen TM, Kautiainen HJ, Keinänen-Kiukaanniemi SM, Kumpusalo EA, Vanhala MJ. Gender difference among smoking, adiponectin, and high-sensitivity C-reactive protein. Am J Prev Med. 2008; 35(6): 598-601.
7. Rogowski O, Shapira I, Berliner S. Exploring the usefulness of inflammation-sensitive biomarkers to reveal potential sex differences in relation to low-grade inflammation in individuals with the metabolic syndrome. Metabolism. 200; 57(9): 1221-1226.
8. Saltevo J, Vanhala M, Kautiainen H, Kumpusalo E, Laakso M. Gender differences in C-reactive protein, interleukin-1 receptor antagonist and adiponectin levels in the metabolic syndrome: a population-based study. Diabet Med. 2008; 25(6): 747-750.
9. Komurcu-Bayrak E, Onat A, Poda M, Humphries SE, Palmen J, Guclu F, Can G, Erginel-Unaltuna N. Gender-modulated impact of apolipoprotein A5 gene (APOA5) -1131T>C and c.56C>G polymorphisms on lipids, dyslipidemia and metabolic syndrome in Turkish adults. Clin Chem Lab Med. 2008; 46(6): 778-784.
10. Tonstad S, Sandvik E, Larsen PG, Thelle D. Gender differences in the prevalence and determinants of the metabolic syndrome in screened subjects at risk for coronary heart disease. Metab Syndr Relat Disord. 2007; 5(2): 174-182.
11. Kuzuya M, Ando F, Iguchi A, Shimokata H. Glutathione peroxidase 1 Pro198Leu variant contributes to the metabolic syndrome in men in a large Japanese cohort. Am J Clin Nutr. 2008; 87(6): 1939-1944.
12. Smith AG, Rose K, Singleton JR. Idiopathic neuropathy patients are at high risk for metabolic syndrome. J Neurol Sci. 2008; 273(1-2): 25-28.
13. Singleton JR, Smith AG. Neuropathy associated with prediabetes: what is new in 2007? Curr Diab Rep. 2007; 7(6): 420-424.
14. Laaksonen DE, Niskanen L, Punnonen K, Nyyssönen K, Tuomainen TP, Valkonen VP, Salonen R, Salonen JT. Testosterone and Sex Hormone - Binding Globulin Predict the Metabolic Syndrome and Diabetes in Middle-Aged Men. Diabetes Care. 2004; 27: 1036-1041.
15. Huang TT, Shimel A, Lee RE, Delancey W, Strother ML. Metabolic Risks among College Students: Prevalence and Gender Differences. Metab Syndr Relat Disord. 2007; 5(4): 365-372.