Research Paper Medical Science

Impact of Lipid Status, Liver Enzymes and Iron Homeostasis on Metabolic Syndrome Among Adult People

Biljana Ilkovska	Department of medical biochemistry, PHO Clinical Hospital dr. Trifun Panovski, Bitola, R. Macedonia
Bisera Kotevska	Department of dermato venereology Tokuda Hospital, R.Bulgaria
Georgi Trifunov	Department of ottorinolaringology, Tokuda Hospital, R.Bulgaria
Branimir Kanazirev	Propedeutics of Internal Medicine, Varna Medical University, Varna, Bulgaria

ABSTRACT

Metabolic syndrome is consisted of a set of metabolic disturbances which support the risk increasing of cardiovascular disease and diabetis mellitus. Aim of this study is to present impact of lipid status, liver enzymes and iron homeostasis on metabolic syndrome among adult people. The study included 240 subjects at the age of 18 to 65 who were divided in two groups(examined and control group). The total number of patients with Metabolic syndrom was 120. In our research it was confirmed that at patients with metabolic syndrome there are increased values of feritin and hepcidin compared to the control group. In our research difference in the values of cholesterol statically was confirmed as significant which is due to the significantly higher values of cholesterol in the group with metabolic syndrome compared to the group of healthy people. We discover that the tests for liver function are higher at women with metabolic syndrome compared to the control group of women.

KEYWORDS lipid status, iron, metabolic syndrome

Introduction

Metabolic syndrome does not represent new medical condition. In early 1920 Swedish doctor Kylin published interesting observations for aggregation of some metabolic risk factors (1). Still the term "metabolic syndrome" was not formilized until 1998 (2). Other terms which are used as synomims to metabolic syndrome are: syndrome X (3), deadly quarter (4) and syndrome of resistance of insulin (5).

Metabolic syndrome is consisted of a set of metabolic disturbances which support the risk increasing of cardiovascular disease and diabetis mellitus (6,7). In 2001 National program for education for cholesterol (NCEP:ATPIII) announced its definition which includes at least three of five criteria for metabolic syndrome (8).

Definition of metabolic syndrome according to ATP III Panel III for treatment of adults clinical identification of metabolic syndrome (8).

1) abdominal obesity, defined as the presence of waist circumference ≥102 cm in men or ≥88 cm in women;

2) fasting plasma glucose ≥ 6.1 mmol/l or drug treatment for elevated blood glucose;

3) serum triglycerides ≥ 1.69 mmol/l or drug treatment for elevated triglycerides;

4) serum HDL cholesterol in men< 1.03 mmol/l and <1.29 mmol/l in women or drug treatment for low HDL-C;

5) blood pressure ≥130/85 mmHg or drug treatment for elevated blood pressure.

Risk factors for appearance of metabolic syndrome are : overweight, physical inactivity, getting older, diabetis mellitus and etc.

Etiology of metabolic syndrome includes: resistance to insulin, increased size of the waist, dyslipidemy, intolerance of glucoses, hypertension, adiponectin and etc.

Aim of this study is to present impact of lipid status, liver enzymes and iron homeostasis on metabolic syndrome among adult people.

Material & Methods,

This study was carried at the Department of medical biochemistry and Diabetes Center of Public Health Organization Clinical hospital d-r Trifun Panovski in Bitola.

The study was approved by the Ethics Committee of Health Organization Clinical hospital d-r Trifun Panovski, and all of the procedures were performed in accordance with ethical approval institutional guidelines. The study protocol followed the ethical guidelines of the most recent Declaration of Helsinki. Written consent was obtained from the participants prior to the start of the study.

The study included 240 subjects at the age of 18 to 65 who were divided in two groups (examined and control group).

The total number of patients with metabolic syndrom was 120, recruited from Diabetes Research Centre of Health Organization Clinical hospital d-r Trifun Panovski, Bitola, R.Macedonia.

Individuals aged 18 years or older were eligible to participate in the study. In this analysis we included subjects with available complete data allowing their classification according National program for education for cholesterol (NCEP:ATPIII) which includes at least three of five criteria for metabolic syndrome.

Exclusion criteria were history of: cirrhosis or chronic hepatitis B and C, clinical evidence of bleeding in the previous 6 months, anemia (hemoglobin <120 g / L), treatment with

iron in the previous year, alcohol consumption - women with daily consumption of alcohol > 40 g / day and men with daily alcohol consumption > 60 g / day, donation of blood in the previous 6 months, haemochromatosis, concomitant infections, malignant disease, chronic diseases other than diabetes mellitus type 2, immunosuppressive therapy, acute infections or invasive procedures (operations, catheterization) in the previous 6 months, neurological, endocrine or other systemic diseases, cardiovascular incident in the previous 6 months and pregnancies.

The remaining 120 patients are healthy people, blood donors from the Department of Transfusion Medicine of Health Organization Clinical hospital d-r Trifun Panovski.

Clinical and laboratory measurements
Study data included a medical history, a physical examination, information provided by a questionnaire, anthropometric measurements, and laboratory measurements.

The medical and drug prescription history were assessed by the examining physicians. All of the participants were asked to respond to a health-related behavior questionnaire, which included the topics of alcohol consumption, smoking, and exercise.In addition, the participants were asked about their physical activities per week, duration of the same in order to produce perspiration such as jogging, bicycling, and swimming (≥1 time/ week).

Blood samples were collected after 12 h of fasting and drawn from an antecubital vein. Serum levels of enzymes, lipid profile, iron, ferritin wer measured by automated chemistry analyzer (Biosystems, Spain).

Hepcidin levels were measured with ELISA kit (DRG Hepcidin-25 bioactive ELISA, Marburg).

The data are presented as mean± standard deviation (SD). The results were done with the SPSS version 13.

Results
The average age of the examined group of patients with metabolic syndrome is 52,87±7,42, the youngest patient with metabolic syndrome is 32 years old and the oldest is 60 years of age. Men from the examined group with average age of 51,03±7,94 are significantly younger than women from the same group who are at the average age of 54,7±6,43 (t=2.78 p=0,006).

Analyses of lipid status
Average values of cholesterol in the whole examined group and in groups male and female respondents are 5, 39±1, 22, 5, 58±1, 26 и 5, 21±1, 16 correspondingly. The average value of cholesterol is insignificantly higher in the group of sick male respondents (p>0,05).

Insignificant differences are registered between men and women from the examined group and regarding the average values of HDL-cholesterol (1,19±0,29 вс 1,32±0,28 p>0,05).

Values of LDL-cholesterol in the examined group are in the range from 1,05 – 6,34, with average value that is medium of 2,95.In male examined group LDL-cholesterol has minimal value of 1,25, maximal 6,34, medium of 2,98, while in the female examined group values of LDL- cholesterol are in the range from 1,05 to 5,72, with medium of 2,94.Statistic analyses confirmed the values of LDL- cholesterol in the group of male with metabolic syndrome significantly higher from female with metabolic syndrome (Z=2,53 p=0,011).

Troglycerides in the examined group have medium from range (0,76 – 6,35). In group with metabolic syndrome men have medium of 2,33 (range 0,81 – 6,35), women have medium value of triglycerides 1,81 (range 0,76 – 4,35). Value of triglycerides is significantly higher at group of men with metabolic syndrome compared to the group women with metabolic syndrome (Z=3,16 p=0,0016).

Values of ApoA in the group with metabolic syndrome are in the range of 56,0 – 171,0, with medium of 87,5. In the group of examined men ApoA has medium of 78 (range 56 – 170), while in the group examined women values ApoA have medium of 82, 5 (range 57 – 171). Differences in values of ApoA between men and women with metabolic syndrome were also statistically confirmed as significant as a result of evidently higher values in the group of women with metabolic syndrome (Z=2,59 p=0,0096).

Average value of ApoB in the whole examined group in both male and female examined group is 170,22±32,13, 179,2±30,79 and161,22±31,13 consequently. Statistic analyses confirmed that the sex has significant influence to the values of ApoB at respondents with metabolic syndrome that is men with this disease have significantly higher average values of ApoB compared to women (t=3,18 p=0,0018).

Table 1. Present mean values ±SD, median, rang of serum concentrations of: cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, ApoA, apoB in patientrs with methabolic syndrom.

Variable (unit)	Total N = 120	Males N = 60	Females N = 60	p-value
Cholesterol (mmol/l) mean±SD, median, rang	5,39 ± 1,22 5,21 2,4 – 8,89	5,58 ± 1,26 5,23 2,91 – 8,89	5,21 ± 1,16 5,17 2,4 – 7,9	t=1,66 p=0,099 ns
HDL-cholesterol (mmol/l) mean±SD, median, rang	1,26 ± 0,29 1,2 0,6 – 2,0	1,19 ± 0,29 1,11 0,6 – 2,0	1,32 ± 0,28 1,3 0,63 – 1,96	t=0,334 p=0,74 ns
LDL–cholesterol (mmol/l) mean±SD, median, rang	2,91 ± 1,31 2,95 1,05 – 6,34	2,95 ± 1,5 2,98 1,25 – 6,34	2,87 ± 1,09 2,94 1,05 – 5,72	Z=2,53 p=0,011*
Triglycerides (mmol/l) mean±SD, median, rang	2,28 ± 1,11 2,11 0,76 – 6,35	2,59 ± 1,26 2,33 0,81 – 6,35	1,97 ± 0,84 1,81 0,76 – 4,35	Z=3,16 p=0,0016**
ApoA(mg/dl) mean±SD, median, rang	94,67 ± 30,09 87,5 56,0 – 171,0	89,42± 30,78 78 56 – 170	99,93 ± 28,67 82,5 57 – 171	Z=2,59 p=0,0096**
ApoB(mg/dl) mean±SD, median, rang	170,22 ± 32,13 167,79 78,0 – 240,35	179,2± 30,79 183,08 108,7 – 240,3	161,22± 31,13 155,42 78 – 232	t=3,18 p=0,0018**

***p<0,05 **p<0,01**
Analyses of enzyme status
All enzymes which were analyzed in the research (ALT, AST и GGT), have significantly higher serum concentrations in a group of men with metabolic syndrome compared to the group of women with metabolic syndrome. Values of the enzyme ALT in the group with methabolic syndrome have medium of 30,2(range 8,1 – 82,0), while in the group of male and female respondents ALT has medium of 39,23 (range

11,95 – 81,6) and medium of 23,7 (range 8,1 – 82) consequently (Z=4,47 p<0,000008).

Medium of the values of the enzyme AST in the group with methabolic syndrome is 26,65 (range 18,3 – 79,70), in male examined group is 28,3 (range 19,3 – 79,7), while in the female examined group the values of AST are considerably lower with medium 25,55 (range 18,3 – 79,0) (Z=2,17 p<0,029).

In the group of respondents with metabolic syndrome the measured serum concentrations of the enzyme GGT are in the range from 7,4 to 101,1, with average of 31,0. This enzyme also presents significantly higher values in the examined group of men compared to the examined group of women. (Z=5,49 p<0,001). GGT enzyme has medium of 40,0 in the group of men and 22,6 in the group of healthy women.

Table 2.Present mean values ±SD, median, rang of serum concentrations of: AST, ALT, gGT in patientrs with methabolic syndrom.

Variable (unit)	Total N = 120	Males n = 60	Females n = 60	p-value
ALT(U/L) mean±SD, median, rang	35,94 ± 19,75 30,2 8,1 – 82,0	43,59 ± 20,97 39,23 11,95 – 81,6	28,27 ± 15,09 23,7 8,1 – 82	Z = 4,47 p = 0,000008**
AST(U/L) mean±SD, median, rang	30,94 ± 13,6 26,65 18,3 – 79,70	33,55 ± 15,56 28,3 19,3 – 79,7	28,33 ± 10,84 25,55 18,3 – 79,0	Z = 2,17 p = 0,029*
gGT(U/L) mean±SD, median, rang	36,63 ± 22,26 31,0 7,4 – 101,1	45,86 ± 22,66 40,0 10,5 - 100	27,41 ± 17,68 22,6 7,4 – 101,1	Z = 5,49 p < 0,001**

***p<0,05 **p<0,01**

Analyses of iron, its transporters feritin, transferin and hormone regulator of iron hepcidin.
The average value of the serum iron in the examined group is 15,79±5,28, that is 17,23±5,22 in the examined group of men and 14,36±4,99 in the examined group of women. For p<0,01 there is significant difference in the average values of the serum iron between men and women from the examined group as a result of significantly higher average values in the group of men with metabolic syndrome (t=3,07 p=0,0026).

Men from the examined group have significantly higher values of feritin than women from the same group (Z=4,04 p=0,00005). Medium that is the average value of feritin in the group of examined men and women is 116,0 (range 34 – 668) and 11,5 (range 11 – 456) consequently.

In the group with methabolic syndrome values of transferin are registered in the range of 172,0 to 582,0, with average value of 244. Male and female respondents have insignificantly different values for (p>0, 05).

Results from our research showed that at the respondents with metabolic syndrome, sex has significant influence to the values of hepcidin (Z=5,54 p<0,001). Men with metabolic syndrome have significantly higher values regarding the respondents from female sex. Value of this hormone regulator of iron, in male examined group has medium of 20, 75 (range 2, 47 – 85, 98), while in the female examined group the medium of hepcidin is 10, 81 (range 2, 93 – 24, 05).

In the whole group of respondents with metabolic syndrome the values of hepcidin are in the range from 2,47 – 85,98, with medium 14,29.

Table 3.Present mean values ± SD, median, rang of serum concentration of: iron, ferritin and hepcidin in patients with metabolic syndrom

Variable (unit)	Total N = 120	Males N = 60	Females N = 60	p-value
Iron (µmol/l) mean±SD, median, rang	15,79 ± 5,28 14,95 5,7 – 28,8	17,23 ± 5,22 16,3 7,6 – 28,8	14,36 ± 4,99 13,5 5,7 – 24,4	t=3,07 p=0,0026**
Ferritin (ng/ml) mean±SD, median, rang	158,47 ± 118,75 129,0 11,0 – 668,0	197,9 ± 142,57 149,5 34 – 668	118,98 ± 70,31 111,5 11 – 456	Z=4,04 p=0,00005**
Hepcidin(ng/mL) mean±SD, median, rang	18,38 ± 15,24 14,29 2,47 – 85,98	25,54 ± 18,33 20,75 2,47 – 85,98	11,23 ± 5,3 10,81 2,93 – 24,05	Z=5,54 p<0,001**

**** p <0,01**

Results from the comparative analyses of respondents from the control group and examined group
In this part of the research results are presented that were received by comparison of the healthy respondents and the respondents with metabolic syndrome.

At the same time parameters where the significant difference by sex has not been confirmed, only the difference between control and examined group has been tested while for those parameters for which there is significant difference regarding sex, the differences between men from the control group and men from the examined group have been compared as well as between women from the both groups.

Analyses of lipid status control group / the group with methabolic syndrome
The average value of cholesterol has value 5, 05±0, 8 in the control group of respondents, and 5,39±1,22 in the group with methabolic syndrome. Difference in the average values of 0, 3 statistically was confirmed as significant (t=2, 6 p=0, 01), which is based on significantly average values of cholesterol in the group with metabolic syndrome compared to the group of healthy respondents.

Results from our research showed that men from control group and the group with methabolic syndrome have significantly different values of LDL- cholesterol, and the remaining analyzed parameters of lipid status: HDL- cholesterol, triglycerids, ApoA and ApoB significantly differ between men from the control group and the group with methabolic syndrome.

Men from the control group have significantly higher average values of HDL- cholesterol compared to the men from the examined group (1,4±0,3 вс 1,19±0,29 t=3,8 p=0,0002).

Triglycerides have significantly lower values in the control group of men compared to the sick group of men (medium 1, 44 vs. 2, 33 Z = 5, 98 p<0,001).

Values of ApoA present significnaly higher values in the group of men without metabolic syndrome compared to the group of men with metabolic syndrome (medium 99 vs78 Z=2,33 p=0,02).

In the control group men significantly lower values ApoB are registered compared to the examined group of men (150, 6±33, 3 вс 179, 2±30, 79 t=4, 89 p=0, 000003).

Women from the control group and the group with metabolic syndrome as well as men insignificantly differ regarding the values of LDL- cholesterol, and significantly differ regarding HDL- cholesterol, triglyceride, ApoA and ApoB.

The average values of HDL- cholesterol in the group of healthy and the group of sick women are 1,58±0,4 и 1,32±0,28 consequently. Statistically seen the difference between two

groups is significant (t=3,87 p=0,00018), as a result of significantly higher average values in the control group of women.

Values of triglycerides are significantly lower in the group without metabolic syndrome (medium 1, 05 vs. 1, 81 Z=5, 68 p<0,001).

Women from the control group have significantly higher values of ApoA compared to the women of the group with metabolic syndrome (medium 133, 5 vs. 82, 5 Z= 4, 47 p=0, 000008).

In the group of healthy women significantly lower values are registered of ApoB compared to the group of women with metabolic syndrome (148, 16 vs. 155, 42 t=2, 03 p=0,044).

Table 4. Present statistical analyzes of correlation between serum concentrations of cholesterol in two groups - control and group with metabolic syndrom

Variable (unit)	Control group N = 120	Group with metabolic syndrome N = 120
	Total N = 120	Total N = 120
Cholesterol (mmol/l) mean±SD, median	5,05 ± 0,8 5,235	5,39 ± 1,22 5,21
tested differences control group/group with metabolic syndrom t=2,6 p=0,01*		

***p < 0,05**

Table 5.Present statistical analyzes of correlation between serum concentrations of HDL-cholesterol, LDL-cholesterol, triglycerides, ApoA, ApoB in two groups - control group and group with metabolic syndrom

Variable (unit)	Control group N = 120		Group with metabolic syndrom N = 120	
	Males N= 60	Females N= 60	Males N=60	Females N=60
HDL-chol. (mmol/l) mean±SD, median	1,4 ± 0,3 1,39	1,58 ± 0,4 1,6	1,19 ± 0,29 1,11	1,32 ± 0,28 1,3
tested differences males control group / males with metabolic syndrom t = 3,8 p=0,0002** females control group / females with metabolic syndrom t = 3,87 p=0,00018**				
LDL-chol. (mmol/l) mean±SD, median	3,025 ± 0,55 3,07	2,88 ± 0,7 2,86	2,95 ± 1,5 2,98	2,87 ± 1,09 2,94
tested differences males control group / males with metabolic syndrom Z=0,5 p=0,58 ns females control group / females with metabolic syndrom Z=0,07 p=0,09 ns				
Triglycerides (mmol/l) mean±SD, median	1,49 ± 0,5 1,44	1,185 ± 0,5 1,05	2,59 ± 1,26 2,33	1,97 ± 0,84 1,81
tested differences males control group / males with metabolic syndrom Z=5,98 p<0,001** females control group / females with metabolic syndrom Z=5,68 p<0,001**				
ApoA(mg/dl) mean±SD, median	112,62± 57,6 99,0	136,47 ± 48,4 133,5	89,42± 30,7 78	99,93 ± 28,67 82,5
tested differences males control group /males with metabolic syndrom Z = 2,33 p=0,02* females control group/females with metabolic syndrom Z = 4,47 p=0,000008**				
ApoB(mg/dl) mean±SD, median	150,6 ± 33,3 150,775	148,04± 39,42 148,16	179,2±30,79 183,08	161,22±31,13 155,42
tested differences males control group/males with metabolic syndrom t=4,89 p=0,000003** females control group/females with metabolic syndrom t=2,03 p=0,044*				

***p < 0,05 **p < 0,01**

Analyses of enzyme status control group / the group with metabolic syndrome

The analyses of the enzyme status between men from the control group and the group with metabolic syndrome showed that both groups men have insignificantly different values of ALT and AST (Z=0,97 p=0,33 и Z=0,42 p=0,67 cconsequently). Significant difference in the values of GGT (Z=4, 49 p=0, 000007) between healthy and sick men is registered. Medium of GGT in the control group of men is 25, 15 and it is significantly lower than the medium from the examined group which has value 40.

Women from the control group and from the group with metabolic syndrome differ significantly regarding the values of ALT, AST и GGT.

In the control group of women significantly lower values are registered of ALT regarding the examined group of women. (medium 19,8 vs 23,7 Z=2,4 p=0,016).

Values of AST are significantly lower in the group of healthy women compared to the group of sick women. (medium 23,1 vs 25,5 Z=2,14 p=0,03).

GGT enzyme has significantly lower values in the group of women without metabolic syndrome compared to the group of owmen with metabolic syndrome (medium 13,95 vs. 22,6 Z=4,14 p=0,000006).

Table 6.Present statistical analyzes of correlation between serum concentrations of ALT, AST, gGT in two groups - control group and group with metabolic syndrome

Variable (unit)	Control group N = 120		Group with metabolic syndrom N = 120	
	Males N= 60	Females N= 60	Males N=60	Females N=60
ALT (U/L) mean±SD, median	39,67 ± 19,8 35,025	24,28 ± 13,3 19,8	43,59 ± 20,97 39,23	28,27 ± 15,09 23,7
tested differences males control group /males with metabolic syndrom Z=0,97 p=0,33 ns females control group/females with metabolic syndrom Z = 2,4 p=0,016*				

AST (U/L) mean±SD, median	31,26 ± 8,8 27,8	25,42 ± 7,9 23,1	33,55 ± 15,56 28,3	28,33 ± 10,84 25,55
tested differences males control group/males with metabolic syndrom Z=0,42 p=0,67 ns females control group/females with metabolic syndrom Z=2,14 p=0,03*				
gGT (U/L) mean±SD, median	39,63 ± 20,05 25,15	18,09 ± 14,0 13,95	45,86 ± 22,66 40,0	27,41 ± 17,68 22,6
tested differences males control group/males with metabolic syndrom Z=4,49 p=0,000007** females control group/females with metabolic syndrom Z = 4,14 p=0,000006**				

***p < 0,05 **p < 0,01**

Analyses of iron, its transporters feritin, and hormone regulator of iron hepcidin in control group / the group with metabolic syndrome

There is significant difference between men from the control and examined group in the values of serum iron, feritin and hepcidin.

The average values of the serum iron in the group of healthy men is 15,03±5,77 and it is significantly (t=2,18 p=0,03) lower than the average value in the group of men with metabolic syndrome which is 17,23±5,22.

Feritin has significantly lower values in the control group of men compared to the group of sick men (medium116 vs. 149,5 Z=3,2 p=0,01).

For p<0,01 significant difference is confirmed in the average values of hepcidin between men from the group of healthy repsodnents and the group with metabolic syndrome (t=5,18 p=0,000001). The average values of hepcidin in the control and group of sick men are 12, 34±7, 37 и 25, 54±18, 33 consequently that is the same are significantly lower than in the group of healthy men.

Between women from control and examined group there is significant difference of values of feritin and hepcidin, and insignificant difference regarding the values of serum iron.

Women in the control group have insignificantly lower average serum values of iron than women in the group with metabolic syndrome (12, 91±6, 1 vs. 14, 36±4, 99 p>0, 05).

In the group of healthy women significantly lower values are registered of feritin compared to the women from the group with metabolic syndrome (medium 56 vs. 111,5 Z=4,8 p=0,000002).

Values of hepcidin in the control group and the group with metabolic syndrome of women are average 6,16±3,2 и 11,23±5,3 consequently. Difference in the average values between two groups of the respondents from 5,07 was statistically confirmed as significant that is important (t=6, 3 p<0,001), that is healthy women have significantly lower values of hepcidin compared to women with metabolic syndrome.

Table 7.Present statistical analyzes of correlation between serum concentrations of iron, ferritin and hepcidin in two groups - control group and group with metabolic syndrom

Variable (unit)	Control group N = 120		Group with metabolic syndrom N = 120	
	Males N= 60	Females N= 60	Males N=60	females N=60
Iron (μmol/l) mean±SD, median	15,03 ± 5,77 13,85	12,91 ± 6,1 12,2	17,23 ± 5,22 16,3	14,36 ± 4,99 13,5
tested differences males control group/males with metabolic syndrom t=2,18 p=0,03* females control group/females with metabolic syndrom t=1,4 p=0,16 ns				
Ferritin (ng/ml) mean±SD, median	120,2 ± 70,67 116,0	69,01 ± 49,36 56,0	197,9 ± 142,57 149,5	118,98 ± 70,31 111,5
tested differences males control group/males with metabolic syndrom Z=3,2 p=0,01** females control group/females with metabolic syndrom Z=4,8 p=0,000002**				
Hepcidin (ng/mL) mean±SD, median	12,34 ± 7,37 10,97	6,16 ± 3,2 5,6	25,54 ± 18,33 20,75	11,23 ± 5,3 10,81
tested differences males control group/males with metabolic syndrom t=5,18 p=0,000001** females control group/females with metabolic syndrom t=6,3 p<0,001**				

***p < 0,05 **p < 0,01**

Discussion

Metabolic syndrome was described for the first time in the first half of the 20th century (6), and the world epidemy of oversize and obesity are the basic reasons for its identification. The central adiposity is the basic characteristic of the syndrome which reflects the fact for the strong bond between the waist and the increased adioposity which influence the distribution of metabolic syndrome (9).

The distribution of metabolic syndrome through the world is different and partially is a reflexion of the age and the ethnicity of people and used diagnostic criteria.

As a whole the distribution of the metabolic syndrome is increased with the age of the population. According to the data of the examination of the national health and nutrition of the USA, the distribution of the metabolic syndrome grows from 7% at respondents at the age of 20-29., 44% at the age of 60-69 and 42% at the age over 70 (10). In France the distribution of patients from 30-39 was <5, 6% at each sex and at the age of 60-64 it was 17,5% (11). The growing industrialization in the world is connected to the larger percentage of obesity of population. In 2000 a metabolic syndrome was diagnosed at 47 million people in the USA which means that it is present at 40% from the adult population (12).

During the last years the interest from the consequences by grown deposing of iron towards people health grows more and more (13). Although, the mechanisms for the potential effect of the iron towards the risk by metabolic syndrome are unclear there are two basic hypotheses.

According to the first hypothesis the increased iron, which is due to overdosed deposing (born or gained) can lead to damage of the liver, heart and other organs. Pancreas beta cells are also important target of toxical iron which causes resistance of glycosis and diabetis. When iron concentration grows in the organism the liver and peripherial resistance towards insluine increases and pancreas secretion of inslulin is decreased (14). Subplus of iron is dangerous as it initiates atherosclerosis carciongenesis diabetis and other diseases connected to the way of life (15).

The second hypothesis for the influence of the iron to the appearance of metabolic syndrome is connected to the capability of the iron to form reactive oxygen radicals and it is considered that the increased oxidative stress is key mechanism on the basis of iron induced resistance although there are still no clear evidences for this hypotehsis (16). Oxidative stress influences to the metabolism of glucoses and iron and causes resistance to insulin with decreased entrance of insulin in the cells and increased synthesis of feritin (17).

The capability of iron to transform into two stabile oxidative forms is potential for creation of reactive oxygen and amino types as hydroxical radicals with Fenton и Haber-Weiss reaction. The oxidative stress can cause death of beta cells of pancreas and leads to diabetes and chronically oxidative stress of the liver muscles and mass tissues causing inflammatory reaction and resistance to insulin in these organs (18).

Stores of irons expressed through concentration of feritin in serum are suggested to be inseparable part of the metabolic syndrome. Feritin is clinic indicator for the level of iron in the organism. The potential reason for increase of feirtin in β- cells of pancreas is especially sensitive to the effects of the oxygen radicals (19). The level of feritin correlates with several components of metabolic syndrome: increased triglycerides reduced HDL-cholesterol obesity. These discoveries refer to the fact that the concentration of feritin can be used as biomarker for metabolic syndrome (13,20,21).

In our research it was confirmed that at patients with metabolic syndrome there are increased values of feritin compared to the control group. Numerous examinations prove increased values of feritin at patients with metabolic syndrome (22-27). High concentration of serum feritin can be potentially used as screening biomarker for revealing of people who were exposed to risk from development of metabolic syndrome and they can be treated even in early stadiums of the diseases through preventative measures (28).

For the first time in 2012 Martinelli N et al. (29) published that the level of hepcidin grows progressively as a result of the increased level of feritin in the serum of patients with metabolic syndrome and it was noticed that people with metabolic syndrome have significantly higher values of feritin and hepcidin compared to people without metabolic syndrome which was confirmed in our research.

We discover that at men from control and examined group there is difference in the value of serum iron and hepcidin. In our research it was confirmed that at the patients with metabolic syndrome from male sex has increased values of serum iron and hepcidin compared to healthy men.

At women from control and examined group we discovered significant differences in the values of hepcidin. In the group of healthy women significantly lower values of hepcidin are registered compared to the women from the group with metabolic syndrome.

We discovered that the sex has significant influence towards the values of serum iron, feritin and hepcidin as a result of the significantly higher values at man compared to women which is due to the lost of iron with period at the women. Men with metabolic syndrome have significantly higher values of hepcidin compared to women in menopause and women in period after menopause. Menopause status influences the concentration of hepcidin with significantly lower values of hepcidin in the group of women with metabolic syndrome in the period of pre meno pause.

Dislipidemy is in the basis of the etiological factors for appearance of metabolic syndrome. The violation of lipoproteins at the metabolic syndrome leads to reaction of the concentration of HDL- cholesterol which as a consequence of the changes in the structure and metabolism of HDL- cholesterol.

In our research difference in the values of cholesterol statically was confirmed as significant which is due to the significantly higher values of cholesterol in the group with metabolic syndrome compared to the group of healthy people. These results are confirmation of the results from other research Nea KR et al (30).

Results from our research show that triglycerides ApoA and ApoB significantly differ between men and women from control group and the group with metabolic syndrome except at LDL-cholesterol difference is insignificant at men and women. We discovered that men and women from the control group have higher values of ApoA compared to the examined group while from the other side ApoB is significantly higher at men with metabolic syndrome compared to men from control group. We discovered higher values ApoB at women with metabolic syndrome and these results are similar to the examination of Lim Y et al (31).

Hypertriglyceridemy is an excellent marker for the state of resistance to insulin and important diagnostic marker for metabolic sydnrome (6). In the research we confirmed these observations and we proved that triglycerides are significantly higher at women and men with metabolic syndrome compared to the control group. These results are similar with the examination of Hea KP et al (30).

HDL-cholesterol is lower at patients with metabolic syndrome compared to control group and that is confirmed in the research of Kasapoglu B et al (32).

The sex significantly influence to the values of LDL-cholesterol triglycerides and ApoB at patients with metabolic syndrome. We confirmed that values LDL-cholesterol triglycerides and ApoB in the group of men are significantly higher compared to women. Kawamoto R et al. (33) in their research of patients with metabolic syndrome discovered higher values of triglycerides at men compared to women which was confirmed in our research.

Values of ApoA are higher in the group of women. Our results are not in correlation with Kawamoto R et al (33) who discover higher concentrations of cholesterol, HDL–cholesterol LDL-cholesterol at women compared to men.

Several examinations discover that the liver enzymes can be connected to the metabolic syndrome through many metabolic disturbances as obesity, dislipedemy, diabetes and hypertension while the insulin resistance is considered as basic reason. Marker for liver steatosis was proved as independent risk factor of metabolic syndrome, diabetes, heart diseases. Increased values of ALT have positive correlation to diseases connected to metabolic syndrome for example diabetes type 2 and heart diseases. Average values of ALT, AST и GGT are statistically significantly higher at patients with metabolic syndrome. GGT is basic in glutnative homeostasis and it is important protector of the cell. GGT plays important role in the protective antioxygen system. Increased levels of GGT can be a marker for oxigent stress and subclinical inflammation. Although the relation between GGT and metabolic syndrome is not clearly understood, some mechanisms including the presence of oxigent stress can explain the connection and GGT can play a role in early diagnosis of metabolic syndrome with high prognostic value for metabolic syndrome and heart diseases (32).

We discover that the tests for liver function are higher at women with metabolic syndrome compared to the control group of women. These results are confirmed in literature data of Hea KP et al (30), who found higher concentrations of AST and ALT at women with metabolic syndrome compared to control group. Analyses of the enzyme status at men from control group and from group with metabolic syndrome proved that both groups of men have insignificant different values of ALT and AST. At healthy and sick men significant difference in values of GGT has been registered with lower values at control group of men compared to examined group. These results are confirmation of the literature data of Kasapoglu B et al (32). The sex is with significant influence to the enzymes ALT, AST and GGT and it confirmed that men have higher serum concentrations compared to women.

CONCLUSION

Ten years in a row metabolic syndrome was connected generally to insulin reisistance.The fact that the increased stores of iron increases the risk of metabolic syndrome led to discovery of new views to this disease. The fact that worries is that

increased incidence of sick with metabolic syndrome is registered and this tendency is defined as pandemics. Data have been collected for a numerous diseases as heart disease, diabetes and many others, whose progression could be connected to increased stores of iron measured through concentration of feritin in serum.

Conflict of interest

The authors state that there is no conflict of interest. The authors have not received any funding or benefits from industry to conduct this study.

Acknowledgements

I would like to express my special thanks to Pharmachem for ELISA kits that sponsored me and for paying my publication fees.

1. Lakka HM, Laaksonen DE, Lakka TA, et al. The metabolic syndrome and total and cardiovascular disease mortality in middleaged men. JAMA. 2002; 288: 2709–16.
2. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. Diabet Med. 1998;15:539-53.
3. Reaven GM. Role of insulin resistance in human disease. Diabetes. 1988;37:1595-607.
4. Kaplan NM. The deadly quartet. Upper-body obesity, glucose intolerance, hypertriglyceridemia, and hypertension. Arch Intern Med. 1989;149:1514-20.
5. DeFronzo RA, Ferrannini E. Insulin resistance. A multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. Diabetes Care. 1991;14:173-94.
6. Kylin E. Studien uber das Hypertonie-Hyperglyka "mie-Hyperurika" miesyndrom. Zentralbl Inn Med. 1923;44:105-27.
7. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet. 2005; 365: 1415–28.
8. Executive summary of the third report of The National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). JAMA. 2001; 285: 2486–97.
9. Ruderman N, Chisholm D, Pi-Sunyer X, et al. The metabolically obese, normal-weight individual revisited. Diabetes. 1998; 47: 699–713.
10. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. JAMA. 2002; 287: 356–59.
11. Azizi F, Salehi P, Etemadi A, et al. Prevalence of metabolic syndrome in an urban population: Tehran Lipid and Glucose Study. Diabetes Res Clin Pract. 2003; 61: 29–37.
12. Regitz-Zagrosek V, Lehmkuhl E, Weickert MO. Gender differences in the metabolic syndrome and their role for cardiovascular disease. Clin Res Cardiol. 2006; 95:136–147.
13. Ford ES, Cogswell ME. Diabetes and serum ferritin concentration among U.S. adults. Diabetes Care. 1999;22:1978–1983.
14. Abraham D, Rogers J, Gault P, et al. Increased insulin secretory capacity but decreased insulin sensitivity after correction of iron overload by phlebotomy in hereditary haemochromatosis. Diabetologia 2006;49:2546–51.
15. Bonkovsky HL, Lambrecht RW, Shan Y. Iron as a co-morbid factor in nonhemochromatotic liver disease. Alcohol. 2003;30:137–44.
16. Datz C, Felder TK, Niederseer D, et al. Iron homeostasis in the metabolic syndrome. Eur J Clin Invest. 2013;43(2):215-24
17. Fernández-Real JM, López-Bermejo A,Wifredo R. Cross-Talk between iron metabolism and diabetes. Diabetes. 2002;51(8):2348-2354.
18. Hämäläinen P, Saltevo J, Kautiainen H, et al. Serum ferritin levels and the development of metabolic syndrome and its components: a 6.5-year follow-up study. Diabetol Metab Syndr. 2014; 26;6(1):114.
19. Rahier JR, Loozen S, Goebbels RM, et al. The hemochromatotic human pancreas: a quantitative immunohistochemical and ultrastructural study. Diabetologia.1987;30:5 –12.
20. Lao TT, Chan PL, Tam KF. Gestational diabetes mellitus in the last trimester - a feature of maternal iron excess? Diabet Med. 2001;18:218– 23.
21. Jiang R, Manson JE, Meigs JB, et al. Body iron stores in relation to risk of type 2 diabetes in apparently healthy women. JAMA. 2004;291:711–17.
22. Hamalainen P, Saltevo J, Kautiainen H, et al. **Erythropoietin, ferritin, haptoglobin, hemoglobin and transferrin receptor in metabolic syndrome: a case control study.** *Cardiovasc Diabetol* 2012, **11**(11)**:**116-2840-11-116.
23. Adediran A, Uche E, Akinbami A, et al. Hemoglobin and ferritin concentrations in subjects with metabolic syndrome. Nutr Metab Insights. 2015:25;8:15-9.
24. Sun L, Franco OH, Hu FB ,et al. Ferritin concentrations, metabolic syndrome, and type 2 diabetes in middle-aged and elderly chinese. J Clin Endocrinol Metab. 2008;93(12):4690-6.
25. Li J, Wang R, Luo D, et al. Association between serum ferritin levels and risk of the metabolic syndrome in chinese adults: a population study. PLoS One. 2013;16;8(9):e74168.
26. Bozzini C, Girelli D, Olivieri O, et al. **Prevalence of body iron excess in the metabolic syndrome.** *Diabetes Care.* 2005; **28:**2061-2063.
27. Tang Q, Liu Z, Tang Y, et al. High serum ferritin level is an independent risk factor for metabolic syndrome in a Chinese male cohort population. Diabetol Metab Syndr. 2015;24:7:11.
28. Abril-Ulloa V, Flores-Mateo G, Solà-Alberich R, et al. Ferritin levels and risk of metabolic syndrome: meta-analysis of observational studies. BMC Public Health.2014;14:483
29. Martinelli N, Traglia M, Campostrini N, et al. Increased serum hepcidin levels in subjects with the metabolic syndrome: A population study. PLoS One. 2012;7(10):e48250.
30. Hea KP, Zhaob H, Qiangc Y, et al. Impact of elevated aspartate and alanine aminotransferase on metabolic syndrome and its components among adult people living in Ningxia, China. Chronic Diseases and Translational Medicine.2015;1:2:124–132.
31. Lim Y, Yoo S, Lee SA, et al. Apolipoprotein B is related to metabolic syndrome independently of low density lipoprotein cholesterol in patients with type 2 diabetes Endocrinol Metab (Seoul). 2015; 30(2): 208–215
32. Kasapoglu B, Turkay C , Bayram Y et al. Role of GGT in diagnosis of metabolic syndrome : A clinic-based cross-sectional survey. Indian J Med Res.2010;132:56-61.
33. Kawamoto R, Tabara Y, Kohara K, et al. Relationships between lipid profiles and metabolic syndrome, insulin resistance and serum high molecular adiponectin in Japanese community-dwelling adults. Lipids Health Dis. 2011; 10: 79.