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## HYPERTRIGLYCERIDEMIC WAIST PHENOTYPE: A MARKER OF CARDIOMETABOLIC RISK IN PATIENTS WITH ARTERIAL HYPERTENSION

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Hypertriglyceridemic waist phenotype in patients with arterial hypertension was examined. Patients were categorized into 3 phenotype groups based on waist circumference means and plasma triglyceride levels: group 1 included patients (n=10) with normal waist circumference (< 90cm in men and < 85 cm in women) and elevated plasma triglyceride levels ( $\geq 1.7$  mmol/l); group 2 included patients (n=25) with increased waist circumference ( $\geq 90$  cm in men and  $\geq 85$  cm in women) and normal triglyceride level (< 1.7 mmol/l); group 3 include patients (n=66) with increased waist circumference (circumference  $\geq 90$  cm in men and  $\geq 85$  cm in women) and increased plasma triglyceride levels ( $\geq 1.7$  mmol/l) that is with hypertriglyceridemic waist phenotype.

The result of our clinical study of patients with arterial hypertension showed that hypertriglyceridemic waist phenotype was associated with elevated SBP, DBP levels; increased body mass, BMI; increased pro-inflammatory cytokine – IL-18 activity; highest glucometabolic risk and atherogenic metabolic risk profile. Our results can suggest that hypertriglyceridemic waist phenotype is a simple and inexpensive marker to help identify patients with high cardiometabolic risk profile, and also can be used as a simple screening approach to predict development of type 2 diabetes mellitus.

Key words: hypertriglyceridemic waist phenotype, glycemic profile, interleukins, cardiometabolic risk, arterial hypertension.

**Objective.** Cardiovascular disease (CVD) has been a leading cause of morbidity and mortality all over the world. Epidemiologic and metabolic studies found strong association of obesity, especially of abdominal type of body fat distribution, to metabolic and cardiovascular pathology. Metabolic syndrome (MS) – a cluster of abdominal obesity, impaired glucose tolerance, dyslipidemia, and arterial hypertension is closely associated with further development of type 2 diabetes mellitus (type 2 DM) and CVD, and therefore has been used to identify subjects with high cardiometabolic risk [1-3]. There is increasing evidence that hypertriglyceridemic waist phenotype is stronger and more valid marker of cardiovascular risk and a better predictor of CVD than MS [4,5]. Therefore, we examined hypertriglyceridemic waist phenotype in patients with arterial hypertension.

**Design and methods.** 104 men (n=45, 43.3 %) and women (n=59, 56.7 %) aged 32-80 years with arterial hypertension were examined. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels were measured twice after 5-minute rest in a sitting position using standardized mercury sphygmomanometer; than average mean of two measurements were calculated and used as a blood pressure level. Anthropometric measurements include: body weight using digital scales and recorded to the nearest 0.1 kg. The patient's height was measured using tape meter. Body mass index (BMI) was calculated as weight in kilograms divided by the square of the height in meters ( $\text{kg}/\text{m}^2$ ). Waist circumference was measured at the umbilicus level, using a tape meter. Fasting blood samples were collected for measurements of carbohydrates profile: glucose, insulin, HbA<sub>1c</sub> plasma levels, and lipid panel. Circulation plasma levels of proinflammatory cytokine – interleukin-18 (IL-18) and anti-inflammatory cytokine – interleukin-10 (IL-10) were detected by ELISA. A hypertriglyceridemic waist phenotype was defined as an elevated waist circumference  $\geq 90$  cm in men and  $\geq 85$  cm in women along with an elevated plasma triglyceride content  $\geq 1.7$  mmol/l.

**Results.** Patients were categorized into 4 phenotype groups based on waist circumference means and plasma triglyceride levels. There were only 3 patients who had normal waist circumference and normal triglyceride levels. Therefore, were excluded them from the study and continue statistical analysis in 3 phenotype groups based on hypertriglyceridemic waist phenotype criteria: group 1 included patients (n=10) with normal waist circumference (< 90cm in men and < 85 cm in women) and elevated plasma triglyceride levels ( $\geq 1.7$  mmol/l); group 2 included patients (n=25) with increased waist circumference ( $\geq 90$  cm in men and  $\geq 85$  cm in women) and normal triglyceride level (< 1.7 mmol/l); group 3 include patients (n=66) with increased waist circumference ( $\geq 90$  cm in men



and  $\geq 85$  cm in women) and increased plasma triglyceride levels ( $\geq 1.7$  mmol/l) that is with hypertriglyceridemic waist phenotype.

Our results suggest that the most of examined patients with arterial hypertension have hypertriglyceridemic waist phenotype. The baseline characteristics of the 3 groups are summarized in Table.

There were no statistically significant differences in patient's age among comparison groups. Patients of group 3 with hypertriglyceridemic waist phenotype had longest duration of arterial hypertension, and the highest blood pressure levels as compared with group 1 and group 2 ( $p < 0.05$  in all cases).

Table

**Baseline characteristics of the patients with arterial hypertension based on hypertriglyceridemic waist phenotype**

Characteristic	Group 1 Normal waist circumference / elevated triglyceride levels n=10	Group 2 Elevated waist circumference / normal triglyceride levels n=25	Group 3 Elevated waist circumference / elevated triglyceride levels n=66
Age, years	51.18±3.09	62.72±1.13	56.98±0.88
Hypertension duration, years	6.36±1.24	9.68±1.28	10.00±0.98
SBP, mmHg	142.91±0.99	159.44±3.23	166.50±1.83
DBP, mmHg	91.64±0.93	100.32±1.48	100.89±0.94
Height, m	1.72±0.02	1.66±0.02	1.70±0.01
Body mass, kg	72.18±3.08	84.16±2.81	89.15±1.72
BMI, kg/m <sup>2</sup>	23.95±0.91	30.21±1.00	31.05±0.61
OT	79.45±1.90	104.04±2.19	104.38±1.34
IL-18, pg/ml	167.73±7.21	172.40±5.61	178.97±2.38
IL-10, pg/ml	87.44±2.03	77.97±1.07	88.79±0.64
Glucose, mmol/l	5.14±0.31	5.92±0.35	6.95±0.12
Insulin, mkU/ml	12.52±2.79	12.31±1.41	14.66±0.95
HOMA	2.90±0.70	2.95±0.33	3.32±0.27
FIRI	2.64±0.64	2.92±0.38	3.04±0.25
HbA1c, %	5.74±0.38	7.18±0.49	6.12±0.20
Total cholesterol, mmol/l	6.08±0.49	4.58±0.13	5.95±0.17
Triglyceride, mmol/l	2.82±0.13	0.99±0.06	2.71±0.05
HDL cholesterol, mmol/l	1.04±0.09	1.27±0.03	1.12±0.04
LDL cholesterol, mmol/l	3.76±0.41	2.87±0.11	3.60±0.14

Patients of group 3 characterized by higher body mass and BMI means than patients with lower waist circumference and plasma triglyceride levels.

A growing body of evidence suggests that MS is associated with a chronic, low-grade inflammation and that several pro-inflammatory cytokines are elevated in parallel with an increasing number of MS components, whereas anti-inflammatory cytokines are consistently lower. IL-18 is a member of IL-1 superfamily, in several studies has been associated with obesity, insulin resistance, arterial hypertension, and dyslipidemia that are with components of MS [6,7]. In our study plasma IL-18 levels were statistically significant highest ( $p < 0.05$ ) in group 3 hypertensive patients with hypertriglyceridemic waist phenotype (Fig. 1).

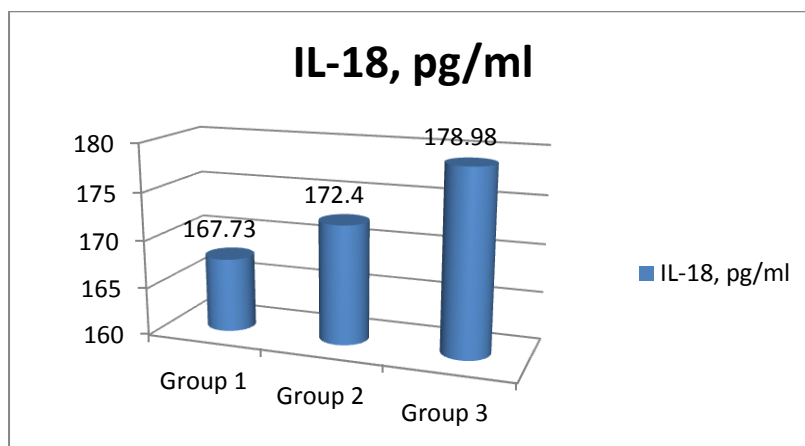


Figure 1. Plasma IL-18 levels in patients with arterial hypertension based on hypertriglyceridemic waist phenotype

Anti-inflammatory cytokine – IL-10 is also involved in pathogenesis of cardiometabolic disorders. The results of several studies show that circulating level of potent anti-inflammatory cytokine IL-10 are elevated in obese women and that low IL-10 levels are associated with MS. Our result showed highest IL-10 plasma levels in group 3 hypertensive patients with hypertriglyceridemic waist phenotype (Fig. 2), but these differences were statistically insignificant ( $p > 0.05$ ).

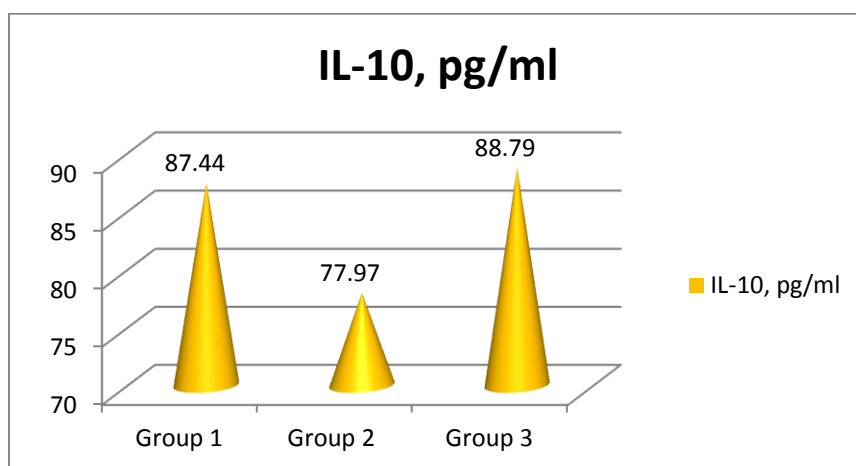


Figure 2. Plasma IL-10 levels in patients with arterial hypertension based on hypertriglyceridemic waist phenotype

Patients in group 3 had significantly higher fasting plasma glucose, insulin levels, and means of insulin resistance index HOMA and FIRI ( $p < 0.05$ ) compared with patients in group 1 and group 2 that confirmed results of previous studies which showed predictive role of hypertriglyceridemic waist phenotype in development of type 2 diabetes mellitus.

Plasma total cholesterol and LDL cholesterol levels were higher, and HDL cholesterol levels were lower in group 3 and group 1 as compared with group 2 patients with arterial hypertension.

**Conclusions.** The result of our clinical study of patients with arterial hypertension showed that hypertriglyceridemic waist phenotype was associated with elevated SBP, DBP levels; increased body mass, BMI; increased pro-inflammatory cytokine – IL-18 activity; highest glucometabolic risk and atherogenic metabolic risk profile.

In conclusion, our results can suggest that hypertriglyceridemic waist phenotype is a simple and inexpensive marker to help identify patients with high cardiometabolic risk profile, and also can be used as a simple screening approach to predict development of type 2 diabetes mellitus.



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**ГИПЕРТРИГЛИЦЕРИДЕМИЧЕСКОЙ ТАЛИИ ФЕНОТИП:  
МАРКЕР КАРДИОМЕТАБОЛИЧЕСКОГО РИСКА  
У ПАЦИЕНТОВ С АРТРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ**

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Изучено фенотип гипертриглицеридемической талии у больных с артериальной гипертензией. Больных разделили на три фенотипические группы на основании значений окружности талии и уровня триглицеридов: в 1 группу вошли пациенты (n=10) с нормальной окружностью талии (< 90 см у мужчин и < 85 см у женщин) и повышенным уровнем триглицеридов в плазме ( $\geq 1,7$  ммоль/л); во 2 группу вошли больные (n=25) с увеличенной окружностью талии ( $\geq 90$  см у мужчин и  $\geq 85$  см у женщин) и нормальным уровнем триглицеридов (< 1,7 ммоль/л); 3 группа состояла из пациентов (n=66) с повышенным показателем окружности талии ( $\geq 90$  см у мужчин и  $\geq 85$  см у женщин) и повышенным уровнем триглицеридов ( $\geq 1,7$  mmol/l) то есть с фенотипом гипертриглицеридемической талии.

Результаты нашего клинического исследования показали, что фенотип гипертриглицеридемической талии ассоциирован с повышенным уровнем САД, ДАД; с увеличением массы тела, ИМТ; усилением активности провоспалительного цитокина – ИЛ-18; наиболее высоким глюкометаболическим риском и атерогенным метаболическим риском. Наши результаты могут свидетельствовать о том, что фенотип гипертриглицеридемической талии является простым и доступным маркером, помогающим выявлять пациентов с высоким кардиометаболическим риском, а также, может быть использован в качестве не сложного скринингового подхода для предупреждения развития сахарного диабета 2 типа.

Ключевые слова: фенотип гипертриглицеридемической талии, гликемический профиль, интерлейкины, кардиометаболический риск, артериальная гипертензия.