GAMMA-GLUTAMYL TRANSPEPTIDASE LEVEL ASSOCIATED WITH METABOLIC SYNDROME AND PROINFLAMMATORY PARAMETERS IN THE YOUNG ROMA POPULATION IN EASTERN SLOVAKIA: A POPULATION BASED STUDY

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SUMMARY

Background: Elevated gamma-glutamyl transpeptidase (GGT) is present approximately in half of all patients with non-alcoholic fatty liver disease (NAFLD). NAFLD is the liver manifestation of metabolic syndrome (MS). This study aimed to explore the relationship between GGT and MS or proinflammatory parameters.

Methods: Data from the cross-sectional HepaMeta study conducted in Slovakia in 2011 among Roma living in rural communities were used. Participants (n = 446) were divided into 2 groups; those with elevated GGT and those with normal GGT levels. MS was diagnosed according to the International Diabetes Federation criteria; presence of central obesity and low density lipoproteins (LDL) or high density lipoproteins (HDL), high triglycerides, hypertension, glucose intolerance or type 2 diabetes. Participants were tested for the presence of MS and its components, and biochemical tests for lipid levels (total cholesterol, HDL, LDL, TG) and inflammatory parameters (high sensitivity C-reactive protein – hs-CRP and ferritin) were performed.

Results: Of 446 Roma participants, only 29 (6.5%) had GGT levels above the normal value. After exclusion of patients with viral hepatitis and alcohol abuse, patients with elevated GGT suffered from MS more often ($p < 0.001$), and patients with more MS components had a higher risk of elevated GGT. We found a significant association between GGT and the individual MS components, except HDL (waist circumference ≥ 94cm in men or 80 cm in women: $p < 0.01$; BMI > 30: $p < 0.001$; fasting glucose ≥ 5.6 mmol/l: $p < 0.001$; arterial hypertension: $p < 0.05$, and TAG ≥ 1.7 mmol/l: $p < 0.001$). Patients with elevated GGT levels had also significantly higher hs-CRP (hs-CRP > 2 mg/l: $p < 0.001$; hs-CRP > 3 mg/l: $p < 0.001$) and ferritin (ferritin > 300 mg/l: $p < 0.01$) levels.

Conclusion: Patients with MS have more significantly elevated levels of GGT. There is a significant association of GGT with individual MS components, except HDL and inflammatory parameters (hs-CRP, ferritin).

Key words: gamma-glutamyl transpeptidase, metabolic syndrome, non-alcoholic fatty liver disease, hs-CRP, ferritin

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INTRODUCTION

Gamma-glutamyl transpeptidase (GGT), a plasma membrane-bound enzyme, is an important catalyst which facilitates glutathione hydrolysis. It is found in many organs, but its presence in the liver has a significant diagnostic use (1). GGT levels are elevated in most diseases of the liver, especially in alcoholic liver disease, non-alcoholic fatty liver disease (NAFLD) and chronic hepatitis (1, 2). GGT, together with obesity and hypertriglyceridemia, are the best markers of NAFLD (3). Approximately 50% of nondiabetic NAFLD patients have elevated GGT levels (4). Elevated GGT level has relatively high sensitivity but low specificity for the diagnosis of NAFLD (5), but we can safely assume that most European patients with elevated GGT, after the exclusion of those

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with chronic viral hepatitis and alcohol overuse, have NAFLD. The aims of this study were to evaluate the prevalence of elevated GGT in Roma aged 15–45 years in communities in eastern Slovakia; analyse the cause of GGT elevation in this population; analyse the association of elevated GGT with metabolic syndrome (MS) and the individual criteria of metabolic syndrome; analyse the relationship between inflammatory markers (hs-CRP and ferritin) with elevated GGT in patients with NAFLD; analyse the influence of some socioeconomic parameters, diet and physical activity on elevated levels of GGT.

MATERIALS AND METHODS

Data from the cross-sectional HepaMeta study conducted in Slovakia in 2011 were used. This project aimed to map the prevalence of viral hepatitis B/C and MS in the population living in eastern Slovakia, including Roma settlements. In addition to the general methodology described in detail elsewhere (6), further paper-specific amendments to the methodology follow.

Only Roma participants (n = 452) were included in this analysis. Participants were considered to have active HBV infection if they were HBsAg positive. Patients with anti-HBc IgG or antiHBsAg positivity were considered to have had encountered HBV in the past or were otherwise vaccinated. GGT levels were considered to be elevated if they were higher than 0.98 μkat/l in men and 0.66 μkat/l in women.

Social Status and Lifestyle Variables

The questionnaire was developed by a group of experts made up of Roma health mediators and community workers as well as public health experts and academics. It was designed to gather information about socioeconomic background based on attributes of living conditions such as housing, family and per capita income, education and health education, occupation and consumer luxury items e.g., automobiles, television, refrigerator, air conditioning available in the family.

For the majority population, trained assistants were present in the outpatient clinic to assist with questionnaires, if needed. For Roma respondents, questionnaires were administered in community centres by community workers or trained assistants who provided help in case of limited literacy (7).

Physical activity was measured by a questionnaire detailing occupational, household, and leisure time physical activity. Sedentary lifestyle assessment was based on occupational or household activity, along with leisure time activity measures, according to the classification of activities specific to other populations, as previously described (8). The variety of physical activities was measured by asking respondents what physical activity, if any, they had performed during the last week. They could select one or more possibilities from the following list: physical activity at work; physical work around the house or home; brisk walking; dancing; sport; no physical activity. Only walking, dancing or sport activities were analysed. Respondents were also asked how often each week they perform physical activity lasting at least 30 minutes, during which they became breathless or sweaty. Possible responses were: every day; 4–6 times a week; 2–3 times a week; once a week; 2–3 times a month; a few times a year or less. Those who reported being physically active 2 or more times a week were considered to be sufficiently physically active (8).

Statistical Analysis

Categorical data is presented in absolute counts and percentages; interval data is presented as a median (interquartile range) because of nonparametric distribution. Measurement of the statistical significance of differences between categorical data was performed using the chi-square test, and for interval data with the Mann-Whitney U test.

RESULTS

The final sample comprised 452 Roma (mean age = 34.7; SD = 9.14; 35.2% men). The number of participants available for individual analyses is stated separately, as not all results were available for each participant. Baseline parameters of the study cohort are summarised in Table 1.

Out of 446 Roma participants with available GGT test results, only 29 (6.5%) had GGT levels above the normal value. Diseases associated with GGT elevation are depicted in Fig. 1. The most common disease in patients with elevated GGT was metabolic syndrome (in 50% of cases) followed by viral hepatitis (15.4% of cases), 15.4% of participants had elevated GGT with no apparent disease, while 11.5% of participants with higher GGT levels confirmed excessive alcohol use, and 7.7% of participants had a combination of the aforementioned conditions. There was a significantly higher association of metabolic syndrome with elevated GGT (p = 0.004).

Laboratory and Clinical Tests in Patients with Elevated GGT

For further analyses all patients with HBs antigen or anti-HCV antibody positivity (56 participants, 12.4%) as well as patients with significant alcohol use (24 participants, 5.3%) together with 12 patients with missing data about viral hepatitis serology or alcohol abuse were excluded. Thus, 354 patients were further analysed. Out of them, 336 participants had a normal GGT serum level and 18 had an elevated GGT serum level.

Table 2 summarizes the clinical data and risk factors for metabolic syndrome. We observed statistically significant difference

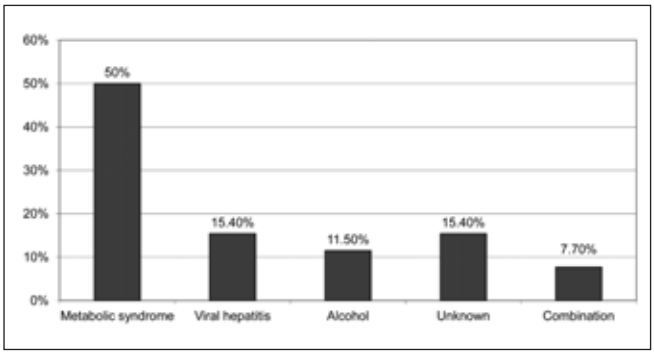

Fig. 1. *Diseases most frequently associated with elevated GGT in the study cohort.*

Table 1. *Baseline parameters of the study cohort by gender*

	Men Median (IQR) N=159	Women Median (IQR) N=293	p
Age (years)	34.83 (15.50)	35.54 (15.45)	0.142
BMI (kg/m^2)	26.30 (8.59)	25.45 (8.26)	0.573
Waist (cm)	90 (23.00)	86 (19.00)	<0.001
sBP (mmHg)	126 (19.67)	116 (18.00)	<0.001
dBP (mmHg)	76 (16.00)	72 (14.00)	0.007
TG (mmol/l)	1.14 (0.84)	1.03 (0.77)	0.016
Cholesterol (mmol/l)	4.63 (1.28)	4.74 (1.21)	0.12
LDL (mmol/l)	2.38 (0.96)	2.51 (0.83)	0.397
HDL (mmol/l)	0.96 (0.36)	1.11 (0.35)	<0.001
Fasting glucose (mmol/l)	4.83 (0.73)	4.59 (0.74)	<0.001
hs-CRP (mg/l)	1.88 (3.80)	1.53 (3.18)	0.153
Ferritin (mg/l)	336.45 (305.00)	73.65 (90.25)	<0.001
Metabolic syndrome (%)	29.7% (47 participants)	29.6% (84 participants)	0.97

Table 2. *Clinical data and risk factors of metabolic syndrome in groups with normal and elevated GGT*

	N	GGT normal Median (IQR) or n (%)	GGT elevated Median (IQR) or n (%)	p
Age (years)	441	35.17 (15.04)	42.41 (15.60)	0.006
BMI (kg/m^2)	354	25.4 (8.55)	32.4 (9.76)	<0.001
sBP (mmHg)	341	118.0 (19.00)	127.0 (33.00)	0.005
dBP (mmHg)	341	72.0 (14.00)	82.0 (19.00)	0.001
Waist (cm)	348	87.0 (20.00)	104.5 (29.00)	<0.001
Weight (kg)	343	65.0 (22)	81.0 (12)	0.001
Metabolic syndrome	352	90 (26.9)	13 (76.5)	<0.001
Fulfilled ≥ 3 MS criteria	336	90 (28.2)	13 (76.5)	<0.001
Fulfilled ≥ 4 MS criteria	336	36 (11.3)	10 (58.8)	<0.001
Fulfilled 5 MS criteria	336	11 (3.4)	5 (29.4)	<0.001
BMI > 25 kg/m^2	341	168 (51.7)	15 (93.8)	0.001
BMI > 30 kg/m^2	343	87 (26.6)	11 (68.8)	<0.001
Arterial hypertension	342	94 (29.0)	10 (55.6)	0.017
Waist circumference**	354	184 (54.8)	16 (88.9)	0.004
Specific treatment for hypercholesterolemia	354	8 (2.4)	4 (22.2)	<0.001

** ≥ 94 cm (men) or 80 cm (women)

in BMI, body weight, waist circumference, and blood pressure. Patients with elevated GMT had also higher risk of having metabolic syndrome and they met significantly more MS criteria.

Biochemical parameters, presented both as interval variables and MS criteria, in patients with elevated and normal GGT levels are summarized in Table 3. Patients with elevated GGT had significantly higher serum levels of cholesterol, TG, glucose, hs-CRP, and ferritin. After exclusion of patients on hypolipidemic treatment, we found significantly higher levels of LDL cholesterol in patients with elevated GGT, although no difference was found in HDL cholesterol. Significantly more patients with elevated GGT met MS criteria for hyperglycemia, hypercholesterolemia, and elevated triglycerides. Interestingly, there was no difference in the incidence of decreased HDL or increased LDL cholesterol between patients with normal and elevated GGT even after the exclusion of patients on hypolipidemic treatment.

As shown in Fig. 2, participants with elevated GGT met a median of 4 metabolic syndrome criteria compared with participants with normal GGT, who met only a median of 2 criteria. Furthermore, Fig. 3 shows that in patients with normal GGT the largest number (over 30%) met only 1 criterion of metabolic syndrome, and only 3.1% met all five MS criteria. In contrast, patients with the elevated GGT largest numbers met 4 or 5 MS criteria.

Lifestyle Components in Patients with Elevated GGT

Based on the extensive questioning of almost all of the study participants we have tried to associate some information about

Table 3. *Biochemical data and risk factors of metabolic syndrome between participants with normal and elevated serum GGT*

	N	GGT normal Median (IQR)	GGT elevated Median (IQR)	p
TG (mmol/l)	354	1.2 (0.74)	1.8 (1.72)	<0.001
Cholesterol (mmol/l)	354	4.7 (1.22)	5.1 (1.25)	0.007
LDL (mmol/l)	354	2.5 (0.86)	3.0 (1.02)	0.03
HDL (mmol/l)	354	1.1 (0.36)	0.9 (0.27)	ns
Fasting glucose (mmol/l)	354	4.7 (0.68)	5.2 (1.99)	0.006
hs-CRP (mg/l)	354	1.6 (3.16)	6.3 (8.50)	<0.001
Ferritin (mg/l)	354	104.2 (175.40)	244.5 (451.10)	<0.001
TAG ≥ 1.7 mmol/l	354	70 (20.8)	11 (61.1)	<0.001
Chol ≥ 5.2 mmol/l	354	94 (28.0)	10 (55.6)	0.012
LDL ≥ 3.4 mmol/l	354	32 (9.5)	3 (16.7)	ns
Elevated HDL***	354	234 (69.6)	16 (88.9)	ns
Fasting glucose ≥ 5.6 mmol/l	354	31 (9.2)	7 (38.9)	<0.001
hs-CRP < 1 mg/l*	354	207 (61.6)	16 (88.9)	0.020
hs-CRP 1–3 mg/l*	354	145 (43.2)	16 (88.9)	<0.001
hs-CRP > 3 mg/l*	354	108 (32.1)	16 (88.9)	<0.001
Ferritin > 300 mg/l	354	58 (17.3)	8 (44.4)	0.004

*hs-CRP < 1 – no CVS risk, *= 1–3 moderate CVS risk, *> 3 – high CVS risk; ***< 1.03 mmol/l (men) or 1.29 mmol/l (women)

eating habits and physical activity with serum levels of GGT. As shown in Table 4, we have not found any statistically significant difference in employment rate, soft drink consumption, diet components, or physical activity in patients with normal and elevated GGT.

DISCUSSION

NAFLD is the hepatic manifestation of metabolic syndrome. Insulin resistance plays a pivotal role in NAFLD pathophysiology followed by abnormal accumulation of fat in the hepatocytes (9). NAFLD is present in approximately 16–23% of the general adult population, but it can occur even in childhood (10). In some patients NAFLD progresses through inflammation to liver fibrosis. This process could be divided into 4 stages according to histology: simple steatosis; steatosis with lobular inflammation; hepatocyte ballooning; presence of Mallory hyaline or fibrosis.

Lobular inflammation with hepatocyte ballooning is the hallmark of nonalcoholic steatohepatitis (NASH) (11, 12). NASH occurs in 2–3% of population and 20–25% patients with NASH progress to liver cirrhosis (13).

We found that 6.5% of Roma had elevated serum levels of GGT. Fifty percent of Roma who had elevated GGT also had metabolic syndrome, 14% had viral hepatitis, 10% confessed to alcohol abuse, and 7% had a combination of at least two of the aforementioned factors. In participants who had negative serology for viral hepatitis B or C, without significant alcohol use and with elevated GGT, metabolic syndrome was present in more than 75% of cases. Metabolic syndrome was the most common disease associated with elevated GGT in the Roma population.

Although elevated GGT has relatively high sensitivity for NAFLD, more tests are required for confirmation of the diagnosis. Foremost, it is necessary to rule out other liver diseases, specifically alcoholic liver disease and viral hepatitis. Insulin resistance or diabetes mellitus and hypercholesterolemia support the diagnosis of NAFLD. Ultrasound of the liver shows remark-

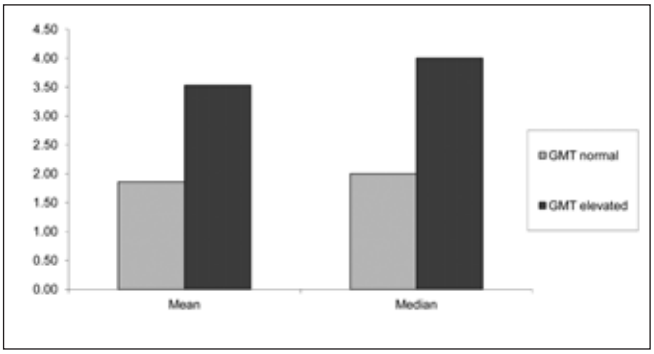

Fig. 2. *Mean and median of fulfilled MS criteria among participants with normal and elevated GGT.*

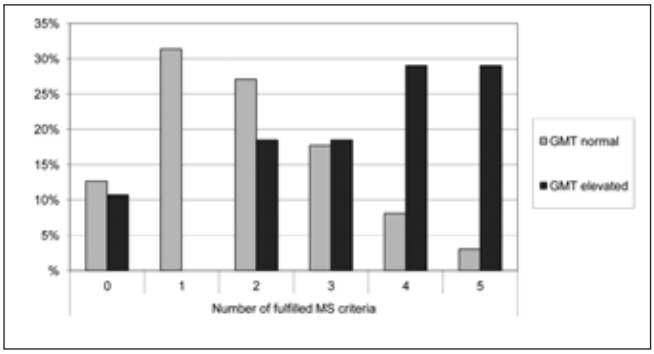

Fig. 3. *Percentage of participants with normal and elevated GGT who fulfilled the criteria of MS.*

Table 4. *Eating habits, physical activity and employment rate in patients with normal and elevated levels of GGT*

	N	GGT normal n (%)	GGT elevated n (%)	p
Employed	350	33 (9.9)	1 (6.3)	ns
More than 1 family in household	350	143 (43.1)	6 (33.3)	ns
Soft drinks	350	245 (73.8)	10 (55.6)	ns
Fruit in diet	347	174 (52.9)	11 (61.1)	ns
Vegetables in diet	345	166 (50.8)	11 (61.1)	ns
Dairy products in diet	342	188 (58.0)	11 (61.1)	ns
Meat products in diet	350	265 (79.8)	12 (66.7)	ns
Meat in diet	341	214 (66.3)	11 (61.1)	ns
Wheat products in diet	342	225 (69.4)	13 (72.2)	ns
Physical activity – walk	354	63 (18.8)	2 (11.1)	ns
Physical activity – dance	354	56 (16.7)	1 (5.6)	ns
Physical activity – sport	354	36 (10.7)	2 (11.1)	ns
No physical activity	354	36 (10.7)	3 (16.7)	ns
Any physical activity over 30min	350	99 (29.8)	6 (33.3)	ns

ably increased echogenity of liver tissue (14). The presence of liver fibrosis is important for the staging of NAFLD. It could be assessed via liver biopsy (invasive) or noninvasive methods, such as transient elastography or commercially available fibrosis biomarkers (e.g., Fibrotest®) (15).

After the exclusion of patients with significant use of alcohol and viral hepatitis, approximately 5% of the study population had elevated GGT. Although GGT is one of the more sensitive markers of NAFLD, it is elevated in about half of patients with NAFLD (4). The Dionysos study results show that NAFLD has been confirmed in about 25% of patients with suspected liver disease and 20% of patients without suspected liver disease ($p = 0.203$). Patients without suspected liver disease underwent the diagnostic procedure because of metabolic syndrome. Based on the available data we can approximate that the NAFLD prevalence in the study cohort is about 10% in 15–45 years old participants. The overall prevalence of NAFLD in the Roma community is probably much higher, because it increases with age and this study had the upper age limit of 45 years. (16). Further research is needed to estimate the prevalence of NAFLD in this specific community, since significant ethnical differences have been previously reported (17).

Prevalence of obesity (BMI > 30 kg/m^2) was 26.1%. This number is comparable to other epidemiological studies performed in Slovakia (18), but is very high compared to the prevalence of obesity in India (19), the country Roma people originated in (20).

Metabolic syndrome was present in 76.5% of participants with elevated GGT compared with only 26.9% of participants with normal GGT ($p < 0.001$). Patients with a higher number of fulfilled MS criteria had a higher risk of having elevated levels of GGT (Fig. 3). Koller et al. showed similar results in a study on 482 patients. The higher the number of MS criteria met, the higher proportion of patients with elevated GGT or increased echogenity on the liver ultrasound, significant correlations were found not only with MS in general but with each individual MS criterion, except decreased HDL cholesterol (21).

We also found significant correlations with the individual components of metabolic syndrome. Patients with elevated GGT had higher mean systolic and diastolic blood pressure and were more frequently diagnosed with arterial hypertension. Similar data have been published by Japanese authors, who report that multiple regression analysis showed that the relationship between GGT and blood pressure was independent of age, obesity and alcohol drinking (22, 23). NAFLD is associated with arterial hypertension even after adjustment for age (24).

Similarly to other studies, significant association of obesity with elevated levels of GGT was observed. In a Norwegian study on 21,782 patients aged 12–59 years, the authors found a significant correlation between BMI and GGT elevation. This correlation was even stronger than the relationship between GGT and alcohol consumption, physical activity, blood pressure, or blood lipids (25). With increasing BMI not only does NAFLD prevalence increase, but also the degree of liver fibrosis (26). The prevalence of NAFLD in the obese is 75% compared with 16% in people with normal body weight (27).

Waist circumference is a relatively strong NAFLD predictor with area under the curve (AUC) of 0.88 (95% CI 0.81–0.94) (28). It also correlates with the degree of fibrosis in children with NASH (29). Participants in this study with a waist circumference of more than 80 cm (women) or 94 cm (men) had NAFLD more frequently.

About one-third of patients with elevated GGT had hyperglycemia compared with only 9.2% of patients with normal GGT ($p < 0.001$). This fact was reported immediately after introduction of GGT testing into routine practice (2). Elevated GGT is present not only in patients with overt diabetes mellitus but also in patients with impaired glucose tolerance (30). Hyperglycemia is, together with age, albumin level, BMI, thrombocyte count, and AST/ALT ratio, an independent predictor of fibrosis in patients with NAFLD (31).

Patients with elevated GGT also had higher levels of cholesterol and triglycerides, but not HDL cholesterol. LDL cholesterol was also higher in patients with elevated GGT, but the proportion of patients with LDL of more than 3.4 mmol/l was not significantly higher. Janzon et al. found positive correlations between GGT, cholesterol and triglycerides as well as with HDL (32). In

the Norwegian study mentioned above, the authors also found a significant relationship between GGT, cholesterol, HLD, and TG (25). However, this study did not confirm the relationship between GGT and HDL cholesterol, probably because of the low HDL levels in up to 70% of the total study population. Higher serum TAG ($p = 0.0154$) and lower levels of HDL-C ($p < 0.001$) are independent predictors of fibrosis in NAFLD patients (33).

Approximately 22% of patients with higher GGT were on hypolipidemic treatment, which is 10-times more than patients with normal GGT ($p < 0.001$). Long-term statin treatment leads to decrease of fat accumulation in hepatocytes and has the potential to stop fibrogenesis (34). Addition of fibrate could lead to a small decrease in biochemical activity (ALT), while the addition of ezetimibe in patients with NAFLD and diabetes mellitus has no effect on liver steatosis (35, 36).

Cardiac and hepatic fat are associated with insulin resistance and impaired suppression of lipolysis, ultimately leading to lipotoxicity. In the heart the lipotoxic effect translates into an impairment of energetic and mechanical efficiency, whereas in the liver a fibrogenic response is favoured by the abundance of inflammatory cells. These features precede and likely contribute to left ventricular overload and cardiac hypertrophy through mechanisms similar to those observed in the progression of liver damage in NAFLD. Collectively, these findings suggest the presence of complex and intertwined relationships between NAFLD, myocardial steatosis and coronary artery disease (37).

High sensitivity CRP reflects the level of basal inflammatory activity, which plays an important part in the pathogenesis of atherosclerosis. Elevated hs-CRP confers a significant additive cardiovascular risk. Several authors have identified important hs-CRP cut-offs:

- hs-CRP < 1 mg/l is not associated with any cardiovascular risk;
- hs-CRP = 1–3 mg/l is associated with moderate coronary heart disease risk;
- hs-CRP > 3 mg/l is associated with high risk of cardiovascular disease (38, 39).

Significantly more participants with elevated GGT had elevated hs-CRP (at all three cut-offs) than participants with normal GGT. Patients with NAFLD had also higher hs-CRP compared with patients without NAFLD in an Indian study by Kuppan et al. (40). Almost 90% of patients with elevated GGT and about one-third of patients with normal GGT aged under 45 years had an hs-CRP level of more than 3 mg/l. This fact could at least partially explain the higher cardiovascular morbidity in the Roma population in Slovakia (41, 42). C-reactive protein and other inflammatory markers could also worsen the insulin resistance and obesity. Exact mechanisms for this effect are not known, however, various targets have been proposed, including damage to the appetite controlling region of the hypothalamus (43).

Roma with elevated GGT had higher ferritin levels compared with Roma with normal GGT. On multiple regression analysis performed by Kowdley et al., ferritin > 1.5 × ULN was independently associated with advanced hepatic fibrosis (OR 1.66; 95% CI 1.05–2.62; $p = 0.028$) and an increased NAFLD Activity Score (NAS) (OR 1.99; 95% CI 1.06–3.75; $p = 0.033$). A ferritin level > 1.5 × ULN is also associated with hepatic iron deposition and worsened histological activity (44). Ferritin is also considered to be an inflammatory marker and was found to be positively associated with carotid atherosclerosis (45).

The diet and lifestyle are the main determinants of metabolic syndrome (46). Surprisingly, the analysis of socioeconomic status, diet and physical activity did not reveal any significant difference between patients with elevated and normal levels of GGT. The main reason behind this is probably the low total count of participants with elevated GGT.

Elevated GGT levels probably have some effect on cardiovascular mortality. English authors observed 6,997 men with no prior history of coronary heart disease, stroke or diabetes for 24 years. Patients with elevated GGT (top quarter of the range) compared with patients with GGT in the bottom quarter of the range had a significantly higher risk for fatal CHD events (OR 1.43; 95% CI 1.09–1.84), stroke incidence (OR 1.56; 95% CI 1.20–2.04) and CVD mortality (OR 1.40; 95% CI 1.16–1.70). Stronger associations were found between GGT and CVD mortality in younger men (< 55 years) and in patients with low and medium CHD risk based on the Framingham risk score (47). Another study of 4,286 women (aged 60–79 years) reported similar results. Patients with elevated GGT had a higher risk of CHD (HR 1.28; 95% CI 1.01–16.2), stroke (HR 1.56; 95% CI 1.02–2.39) or a combination of endpoints (HR 1.31; 95% CI 1.06–1.62). In the entire meta-analysis cohort, with data pooled from 10 studies, 1 U/l higher GGT (on a log scale) was associated with a 20% increase in the risk of coronary heart disease, a 54% increase in the risk of stroke and a 34% increase in the risk of coronary heart disease and stroke combined (48). Austrian authors followed 2,556 subjects with and 699 subjects without angiographic evidence of CAD in the Ludwigshafen Risk and Cardiovascular Health (LURIC) study. Compared with subjects in the lowest quartile of GGT, patients in the second, third and fourth quartile had a higher risk for all-cause mortality; unadjusted hazard ratios (95% CI) were 1.2 (0.9–1.5), 1.4 (1.1–1.8) and 1.9 (1.5–2.3), respectively. Hazard ratios (CI) for death from cardiovascular causes were 1.4 (1.0–2.0), 1.8 (1.4–2.5) and 2.2 (1.6–2.9), respectively. The authors concluded that serum GGT is predictive of all-cause and cardiovascular mortality in individuals with CAD independently of other cardiovascular risk factors (49). Elevated GGT in these instances is probably the manifestation of NAFLD/NASH, which on its own significantly increases the risk of fatal and nonfatal cardiovascular events and stroke (50).

CONCLUSION

Approximately half of patients with NASH have elevated levels of GGT. In this study, which included Roma aged 15–45 years from segregated communities, elevated GGT was associated with MS. Patients with elevated GGT had higher chance of meeting more MS criteria, and elevated GGT was associated with individual MS components, HDL excepted. Inflammatory markers (hs-CRP and ferritin) were associated with elevated GGT as well. More research is needed to assess the influence of elevated GGT on mortality in this community and to assess the influence of pharmacological and nonpharmacological interventions on the prognosis.

Acknowledgement

This work was partially supported by the Agency of the Slovak Ministry of Education for the Structural Funds of EU CEMIO-ITMS:

26220120058 (30%), the project VEGA grant 1/1072/12, the Visegrad fund, and by Roche Slovakia, s. r. o. This paper was also partially funded within the framework of the project "Social determinants of health in socially and physically disadvantaged and other groups of population" (CZ.1.07/2.3.00/20.0063).

Conflict of Interests

None declared

APPENDIX

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