

# Metabolic Syndrome and NAFLD in a Social Reintegration Facility Environment - Project Results

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Original Article

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Source: *Clinical Social Work and Health Intervention*  
Pages: 59 – 65

Volume: 12  
Cited references: 19

Issue: 5

## Reviewers:

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## Keywords:

Metabolic Syndrome. Non - Alcoholic Fatty Liver Disease. Social Reintegration Facility. Fibrosis  
Indexes. Transient Elastography.

## Publisher:

International Society of Applied Preventive Medicine i-gap

CSWHI 2021; 12(5): 59 – 65; DOI: 10.22359/cswghi\_12\_5\_09 © Clinical Social Work and Health Intervention

## Abstract:

**Introduction:** Metabolic syndrome (MS) is a metabolic disease characterized by a simultaneous occurrence of several risk factors (RF) for the development of cardiovascular diseases. NAFLD - Non-alcoholic fatty liver disease - is characterized by the presence of hepatic steatosis, i.e. excessive accumulation of fat in liver tissue that is associated with insulin resistance.

**Objectives:** To determine the presence of MS and liver diseases in clients of the Social Reintegration Facility in Zakovce.

The project "*Screening of liver diseases in Social Reintegration Facility*" ran from 1/2020 to 10/2020. It was carried out within the institutional project of the St. Elizabeth University of Health and Social Sciences (VSZaSP sv. Alzbety) and the Slovak Society of Practical Obesity (SSPO).

**Participants and methods:** A total of 229 clients and employees of the Social Reintegration Facility of the Institute of Christ the High Priest in Zakovce: 188 clients (82%); 41 employees (18%). Men made up 63% of the sample (145); women 37% (84). The mean age of the clients was 51.4 years, the mean length of their stay in the facility was 5.87 years. We clinically examined the clients and employees, and we collected venous and capillary blood. We examined the stiffness of liver tissue with transient elastography, and we used a special CAP software to quantify the presence of steatosis.

**Results:** In the group of examined clients and employees of the Social Reintegration Facility in Zakovce, we were in particular looking for the presence of liver diseases. However, we also found the presence of other diseases of civilization that have a statistically significant effect on the indicators of MS, FLI, NFS, APRI, FIB-4, FS and CAP. Other research results are described by the authors in more detail in the article.

**Conclusion:** NAFLD is considered to be a slowly progressing chronic liver disease in both, adults and children. Besides taking care of our outpatient clinic patients, we should not forget about clients of the social reintegration facilities, in whom - due to the presence of several risk factors - the incidence of liver diseases and other diseases of civilization is even higher compared to the general population.

## Introduction

Every year, 39.5 million people die from chronic diseases. If the current state is maintained, the number of deaths from chronic diseases will increase to 55 million by 2030 (1). In terms of causes of death, diseases of civilization occupy a dominant place in the Slovak population (2). Metabolic syndrome (MS) is a metabolic disease characterized by a co-occurrence of several risk factors (RFs) for the development of cardiovascular diseases. It is a disorder of glucose metabolism associated with hyperglycaemia; development of insulin resistance; development of type 2 diabetes mellitus (type 2 DM) associated with obesity. Atherogenic dyslipoproteinemia, arterial hypertension, generalized atherosclerosis belong here (3).

The same risk factors have been demonstrated for metabolic syndrome and NAFLD. This finding raises a question of whether NAFLD is a symptom or a consequence of the metabolic syndrome. Most studies have concluded that a cardiovascular

disease, similarly to NAFLD, is a consequence or a complication of the metabolic syndrome. NAFLD - Non-Alcoholic Fatty Liver Disease - is characterized by the presence of liver steatosis, i.e. excessive accumulation of fat in liver tissue (steatosis must be present in more than 5% of hepatocytes) which is associated with insulin resistance. NAFLD is considered a benign, non-progressive form of the disease, while NASH - Non-Alcoholic Steatohepatitis - is a progressive form with the development of fibrogenesis with a high risk of liver cirrhosis and hepatocellular carcinoma of the liver (4). Patients with NAFLD carry an independent risk factor for cardiovascular disease; the risk of mortality from cardiovascular diseases is higher in people with NASH compared with people with only simple steatosis (5).

## Research objective

The aim of the research was: **a)** to document the presence of fibrosis and CAP in clients of so-

cial reintegration facility through examination by transient elastography; **b**) to find a correlation between the degree of fibrosis and the degree of CAP; **c**) to determine whether there is a correlation between BMI, FLI, CAP and FS; **d**) to determine whether associated diseases affect parameters such as MS (metabolic syndrome), FLI, NFS, APRI, FIB-4, FS and CAP; **e**) to determine whether there is a correlation between MS and NFS and CAP indicators; **f**) to determine whether MS, Fibroscan and CAP values increase with increasing BMI; **g**) to determine the correlation between the level of NH<sub>3</sub> (ammonia) and fat spectrum indicators (CHOL, TAG, LDL, HDL); **h**) to determine the correlation between NH<sub>3</sub> level and the CAP level.

### The research sample group and methodology:

The project "*Screening of liver diseases in Social Reintegration Facility*" ran from 1/2020 to 10/2020. It was carried out within the institutional project of the St. Elizabeth University of Health and Social Sciences (VSZaSP sv. Alzbety) and the Slovak Society of Practical Obesity (SSPO). We examined a total of 229 clients and employees of the Social Reintegration Facility of the Institute of Christ the High Priest in Zakovce: 188 clients (82%) and 41 employees (18%). Men made up 63% of the sample (145); women 37% (84). The mean age of clients in Zakovce was 51.4 years, the mean length of their stay in the facility was 5.87 years. We determined the nutritional status of the clients by determining their BMI: 95 clients (including employees) had physiological weight (41.4%); 69 were overweight (30.1% of the sample); 34 were obese (14.8%); 7 clients suffered from malnutrition (3%). At the beginning, we clinically examined all the clients and employees interested in the examination. We took a medical history (what diseases clients are being treated for, what medications they take, whether they are allergic to any medications or food). In addition to anamnestic data, we asked the clients/employees about the length of their stay in the facility, we determined their height, weight, waist circumference. We also collected venous and capillary blood. Due to the larger number of clients and employees, we visited the facility in Zakovce a total of 20 times. From the venous blood samples, we examined the follow-

ing biochemical parameters of the clients and employees: fat spectrum (cholesterol; LDL-cholesterol; HDL-cholesterol, triacylglycerols); so-called liver function tests (AST, ALT, GGT, ALP); albumin; bilirubin; glycemia; creatinine; levels of vitamin D; folic acid. From the capillary blood samples, we examined the level of ammonia (NH<sub>3</sub>) using the ARKRAY device.

Ammonia induces pathological changes in human hepatic stellate cells (activates stellate cells in vitro); disrupts intrahepatic hemodynamics; increases portal hypertension; enhances the formation of liver fibrosis in vivo; is a "target" in the treatment of chronic liver diseases (6).

We entered individual data into a so-called **hepcalculators** (developed thanks to the initiative of WORWAG Pharma GmbH in cooperation with the Slovak Society of Hepatology). The calculator automatically evaluates the entered data and calculates the following values for each patient: BMI, presence/absence of metabolic syndrome; indexes of liver damage FLI (fatty liver index); APRI, NFS (naflD fibrosis score), FIB-4. This helps to save time when processing data.

To examine the stiffness of liver tissue we used **transient elastography (TE)**. It is a non-invasive painless method that measures liver stiffness. The principle of elastography is based on the finding that fibrotic liver is less deformable by the action of an external forces, i.e. it is less elastic compared to a normal liver (Koller, Rac, 2015). We used special software to quantify the presence of steatosis (a so-called **CAP module** - controlled attenuation parameter).

CAP measurement results are given in dB / m. The measuring range is from 150 dB / m to 400 dB / m. Based on statistical recalculations, cut-off values with a sensitivity of  $\geq 90\%$  were determined for all degrees of steatosis:  $S \geq 1,215$  dB / m,  $S \geq 2,252$  dB / m,  $S \geq 3,296$  dB / m (7). dB / m values of individual degrees of hepatic steatosis in NAFLD as follows: S0: 150-240, S1: 240-270, S2: 270 - 303, S3 303-400. There are accurate scales for assessing hepatic steatosis not only for NAFLD, but also for viral hepatitis and liver diseases of various etiologies (7, 8).

For the needs of this screening project it was possible to purchase a PocketChem™ BA PA-4140 - a Japanese instrument from the ARKRAY company for determination of the ammonia levels; the NH<sub>3</sub> tests themselves; to rent a Fibroscan

530 Compact instrument with M and XL probes and built-in CAP function from the Czech Republic for one month. We also thank the PRO.MED.CS company for supporting the project.

## Results

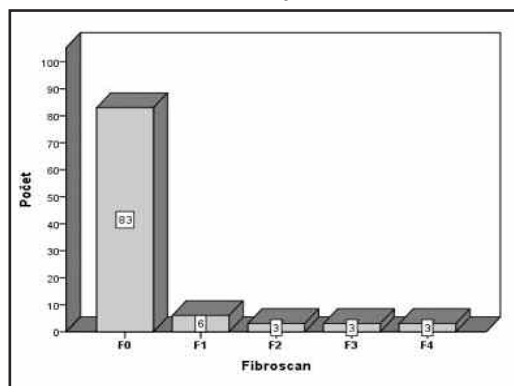
In the group of examined clients and employees of the Social Reintegration Facility in Závokce, we were in particular looking for the presence of liver diseases (with a focus on non-alcoholic fatty liver disease). However, in our research sample group, 63/229 respondents (27.5% of the sample) stated that they were being treated for cardiovascular diseases; 13/229 respondents (5.7%) were being treated for type 2 diabetes mellitus; 12/229 (5.2%) were being treated for lung diseases; 46/229 (20%) are taking psychiatric medications. 156/229 respondents (68.1%) are being treated for other diseases (e. g. diseases of the gastrointestinal tract, neurological diseases, diseases of the musculoskeletal system, etc.). 78/229 respondents (34%) are being treated for several diseases at the same time.

From the above, it is clear that diseases of civilization do not avoid Social Reintegration Facilities and that we must comprehensively assess the health status of the clients, although the project we carried out in this facility was primarily focused on liver diseases.

Based on the calculated fibrosis indexes, we selected a group of 98/229 clients in whom we performed examination by transient elastography. We hypothesized that they may have had liver damage in the sense of fibrosis: 83/98 examined had no liver fibrosis present (F0 / Metavir); we recorded grade F1 liver fibrosis in 6 clients; grade F2 in 3 clients; grade F3 in 3 clients; grade F4 (which is a synonym for liver cirrhosis) in 3 clients. The results are shown in graph no. 1.

We investigated *whether there was a correlation between the degree of fibrosis and the degree of CAP*. According to the Cohen scale (Pearson = 0.137), the correlation between CAP values and Fibroscan values was weak. The results are shown in table 1. On the CAP module, we distinguish the degrees of hepatic steatosis according to the percentage of liver impairment as follows: S0 (0 - 10% of hepatic steatosis); S1 (11 - 33%); S2 (34 - 66%); S3 (67 - 100%).

**Graph no. 1** Degrees of liver fibrosis determined by Fibroscan



\*pocet = number

In our research sample group: 42/99 patients had steatosis grade 0 (42.4%); 23/99 had steatosis grade 1 (23.2%); 11/99 had steatosis grade 2 (11.1%); 23/99 had steatosis grade 3 (23.2%).

**Table 1** Correlation between degree of fibrosis and degree of CAP Correlations

		CAP	Fibroscan
CAP	Pearson Correlation	1	.137
			Sig. (2-tailed)
			.179
N		99	.98

In the research, we investigated *whether there is a correlation between BMI, FLI, CAP and FS*. We found a statistically significant correlation between BMI and FLI, CAP and FS indicators.

At the same time, we wanted to determine *whether the associated diseases affect indicators such as MS, FLI, NFS, APRI, FIB-4, FS and CAP*. There is a statistically significant correlation between the incidence of associated diseases and indicators: MS, FLI, NFS, APRI, FIB-4, FS, CAP. The only exception is the Fibroscan (FS) indicator (Pearson = 0.188,  $p = 0.064$ ). We continued by *identifying correlations between MS and NFS and CAP indicators*. The correlation between MS and NFS and CAP indicators was confirmed. With the presence of MS, the value of both NFS and CAP increases. For NFS: Pearson = 0.266 \*\*,  $p = 0.0001$ , for CAP: Pearson = 0.359 \*\* and  $p = 0.001$ .

Another aim of the research was *to find whether the values of MS, Fibroscan and CAP increase with increasing BMI*. With statistical significance, a positive correlation was confirmed for all 3 markers. For MS and CAP, statistical significance was at alpha level = 0.01; for Fibroscan at alpha level = 0.05. With increasing weight (BMI), the incidence of MS and the degree of Fibroscan and CAP increase. On a device from the ARKRAY company, using the microdiffusion method, out of a drop of capillary blood we determined the ammonia level in 194/229 clients (85% of the group); out of which only 5% of the group (10/194) had a physiological value of NH<sub>3</sub> (55-60 μmol/l). The mean level of NH<sub>3</sub> in the clients but also in the employees of the facility was 181.8 μmol/l.

In our research, we set several goals associated with the level of NH<sub>3</sub>. One of them was: *to find out whether there was a correlation between ammonia level (NH<sub>3</sub>) and fat spectrum indicators (CHOL, TAG, LDL, HDL)*. We did not find a correlation in the monitored group.

At the same time, we analyzed individual parameters of the fat spectrum. We found an increased level of cholesterol in 106/221 clients (47.9%); 100/225 clients (46.4%) had an increased level of triacylglycerides (TAG); we found an increased level of LDL in 132/190 patients (69.4%); a decreased level of HDL was found in 72/191 clients (37.7%). On the whole, we can state that dyslipoproteinemia was very common in the clients, which is a risk factor not only for fatty liver disease but also for cardiovascular diseases. Another goal was *to determine possible correlations between the level of NH<sub>3</sub> and the degree of CAP*. According to the Cohen scale (Pearson = 0.083) the correlation between NH<sub>3</sub> and CAP was trivial / (negligible).

## Discussion

NAFLD is the most common liver disease in economically developed countries. The prevalence ranges from 17 to 46%, depending on diagnostic procedures, ethnicity, age, gender (9). In children, the prevalence of NAFLD is related to the age: 3-10%, but in obese children it reaches a value of 40-70% (10).

In Europe, in 2016, 73 million people suffered from NAFLD, out of which 2.5 million suffered from advanced fibrosis. By 2030, an in-

crease of NAFLD to 84 million can be expected. The alarming assumption is that by 2030, in Europe the number of people suffering from advanced fibrosis will double - from 2.5 million to 5 million (11). The prevalence of NAFLD increases with age, as older patients have more risk factors for metabolic syndrome (9). It is generally believed that the progression of NAFLD to steatohepatitis or to fibrosis results rather from associated diseases and their duration than from the age itself. Risk factors for the development of NAFLD are: obesity, type 2 diabetes mellitus (DM), hypertriglyceridemia (12, 13, 2).

**The key etiopathogenetic factors for NAFLD are:** high-calorie food intake, excessive intake of saturated fats; refined sugars; sweetened beverages; fructose; sedentary lifestyle; low physical activity; a so-called western type of diet (4). Excessive intake of fructose may increase the risk of developing NASH and advanced fibrosis. An unhealthy lifestyle plays an important role in the development and progression of NAFLD. Therefore, an evaluation of eating habits and physical activity is part of an extensive NAFLD screening.

NAFLD, especially when associated with type 2 DM and metabolic syndrome is supposed to be the most common chronic disease worldwide affecting 15-40% of the world's population (14). Cirrhosis in NAFLD was once referred to as cryptogenic. Today, it is the 3rd most common indication for liver transplantation (right after alcoholic cirrhosis and cirrhosis based on chronic hepatitis C). It is expected to dominate the indications for liver transplantation (15).

In the group of examined clients and employees of the Social Reintegration Facility in Zakovce, we were mainly looking for the presence of liver diseases (with a focus on NAFLD). During the examination of the clients we found not only frequent occurrence of dyslipoproteinemia, but also of other diseases of civilization. Within the research, we wanted to determine whether the associated diseases (cardiovascular and other diseases of civilization) affect indicators such as MS, FLI, NFS, APRI, FIB-4, FS and CAP. There is a statistically significant correlation between the incidence of associated diseases and indicators: MS, FLI, NFS, APRI, FIB-4, FS, CAP. The only exception is the Fibroscan (FS) indicator (Pearson = 0.188, p = 0.064).



Another aim of the research was to find whether the values of MS, Fibroscan and CAP increase with increasing BMI. With statistical significance, a positive correlation was confirmed for all 3 markers. For MS and CAP, statistical significance was at alpha level = 0.01; for Fibroscan at alpha level = 0.05. With increasing weight (BMI), the incidence of MS and the degree of Fibroscan and CAP increase (16).

The aim of the treatment of patients diagnosed with NAFLD / NASH is to slow down or to stop the progression of the disease; the development of liver fibrosis/cirrhosis; subsequent serious complications (4).

Epidemiological studies confirm a correlation between the occurrence of NAFLD and unhealthy lifestyle (17). The treatment strategy for NAFLD is mostly based on regimen measures and treatment of the individual components of the metabolic syndrome (18). For morbidly obese patients, bariatric surgery is a suitable alternative. Thorough treatment of the present risk factors is needed. Healthy eating takes on a new dimension in the context of the COVID-19 pandemic. It has become a global health and social problem with specific contexts in the field of gastroenterology and hepatology. There is a link between COVID-19 infection and NAFLD (19).

Physical activity is important not only in the treatment of NAFLD, but also in its primary prevention. Physical activity supports the production of active body mass; prevents undesired reduction of muscle mass during a reduction diet; reduces diet-induced decrease in resting energy expenditure; favourably affects the amount of postprandial energy expenditure; increases the mobilization of fats from fat stores. As important as the exercise itself is the limitation of sedentary way of spending free time outside of the exercise. Sedentary lifestyle and low cardiorespiratory fitness are among the most important independent predictors of premature mortality.

## Conclusion

NAFLD is considered to be a slowly progressing chronic liver disease in both, adults and children. Over the last 30 years, NASH has become a serious health problem due to the obesity epidemic and metabolic syndrome. NAFLD/NASH is considered to be an organ/liver manifestation of the metabolic syndrome and is likely to play

a key role in the pathogenesis of systemic atherosclerosis.

NAFLD should not be only perceived in terms of the risk of liver damage progression but also as an independent risk factor for cardiovascular diseases or diabetes. On the contrary, patients at high risk of developing cardiovascular diseases should be screened for NAFLD (12). Among other extrahepatic manifestations of NAFLD as an independent risk factor: colorectal cancer; kidney disease; some endocrinopathies; sleep apnoea syndrome; osteoporosis are intensively investigated (5).

Besides taking care of our outpatient clinics patients, we should not forget about clients of the Social Reintegration Facilities, in whom - due to the presence of several risk factors (including stress and difficult life circumstances that brought them to such facility) - the incidence of liver diseases and other diseases of civilization is even higher compared to the general population.

Our big thanks belong to Father Marian Kuffa, social workers and nurses who take exemplary and dedicated care of the clients of the Social Reintegration Facility in Zakovce and who were very helpful during the project implementation.

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