THE ETIOLOGY OF CHRONIC LIVER DISEASE AND CIRRHOSIS IN HUNGARIAN MEN

by BEÁTA ÉVA PETROVSKI

Supervisor: ZOLTÁN VOKÓ, MD., Ph.D.

DOCTORAL SCHOOL OF HEALTH SCIENCES

UNIVERSITY OF DEBRECEN

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INTRODUCTION

Chronic liver disease (CLD) and cirrhosis mortality in Europe and worldwide.

According to the WHO report 2004, the diseases of the digestive system accounted for approximately 3.5% of all deaths worldwide (3.8% in men and 3.2% in women). Cirrhosis of the liver was the 18th leading cause of death worldwide, accounting for 1.3% of all deaths.

Unlike in Western societies where mortality from CLD and cirrhosis was low between the 1970s and 1990s, the Central and Eastern European (CEE) countries, including Hungary, experienced an increasing occurrence of deaths due to these diseases, reaching a maximum in 1995, when the relative risk of death increased to 7.4 times and 6.2 times the European Union (EU) average in men and women, respectively. Although the premature mortality from CLD and cirrhosis decreased considerably from 1995 in Hungary, such decrease was observed in other EU member states as well. This unfavourable tendency remained to the present if compared to both the EU_{15}[1] and EU_{12}[2] member states.

CLD and cirrhosis morbidity in Hungary

According to the data from the General Practitioners' Morbidity Sentinel Station Program[3] (GPMSSP) from 1998, the prevalence of CLD and cirrhosis was extremly high (1.5-2.5 times higher) among men living in Zala county (35-64 years of age, 5-6%) compared to the other three counties participating in the project. In the oldest age group (65-X years of age) the difference was even more significant. In women, the difference in the prevalence of liver cirrhosis was the highest in the age group 55-64 years, with the highest prevalence observed in the eastern county Hajdú-Bihar (1.5%) and the lowest in other eastern county Szabolcs-Szatmár-Bereg (0.5%). Considerable regional differences among eastern and western representative counties were observed. Counties joining the GPMSSP later - Bács-Kiskun and Heves, showed similar distribution as the other eastern counties, while the prevalence distribution in the western, Baranya and Komárom-Esztergom, counties corresponded to the distribution in other western counties in Hungary.

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[1] Countries that joined the EU before 2004
[2] Countries that joined the EU between 2004-2007
[3] The program was established in 1997 and started in 1998 in four counties – Hajdú-Bihar, Győr-Moson-Sopron, Szabolcs-Szatmár-Bereg és Zala. Between 2002-2004, four other counties: Bács-Kiskun, Komárom-Esztergom, Baranya, Heves –, and in 2007, three other counties: Borsod-Abaúj-Zemplén, Jász-Nagykun-Szolnok, Nógrád – joined the program.

The prevalence of CLD and cirrhosis has not changed significantly over the last 12 years compared to the situation in 1998. According to the 2010 data from the GPMSSP, the prevalence of the disease was still highest among men in Zala county; although it was not affecting the 35-64 years age group anymore as seen in 1998, but due to the cohort effect, it shifted to the 10 years older population (45-74 years age group), reaching the highest point in the 65-74 years old (8%). The disease frequency was higher among men living in Szabolcs-Szatmár-Bereg- (65-74 years age group) and Hajdú-Bihar county (55-64 years old) (the disease prevalence in both counties was approximately 3%). In the other GPMSSP participant counties, the disease frequency was below 3%, the lowest being in Borsod-Abaúj-Zemplén and Jász-Nagykun-Szolnok counties (approximately 1%).

The cirrhosis prevalence in Zala county was also highest in the 65-74 years age group in women, with the similar cohort effect as seen in men. The age distribution and the observed prevalence differences of the disease were similar among women and men, with the prevalence of the disease being much lower in women compared to men.

Risk factors affecting the etiology of CLD and cirrhosis

Alcohol comsumption. The alcohol consumption in the WHO European Region is the highest in the world. The risk and the mortality of CLD and cirrhosis in parallel to the quantity of alcohol consumed. Regarding mortality from cirrhosis, Hungary takes the 3rd place, while in terms of alcohol-related liver disease Hungary takes the 1st place in the Eur-C countries.[4]

The negative trends observed in Hungarian men, however, are not simply due to the amount of alcohol consumed, since the alcohol consumption in western European countries, although not as high as in our contry, is still significant. Therefore, other risk factors should be considered in the disease development. Consumption of alcohol from uncontrolled sources is significant in Eastern Europe.

Smoking. Cigarette smoking has been shown to be hepatotoxic and a risk factor for CLD.

Socioeconomic status. Besides behavioral factors, CLD has repeatedly been reported to be associated with low socio-economic status (SES). A study made in the United States between 1935-1997 analysed the relationship between socio-economic factors and liver disease. Significant differences were found in the mortality from liver disease in the categories of marrital status, SES and education. The SES of the subjects could be

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[4] European countries with low child-, but high adult mortality: Belarus, Estonia, Hungary, Kazahstan, Letonia, Litvania, Moldavia, Russian Federation and Ukraine.

connected with certain forms of behavior. Low SES individuals conducted unfavourable health behaviours. Besides health behaviour, other risk factors related to the SES can affect the health of the individuals.

Hepatitis virus infection. Viral hepatitis infection (hepatitis B (HBV) or C (HCV)) alone or synergistically with alcohol consumption may accelerate the development and progression of liver disease.

Selenium (Se) has been identified in connection with the onset and progression of many diseases. Many studies have found significantly lower serum and plasma Se levels in patients with different degrees of hepatocellular injury compared to healthy individuals. Studies exploring the effect of Se in non-alcoholic liver disease have been very controversial.

Other risk factors may play a role in the development of CLD and cirrhosis, however, in the present study we did not study the effect of these risk factors (viruses: e.g. Cytomegalovirus and Epstein Barr Virus; toxic chemicals and drugs: e.g. amiodarone, methotrexate; genetic disorders: e.g. Wilson's disease, hemochromatosis; other diseases: type 2 diabetes, high cholesterol; auto immune diseases: autoimmune chronic hepatitis, primary biliary cirrhosis) in the etiology of the disease.

Aims of the study

1. To determine how the prevalence of CLD and cirrhosis depend on lifestyle factors (alcohol consumption (quantity, quality), alcohol-related problems, smoking, physical activity), viral hepatitis (B, C, E) infection and socio-economic factors (educational level, marrital- and financial status).

2. To find out how lifestyle factors can explain the relationship between socio-economic factors and liver disease.

3. To determine whether the serum Se level is related to the level of liver injury.

4. To find out whether serum Se level can be affected by age, socio-economic-, lifestyle- factors or nutritional status in the general population.

MATERIALS AND METHODS

Source population. A study investigating the etiology of CLD and cirrhosis started on December 1, 2005 (in the framework of the Ányos Jedlik Program; NKFP1-00003/2005), as an open cohort inside the GPMSSP program. Four counties – Győr-Moson-Sopron, Hajdú-Bihar, Szabolcs-Szatmár-Bereg, Zala – provided the source population of men between 45-64 years of age (on December 31, 2004.) in one of the participating 55 district general practitioners (GP) practices.

Case and control selection, case verification. Potential cases were patients (45-64 years men on 31.12.2004) who were registered at one of the participant GP practices on May 1, 2005 and had been reported to have CLD or cirrhosis in the regular monitoring programme. A total of 692 subjects in four counties have been reported. Only those subjects were included as cases who had at least two of the following symptoms on physical examination: spider nevus, ascites, palmar or plantar erythema, jaundice, enlarged, firm liver with rounded or nodular edge, and had at least one positive laboratory test result of increased level of glutamate-oxaloacetate transaminase (GOT), glutamate-pyruvate transaminase (GPT), gamma-glutamyl-transpeptidase (γGT), alkaline phosphatase, total bilirubin or decreased serum albumin. Controls were randomly selected from the source population (1181 subjects). Case verification was performed among controls as well, from which 100 subjects fulfilled the case criteria.

Type of studies. Case-reference study was performed to examine the relationship between CLD and cirrhosis, and lifestyle factors, viral hepatitis and SES. Cross-sectional study of the relationship between serum Se level and liver damage, as well as lifestyle and socio-economic factors was also carried out.

Data collection and tasks. Since the study included men only, only the year of birth was recorded as demographic data. According to the study protocol, GPs completed a physical examination on patients and collected fasting blood sample. The blood was sent to one of the previously designated accredited laboratories, where the serum GOT, GPT, γGT, alkaline phosphatase, albumin and total bilirubin, as well as other laboratory parameters such as Se, HBV, HCV and hepatitis E (HEV) viral serology were measured.

Blood samples were tested for the presence of antibodies to hepatitis C and E antigen (anti-HCV and anti-HEV), hepatitis B surface antigen (HBsAg) and antibodies to hepatitis B core antigen (anti-HBc) (ELISA method, Biomerieux, France and DiaPro, Italy) at the National Center for Epidemiology. A person was considered HBV infected if the HBsAg or the anti-HBc was found positive. Similarly, people positive for anti-HCV and anti-HEV were considered hepatitis C and E virus infected, respectively.

Serum Se concentration was measured using inductively coupled plasma-mass spectrometry.

Patients were divided into four categories based on their alcohol consumption: heavy drinkers, moderate drinkers, occasional drinkers and abstinent. Participants who consumed more than 14 units (1 unit = 15 grams) of alcohol in the previous week or consumed more than 5 units on any day of the last week were considered heavy drinkers. Those who consumed alcohol in the previous week, but did not qualify as heavy drinkers were considered moderate drinkers. Occasional drinkers were those who had consumed alcohol before, but not during the previous week. Men who never consumed alcoholic beverages were considered abstinent.

The CAGE (Cut-Annoyed-Guilty-Eye) questionnaire on problem drinking was part of the self-administered questionnaire. Based upon answers to four questions, a person answering positively to at least two questions was identified as a problem drinker. Non-problem drinkers were those who gave less than 2 positive answers. Besides the quantity and the form of alcohol consumed, questions were asked about the source of wine and spirits consumed. The quality of the alcohol consumed (wine or spirits) was categorised as controlled or uncontrolled based on the source it was obtained from (commercial production, shops, black market, house-made or self-made).

Smoking was categorised as never smoker, former smoker, occasional smoker (smokes but not every day), daily smoker (everyday but less than 20 cigarettes per day) and heavy smoker (at least 20 cigarettes per day).

Based upon the type and frequency of the activity, physical activity was classified as sufficient physical activity (at least 150 minutes per week spent on walking/moderate/intensive activity in the previous 7 days), insufficient physical activity (less than sufficient but more than inactive) and inactive (no time spent on walking/moderate/intensive activity in the past 7 days).

Participants were also divided into three marrital status groups: maried or living with a partner; single, separated or divorced; and widowed. Participants assessed their own

financial status (subjectively) as: good or very good, satisfactory, and bad or very bad. Participants also selected their highest level of education: elementary school or less, high school without certificate of final examination, high school with certificate of final examination, and college or university degree.

The nutritional habits were based upon the fat used for cooking and categorised as: uses neither animal nor vegetable fat, uses animal fat, vegetable fat; or both of them; does not bake/cook at home.

The subjects' body mass was classified according to the body mass index (BMI) into four categories: <18.5, 18.5-24.99, 25-29.99, and ≥ 30 kg/m^2.

The participants were divided into two age groups: 45-54 years and 55-64 years.

Written informed consent was obtained from all participants. The protocol was approved by the Regional and Institutional Ethics Committee, Medical and Health Science Centre, University of Debrecen.

Statistical analysis. The chi-square ($\chi2$) test was used to analyse the differences in the distributions of categorical variables. To study the relationship between the CLD/cirrhosis and the potential risk factors, simple logistic regression models were first fitted for each risk factor. Crude odds ratios (ORs) and their 95% confidence intervals (CIs) were obtained from these models. To study whether the effect of socio-economic factors was fully mediated by health behaviour, a multiple regression model was fitted for the socio-economic factors, behavioural factors and age as explanatory variables. Finally, a study whether the remaining effects of socio-economic factors could be explained by HBV or HEV infection was performed.

Due to presence of skewed distributions in the examined serum Se and liver biochemical markers (GOT, GPT, GOT/GPT, γGT, alkaline phosphatase, albumin and total bilirubin), medians and interquartile ranges (IQR) were implemented.

Kruskal-Wallis variance analysis (ANOVA) was used to compare the levels of the Se and biochemical markers between the cases and controls. To differentiate the liver injury, we categorized the case and control participants by tertiles of the GOT/GPT ratio. Simple linear regression analysis was performed to examine the relationship between serum Se and biochemical markers in the control and in the CLD group separately. Simple and multiple linear regression analysis were also used to examine the relationship between Se and other risk factors (lifestyle, SES, age, nutritional status) in the control group. The statistical software package Stata was used for the analysis.

RESULTS

The GPs reported 692 case out of which 407 (58.8%) agreed to participate and only 187 (45.9%) fulfilled the diagnostic criteria. From the source population, 1181 persons were randomly selected as potential controls out of which 892 persons (75.5%) agreed to participate in the study. A hundred controls (11.2%) fulfilled the diagnostic criteria for being a case; these were included as cases and controls in the case-reference study according to the planned study design. In the cross-sectional study, only healthy subjects were included in the control group.

The results of the case-reference study showed that heavy alcohol consumption was associated with more than 2-fold increased risk of developing CLD/cirrhosis (OR: 1.8; CI: 1.2-2.8) compared to the abstinent group. Similar increased risk was found within the smokers group, as well. While former smoking increased the risk for developing disease by 1.7 times (OR: 1.7; CI: 1.2-2.5), heavy smoking (more than 20 cigarettes) increased the risk by 1.8 times (OR: 1.8; CI: 1.2-2.7) compared to non-smokers. Problem drinking increased the risk of CLD/cirrhosis more than four times (OR: 4.2; CI: 3.1-5.7) compared to non-problem drinking.

Half of the participants, both cases and controls, obtained their wine from uncontrolled sources, and close to a quarter of the participants obtained their spirits from uncontrolled sources. Regarding physical activity, majority of the participants did satisfactory activity (among cases 89.2% and controls 91.9%). In the crude analysis we found that neither the source of consumed alcohol (wine: OR: 1.0; CI: 0.76-1.4; spirits: OR: 0.74; CI: 0.49-1.1) nor the physical activity of the participants (not sufficient: OR: 0.48; CI: 0.15-1.5; sufficient: OR: 0.41; CI: 0.16-1.1) were related to liver disease. Among the socio-economic factors, being single, separated or divorced significantly increased the risk of CLD/cirrhosis compared to being maried or living with a partner (OR: 1.7; CI: 1.2-2.5). Participants with higher education (high school with certificate, college or university degree) had CLD/cirrhosis risks reduced by 40 and 70% compared to participants with only elementary education. Persons who perceived their financial status as bad or very bad had an 80% increased risk of the disease compared to those with good or very good perceived financial status.

The effect of marrital status (OR: 1.9; CI: 1.2-3.1) and the effect of education (OR: 0.35; CI: 0.16-0.77) did not change after adjustment for health behavioural factors, while the effect of perceived financial status disappeared (OR: 0.98; CI: 0.50-1.9).

The prevalence of HBV infection was 9.8% and the prevalence of HEV infection was 8.2% among cases. The corresponding figures among controls were 9.7% and 9.7%, respectively. Only 5 persons had HCV infection - 1.04% of the cases (3 subjects) and 0.25% of the controls (2 subjects).

Neither the HBV (OR: 1.0, CI: 0.67-1.7) nor the HEV (OR: 0.89, CI: 0.55-1.5) infection were associated with the disease. Since HEV infection was neither associated with CLD/cirrhosis nor with marrital status or education, it could not explain the remaining effects of the socio-economic factors. The HBV infection showed statistically significant association with education. The prevalence of the viral infection was 13.4% among persons with only elementary education and 7.5% among those who had college or university degree. Nevertheless, adding HBV to the multivariate model did not change the effect estimates of education and marrital status.

In the the cross-sectional study, 281 cases (out of 287 subjects) and 778 controls (out of 792 subjects) were involved in it. Compared to the controls, the cases were older (P=0.002), there were more obese subjects among them, had lower level of education (P<0.001), were more likely to perceive their financial status as bad or very bad (P=0.02), were heavier drinkers (P<0.001) and heavier smokers (P=0.009). There were higher prevalence of obesity in the control group (P=0.009).

Regarding the type of fat used for cooking, no significant difference was found between the cases and the controls (P=0.2).

The lowest serum Se level was found in the highest GOT/GPT ratio tertile in both the cases (median: 0.80 µmol/L, IQR: 0.67 – 0.93 µmol/L) and the controls (median: 1.03 µmol/L, IQR: 0.93 – 1.15 µmol/L).

The high GOT/GPT ratio in the upper tertiles of the control group was due to decreased GPT level, whereas both GOT and GPT levels were increased among the cases – the GOT level was the highest in the 3rd tertile of GOT/GPT ratio (median: 63 U/L, IQR: 37-94 U/L), while the GPT level was the highest in the 1st tertile of the GOT/GPT ratio (median: 42 U/L, IQR: 27-55 U/L). The γGT level was increased in all tertiles of the cases.

The levels of the biochemical markers differed significantly between the examined groups (P<0.001).

Among the cases, there was a statistically significant relationship between the Se level and albumin and bilirubin. The serum Se level decreased with the increase in serum GOT level, although the result was not statistically significant. The increase in the GOT/GPT ratio was however, significantly related to the decrease in the Se level.

In the control group, the Se level significantly decreased with increases in bilirubin, GOT and GOT/GPT ratio; in contrast, the Se level increased with increases in GPT. In this group, the younger, better-educated men had significantly higher level of Se, while regular smokers and heavy drinkers had significantly lower level of Se. The use of vegetable fat for cooking was associated with increased Se level. The relationships remained essentially the same after adjusting for all studied factors.

CONCLUSION

The study was performed to explore the etiology of high premature mortality due to CLD and cirrhosis in Hungary.

Since the premature death from this disease is significantly higher in men compared to women, and the frequency of the disease gradually increases after 45 years of age, the study included men between 45-64 years age.

The selection of participating counties took into account the regional differences in disease frequency between eastern and western counties. An important aspect was the exstensive experience of the GP practices in the GPMSSP.

The study design took into account past experiences from the GPMSSP. Accordingly, a 25% response rejection rate, as well as 3-10% hidden morbidity were pre-assumed. Approximately 70% of the planned sample size agreed to participate in the study. After the case verification, 11% hidden morbidity was found in the control group.

Out of the reported cases, 46% were actually diagnosed as cases, and more than half of them were misdiagnosed, which is significantly higher than the previous experience from the GPMSSP (15%). The high level of overdiagnosis draws the attention of a problem of the credibility of the Hungarian health statistics data regarding CLD, as well as raises the awareness that the GPs not necessarily apply standardised diagnostic criteria for liver disease in their daily practice. There is a possibility that the participating GPs presumed their patients being liver diseased without any signs or symptoms of the disease simply because they knew they were heavy drinkers. These distortions were corrected at the beginning of the study by excluding the individuals who had connection to risk factors examined in the study (example: living in an Alcohol Rehabilitation Center). In addition, the cases that were reported by the GPs that did not meet the diagnostic criteria were also excluded from the study.

A limitation of our study is the lack of use of instrumental tests (abdominal ultrasound, liver biopsy) for the diagnosis of the disease type. The reason for this is in part of ethical nature. Nevertheless, the advantages of our study are the uniform use of disease and exposure factors that were determined by standard methods, as well as the verification of the quality of fieldwork performed.

The behavioural and socio-economic risk factors showed strong correlation with CLD. Heavy and problem drinkers, former or heavy smokers, single, separated or divorced, having bad or very bad perception of the financial status were all associated with

increased, while higher education was associated with decreased risk of developing CLD/cirrhosis. Regarding the behavioural factors (alcohol consumption, smoking), our results are in line with previous findings from other studies.

The socio-economic factors showed strong correlation with CLD/cirrhosis in the simple logistic regression analysis. If we assume that lifestyle factors mediate the effects of the socio-economic factors, then this effect would have been eliminated after adjustment for lifestyle factors. The effect of the marrital status and education remained unchanged however, after adjustment for lifestyle factors, while the effect of the financial situation disappeared. Indeed, the effect of the financial factors prevailed and could be fully explained through the health behavioural factors. There are several theories which can explain this phenomenon. Socio-economic factors can affect the disease, at least in part, through lifestyle factors. Subjects with low SES (low education, poor/very poor financial situation) usually have a lifestyle that negatively affects their health. Since the effect of education and marrital status remained unchanged even after adjustment for lifestyle risk factors, it can be concluded that education and marrital status are not related the risk of liver disease only thorugh the studied life-style factors. There are probably other risk factors that may be related to the SES and liver disease that can mediate an unfavourable effect of the SES.

Interestingly, the effect of bad perceived financial situation could be entirely explained by the behavioural factors. The financial situation was assessed by applying subjective methods which have been shown by several studies to be clearly related to health status, just like more objective measures of the financial status. On the other hand, the high morbidity and premature mortality in men with low SES may not simply be attributed to health behavioural risk factors.

Since estimation of the disease status and presence of risk factors happened at the same time, it is possible that a given risk factor is not the cause of the disease, but rather the result of it. This can affect the results obtained regarding the association of liver disease with marrital and financial status. The participation rate might have resulted in a bias, too. Although its effect on our results was probably limited, because it was not our intention to estimate the prevalence of the risk factors in the whole population, but rather study their relationship with the severity of the liver disease.

It has been shown that not only the amount of the alchohol consumed should be considered in the development of liver disease, but also the quality of the alcohol. However, our proxy measure of the quality of alcohol consumed - the source it was obtained from - was not

related to the risk of CLD/cirrhosis. The lack of association can probably be attributed to high rate of missing data about the source of alcohol consumed.

The association between HBV and liver disease development is well established. It is widely accepted that viral hepatitis and alcohol, independently or combined, can have a liver damaging effect. Furthermore, HEV infection can cause acute exacerbations in both recognized and unrecognized asymptomic HBV-related CLD. Almost every 10th person was HBV or HEV infected in our study population. However, we did not find significant association between hepatitis infection and CLD/cirrhosis. An explanation for that may be the use of prevalent cases of CLD/cirrhosis, thus cases with rapid progression were less likely to be included in the study. This may result in an underestimation of the effect of viral hepatitis.

The serum GOT/GPT ratio is considered a marker of the severity of CLD. We categorized the case and control groups according to the GOT/GPT ratio by tertiles. The decrease in the serum Se level followed in parallel the liver disease severity. The serum Se was significantly lower in the case group compared to all tertiles of the control group. The results of our serum Se level measurements when compared to other study results would represent a middle range, considering the fact that the participants' Se levels (referring to the medians: 0.76-1.27 µmol/L) regardless the presence or absence of the liver disease. Meanwhile, the GOT/GPT ratio increase was followed by a parallel decrease in the serum Se level. In the highest tertile of the cases, part of the diseased patients had low serum Se level (<0.76 µmol/l).

The serum Se level strongly correlated with the level of liver injury, as characterized by the serum albumin, bilirubin and GOT/GPT ratio. A decreased Se level significantly correlated with an increased GOT, GOT/GPT ratio and bilirubin in the control group. These findings are consistent with most of the studies performed to date, although a recent study indicated that serum Se levels are decreased in cirrhotic patients, but not influenced by the disease severity. Our results suggest that the serum Se level is closely related to the amount of liver damage and the changes in liver biochemical markers. The changes in the Se level can be detected even at the early stages of liver disease, before clinical symptoms appear.

The Se concentration in non-alcoholic liver disease significantly decreased with age, in heavy drinkers and regular smokers compared to the abstinent subjects. An association was further found between blood Se concentration and nutritional factors such as vegetable fats, or vegetable and animal fats use in which the Se level was higher. These findings were also in agreement with the results from other similar studies.

The socio-economic fators showed correlation with Se - higher educational status correlated with increased Se concentration in the serum compared to status with elementary school education. The financial status did not show any association with the Se level in our study.

A limitation of our study is its cross-sectional design. The relationship between serum Se and CLD in our results reflects both the effect of the disease on the Se level and the effect of Se on the risk and progression of disease. Selenium supplementation has been known to prevent liver diseases, or delay its progression. Although smoking and alcohol consumption should be given first priority in any public health program, our findings raise the awareness that a higher CLD burden in subjects with unfavourable SES may be accounted to other unknown risk factors. Discovering these factors would increase our understanding of the CLD epidemiology, and probably provide us with more tools for prevention of CLD.

Main findings and results

1. We performed a comprehensive epidemiological study involving the independent and interdependent effect of risk factors in the etiology of CLD and cirrhosis in Hungary.

2. We found that socio-economic factors such as education and marrital status do not affect the liver disease in an expected way, through the examined health behavioural factors.

3. Our study results may serve as a reference for the serum Se level in the Hungarian population.

4. We found that the Se level changed in parallel with the biochemical markers of liver damage. This pattern was observed in the control group as well. In the population with no symptoms of liver disease serum Se level was associated with the socio-economic and health behavioural factors.

Candidate: Beáta Éva Petrovski

Neptun ID: JECKCY

Doctoral School: Doctoral School of Health Sciences

List of publications related to the dissertation

1. **Petrovski, B.É.**, Pataki, V., Jenei, T., Ádány, R., Vokó, Z.: Selenium levels in men with liver disease in Hungary.
   J. Trace Elem. Med. Biol. Epub ahead of print (2012)
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3. Tóth, R., Fiatal, S., **Petrovski, B.**, McKee, M., Ádány, R.: Combined effect of ADH1B rs1229984, rs2066702 and ADH1C rs1693482/ rs698 alleles on alcoholism and chronic liver diseases.
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Katona C., Antal D., Puskás É., **Petrovski B.**: Az emlőrák és méhnyakrák szűrés igénybevételében megjelenő társadalmi-gazdasági egyenlőtlenségek a magyarországi nők körében. DE OEC TDK Konferencia, Debrecen, 2012. február 15-17. (hallgatói előadás/témavezetés)

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