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Prevalence of Liver Disease in Russia's Largest City: A Population-based Study

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Abstract **Background and aim:** Difficulties in accessing data from individual countries, especially Russia, hinder global evaluation of liver disease in Europe. The aim of this study is to estimate the prevalence of liver disease in Moscow, Russia's capital and most densely populated urban area. **Methods:** We recruited 5,000 random Moscow residents over the age of 18 in a population-based cross-sectional study. Participants were screened for liver disease between October 2012 and November 2012. Socio-demographic, health and lifestyle information was obtained via questionnaire; alcohol screening was done using CAGE and AUDIT tools; BMI was measured by physical exam; liver tests (ALT, AST, GGTP, bilirubin, ALP, ALT/AST), anti-HCV, HBsAg, and γ-globulins were checked by laboratory analysis; an abdominal ultrasound was performed for all patients. Provisional diagnoses were formed for all participants according to our established algorithm. **Results:** In total, 4,768 participants completed screening. Socio-demographic data: male 1,671 (33.42%), female 3,329 (66.58%), average age 45 years, average BMI 26.2 kg/m^2. Average BMI >25 kg/m^2 was observed among the following occupational groups: retired, disabled, military and businessmen. Health care workers and students were the "slimmest" occupational groups, with only 24.7% and 21.8% having BMI >25 kg/m^2 respectively. The CAGE and AUDIT questionnaires revealed that a huge number of participants (74.64% of all participants) should reduce the quantity of alcohol they consume, and that 9.8% abuse alcohol or are alcohol dependent. Overall, 1,459 subjects (30.6%, m:f=2:1) had at least one abnormality in liver function tests. We found the following prevalence of liver diseases in Russia's largest city: NAFLD 7.4% (n=352), ALD 6.9% (n=329), hepatitis C 6.7% (n=322), hepatitis B 1.9% (n=91), DILI 0.82% (n=39), cholestasis 0.69% (n=33), AIH 0.78% (n=37), other forms of liver disease 5.4% (n=258). **Conclusions:** According to our study, more than one quarter of Moscow residents have abnormal liver tests that may indicate liver disease. NAFLD, ALD and hepatitis C were the main causes of abnormal tests. The primary risk factors for abnormal liver tests as determined by multivariable analysis were: young age (30-59 years, p<0.001), alcohol abuse (AUDIT score >16, p<0.04), and hypercholesterolemia (p=0.016). 80.3% of patients with abnormal liver tests required etiotropic treatment.

Keywords: *Russia, prevalence, liver disease, epidemiology*

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1. Introduction

Diffuse liver disease is the most significant gastroenterological illness nowadays. The rate of liver disease is increasing around the world and approximately 29 million persons in the European Union suffer from a chronic liver condition [13]. Liver disease can be silent and asymptomatic for decades and first present an advanced stage (for example, as complications of portal hypertension). Liver cirrhosis accounted for 1.8% of all deaths in Europe in 2000-2002 [13]. Alcohol abuse and non-alcoholic fatty liver disease (NAFLD) are two factors with the potential to keep levels of liver cirrhosis relatively high in European countries.

Data on the prevalence of liver disease in Russia are usually incomplete and are not included in official reports published by the World Health Organization (WHO) or other international organizations. Some groups of the Russian population − including pregnant women, blood donors, health care workers, and military personnel − are regularly screened for viral hepatitis, but there is no standard screening process for the general population.

Liver disease is becoming increasingly common among the working age populations [2,3,7,9,13]. We reviewed current data about liver epidemiology and found that the true prevalence of liver disease in the world is not known and that further investigation is needed.

The aim of our research was to estimate the prevalence of liver disease in Moscow, Russia's capital city and most densely populated urban area. To do so, we collected demographic data from the study population, calculated the frequency of abnormal liver tests and made preliminary diagnoses for participants with abnormal tests.

We analyzed liver disease risk factors and selected the most important factors in order to make suggestions about liver disease prophylaxis and early detection in Russia.

2. Methods

Our study was a population-based cross-sectional study based in Moscow, Russia. A total of 5,000 random Moscow residents between the ages of 18 and 75 years old were enrolled (power - 90.6%). Of these subjects, 4,768 completed all required evaluations. 232 subjects were excluded from the study because of incomplete data.

Study recruitment was organized around the social project "Test your liver", which was sponsored by the Russian Scientific Liver Society. Participants received information about the project via outdoor advertising, banners, booklets, and the websites of major Russian medical organizations (rsls.ru, gastro.ru, gastrohep.ru). The participant flow diagram for recruitment and retention is presented in Figure 1.

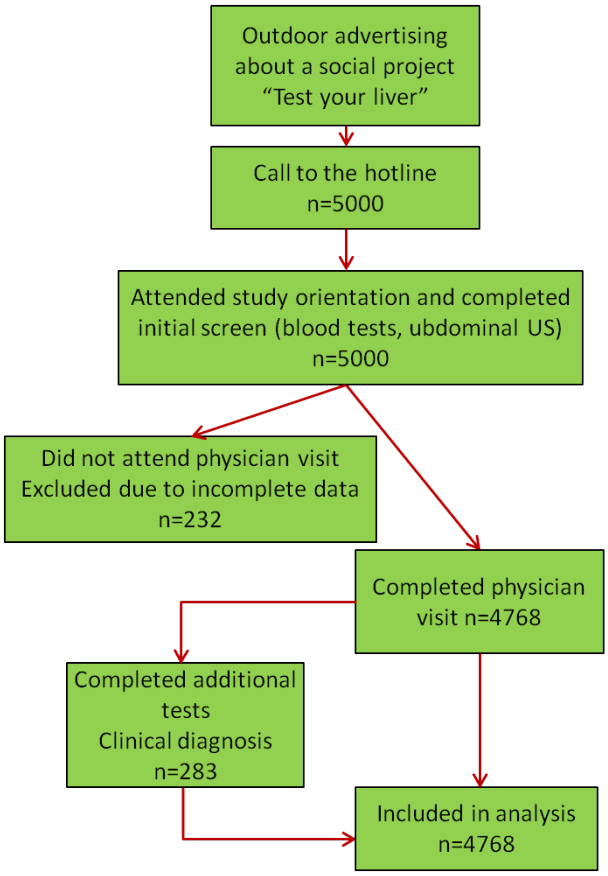

Figure 1. Participant flow of recruitment and retention for the population-based cross-sectional study

The following information was collected from each participant:

1. Demographic data including age and sex.
2. Professional occupation (laborer, office professional, retired, disabled, homemaker, student, healthcare worker, academic or cultural worker, manager/business owner, educational worker, military or other).
3. Health related behaviors: tobacco use, alcohol screening using the CAGE and Alcohol Use Disorders Identification (AUDIT) tests, dietary habits as measured by food diary.
4. Medication history: any prescription medications, herbal medicines or dietary supplements used during the last 3 months.
5. Physical examination: including height, weight and body mass index (BMI), the ratio of weight in kg to height in square meters.
6. Laboratory screening tests to identify common forms of liver disease: complete blood count, chemistry panel (ALT, AST, total bilirubin, direct bilirubin, GGT, AP, triglycerides, cholesterol, glucose), protein electrophoresis, anti-HCV, and HBsAg [5,8,12].
7. Abdominal ultrasound.
8. As needed: additional physical examination from a general practitioner.

The 4,768 subjects who completed the full protocol were divided into 2 groups for further analysis. Group A included participants with abnormal liver function tests and group B included participants without such changes. Univariable and multivariable statistical analysis with binary logistic regression was done to compare the groups.

3. Results

Our population-based sample of Moscow residents included 5,000 people. Women made up 66% of our sample (n=3329) and men made up 33.4% of the sample (n=1671). From this, we concluded that women were more concerned about their health and thus more likely to enroll.

Participants were broken into three age categories: young age (18-44 years) – 47.5% of sample, middle age (45-59 years) – 33.4%, and advanced age (60-75 years) – 19,1%.

Further analysis of the 4,768 participants who complied all study requirements revealed 1,461 persons (30.6% of total) with possible liver disease (study Group A). Based on this finding, we estimate that more than one in four Moscow residents have abnormal liver tests that may indicate liver disease. Group B, participants with normal liver tests, included 3,307 people (69.4% of total). A male predominance was found among participants with abnormal liver tests: 49.7% of Group A was male, whereas only 25.5% of Group B was male ($p<0.001$). This is very interesting because the overall male to female ratio of the study population was 1:2.

A great amount of clinical research around NAFLD and alcoholic liver disease (ALD) risk factors has been done in the last several years. Based on initial diagnoses assigned in our study, the proportion of such diseases was very large: 24.1% for NAFLD and 18.1% for ALD (42.2% total). NAFLD was directly associated with obesity and metabolic syndrome. These pathological conditions become more frequent with age, but according to recent data NAFLD is not associated with advanced age [1]. In our study we found the same results: advanced age is an independent preventive factor for abnormal liver tests.

We also analyzed sex, BMI, CAGE and AUDIT scores (used to screen for alcohol abuse), smoking, and specific laboratory measurements (cholesterol, triglycerides, glucose, GGT, gamma-globulins) as independent risk factors for liver disease.

3.1. Sex

Male sex was a significant risk factor for liver disease (p<0.001). However, male sex became insignificant during multivariable analysis (p=0.244) and was ultimately excluded from the logistic regression model. We can explain this with the generally known fact that male sex is an independent and significant risk factor for ALD [1,6,10,14] and therefore for alcohol abuse, and during multivariable analysis alcohol abuse (AUDIT score) in our study was singled out as a stronger factor.

3.2. BMI

Findings from published research show that BMI is an independent risk factor for NAFLD development [1,7,8,11]. In our study overweight and obesity were also identified as a significant causes of elevated liver tests. However, in multivariable analysis BMI was not found to be significant. We suppose this is connected with the fact that obesity is not widespread in Russia. The average BMI of Moscow residents is not very high: 26.5 kg/m^2 for males and 26.3 kg/m^2 for females in our study. BMI in Group A, the patients with abnormal liver tests, was significantly higher than that of group B, the patients with normal liver tests (p<0.001), with average BMIs being 26.84±4.99 kg/m^2 for Group A and 25.63±5.02 kg/m^2 for group B. The frequency of persons with normal or underweight BMI in Group B was significantly higher, at 47.7%, than that of Group A, at 2.7% (p<0.001). The frequency of overweight and obese persons was significantly higher in Group A than in Group B (p=0.007, p<0.001 accordingly) (Figure 2, Table 1). We can conclude that overweight or obesity of all grades is a significant risk factor for pathological processes in the liver.

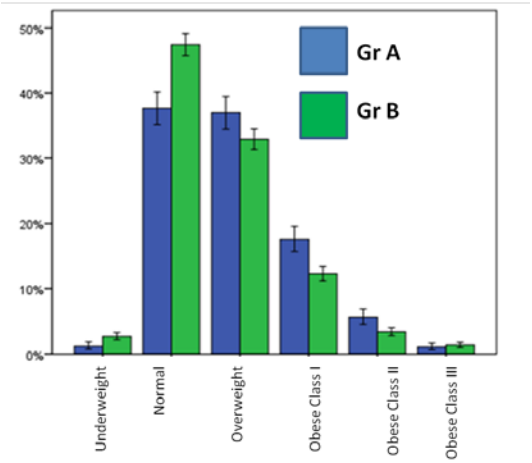

Figure 2. Comparison of the groups according BMI (95%)

Table 1. Comparison of Groups A and B by average BMI (95%)

BMI	Group A (n=1461)	Group B (n=3307)	p*
Average ± SD	26.84±4.99	25.63±5.02	<0.001
Underweight	17 (1.2%)	88 (2.7%)	<0.001
Normal	547 (37.6%)	1562 (47.4%)	<0.001
Overweight	537 (37%)	1084 (32.9%)	0.007
Obese Class I	255 (17.5%)	405 (12.3%)	<0.001
Obese Class II	82 (5.6%)	111 (3.4%)	0.004
Obese Class III	15 (1%)	44 (1.3%)	0.477

In our study we also looked at possible relationships between BMI and professional occupation. We found that the groups with the highest average BMI are disabled people, retired people and military personnel – 28.04 kg/m^2, 27.93 kg/m^2 and 26.68 kg/m^2 respectively.

3.3. Laboratory Data

Significant Liver tests abnormalities were detected more frequently in persons with elevated blood glucose, cholesterol and triglyceride levels (p<0.001). These factors were previously investigated in different international studies and are independent significant risk factors for NAFLD [1,4,7].

3.4. Smoking

Smoking prevalence varies greatly from country to country, ranging from 4% in Libya to 54% in Nauru. The most "smoking" countries are Guinea, Namibia, Kenia, Bosnia and Herzegovina, Mongolia, Yemen, Turkey, and Romania. Russia is 33rd place in the world ranking.

Only 8% of the participants surveyed in our study were smokers. There was no difference in smoking rates between Groups A and B: Group A had 8.7% smokers, group B had 7.3% (p=0.101). This figure is much lower than data published by WHO in 2011 that reports that 37% of Russians smoke. We assume this difference is due to the active population recruited for the study (more than 50% of participants were female) and the positive results of smoking cessation campaigns taking place in Russia since 2010.

3.5. Alcohol

The CAGE and AUDIT questionnaires revealed that a huge number of participants (74.64% of all participants) should reduce the quantity of alcohol they consume, and that 9.8% abuse alcohol or are alcohol dependent. The percentage of such persons in Group A was significantly higher than that in Group B, those with suspected "normal" livers. Our data match official Russian statistics published by WHO in 2010 that report that 8.9% of Russians over 12 years of age abuse alcohol.

3.6. Anti-HCV and HBsAg Prevalence

After screening 5,000 people we found that 6.7% (n=322) were anti-HCV positive, a finding that was reported in 2011 at the International Epidemiological Symposium [15]. 1.9% of participants (n=91) were HBsAg positive. We analyzed ALT and AST elevation frequency in these persons and could roughly conclude that they have virus replication [10,12]. This represents 50.9% of anti-HCV positive and 14.3% of HBsAg positive participants in our study. These participants need further investigation and antiviral treatment.

We compared anti-HCV and HBsAg prevalence between health care workers and those with other occupations and didn't find any difference: 6.5% of health care workers are anti-HCV positive compared with 6.9% of people from other occupations (p=0.841). HBsAg prevalence is 0.7% among health care workers, and 1.9% among other occupations (p=0.523). This is probably due to lack of differentiation of health care workers into groups with high and low risk of infection. On the other

hand, it shows that professional groups at risk consist not only of providers with direct blood contact (surgeons, emergency room physicians, surgical and triage nurses, etc.), but also providers who rarely do invasive procedures and don't have proper safety training.

4. Conclusions

According to our study about 30.6% (n=1461) of Moscow residents have elevated liver function tests (ALT, AST, GGT, AP, total bilirubin, anti-HCV, HBsAg) with a significant male predominance - 49.7% of all males and 25.5% of all females (p<0.001).

Preliminary diagnoses were assigned based on established guidelines [11]. Using these diagnoses, we concluded that the prevalence of liver disease in our study was (n=4768): NAFLD 7.4% (n=352), ALD 6.9% (n=264), hepatitis C 6.7% (n=322), hepatitis B 1.9% (n=91), DILI 0.82% (n=39), cholestasis 0.69% (n=33), AIH 0.78% (n=37), other 5.4% (n=323) (Figure 3).

The main risk factors for abnormal liver tests as determined by multivariable analysis were young age (30-59 years, p<0.001), alcohol abuse (AUDIT score > 16, p<0.04), and hypercholesterolemia (p=0.016). Univariable analyses revealed additional risk factors to be male sex (p<0.001), BMI >25 kg/m^2 (p<0.001), hyperglycemia (p<0.001), and hypertriglyceridemia (p<0.001).

About 80.3% of patients with abnormal liver tests required etiotropic treatment.

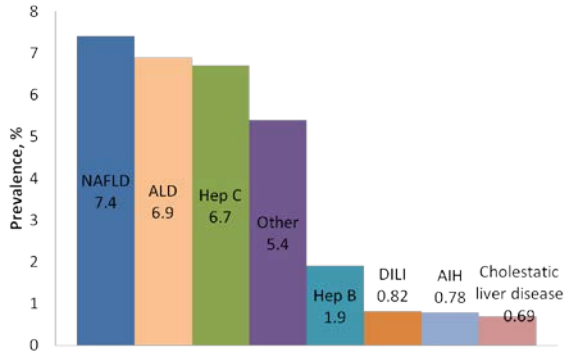

Figure 3. Liver disease prevalence in Russia's largest city (n=4,768)

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