

Original article ■

Epidemiological Characteristics of Carriers of Antibody Against Hepatitis C Virus in the Population of Nišava District

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SUMMARY

The aim of the paper was to determine the disease trends and characteristics of anti-HCV antibody carrier status for the purpose of better prevention and disease control.

The materials used were annual reports, reports of diseases and deaths from infectious diseases, and epidemiological surveys of the Public Health Institute Niš in the period from 2002 to 2011 in the Nišava District. A descriptive epidemiological method was used. Rates were non-standardized and were calculated per 100.000 residents.

There was an upward trend ($y = -5.4 + 8.21x \pm R^2 = 0.53$) of HCV carriers. Most carriers were male (68.34%), from urban areas (81.66%), aged $37.75 \pm SD 16.80$ years on the average, and unemployed (39.45%) (out of which the inmates of the Correctional Facility in Niš making up 26.11%). More than half of the registered carriers (59.05%) were not able to report the precise mode of transmission. Then followed hemodialysis patients (15.83%), injecting drug users (11.06%), blood donors (4.77%), pregnant women (3.52%), mother-to-child transmission cases (2.26%), and health professionals (0.75%). There were 14.82% of hospitalized cases. In 4.52%, a coinfection with hepatitis B virus was found.

HCV carrier status in the Nišava District showed an upward trend. Low incidence rates might have been the result of underreporting. Since there is no anti-HCV vaccine, it is necessary to focus on the activities of health education of all categories of people at risk, as well as on the service providers in different sectors, risk factors, modes of transmission and protection measures.

Key words: epidemiology, carriers, HCV antibodies, trend

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INTRODUCTION

The cause of hepatitis C infection is hepatitis C virus (HCV), from the flavivirus group. According to the World Health Organization (WHO), 3% of the world population (or 170 million people) are infected with HCV and the number of infections will be three times higher in 2020. The route of transmission is contact. The clinical picture is mild or the disease runs asymptotically. Over 80% of the infected can become permanent or chronic carriers of the disease. It is believed that at least 20% of people who are chronic carriers will develop cirrhosis (1-4). Standardized mortality rates from liver diseases are 16-45 times higher if there is a HCV infection. The highest prevalence rates of the diseases associated with HCV are reported in developing countries such as Egypt - 22%, Pakistan - 4.8%, and China - 3.2% (5). Most HCV infection incidents in the USA are reported in injecting drug users (IDUs), while in some groups, among them (HIV-positive), the seroprevalence of HCV infection is as high as 80-90% (6, 7).

There is still no vaccine against hepatitis C. Consequently, the prevention is of utmost importance. HCV identification has been going on since 1989. The diagnosis of hepatitis C is made on the basis of elevated transaminases, biopsy, serum markers of HCV presence and serum HCV RNA. For the time being, routine diagnosis involves only the demonstration of antibodies against HCV. Since these are not protective antibodies, their presence in the blood can be interpreted as past or ongoing HCV infection, as well as the presence of acute or chronic hepatitis C. Anti-HCV antibodies can persist for life. Due to a low titer of viral antigens in the serum, an active HCV infection can be established only by the presence of RNA sequences of the viral genome by PCR (8-10).

The Center for Disease Control and Prevention in Atlanta has made the recommendations for the control and prevention of HCV. Many countries have implemented monitoring of infection with this virus (11). Reporting of hepatitis C, as well as of anti-HCV antibody carriers, has been applied since 1997 in the Nišava District.

AIM

Our aim in this paper was to determine the disease trends and characteristics of anti-HCV antibody carrier status for the purpose of better prevention and disease control.

MATERIAL AND METHODS

The material used were annual reports of the Public Health Institute (PHI) Niš, reports of diseases and deaths from infectious diseases, and epidemiological surveys of the Department of Sexually Transmitted Infections. The period from 2002 to 2011 in the Nišava Di-

strict area was reviewed. A descriptive epidemiological method was used. The rates were non-standardized and were calculated per 100.000 residents. For the statistical analysis of data, the Microsoft Office Excel 2003 and PASW Statistics18 software packages were used.

RESULTS

In the period from 2002 to 2011 there were 398 registered carriers of anti-HCV antibody. Unadjusted rates of the carrier status reached 99.42/100.000 people. The majority of HCV carriers were reported in 2011 - 104 (26.13%), while the lowest number of carriers was reported in 2008 - 11 (2.76%). Half of the patients were reported in the last two years (202 or 50.75%). In this period, in the Municipality of Niš, 90.45% of anti-HCV antibody carriers were reported, while all other municipalities together had less than 10%. The rate of carriers in the Municipality of Niš was 143.70, and the lowest one was in the Municipalities of Svrlijig - 17.36, and Ražanj - 17.59/100.000. In the municipality of Niš, double-digit numbers of cases were registered each year, while in other municipalities there were periods without a single case of anti-HCV antibody carrier status.

In Figure 1, anti-HCV antibody carrier status in the Nišava District shows an upward trend ($y = -5.48 \cdot 21x \pm R^2 = 0.53$).

The majority of HCV carriers were in the age group of 20-29 and 30-39 years, with 28.89% of patients (Figure 2). The average age of carriers was $37.75 \pm SD 16.80$ years. The carriers with the highest rate were men aged 30-39 (345.10) and 20-29 years (316.69), while the highest rate among women was observed in the age group 20-29 years (120.98). The highest rate of childhood carriers was reported for children aged 0-4 years (76.62/100.000 residents). Secondary school children (15-19 years old) had the rate of 60.88/100.000.

Most of the reported cases were men (272 or 68.34%). The unadjusted rate of carriers of HCV antibodies in men was 138.24/100.000, being 2.23 times higher than the non-standardized rate of carriers in women (61.90/100.000 individuals). A similar gender ratio of rates was observed in the Municipality of Niš (2.32:1 man-to-female ratio).

According to the place of residence, 81.66% of the carriers resided in urban areas (Table 1). Urban carriers of antibodies to HCV in the Municipality of Niš accounted for 77.64% of the reported carriers in the Nišava District, while the percentage was 12.81% in rural populations. Rural residents were reported more often in the Municipalities of Aleksinac (2.01% vs. 1.26%), G. Han (0.75%, vs. 0%) and Merošina (1.01% vs. 0.25%), while the Municipalities of Niš, Ražanj and Svrlijig had more urban carriers. The municipalities of Doljevac and Sokobanja had the same number of carriers of HCV antibodies in rural and urban areas. Although there were no seasonal occurrences, the majority of anti-HCV anti-

body carriers were reported in February (11.31%), with the lowest number reported in August (5.53%).

The unemployed occupied the first place compared to all other carriers of HCV antibodies, with 39.45% (Figure 3). In this group, there were 41 inmates of the Correctional Facility in Niš (26.11% of them were unemployed) and 33 IDUs (21.02%). Retired persons, aged 29 to 83 years, were in the second place with 18.84%. In the group of retired persons aged 29 to 60, there were 64.52% nephrology patients. The individuals whose occupation could not be classified immediately followed (18.34%). In the group of 73 workers with no particular occupation there were also 10 patients of the Special Psychiatric Hospital (SPH) in Gornja Toponica, 8 blood donors, 7 drug users and 7 prison inmates. There were 3.27% preschool children, 0.50% school children, 1.01%

secondary school children, and 3.02% students. Three health professionals (1 doctor, 2 nurses) constituted 0.75% of anti-HCV carriers.

The percentage of hospitalized anti-HCV carriers was 14.82%. In 18 individuals (4.52%), a co-infection with hepatitis B virus was found.

Out of 330 HCV carriers, 59.05% belonged to the group of tested outpatients, without any information about the mode of transmission (Table 2). In this group of 235 tested carriers, 20.85% were the Correctional Facility inmates, while 5.11% were the patients of the SPH in Gornja Toponica. Out of the carriers with a known mode of transmission, patients on hemodialysis made up 15.83%, injecting drug users 11.06%, and blood donors 4.77%. Anti-HCV carriers were also 14 pregnant women (3.52%).

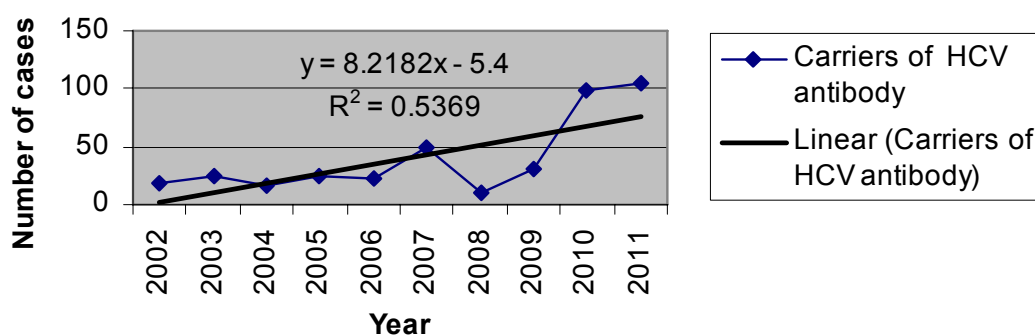


Figure 1. The trend of carrying HCV in Nišava District from 2002 to 2011

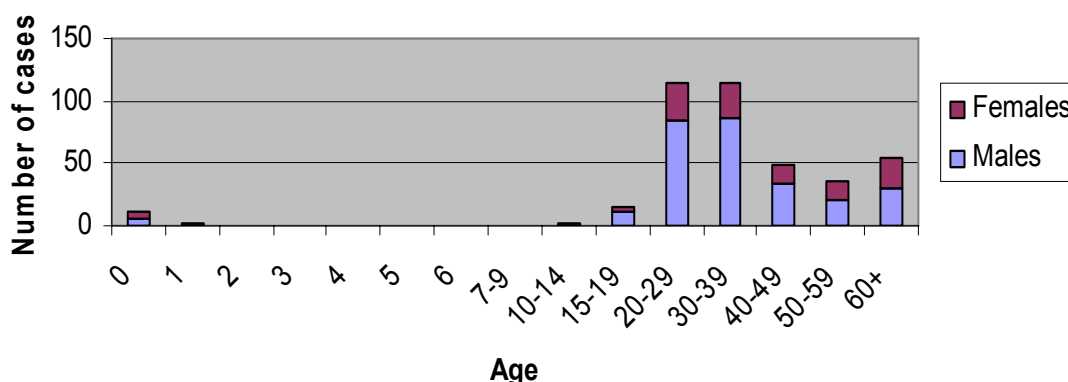


Figure 2. Distribution of carriers of HCV by sex and age in Nišava District from 2002 to 2011

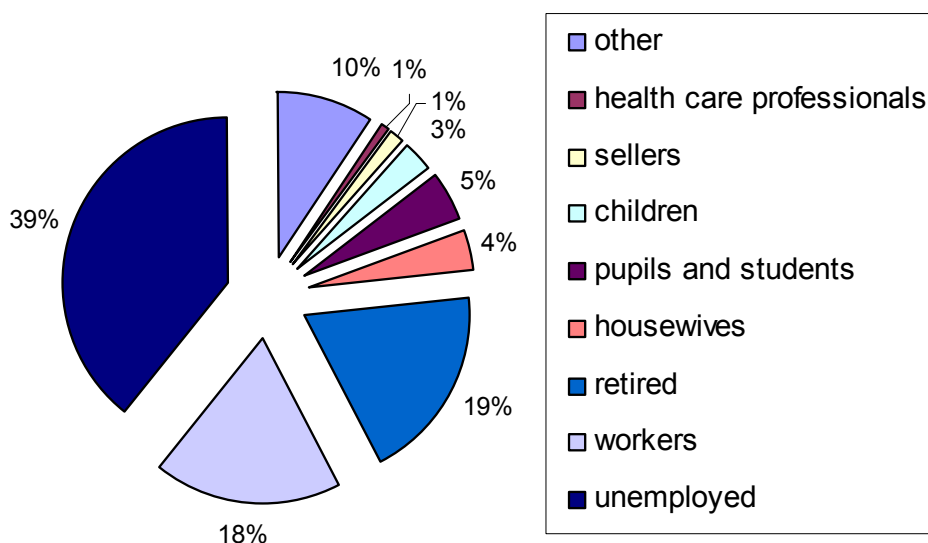


Figure 3. Profession of carriers of HCV antibodies in Nišava District from 2002 to 2011

Table 1. Distribution of carriers of HCV antibodies by place of residence in Nišava District from 2002 to 2011

Municipality	Village	%	City	%
Aleksinac	8	2.01	5	1.26
Gadžin Han	3	0.75	0	0.00
Doljevac	2	0.50	2	0.50
Merošina	4	1.01	1	0.25
Niš	51	12.81	309	77.64
Ražanj	0	0.00	2	0.50
Svrljig	1	0.25	2	0.50
Sokobanja	4	1.01	4	1.01
Total	73	18.34	325	81.66

Table 2. *Transmission groups of carriers of HCV antibodies in Nišava District from 2002 to 2011*

Transmission groups	Number of cases	%
Outpatient - polyclinic tested	235	59.05
Hemodialysis	63	15.83
Hemophilia	1	0.25
Heterosexuals	5	1.26
Injecting drug users	44	11.06
Other	1	0.25
Sexual partner	1	0.25
Mother	9	2.26
Pregnant	14	3.52
Health professionals	3	0.75
Recipient blood	1	0.25
Blood donors	19	4.77
Bone marrow transplantation	1	0.25
Carriers of HIV antibody	1	0.25
Total	398	100.00

DISCUSSION

The status of anti-HCV antibody carrier in the Nišava District from 2002 to 2011 showed an upward trend. The increase was especially conspicuous in the last two observed years. Up to 2002, the trend had been negative ($y=78.6-9.6x \pm R^2=0.26$), probably because of the fact that in early years (1997 and 1998) all cases were reported as new ones. The overall incidence trend from 1997 to 2011 was $y=33.65-1.19x \pm R^2=0.03$. In the Municipality of Niš, the trend was also steeply ascending in the period from 2002 to 2011 ($y=-4.67-38x \pm R^2=0.54$), while in other municipalities it was from $y=0.09x-0.2$ in the Municipality of Gadžin Han, to $y=-0.2$ to $0.27x$ in the Municipality of Aleksinac. In the Republic of Serbia, the number of carriers of hepatitis C was increasing, with the rate of registered carriers of hepatitis C virus higher in 2011 in central Serbia than in Vojvodina (5.38: 4.5/100.000). Carriers of HCV in the Nišava District accounted for 27.73% of the total reported number of anti-HCV antibody carriers in Serbia in 2011 (12). Increased reporting of anti-HCV antibody carriers in the last two years in the population of Nišava District could be attributed to increased surveillance of hepatitis by the Center for Disease Control

and Prevention on the one hand, and increased surveillance of reporting of isolated infectious agents in private and government laboratories by the sanitary inspection of Nišava District. Nevertheless, underreporting of carriers was possible due to frequent lacks of laboratory reagents and the fact was that infections usually went with asymptomatic or atypical clinical presentation, with the health care system undertaking insufficient screening of high-risk groups. There is no vaccine against HCV infection, which further complicates its prevention.

For example, in the cross-sectional study performed in the Subcarpatian and Southeastern Romania the recorded prevalence of anti-HCV antibodies was 4.58 (13). In Azerbaijan, the prevalence of anti-HCV antibodies was 4% (14).

In the study population, the unemployed accounted for nearly 40% of carriers. Pupils and students are in the fifth place (4.52%) (with students prevailing). In Pakistan, among the students of medical and dental colleges in Lahore, the seroprevalence of HCV carriers was 2.1% (15). Three health professionals were the carriers of HCV. A pediatrician first tested for hemodialysis was negative, but two years later as a patient of the Clinic for Infectious Diseases and Department of Nephrology he was positive to anti-HCV antibodies. A nurse and a kin-

dergarten teacher were sent from the health center to get tested for hepatitis B and C when it was discovered that they were the carriers of anti-HCV antibodies. In a medical center in Jerusalem, the prevalence of anti-HCV antibodies of health workers in 1994 was significantly higher (1.25%) than in the general population of Israel (0.15%) (16).

In the Nišava District in the period from 2002 to 2011, coinfection with hepatitis B and C virus was found in 18 people (4.52%). In the neighboring Bulgaria, the percentage of coinfection was 0.68%. Coinfection with hepatitis B and C multiplied several times the risk of developing hepatocellular carcinoma (17-20).

The studied outpatient group included 12 patients of the Special Psychiatric Hospital in Gornja Toponica and 49 inmates of the Correctional Facility (OCA) in Niš. The report of the Helsinki Committee for Human Rights (HC) set out that in the Correctional Facility in Niš, in the period from April to June 2006, there were 55 anti-HCV positive inmates and 17 drug addicts, with 9 more drug addicts in the period from July to September. There were no HIV positives. In the prison, there was the problem with more inmates using one syringe, raising the possibility for further infections among the inmates (21). In the cross-sectional study, performed in Iran, it was found that HCV infection was 70 times more common among prisoners than in the general population (22).

In Niš, the prevalence of hepatitis C virus infection in a sample of IDUs in 2010 rose by 2.1% compared to 2008 (58.4%: 60.5% in 2010) (23). In the population of Nišava District in the period from 2002 to 2011, IDUs accounted for 11.06% of anti-HCV carriers. In the population of Nišava District in 2008, not a single IDU case was reported as the carrier of anti-HCV antibodies, while the highest number was recorded in 2007 and

2010 - 25% in each year. The average age of IDUs was 28.77 years \pm SD 5.94 (similar to the average age of IDUs in the above study - 29,69 \pm 5.01). The youngest was 18 and the oldest 50 years old, with 75% of IDUs belonging to the group of unemployed.

CONCLUSION

Anti-HCV carrier status in the Nišava District showed an upward trend. Low incidence rate of 0.10% for carriers of HCV antibodies could be the consequence of underreporting. Males accounted for 68.34% of all carriers. The average age of an anti-HCV carrier was 37.75 years \pm SD 16.80. Urban residents accounted for 81.66% of carriers. The unemployed occupied the first place among the carriers of HCV antibodies with 39.45%. In this group, the inmates of the Correctional Facility in Niš accounted for 26.11%. The groups with high expectancy of anti-HCV carrier status were present in the population of Nišava District - hemodialysis patients with 15.83%, and injecting drug users with 11.06%. Pregnant women were the carriers of anti-HCV antibodies in 3.52%, while the transmission from mother to child was reported in 2.26%. The use of non-sterile injecting equipment significantly increases the number of infected with HCV. Since there is no anti-HCV vaccine, it is necessary to strengthen the activities of the health education in all categories of people at risk, as well as the continuing education of providers in different health care sectors. It is necessary to perform repeatedly the studies of seroprevalence and behavior (life-style) in order to monitor the trends of HCV epidemics, in order to spot changes in behavioral patterns, level of knowledge, and to use better preventive and therapeutic services in further planning of strategies and programs of control and prevention of this disease.

References

1. Memon MI, Memon MA. Hepatitis C: an epidemiological review. *J Viral Hepat* 2002;9(2):84-100. Ahmad W, Ijaz B, Gull S et al. A brief review on molecular, genetic and imaging techniques for HCV fibrosis evaluation. *Virology* 2011; 8: 53. <http://dx.doi.org/10.1046/j.1365-2893.2002.00329.x>
2. Jovanovic M, Konstantinovic Lj, Katic V et al. Histopathological and immunocytochemical changes in the liver of patients with chronic hepatitis C. *Vojnosanit Pregl* 2004; 61(1): 29-34. (in Serbian) <http://dx.doi.org/10.2298/VSP0401029J>
3. Kostic V, Jovanovic M, Konstantinovic Lj et al. Liver damage caused by Hepatitis C viral infection and ethyl alcohol consumption. *Vojnosanit Pregl* 2006; 63(4): 393-6. (in Serbian) <http://dx.doi.org/10.2298/VSP0604393K>
4. Ford N, Kirby C, Singh K et al. Chronic hepatitis C treatment outcomes in low- and middle-income countries: a systematic review and meta-analysis. *Bull World Health Organ* 2012; 90: 540-50.
5. Gunn RA, Murray PJ, Ackers ML et al. Screening for chronic hepatitis B and C virus infections in an urban sexually transmitted disease clinic. *Sex Transm Dis* 2001; 28: 166-70. <http://dx.doi.org/10.1097/00007435-200103000-00008>
6. Centers for Disease Control and Prevention. Integrated Prevention Services for HIV Infection, Viral Hepatitis, Sexually Transmitted Diseases, and Tuberculosis for Persons Who Use Drugs Illicitly: Summary Guidance from CDC and the U.S. Department of Health and Human Services. *MMWR* 2012;61(rr05): 6. <http://www.cdc.gov/mmwr/pdf/rr/rr6105.pdf>
7. Krstic Lj. Medical virology. *Cigoja*, 2000:138-44, 207-10. (in Serbian)

8. Konstantinovic Lj. Viral hepatitis C. Prosveta ,1997:67-72. (in Serbian)
9. Stankovic-Djordjevic D, Otasević M, Tasic G et al. Hepatitis C Virus Infection - Virusological And Pathophysiological Aspect. Acta medica Medianae 2002; 1: 43-52. (in Serbian)
10. Centers for Disease Control, Prevention. Recommendations for prevention and control of hepatitis C virus (HCV) infection and HCV-related chronic disease. MMWR Morb Mortal Weekly Rep 1998; 47(RR-19):1-39. <http://www.cdc.gov/mmwr/PDF/RR/RR4719.pdf>
11. Record of infectious diseases in 2011 in the territory of Republic of Serbia. Public Health Institute of Serbia, Belgrade, 2012: 53-4.
12. Voiculescu M, Iliescu L, Ionescu C et al. A cross-sectional epidemiological study of HBV, HCV, HDV and HEV prevalence in the subcarpathian and south-eastern regions of Romania. J Gastrointest Liver Dis 2010; 19 (1): 43-48. <http://www.rjge.ro/jgld/2010/1/6.pdf>
13. (No authors listed). Epidemiological assessment of the hepatitis B and C infectious disease markers in Baku and Nakhtchivan healthy population. Georgian Med News. 2010; (184-185):40-4. (in Russian)
14. Sarwar Bhatti M, Quraishi M, Mahmood ChZ, Javaid K. Seroprevalence of HBsAg and HCV antibodies in healthy individuals of high socioeconomic status. Biomedica 2007; 23: 131-3. <http://www.thebiomedicapk.com/articles/119.pdf>
15. Rosen E, Rudensky B, Paz E et al. Ten-year follow-up study of hepatitis B virus infection and vaccination status in hospital employees. J Hosp Infect 1999; 41(3): 245-50. [http://dx.doi.org/10.1016/S0195-6701\(99\)90023-3](http://dx.doi.org/10.1016/S0195-6701(99)90023-3)
16. Atanasova MV, Haydouchka IA, Zlatev SP et al. Prevalence of antibodies against hepatitis C virus and hepatitis B coinfection in healthy population in Bulgaria. A seroepidemiological study. Minerva Gastroenterol Dietol 2004;50(1):89-96.
17. Liu Z, Hou J. Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) Dual Infection. Int J Med Sci 2006; 3: 57-62. <http://dx.doi.org/10.7150/ijms.3.57>
18. Zhang JY, Dai M, Wang X et al. A case-control study of hepatitis B and C virus infection as risk factors for hepatocellular carcinoma in Henan, China Int J Epidemiol 1998;27:574-8. <http://dx.doi.org/10.1093/ije/27.4.574>
19. Semnani S, Roshandel G, Abdolahi N et al. Hepatitis B/C virus co-infection in Iran: A seroepidemiological study. Turk J Gastroenterol 2007; 18 (1): 20-1.
20. Jelic M, Lukic Samardzija G, Obradovic M, Markovic Z. Prisons in Serbia - April 2005 - April 2006. Helsinki Committee for Human Rights in Serbia. Belgrade, 2006: 14-8.
21. Javadi AA, Avijgan M, Hafizi M. Prevalence of HBV and HCV infections and associated risk factors in addict prisoners. Iranian J Publ Health, 2006; 35 (4): 33-6. http://journals.tums.ac.ir/upload_files/pdf/_/2900.pdf
22. Ministry of Health of Republic of Serbia, HIV Project Implementation Unit financed by the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM), Public Health Institute of Serbia, „Dr Milan Jovanovic Batut”, National HIV/AIDS Office. Research among populations most at risk to HIV and among people who live with HIV. Basic results of supervised researches from 2009 to 2010. Ministry of Health of the Republic of Serbia, Belgrade, 2010.

EPIDEMIOLOŠKE KARAKTERISTIKE NOSILAŠTVA ANTITELA NA VIRUSNI HEPATITIS C U POPULACIJI NIŠAVSKOG OKRUGA

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Sažetak

Cilj rada bio je utvrđivanje trenda oboljevanja i karakteristike nosilaštva antitela na virusni hepatitis C radi boljeg sprovođenja prevencije i suzbijanja ove bolesti.

Kao materijal korišćeni su godišnji izveštaji, prijave zaraznih bolesti, epidemiološke ankete Instituta za javno zdravlje Niš za period 2002-2011. godine na području Nišavskog okruga. Korišćen je deskriptivni metod rada. Stope su nestandardizovane i izračunavane su na 100000 stanovnika.

Nosilaštvo HCV antitela pokazuje uzlazni trend ($y = -5,4 + 8,21x \pm R^2 = 0,53$). Većinu nosilaca čine osobe muškog pola (68.34%), iz gradske sredine (81.66%), prosečne starosti 37.75 godina \pm SD 16.80, nezaposleni (39.45%). Među nezaposlenima, štićenici Kazneno-popravnog zavoda čine 26.11%. Više od polo-

vine registrovanih nosilaca (59.05%) nema utvrđen način transmisije; slede bolesnici na hemodijalizi (15.83%), intravenski korisnici droga (11.06%), dobrovoljni davaoci krvi (4.77%), trudnice (3.52%), transmisija sa majke na dete (2.26%) i zdravstveni radnici (0.75%). Hospitalizovano je 14.82%. Kod 4.52% nađena je koinfekcija sa hepatitis B virusom.

Nosilaštvo HCV antitela u Nišavskom okrugu pokazuje uzlazni trend. Niske stope incidencije mogu da budu posledica podregistracije. Pošto protiv HCV infekcije ne postoji vakcina, potrebno je pojačati aktivnosti na edukaciji svih kategorija lica u riziku, kao i pružalaca usluga u različitim sektorima, o faktorima rizika, načinima transmisije i merama zaštite.

Ključne reči: epidemiologija, nosilaštvo, HCV antitela, trend