HANTAVIRUS INFECTION - EPIDEMIOLOGICAL CHARACTERISTICS IN THE AREA OF THE REPUBLIC OF CROATIA DURING THE COVID-19 PANDEMIC

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ABSTRACT

Introduction: Hantaviruses are the causative agents of hemorrhagic fever with renal syndrome (HGBS). People are most often infected by inhaling a contaminated aerosol, but infection can also occur through contaminated food or water. On average, eighteen people fall ill with HGBS per year outside of epidemics. Men between the ages of 20 and 40, especially farmers, soldiers, foresters and hikers, are most often affected. Famous hotspots in Croatia are Lika, Gorski kotar and Medvednica. Objective: To analyze the frequency and epidemiological characteristics of hantavirus infections in the Republic of Croatia during the COVID-19 pandemic. Materials and methods: Data on the incidence of HGBS according to counties, seasonal occurrence, age groups and gender were analyzed, as well as the connection of recommendations for being in nature as part of the suppression of the Covid-19 pandemic to a potential increase in the number of HGBS patients. Retrospective analysis was used to process the data collected at the Croatian Institute of Public Health, and descriptive methods were used to perform statistical analyzes in the Microsoft Excel software system. Results: In the period from 2019 to 2021, there were 547 patients with HGBS, with men suffering more often than women (78.0% vs. 22.0%). The highest activity was recorded in Primorje-Gorski Kotar and Lika-Senj counties from March to August in the age groups of 30 to 39 years. In 2021, 332 patients were reported, which is more than the average, and this can be connected to the more frequent stay of people in nature due to recommendations to reduce the number of patients with the COVID-19 disease. Conclusion: The study of the epidemiological features of hantavirus infections is important for public health because it enables the identification of areas with a higher risk of infection, the recognition of epidemics and the adoption of appropriate control and prevention measures.

Keywords: Hantavirus, Epidemiology, COVID-19, Croatia

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INTRODUCTION

Hantaviruses are a group of serologically and phylogenetically related RNA viruses of the genus Hantavirus, family Bunyaviridae (1). So far, 40 species have been described, 20 of which cause disease in humans. Hantaviruses are the causative agents of two important syndromes: hemorrhagic fever with renal syndrome (HGBS) caused by Dobrava (DOBV), Hantaan (HTNV), Puumala (PUUV) and Seoul viruses (SEOV) and hantavirus pulmonary syndrome (HPS) whose most common causes are: Sin Nombre virus (SNV), Andes virus (ANDV), Bayou virus, Black Creek Canal virus, Laguna Negra virus and New York virus. In nature, they are maintained in chronically infected rodents and small mammals (2).

Hantavirus reservoirs are small rodents: wood vole (*Clethrionomys glareolus*), yellow-throated mouse (*Apodemus flavicollis*), striped field mouse (*Apodemus agrarius*) and common wood mouse (*Apodemus sylvaticus*). After infection, rodents excrete the virus with saliva, feces and urine. Infection in humans most often occurs by inhalation of a contaminated aerosol, but the virus cannot be introduced into the body of a new host either through food or water, i.e. through contaminated food or water. Interhuman transmission of HGBS has not been proven. The disease occurs in groups of people aged 20 to 40, and the most frequently affected professional groups are farmers, soldiers, foresters, and hikers. The disease occurs sporadically, most often in rural areas where there are suitable places for small rodents that transmit the virus (3). The first signs of the disease appear after an incubation period of an average of 2 weeks (5-40 days). HGBS most often begins with a general infectious syndrome and renal symptoms dominate. About 100,000 cases of HGBS are reported annually in the world, of which 70-90% (40,000 - 60,000 cases) on the territory of China. In Europe, approximately 9,000 cases of HGBS occur annually, and the most common proven type of hantavirus is PUUV (4). Croatia, as a country with diverse ecosystems, offers a favorable habitat for rodents, which are natural reservoirs of hantaviruses (5). In Croatia, the areas of Lika, Gorski Kotar and Medvednica are known to be endemic natural foci of hantavirus (6). Hemorrhagic fever with renal syndrome is an endemic disease in Croatia and was first described in 1952, after which sporadic cases were continuously recorded (7). In 1995, only two smaller epidemics were registered: in 1967 at the Plitvice Lakes, when 14 forest workers fell ill, and in 1989, near the Pleso airport, when 14 soldiers fell ill (8). The first major epidemic was recorded in 1995

simultaneously in several localities (Mala Kapela, Dinara, Slavonia) with 125 cases reported (9). Then, in 2002, the largest HGBS epidemic broke out so far, with more than 300 patients in almost the entire the territory of Croatia (10). The last epidemic was in 2012 in Sljemen with 152 reported cases (11). In the inter-epidemic period, about 10-20 cases of HGBS are registered annually, according to the register of infectious diseases of the Croatian Institute of Public Health since 2000, the average number of patients per year is 18.

In the period from 2019 to 2022 years, isolation measures and recommendations for people to stay in mountains, forests and solitude were applied in order to suppress the COVID-19 pandemic. However, as a possible consequence of such measures, an increase in the number of people suffering from hantavirus infections was recorded, with a total of 332 cases in 2021. The study of the epidemiological characteristics of hantavirus infections in Croatia is of great importance for public health, as it enables the identification of areas with a higher risk of infection, the timely recognition of epidemics and the adoption of appropriate control and prevention measures.

OBJECTIVE

The aim of the study is to analyze the frequency and epidemiological characteristics of hantavirus infections in the Republic of Croatia during the COVID-19 pandemic.

MATERIALS AND METHODS

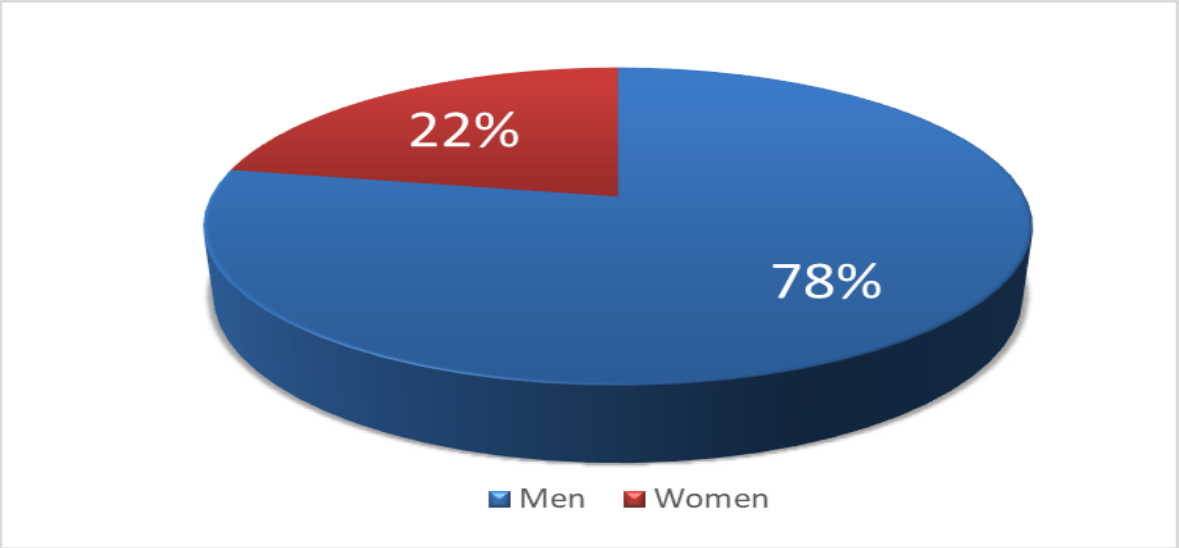
Data on the incidence of HGBS from 2019 to 2022 years were analyzed according to counties, seasonal occurrence, age groups and gender, and the connection of recommendations for spending time in nature as part of the fight against the Covid-19 pandemic to a potential increase in the number of HGBS patients. Retrospective analysis was used to process the data collected at the Croatian Institute of Public Health. Registration of patients and verification of applications is conducted in the National Public Health Information System, from which the data is transferred to the Register of Infectious Diseases of the Republic of Croatia, which is coordinated by the Croatian Institute for Public Health. Data from the Registry of Infectious Diseases collected by the Epidemiology Service of Infectious Diseases were used to investigate the incidence of HGBS.

Descriptive methods in the Microsoft Excel software system were used for statistical analysis, and in this way a complete insight into the epidemiological features of hantavirus infection in Croatia was obtained

over a period of four years.

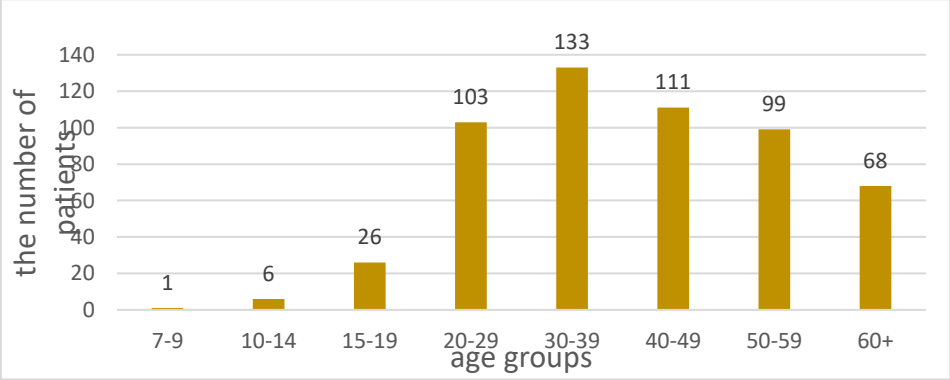
RESULTS

The study included a total of 547 subjects between the ages of 7 and 65 years old. There were 426 (78%) men and 124 (22%) women. (Picture 1)



Picture 1. Distribution of respondents by gender

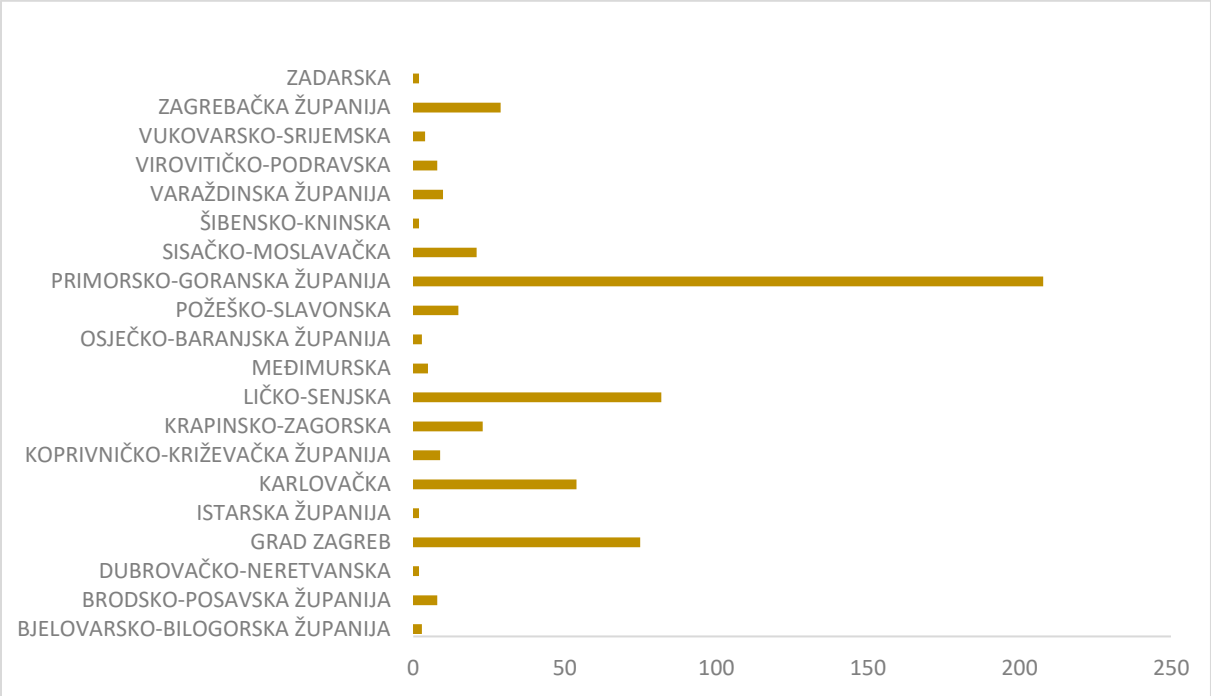
Regarding age, the respondents were divided into the following age groups: 7-9 years (1/0%), 10-14 years (6/1%), 15-19 years (26/5%), 20-29 years (103/19%), 30-39 years (133/24%), 40-49 years (111/20%), 50-59 years (99/18%) and 60+ years (68/13%). (Picture 2)



Picture 2. Distribution of patients with hemorrhagic fever with renal syndrome according to age

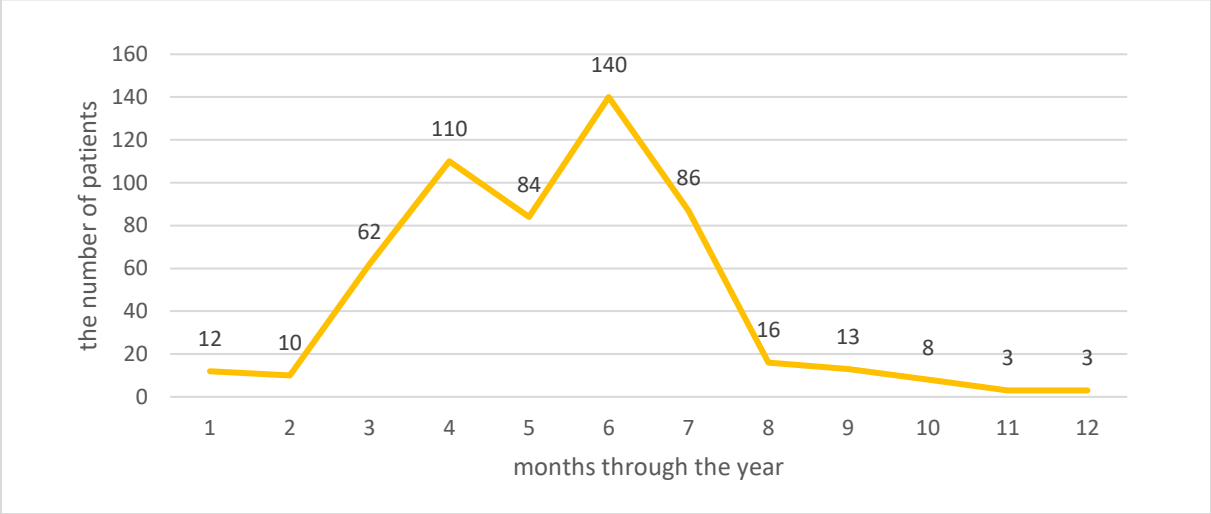
The largest number of patients was in the age group of 30-39 years of age, and the average age of the patients was 37.9 years. According to the geographical distribution,

the highest number of patients was from the Primorje-Gorski Kotar County (207), followed by the Ličko-Senjska County (81), the City of Zagreb (74), the Karlovac County (53) and the Zagreb County (28). (Picture 3)



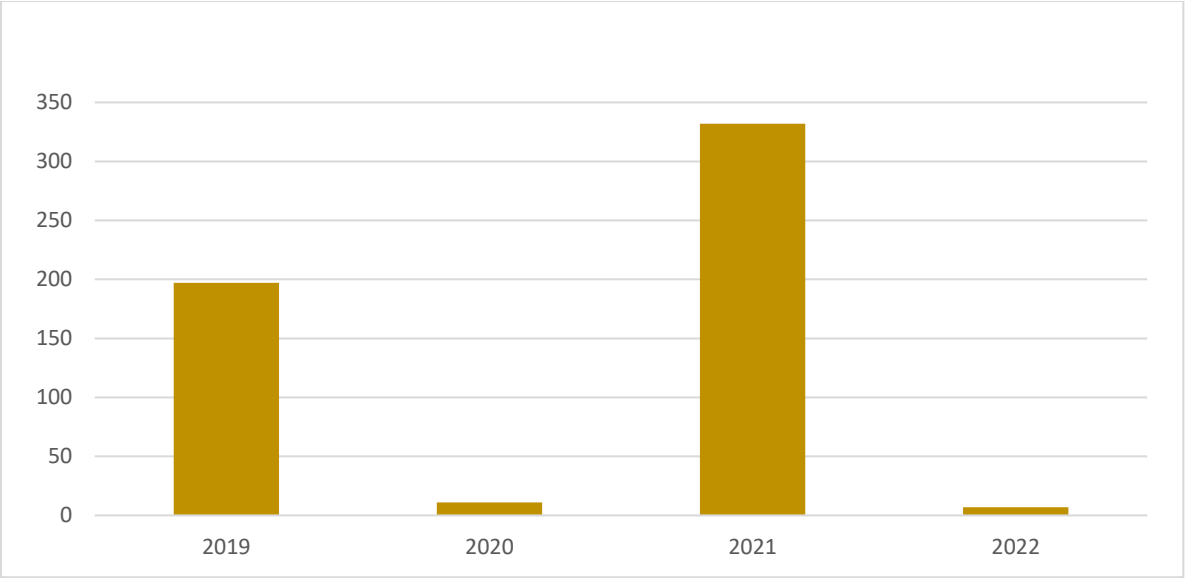
Picture 3. Distribution of hemorrhagic fever patients with renal syndrome by county in the Republic of Croatia

When we study the incidence of the number of patients with regard to seasons and months of the year, we see that the largest number of patients was recorded in June (140 persons), followed by April (110 persons), July (86) and May (84). The largest number of patients is in spring and summer (Picture 4).



Picture 4. Number of patients with hemorrhagic fever with renal syndrome by month, from 2019 to 2022 years

In the period from 2019 to 2022, which is also marked by the COVID-19 pandemic, the largest number of patients was in 2021, when 332 patients with HGBS were reported, then in 2019, 197 patients were reported, while in 2020, 11 patients and 7 patients in 2022. (Picture 5)



Picture 5. Number of patients with hemorrhagic fever with renal syndrome from 2019 to 2020 years

DISCUSSION

The study results indicate a significant number of HGBS patients in Croatia during the observed period from 2019 to 2022 years. A total of 547 people were infected during the period of four years. Next, the

data show differences in the incidence of HGBS between the sexes. Men made up the majority of patients (78%), while the proportion of women was smaller (22%). The age group of 30-39 years was the most affected by HGBS, with 133 patients (24%). These results are expected and similar to the researches published in Slovenia, Germany, America and Southeast Europe (12-19) and earlier epidemics in Croatia (men 76.6%-79%; average age 36.6-40 years) (7-10). According to previous studies, men are more likely to suffer from HGBS due to occupational exposure to rodents, as many as 40% of hospitalized patients cited occupational exposure as a risk factor (8-10). These data point to the need for a targeted approach to prevention, to strengthen protection and education for that specific profession and excursionists. Analyzing the geographical distribution of the sick, we notice that the most cases were recorded in Primorje-Gorski Kotar County (207), Lika-Senj County (81), the City of Zagreb (74), Karlovac County (53) and Zagreb County (28), which was expected since that precisely these are endemic hotspots (8-10). It is also interesting to note that the disease occurs throughout the year, but the highest number of cases is recorded from March to August, when rodent activity is at its highest. This information is certainly useful for planning surveillance interventions aimed at reducing the number of patients. Furthermore, the analysis of the time period from 2019 to 2022 years shows a significant increase in the number of cases in 2021, with 332 cases of HGBS reported, indicating a potential link between the measures to control the pandemic of COVID-19, which included isolation and recommendations that people living in mountains, forests and solitude and the increased number of people suffering from hantavirus infections in 2021. Although the suppression of the COVID-19 pandemic was necessary to protect public health, it is possible that certain consequences of such measures affected the risk of hantavirus infection.

CONCLUSION

In the period from 2019 to 2021 years, there were 547 patients with HGBS in the Republic of Croatia, with men suffering from it more often than women (78.0% vs. 22.0%). The highest activity was recorded in Primorje-Gorski Kotar and Lika-Senj counties from March to August in the age groups of 30 to 39 years. In 2021, 332 patients were reported, which is more than the average, and this can be connected to the more frequent stay of people in nature due to recommendations to reduce the number of patients with the COVID-19 disease. The conducted analysis emphasizes the

importance of studying the epidemiological characteristics of hantavirus infections for public health, enabling the identification of high-risk areas, the recognition of epidemics and the adoption of appropriate control and prevention measures.

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INFEKCIJA HANTAVIRUSOM - EPIDEMIOLOŠKE ZNAČAJKE NA PODRUČJU REPUBLIKE HRVATSKE U VRIJEME PANDEMIJE COVID-19

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SAŽETAK

Hantavirusi su uzročnici hemoragijske groznice s bubrežnim sindromom (HGBS). Ljudi se najčešće zaraze udisanjem kontaminiranog aerosola, no do infekcije može doći i putem kontaminirane hrane ili vode. Od HGBS-a godišnje u prosjeku oboli osamnaest osoba izvan epidemija. Najčešće obolijevaju muškarci u dobi od 20 do 40 godina, osobito poljoprivrednici, vojnici, šumari i planinari. Poznata žarišta u Hrvatskoj su Lika, Gorski kotar i Medvednica. Cilj: Analizirati učestalost i epidemiološka obilježja hantavirusnih infekcija u Republici Hrvatskoj tijekom pandemije COVID-19. Materijali i metode: Analizirani su podaci o incidenciji HGBS-a po županijama, sezonskoj pojavnosti, dobnim skupinama i spolu, te povezanost preporuka za boravak u prirodi u sklopu suzbijanja pandemije Covid-19 s potencijalnim porastom u broju pacijenata s HGBS. Retrospektivnom analizom obrađeni su podaci prikupljeni u Hrvatskom zavodu za javno zdravstvo, a deskriptivnim metodama statističke analize u programskom sustavu Microsoft Excel. Rezultati: U razdoblju od 2019. do 2021. godine bilo je 547 pacijenata s HGBS-om, pri čemu su češće obolijevali muškarci nego žene (78,0% naspram 22,0%). Najveća aktivnost zabilježena je u Primorsko-goranskoj i Ličko-senjskoj županiji od ožujka do kolovoza u dobnim skupinama od 30 do 39 godina. U 2021. godini prijavljeno je 332 oboljelih, što je više od prosjeka, a to se može povezati s češćim boravkom ljudi u prirodi zbog preporuka za smanjenje broja oboljelih od bolesti COVID-19. Zaključak: Proučavanje epidemioloških obilježja hantavirusnih infekcija važno je za javno zdravstvo jer omogućuje prepoznavanje područja s povećanim rizikom od infekcije, prepoznavanje epidemija i donošenje odgovarajućih mjera kontrole i prevencije.

Ključne riječi: Hantavirus, Epidemiologija, COVID-19, Hrvatska

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