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Short Communication

Hemorrhagic Fever with Renal Syndrome in Montenegro

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SUMMARY: The objective of the study was to analyze the epidemiological features of hemorrhagic fever with renal syndrome (HFRS) in Montenegro. The study included 169 cases of HFRS diagnosed in the period between 1995 and 2005 according to the clinical symptoms and serological confirmation. For the analysis of the demographic characteristics of the cases, as well as of the chronological and topographical features of the disease, a descriptive epidemiological method was employed. The average incidence rate in the observed period was 2.6 per 100,000. In the observed period, 8 people died; the average case fatality rate was 4.8% (range: 0.1 - 15%). Among the diseased persons, 116 were males and 53 were females; most of the cases were adults. The greatest number of HFRS cases occurred during the summer months. The highest incidence rates were registered in the northeastern, rural part of the country. The most frequent type of hantaviruses in Montenegro were Dobrava-Belgrade and Hantaan, carried by rodent species, i.e., the yellow-neck mouse and the striped-field mouse. It is likely that HFRS in Montenegro will become more common in the near future, unless public health control measures are taken.

Hemorrhagic fever with renal syndrome (HFRS) is zoonosis and has a sudden onset characterized by high fever, renal insufficiency, and hemorrhage. The disease is caused by serotypes Hantaan (HTN), Seoul (SEO), Puumala (PUU), and Dobrava-Belgrade (DOB), which are grouped into a genus known as the hantaviruses, members of the family *Bunyaviridae* (1,2). Although rodents are the major reservoir, antibodies against hantaviruses are present in wild and domestic animals (3,4). Humans become infected through contact with urine, saliva, or feces from infected rodents, primarily via inhalation of virus-contaminated aerosols of rodent excreta (4,5). Hantaviruses that can cause this illness are spreading throughout Europe, including the Balkan region (5).

The objective of this study was to analyze the epidemiological features of HFRS in Montenegro. The study included all cases of HFRS diagnosed in Montenegro in the period between 1995 and 2005 reported to the Institute of Public Health in Podgorica. Data from the epidemiological questionnaires for each patient were analyzed. In the observed period, the average Montenegro population consisted of approximately 640,000 inhabitants (6). The analysis was carried out according to the demographic characteristics of the patients, as well as according to the chronological and topographical features of the disease.

In the period between1995 and 2005 in Montenegro, 169 people were diagnosed with HFRS according to the clinical symptoms of presenting cases, as well as by serological confirmation using an indirect immunofluorescence test for specific IgG conducted at the Institute for Virology and Immunology "Torlak" in Belgrade (Serbia). The average incidence rate in the observed period was 2.6 per 100,000, and varied from 16.3 per 100,000 (the highest value) in the epidemic year 1995 to 4.7 per 100,000 in the 2002 epidemic, and to zero in 1997 and 1998. In the observed period, 8 of 169 patients died. The case fatality rate was 4.8% (range: 0.1 - 15%).

The first outbreak of HFRS in Montenegro occurred in 1967, after which, four epidemics were registered in 1986, 1989, 1995, and 2002. There is some periodicity in the occurrence of these outbreaks of HFRS in Montenegro. Outbreaks are thought to be associated with changes in rodent population densities, which may vary greatly across time, both seasonally and from year to year; this expectation holds for other regions in Europe as well, where cycles respond to such extrinsic factors as climatic change, predation, competition among different rodent species, and other factors (7-9). However, there is little information on the rodent population density in Montenegro and other Balkan regions such as Bosnia, Herzegovina, and Croatia, where HFRS threatened civilians and soldiers during the war in the former Yugoslavia, as well as post-war peacekeeping forces (10,11).

Higher incidence rates were registered in the northeastern part of the country, in the municipalities of Berane, Plav, Mojkovac, Pluzine, and Kolasin (Figure 1). These are rural

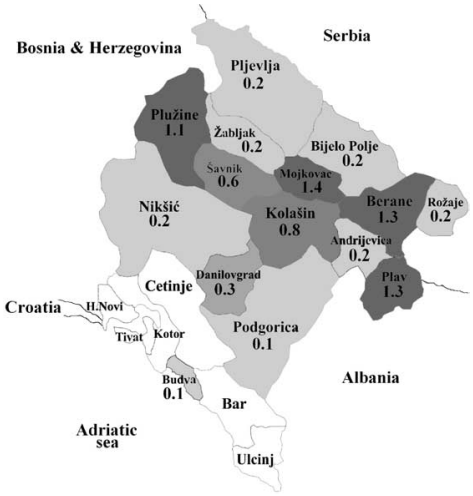

Fig. 1. Spatial distribution of HFRS in Montenegro in the period between 1995 and 2005.

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Table 1. Age distribution of HFRS cases in Montenegro in the period between 1995 and 2005

Age (y)	0-4	5-9	10-19	20-29	30-39	40-49	50-59	>60	Total
No. of cases	2	3	27	29	33	34	23	18	169
Rate (%)	1.2	1.8	16.0	17.2	19.5	20.1	13.6	10.7	100

Adult 86.4%; others 13.6%.

regions of Montenegro with mountains of over 1,000 m above sea level. In the seaside region, there were no registered cases of HFRS, with the exception of one patient in Budva, who was most probably infected in another municipality. In Podgorica, the capital of Montenegro, people acquired the infection outside the town. Epidemiological investigation has connected viral exposure to human activities such as agricultural work, threshing, hunting, and sleeping on the ground. Indoor exposure was linked to an invasion of homes by field rodents into houses during periods of cold weather and to the nesting of rodents in or near the dwellings of persons living in relatively poor housing conditions (7,12).

The seasonal distribution of the disease in summer and early autumn could be accounted for by human activities in the mountainous regions of Montenegro, as well as by rodent activity (7,12). The majority of male cases (116 out of 169 cases; 68.4%) in the adult age group between 10 and 59 (86.4%) (Table 1) were connected with professional exposure (e.g., working in a forest, hunting, etc.) in positions almost exclusively occupied by men, as in other parts of Europe (13-15).

Serological analysis by indirect immunofluorescence assay using HTN, SEO, PUU, and DOB antigens revealed that the most frequent serotypes (90%) in Montenegro were DOB and HTN, whereas PUU and SEO together accounted for less than 10% of the cases. This pattern is similar to those of other European regions (5,10,16-21). The present results are in concordance with the distribution of the most prevalent rodent reservoirs of hantaviruses in Montenegro, i.e., the *Apodemus flavicollis* (yellow-neck mouse) and *Apodemus agrarius* (striped-field mouse), and less frequently *Clethrionomys glareolus* (red bank vole); this trend is also similar to that observed in other regions in Europe (7,11,12,17).

In Montenegro as in many other parts of the world, the aerosol route is the most common means of transmission of this pathogen between rodents, and from rodents to humans; however, contaminated food and water cannot be excluded as transmission routes (7,12).

No disease was registered in urban dwellings, and thus we can conclude that in Montenegro, the rural type of HFRS is dominant. In some countries (e.g., Japan, China, and Korea), HFRS occurs in large cities (22-24), although in Japan, there have been no registered cases since 1984.

Rodent control is crucial for the prevention of HFRS. Environmental changes may affect the geographic distribution abundance and dynamics of rodent reservoirs, and in turn influence the epidemiology of hantaviruses. It could be expected that these diseases will become more common in the near future, unless public health control measures are improved.

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