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Investigation of Seroprevalence of Crimean-Congo Hemorrhagic Fever in Samsun Region

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ABSTRACT

Crimean-Congo Hemorrhagic Fever (CCHF) is a highly deadly infection transmitted to humans by ticks, has an acute course, and progresses with bleeding. The disease entered Turkey for the first time in 2002 and has continued until today. The primary source of transmission of the disease to humans is ticked and contact with the body fluids of infected animals or humans. Since animals have the subclinical disease, they have an important place, especially in human transmission. In this study, serum of people living in the urban and rural areas of Vezirkopru district and the rural areas of Kavak district are endemic in terms of CCHF disease in Samsun, without a history of tick bite and who came to the hospital for health check-ups were used.

While serums were collected from the district urban and rural areas in Vezirkopru, only rural areas in the Kavak district were collected between January 2020 and March 2020. A total of 336 (168 Vezirkopru, 168 Kavak) serums were tested for CCHF Virus IgG antibodies. As a test result, 15 (8.9%) serum collected from Vezirkopru and 12 (7.1%) serum collected from Kavak were positive. When the studies conducted throughout Turkey are examined, the seroprevalence rate determined in the region was found to be close to the endemic regions.

Keywords

Crimean-Congo hemorrhagic fever virus, ELISA, Human seroprevalence, Ticks.

Introduction

Crimean-Congo hemorrhagic fever (CCHF) is an acute, highly contagious, and life-threatening viral infection with a case fatality rate of up to 30%. The causative agent is in the genus Orthonairovirus from the family Nairoviridae. The virus is transmitted to humans by the bite of an infected tick or by direct contact with infected body fluids of patients [1-3].

The disease is among the most widely distributed hemorrhagic fever viruses, with cases reported in Africa, the Middle East, Asia, and Southern and Eastern Europe [4].

CCHF disease was first defined in 1944 as an acute febrile illness with severe bleeding seen in more than 200 agricultural workers and soldiers in the Steppe region of Western Crimea. The viral etiology of this disease has not been clarified for a long time. As a result, it was understood that the disease was caused by the same virus seen in Central Asian Republics and known for years. With diagnostic methods and international studies, Crimean Hemorrhagic Virus, similar to Congo Fever viruses, endemic in Asia and Russia and progresses with severe bleeding and high mortality in Africa, has been identified. The first isolation of Congo Virus was isolated from a patient in Kisangani, Republic of the Congo, in 1956. It was under preparation in the 1970s as the Crimean Congo Hemorrhagic Fever (CCHF) virus [5,6]. CCHF records are tick-borne and are most common in Africa, Asia, Eastern Europe, and the Balkan peninsula. CCHF has been reported in Turkey since 2002 [7-9].

CCHF outbreaks threaten public health in endemic areas due to their epidemic potential, high mortality rate, potential bioterrorism agents, and difficulties in treatment. In order to develop treatment options, diagnostic methods, and potential vaccines, it is necessary

to understand the genetic changes, virulence factors, and biology of the virus well [10].

Today, virus isolation in vitro cell cultures is the gold standard for detecting the CCHF disease virus. However, this is not always possible given the laboratory requirements and the working expert conditions. Another test method, RT-PCR, is used in diagnostic and epidemiological studies in many developed countries. Antibodies in serum used in serological diagnostic tests generally appear in the first nine days. IgM and IgG antibodies are the essential criteria in viral diagnostic tests. Both types of antibodies can be seen up to seven days after the disease appears. However, specific IgMs remain detectable four months after the disease has passed.

In contrast, IgGs can be detected in the blood for at least five years. IgM plays a decisive role in detecting new infections and IgG in the detection of past infections. [11-12].

Method

Collection of serum samples

For this purpose, Kavak and Vezirkopru, two districts where CCHF is endemic, were selected. The serums taken for health check-ups tests from individuals who applied to both district state hospitals between January and March 2020 were portioned to be used in the study. In this way, a total of 336 serums, 168 from both districts, were collected. The collected serums were stored at -20°C for later use.

Performing ELISA tests

Serum stored at -20°C was taken and thawed at room temperature. After thawing at room temperature, the serum was kept in a water bath at 56°C for 30 minutes for inactivation. After this process, Indirect ELISA was performed with the VectoCrimean-CHF-IgG (Vector Best, Russia) ELISA kit in line with the manufacturer's instructions. Sample (S), positive control (Pc), and negative control (Nc) were used in each plate. Optical densities at 450 nm wavelength were determined, and results were calculated using an automated ELISA reader (BIOTEK-ELX800).

Statistical analysis

Statistical analyzes were performed after the data obtained from the study were uploaded to the computer environment via "SPSS (Statistical Package for Social Sciences) for Windows 25.0 (SPSS Inc, Chicago, IL)". Descriptive statistics were presented as mean±standard deviation, minimum and maximum values, frequency distribution, and percentage. Chi-square test and chi-square test with continuity correction were used to evaluate categorical variables. The suitability of the quantitative variables to the normal distribution was examined using the histogram, coefficient of variation, skewness and kurtosis level, and the Kolmogorov-Smirnov Test. The Mann-Whitney U test was used to determine statistical significance between two independent groups for the variables found not to fit the normal distribution.

Ethical Consideration

This study was carried out with the approval University of Health Sciences Samsun Education and Research Hospital Non-Interventional Clinical Research Ethics Committee dated 24.03.2021 and decision number 2021/6/2.

Results

A total of 336 participants, 153 men and 183 women, aged 10-89 years, who applied to Vezirkopru and Kavak state hospitals for control and had no history of tick bite, were included in the study. Of the 336 samples tested, 27 were positive (8%). Twelve of the IgG positives were male and 15 were female.

One hundred sixty-eight serum samples (73 men and 95 women) were collected from Vezirkopru district urban and rural areas. The mean age of the participants who applied to Vezirkopru State Hospital was 47.94 (14 years, 88 years). As a result of the indirect ELISA tests, 15 (8 women and 7 men) (8.9%) of the serum obtained from Vezirkopru were IgG positive. Of the positive sample results obtained from Vezirkopru, seven were rural, and eight were urban. Although the mean age (55.6 years) of IgG positive samples taken from Vezirkopru was higher than the mean age of IgG negative samples (47.1 years), there was no statistically significant difference between them (p=0.077). There was no statistically significant difference between IgG positive and IgG negative samples taken from Vezirkopru in terms of gender (p=1,000). There was no statistically significant difference between rural and urban aspects between IgG positive and IgG negative samples taken from Vezirkopru (p=0.553).

A total of 168 serum samples (80 men and 88 women) were collected from the rural areas of Kavak. As a result of indirect ELISA tests, 12 (7 women and five men) of 168 serum samples taken from Kavak (7.1%) were IgG positive. The age data of the samples taken from Kavak State Hospital were not known. In addition, all of the samples taken from Kavak were obtained from rural areas. There was no statistically significant difference between IgG positive and IgG negative samples taken from Kavak in terms of gender (p=0.898).

According to the results of all samples (n:336) included in the study from Vezirkopru and Kavak, there was no statistically significant difference between IgG positive and IgG negative samples in rural-urban (p=0.548). Rural and urban sample results are shown in table 1.

Discussion

CCHF IgG positivity was found in 75 of them in a study collecting 750 serum in the Tokat region. In this study, 240 serums were obtained from the control group, 150 serum from healthcare workers, 26 serum from people working with animals, 193 serum from relatives of CCHF patients, and 106 serum from individuals with a history of tick bites. As a result of the study, 11 positivity was found in the control group, 3 in the health workers, 6 in the people working with animals, 44 in those relatives of CCHF

Table 1: The table shows the results of the sample of the Vezirkopru and Kavak districts.

Variables	Samples results				p
	Positive		Negative		
	N=	%	N=	%	
Areas					
Kavak Rural	12	44,4	156	50,5	0,548*
Vezirkopru Rural	7	25,9	54	17,5	
Vezirkopru Urban	8	29,6	99	32,0	
Total	27	100	309	100	336

* Pearson Chi-Square

patients. In comparison, 11 positivity was found in those with a history of the tick bite [2].

In a serosurvey study conducted in Kirklareli, CCHF IgG positivity was found in 10.9% of the samples taken from 193 participants living in rural areas. They detected 10.9% CCHF IgG positivity from these blood samples [13].

A study conducted with 3557 serums in the Central and North Anatolian region detected a 10% IgG positivity [14].

CCHF virus genomic RNA was detected in ticks in Vezirkopru. This IgG positivity indicates that the virus may still be circulating in the area [15].

In a study examining 625 healthcare workers living in Giresun, Gumushane, Artvin, Erzincan, 13.6% positivity was obtained in healthcare workers. In particular, they stated in their study that the average age of positive cases was higher than that of negative cases and that 78.6% of the positive cases were from people living in rural areas [16].

A 2.3% positivity rate was reported in a study conducted with 1066 serums representing a population of 48.500.000 in Istanbul, Samsun, Erzurum, Yozgat, Aydin, Adana, and Gaziantep regions. Accordingly, the distribution of positivity by provinces is as follows: Istanbul (2%), Samsun (1%), Erzurum (1.3%), Yozgat (7.5%), Aydin (1.3%), Adana (0.7%), and Gaziantep (1.1%) was determined. In the light of this information, the positivity rate was 1.8% for urban areas and 4.1% for rural areas [17].

In another study, 372 serums were studied in the Erzincan region. The total positivity rate was found to be 14%. The serum samples were taken from those who had a history of the tick bite (174), who were engaged in working with livestock (145), and who lived in the city and had no contact with animals (53). This result determined positivity rates as 16.7%, 12.4%, and 9.4%, respectively [18].

In the study conducted with the serum of 1000 healthy blood donors in the Konya region, a positivity rate of 0.8% was found [19].

A high rate of 19.7% was found in a study conducted with a total of 293 serums in Aydin. The results of this study were compared with other regions, and the region was stated as endemic in terms of CCHF disease [20].

Our study used the serum of 336 participants who applied to the district state hospital for health check-ups, living in Vezirkopru district urban and rural areas and Kavak district rural, to determine CCHF IgG seroprevalence. In this study, 8.9% of Vezirkopru and 7.1% of Kavak were found positive. The result of this study suggests that the CCHF virus is still circulating in the region.

Limitations

This study has some limitations: In serum samples taken from Kavak State Hospital, samples taken from the urban area were excluded from the evaluation. In addition, detailed age data of the samples taken from the rural area of Kavak were not known.

Conclusion

CCHF virus is transmitted by ticks, fluids such as blood of infected animals; The incidence is higher in occupational groups such as veterinarians and butchers who live in rural areas and people working with animals. Therefore, the presence of antibodies in the population should be monitored by performing seroprevalence studies at regular intervals. The necessary information should be given to the individuals by experts to prevent the disease. In addition, hospitals located in regions where the disease is endemic should have appropriate laboratories to detect CCHF.

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