Recommended precaution procedures protect healthcare workers from Crimean-Congo hemorrhagic fever virus

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S U M M A R Y

Objectives: The Crimean-Congo hemorrhagic fever (CCHF) virus can spread from person to person and may cause nosocomial outbreaks among healthcare workers (HCWs). The US Centers for Disease Control and Prevention have recommended the use of personal protective equipment (PPE). We investigated the compliance of HCWs with PPE usage during the follow-up of patients, and also the number of risky contacts that occurred between patients and HCWs. We also aimed to determine the seroprevalence of CCHF virus in HCWs.

Methods: This study was conducted at Cumhuriyet University Education and Research Hospital, a medical center located in a highly endemic area for CCHF where a total of 1284 confirmed CCHF patients were followed-up between 2002 and 2012. All HCWs who were at risk of CCHF virus contact and infection were included in the study. The compliance of the HCWs with PPE usage and the number of contacts that had occurred were recorded. HCW serum samples were analyzed for CCHF virus IgM and IgG by ELISA.

Results: The total rates of PPE usage were 93.7% for gowns, 77.4% for gloves, and 38.9% for masks; the highest compliance was detected in the infectious diseases ward: 100%, 88.6%, and 82.9%, respectively. A total of four HCWs had a history of high-risk contact with contaminated material (two percutaneous exposure and two mucosal contacts), but the number of low-risk contacts was quite high. The total seroprevalence rate was only 0.53%.

Conclusions: Although the HCWs at our medical center have dealt with an extremely high number of CCHF patients during the last decade, the total seropositivity for CCHFV IgG was only 0.53%. This low rate may be a result of high compliance with PPE usage and also regular education programs.

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1. Introduction

Crimean-Congo hemorrhagic fever (CCHF) is a potentially fatal viral infection mostly reported from Africa, Asia, Eastern Europe, and the Middle East.1,2 The CCHF virus (CCHFV) is a tick-borne virus belonging to the genus Nobiviruses of the Bunyaviridae family. This virus generally causes an acute febrile illness in humans, often accompanied by hemorrhagic manifestations, and has a mortality rate of 5–30%.3 Humans are infected mostly by tick bites (Hyalomma spp) or by direct contact with the blood or tissue of viremic livestock.4,5 However, CCHFV may also spread from person to person and can cause nosocomial outbreaks with a high mortality rate among healthcare workers (HCWs). The activities with a high risk of viral transmission include needle-stick injury, interventions for gastrointestinal bleeding, emergent operations for unsuspected cases, and unprotected handling of infected materials.6,7 Other routes of transmission such as close contact and respiratory contact are the subject of debate. The US Centers for Disease Control and Prevention have recommended that if a patient with a viral hemorrhagic fever has respiratory symptoms, a face shield or surgical mask and eye protection should be used by HCWs to prevent droplet contact. However, epidemiological studies indicate that such infections are not readily transmitted from person to person by airborne route.8–11

CCHF cases were first identified in Turkey in 2002, and, according to the literature, this country is now one of the most risky areas for the disease.1,12–15 However, the mortality rate of
CCHF in Turkey is reported to be lower than in other areas.\textsuperscript{7,12} It is known from molecular epidemiology and phylogenetic studies that there are different genetic strains and this may explain the differences in mortality rates in different regions of the world.\textsuperscript{7,12,16–18} The majority of cases in Turkey have been reported from the northeastern provinces (Tokat, Sivas, Gumushane, Amasya, Yozgat, and Corum), and our hospital is located in this highly endemic region, serving as a tertiary care reference hospital. A total of 1284 confirmed CCHF cases have been followed-up at our hospital since 2002.

We conducted this study to determine the compliance with personal protective equipment (PPE) usage of HCWs during the follow-up of patients with CCHF; HCWs worked on the wards or handled contaminated materials from these patients in the laboratory. Furthermore, we recorded the number of risky contacts between the patients and HCWs, and also analyzed the serum seropositivity for CCHFV IgM and IgG of all HCWs at risk, and thus aimed to determine the possible risk factors for seropositivity among HCWs in Turkey.

2. Materials and methods

This study was conducted at Cumhuriyet University Education and Research Hospital. This hospital is located in a high-risk region for CCHF where the disease is endemic, and serves as a tertiary care reference hospital for the northeastern part of the country. Acute and convalescent phase serum samples of the patients were sent to the virology laboratory of Rekif Saydam Hygiene Center in Ankara for serologic and virologic analysis. The serum samples of the patients with epidemiological risk factors or with clinical and laboratory findings compatible with CCHF were analyzed for CCHFV RNA by reverse-transcriptase PCR and CCHFV-specific IgM by ELISA; if at least one revealed a positive result, the patient was defined as a confirmed CCHF case. A total of 1284 confirmed CCHF patients were followed up at our hospital between 2002 and 2012; 91 of these patients (7.09%) died.

Our aim was to analyze all the HCWs at risk of viral infection. Therefore the study group included all the HCWs (physicians, nurses, housekeeping staff, and laboratory technicians) who have worked on the wards, and also HCWs in the laboratory who may have handled contaminated material. The following departments were included: infectious diseases, pediatric infectious diseases, emergency department, internal medicine, hematology, intensive care unit (ICU), and the laboratories. A face to face interview questionnaire was used for data collection and was completed with the HCWs 3 months after the care of the last definitive case (December 2012). An interviewer explained the study purposes to all the HCWs and obtained their consent. All the HCWs who had been at risk accepted participation in the study. The questionnaire was used to collect information on HCW characteristics, including age, sex, occupation, working department, time HCW had worked in the selected department, history of tick exposure, history of travel to an endemic region, living in an endemic region, and history of any risky activity (animal husbandry, farming, hunting, and butchery), and also on compliance of the HCWs with the recommended precaution procedures. Recommendations for infection control while providing care to patients with suspected or confirmed CCHF include the following: isolation of the patient and standard infection control precautions, i.e., basic hand hygiene, use of PPE (gloves, gown, and mask), and also the use of face shields and eye protection when caring for patients with respiratory symptoms to prevent droplet contact. Samples taken from CCHF patients should have been handled by trained and equipped laboratory staff.\textsuperscript{5,7,19,20} In addition, HCWs were questioned in detail regarding their exposure to the blood or sanguineous body fluids (saliva, sweat, vomit, feces, and urine) of CCHF patients and also other possible low-risk contacts that could result in the possibility of viral transmission. The contacts that occurred between the patients and the HCWs were recorded in detail and were grouped into the following: percutaneous exposure, mucosal contact with blood or sanguineous body fluids, skin (intact) contact with blood or other sanguineous body fluids, physical contact with a CCHF patient without wearing gloves, and proximity to a CCHF patient closer than one meter (without mask).

Three months after the last definitive case (December 2012), serum samples were obtained from the HCWs and were analyzed for CCHFV IgM and IgG by ELISA (Vectocrimean-CHF-IgM and IgG, Vector-best, Koltsovo, Novosibirsk, Russia), in accordance with the manufacturer’s recommendations; this was carried out in the Department of Medical Microbiology, Cumhuriyet University School of Medicine.

2.1. Statistical analysis

SPSS version 14 for Windows (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. Parametric data were expressed as the median (min–max) and categorical data as percentages. Proportions for categorical variables were compared using the Chi-square test. A p-value of <0.05 was considered significant in all analyses.

3. Results

A total of 190 HCWs, including 57 (30.0%) nurses, 47 (24.7%) physicians, 45 (23.7%) laboratory technicians, and 41 (21.6%) housekeeping staff participated in the study. Their median age was 31 years (range 20–55 years) and 104 (54.7%) were women. The basic characteristics of the study participants are shown in Table 1.

Compliance of the HCWs with PPE usage during the follow-up period was also analyzed. There were no statistically significant differences between the male and female participants (p > 0.05). The use of gloves in the older age group (≥31 years) was lower (p = 0.003), but there were no statistically significant differences

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, median (min–max)</td>
<td>31 (20–55)</td>
</tr>
<tr>
<td>Gender, n (%)</td>
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<tr>
<td>Female</td>
<td>104 (54.7)</td>
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<tr>
<td>Male</td>
<td>86 (45.3)</td>
</tr>
<tr>
<td>Occupation, n (%)</td>
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</tr>
<tr>
<td>Nurse</td>
<td>57 (30.0)</td>
</tr>
<tr>
<td>Physician</td>
<td>47 (24.7)</td>
</tr>
<tr>
<td>Housekeeping staff</td>
<td>41 (21.6)</td>
</tr>
<tr>
<td>Laboratory technician</td>
<td>45 (23.7)</td>
</tr>
<tr>
<td>Department, n (%)</td>
<td></td>
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<tr>
<td>Infectious diseases</td>
<td>35 (18.4)</td>
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<tr>
<td>Pediatric infectious diseases</td>
<td>20 (10.5)</td>
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<tr>
<td>Emergency department</td>
<td>26 (13.7)</td>
</tr>
<tr>
<td>Internal medicine</td>
<td>21 (11.1)</td>
</tr>
<tr>
<td>Hematology</td>
<td>14 (7.4)</td>
</tr>
<tr>
<td>ICU</td>
<td>23 (12.1)</td>
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<tr>
<td>Laboratory</td>
<td>51 (26.8)</td>
</tr>
<tr>
<td>Years of work, median (min–max)</td>
<td>5 (1–21)</td>
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<td>History of tick exposure, n (%)</td>
<td>4 (2.1)</td>
</tr>
<tr>
<td>Living in an endemic region, n (%)</td>
<td>7 (3.7)</td>
</tr>
<tr>
<td>History of travel to an endemic region, n (%)</td>
<td>93 (48.9)</td>
</tr>
<tr>
<td>History of risky activity, n (%)</td>
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<tr>
<td>Animal husbandry</td>
<td>4 (2.1)</td>
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<tr>
<td>Farming</td>
<td>3 (1.6)</td>
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<tr>
<td>Hunting</td>
<td>5 (2.6)</td>
</tr>
<tr>
<td>Butchery</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>Total, N (%)</td>
<td>190 (100)</td>
</tr>
</tbody>
</table>

ICU, intensive care unit.
for the use of gowns or masks between the younger and older age groups \( (p > 0.05, \text{ Table } 2) \). While there were no differences between the occupational groups with regard to gown use \( (p = 0.13) \), the use of gloves and masks were lower among laboratory technicians \( (p = 0.001, p = 0.001, \text{ respectively}) \). Total rates of PPE usage among the HCWs were found to be 93.7% for gowns, 77.4% for gloves, and 38.9% for masks; the highest compliance was found among the HCWs of the infectious diseases ward: 100%, 88.6%, and 82.9%, respectively. However, PPE usage in the hematology department was significantly lower than in the other departments \( (p < 0.05, \text{ Table } 2) \).

A history of needle-stick injury contaminated with blood was reported by two HCWs, and a history of mucosal contact with blood or sanguineous body fluids was reported by two others. Ribavirin prophylaxis was provided to all but the two HCWs with mucosal contact, who refused this therapy. None of the four HCWs developed any signs or symptoms of the disease (fever, headache, vomiting, bleeding), or had any laboratory findings (alanine/ aspartate transaminase elevation, leukopenia, thrombocytopenia) compatible with CCHF disease. The low-risk contacts were also recorded and are shown in Table 3. None of the HCWs were positive for CCHF IgM and only a nurse working on the internal medicine ward was positive for CCHF IgG (very high level of positivity was observed according to cut-off values). She reported no history of tick bites and no history of febrile disease, but had a history of travel to an endemic region. Therefore, this may not be false-positivity; she might have experienced a subclinical infection as reported previously in Turkey. The total seroprevalence rate was found to be only 0.53%.

### 4. Discussion

Nosocomial transmission of CCHFV to HCWs has been reported from different countries. In particular, percutaneous exposure, interventions for gastrointestinal hemorrhage, emergency surgical interventions, mouth to mouth resuscitation, and unsafe handling of infected materials or patients have been reported as high-risk activities for viral transmission. These studies suggest that CCHF patients should be isolated and that HCWs should use PPE, including gowns, gloves, surgical masks or face shields, and eye protection, while giving care to the patients or handling their blood and other sanguineous body fluids. In most of the nosocomial outbreaks, unsuspected cases who were admitted with massive bleeding were the origin of infection in the healthcare setting. In endemic areas, each patient with a febrile hemorrhagic syndrome should be considered to have a viral hemorrhagic fever until the definitive diagnosis. The availability of appropriate protective equipment and education of HCWs about safe clinical practices and infection control is the mainstay of the prevention of nosocomial spread. Almost all of the CCHF patients were admitted to our hospital through the emergency unit, where the first evaluation of these patients was performed. Therefore, the standard isolation procedures should be applied in the emergency department before transfer of the patient to the infectious diseases department. Patients with CCHF were infrequently hospitalized in other clinics, such as hematology, internal medicine, and ICU, with a diagnosis of severe sepsis or for other hematologic diseases. A total of four patients \( (4/190; 2.1\%) \) were initially hospitalized on other wards and then transferred to the infectious diseases ward. From the first years of the CCHF epidemic in Turkey, all HCWs in our hospital at risk of nosocomial transmission have been educated regarding transmission routes and standard precaution methods. This education has been repeated each year just before the outbreak season.

Gaps in infection control practices are the common factors in the occurrence of nosocomial outbreaks. A study conducted in Iran reported a 3.87% seroprevalence rate among HCWs with a history of exposure to patients with CCHF directly or with their blood or sanguineous fluids, and no seropositivity among HCWs with any history of exposure. In another trial, the compliance with gloves and mask use was 44% among HCWs who were in close contact with patients with CCHF. The compliance rates among our

### Table 2

Compliance with personal protective equipment usage of 190 healthcare workers

<table>
<thead>
<tr>
<th>Rate of adherences to protective equipments usage, n (%)</th>
<th>Gown</th>
<th>p-Value</th>
<th>Gloves</th>
<th>p-Value</th>
<th>Mask</th>
<th>p-Value</th>
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</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Female</td>
<td>99 (95.2)</td>
<td>0.34</td>
<td>79 (76.0)</td>
<td>0.61</td>
<td>47 (45.2)</td>
<td>0.76</td>
</tr>
<tr>
<td>Male</td>
<td>79 (91.9)</td>
<td>0.88</td>
<td>68 (79.1)</td>
<td>0.003</td>
<td>28 (32.6)</td>
<td>0.78</td>
</tr>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>20–30</td>
<td>85 (93.4)</td>
<td>0.13</td>
<td>79 (86.8)</td>
<td>0.001</td>
<td>35 (38.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>≥31</td>
<td>93 (93.9)</td>
<td></td>
<td>68 (68.7)</td>
<td></td>
<td>40 (40.4)</td>
<td></td>
</tr>
<tr>
<td>Job</td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Nurse</td>
<td>52 (91.2)</td>
<td></td>
<td>41 (71.9)</td>
<td></td>
<td>27 (47.4)</td>
<td></td>
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<tr>
<td>Physician</td>
<td>47 (100)</td>
<td></td>
<td>43 (91.5)</td>
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<td>24 (51.1)</td>
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<tr>
<td>Laboratory technician</td>
<td>40 (88.9)</td>
<td></td>
<td>27 (60.0)</td>
<td></td>
<td>5 (11.4)</td>
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<tr>
<td>Housekeeping staff</td>
<td>39 (95.1)</td>
<td></td>
<td>36 (87.8)</td>
<td></td>
<td>18 (43.9)</td>
<td></td>
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<td>Department</td>
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<tr>
<td>Infectious diseases</td>
<td>35 (100)</td>
<td>0.001</td>
<td>31 (88.6)</td>
<td>0.005</td>
<td>29 (82.9)</td>
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<td>20 (100)</td>
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<td>10 (50.0)</td>
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<td>Emergency department</td>
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<td>22 (84.6)</td>
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<td>9 (34.6)</td>
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<tr>
<td>Internal medicine</td>
<td>20 (95.2)</td>
<td></td>
<td>18 (85.7)</td>
<td></td>
<td>6 (28.6)</td>
<td></td>
</tr>
<tr>
<td>Hematology</td>
<td>8 (57.1)</td>
<td></td>
<td>8 (57.1)</td>
<td></td>
<td>3 (21.4)</td>
<td></td>
</tr>
<tr>
<td>ICU</td>
<td>23 (100)</td>
<td></td>
<td>22 (95.7)</td>
<td></td>
<td>9 (39.1)</td>
<td></td>
</tr>
<tr>
<td>Laboratory</td>
<td>46 (90.2)</td>
<td></td>
<td>32 (62.7)</td>
<td></td>
<td>16 (31.4)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>178 (93.7)</td>
<td></td>
<td>147 (77.4)</td>
<td></td>
<td>74 (38.9)</td>
<td></td>
</tr>
</tbody>
</table>

ICU, intensive care unit.
participants were higher than those of the participants in Iran, with the highest rate on the infectious diseases ward and the lowest rate on the hematology ward. Although these patients stay for a short time in the emergency department and are immediately transferred to the infectious disease clinic, some applications, i.e., intravenous catheterization, urinary catheterization and monitoring, may be applied to these patients before hospitalization; however most of the interventions and all treatments, i.e., replacement of intravenous fluids, blood, and blood products transfusion, take place on the infectious diseases ward. Therefore, it is not surprising that the highest compliance rate to PPE usage among HCWs was recorded in this clinic.

The substantial impact of education on adherence to the use of recommended barrier precautions has been reported. Occupational groups were compared for compliance with PPE usage, and laboratory technicians had the lowest compliance rates for the use of gloves and masks. The compliance rates to all three PPE (gowns, gloves, and masks) were higher among physicians, which may be associated with better education and awareness. They had been trained on methods of infection control at medical school to a greater extent than the other HCWs. Training programs on infection control issues are required to improve the awareness of all HCWs, and this training should include all students in any health-related programs. Nosocomial outbreaks have been reported in several studies, with higher mortality rates. Percutaneous exposure to contaminated material is believed to have the highest risk for viral transmission from person to person. A needle-stick injury occurred in two HCWs in our study. Both injuries occurred during peripheral venous blood sampling for routine control tests. At the time of injury, both patients were in the convalescence period of CCHF disease and both HCWs were using gloves. Although the efficacy of ribavirin for the prophylaxis and therapy of CCHF is still unclear, ribavirin prophylaxis was offered. They were observed for the development of clinical signs and laboratory findings of CCHF disease, and neither HCW developed any signs or symptoms. Even though a high rate of transmission with percutaneous exposure has been reported in the literature, two HCWs did not develop the disease and CCHFV IgM and IgG tests were negative. Because both of the patients involved were in the convalescence period, both HCWs were wearing gloves, and both HCWs took ribavirin prophylaxis, clinical disease or seropositivity did not occur.

There is concern regarding transmission via respiratory contact. Epidemiologic studies indicate that viral hemorrhagic fever infections are not readily transmitted by airborne route. A history of mucosal contact with blood or sanguineous body fluids was reported by two of our participants. A physician and a nurse reported probable mucosal contact with the oropharyngeal secretions of a patient with mucosal bleeding while applying cardiopulmonary resuscitation. Both HCWs were wearing gowns and gloves, but neither used a mask during the procedure. This patient was initially hospitalized with a suspicion of a hematologic disorder on the internal medicine ward, and the probable mucosal contact occurred on this ward before the patient was diagnosed with CCHF. Although ribavirin prophylaxis was recommended, both HCWs refused to take the pills. They also did not develop CCHF disease and were seronegative for CCHFV IgM and IgG. In addition, 45 HCWs (23.7%) related getting close (nearer than one meter) to CCHF patients, without wearing masks, but CCHFV IgM and IgG serologies were negative in all of them. While the usage rates of gowns and gloves were very high, the usage rate of masks was low. However, the seroprevalence rate was very low and this may be explained by high compliance of HCWs to PPE usage except masks. Furthermore, this may support the idea that CCHFV is not readily transmitted from person to person by airborne route. A similar study from Turkey reported the lack of airborne transmission of CCHFV to HCWs. However, if a patient with a viral hemorrhagic fever has respiratory symptoms, or aerosol-generating procedures are used, additional precautions (N95 or FFP2 respirator) are indicated to prevent possible exposure to airborne particles that may contain the virus. The spread of CCHFV from person to person through close contact and direct contact with blood and other sanguineous body fluids of patients has also been reported. Direct contact with blood, clothes, and sheets were reported as the probable transmission route in three cases in a nosocomial outbreak, and direct cutaneous contact with contaminated blood was reported in a case in another study. In a seroprevalence study, more frequent seropositivity was demonstrated among HCWs who reported intact skin contact with body fluids. A total of 32 HCWs reported an intact skin contact with blood or body fluids and 25 HCWs reported physical contact with CCHF patients without wearing gowns; none of them developed clinical infections or seropositivity.

The phylogenetic and molecular epidemiology analysis of CCHFV has demonstrated the existence of different genetic strains and higher mortality rates in Asian strains. The mean mortality rate in our country was about 5% and this rate is lower than those of other countries. A study from Iran reported a 3.87% seroprevalence rate among HCWs who had a history of exposure to patients with CCHF; their blood, or sanguineous fluids. We observed a lower seropositivity rate among HCWs in the presented study. CCHF strains in Turkey are significantly similar to strains in Russia and Kosovo, and the lower mortality rate might be due to the differences in genetic lineage. In addition, these strains may be less transmissible, explaining the lower seropositivity among HCWs working at risk in Turkey.

In conclusion, we found the compliance of HCWs with the usage of PPE to be high. Although our center is one of the hospitals with the highest number of CCHF patients during the last decade, the seroprevalence rate among HCWs at risk was very low. This may be due to the higher compliance rates and also due to regular education. However, further studies are needed to evaluate whether the recommended PPE usage is sufficient to prevent nosocomial transmission among HCWs working in countries with more dangerous strains.

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Conflict of interest: The authors have declared that no competing interest exists.

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