



Short Communication

Absence of IgG antibodies among high-risk contacts of two confirmed cases of Crimean-Congo haemorrhagic fever in the autonomous region of Madrid (Spain)



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ABSTRACT

Crimean-Congo haemorrhagic fever (CCHF) is a widely distributed tick-borne disease. In Spain, the disease has emerged as outbreak associated with high-risk exposures. Our goal was to evaluate the prevalence of antibodies against the CCHF virus (CCHFV) in high-risk contacts. A cross-sectional study was conducted. Three hundred eighty-six high-risk contacts were identified comprising family contacts and hospital workers who had attended the cases. Fifty-seven cases with closer exposure were selected. However, forty-nine cases participated in the study. IgG antibodies were detected by immunoenzymatic techniques. All determinations tested negative for anti-CCHFV IgG antibodies. Most of the responders were women (73.5%), and belong to the intensive care department (53.1%). In relation to other possible sources of exposures, 18.4% travelled to countries with CCHF transmission risk. No CCHF positivity was recorded among selected high-risk contacts. This highlights the importance of standard precautions which might have protected healthcare workers and care providers from CCHF infection.

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Introduction

Crimean-Congo haemorrhagic fever (CCHF) is a widely distributed viral tick-borne disease. It is endemic in all countries south of the 50th parallel north, the geographic limit of *Hyalomma*, the main vector. In Spain, infected vectors have been detected in livestock-rearing regions [1].

The causative agent is a RNA virus which can be transmitted by the bite of infected ticks or by contact with the blood or tissues of infected patients or livestock. Nosocomial infection has been

reported due to occupational exposure to contaminated body fluids in healthcare settings and can generate outbreaks.

Clinical manifestations appear after an incubation period of 1–13 days and often include high fever, headache and myalgia, among other symptoms, which can progress to extensive bleeding, multi-organ failure and shock. Fatality rate ranges from 5% to 40% [2]. There is no specific treatment though ribavirin could be recommended in some situations with variable results [3].

Polymerase chain reaction (PCR) enables diagnosis in the acute stages of the disease. ELISA and immunofluorescence techniques can be used to determine immune response. Active infection can be detected by measuring IgM or IgG following the acute phase of infection 4–9 days after symptom onset [4]. IgM levels decrease gradually until they become practically undetectable in or around

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Fig. 1. Selection criteria of the study population. Seroprevalence of antibodies against CCHFV among high-risk contacts: Madrid Autonomous Region, 2017.

the fourth month post-infection. IgG response follows a bimodal pattern and can be detected until at least 5 years post-infection [5].

Human infection can occur asymptomatically, according to serological studies carried out in endemic countries, such as Turkey, with a seroprevalence rate of 13.6% in high-risk populations [6]. Considering the particularly high fatality rates of this disease and its epidemic potential, as well as the considerable economic implications due to the cost of high-level isolation measures [7–9], the possibility of inadvertent transmission of the virus to close contacts of CCHF cases should be ascertained [10].

In August 2016 the first outbreak of CCHF happened in Spain, with two cases associated. The first case was infected by a tick bite and the second one was a nurse who cared for the index case during his stay in Infanta Leonor Hospital of Madrid (hospital 1) and was in contact with his body fluids. CCHF was suspected after the death of the first case and the development of similar symptoms in the nurse, indicating secondary transmission. She was initially assisted in Gregorio Marañón University Hospital of Madrid (hospital 2), and was transferred to the referral hospital for highly communicable infectious diseases after the microbiological confirmation of CCHF. Nosocomial transmission could have happened in both hospitals 1 and 2. More detailed information on the two cases and contact classification and management is available elsewhere [11].

Our goal was to evaluate the inadvertent transmission of the CCHF virus to high-risk contacts of both confirmed cases of CCHF in the Autonomous Region of Madrid (Spain).

Methods

The study population comprised family members and hospital workers who met the definition of high-risk contact which includes met at least one of the following criteria: (a) Close contact (within 1 m), without appropriate Personal Protective Equipment (PPE) (or with incidents in the use of PPE), with a confirmed case that he was coughing, vomiting, bleeding or having diarrhoea; (b) Direct contact with clothes, bedding or fomites contaminated with blood, urine or fluids from a confirmed case, without the appropriate PPE (or with incidences in the use of PPE); (c) Percutaneous wound (for example, with a needle) or exposure of the mucous membranes to body fluids, tissues, or laboratory samples of a confirmed case; (d) Health care for a confirmed case or handling its samples without proper PPE (or with incidents in the use of PPE) by nurses, laboratory, ambulance, doctors and other personnel; (e) Contact with the body of a person deceased by CCHF or with clothing or fomites of the body, without the appropriate PPE (or with incidents in the use of PPE) [12,10]. Nevertheless, given the heterogeneity of the exposure, a second criteria was applied to high-risk contacts in order to select those with closer contact, based on the type and duration of the exposure.

Data collection was carried out from 5 to 20 October of 2017. The Occupational Risk Prevention Departments of hospitals 1 and 2 identified the individuals who met the selection criteria, asked them to participate in the study and obtained their informed consent. Participation consisted in completing a questionnaire and drawing a blood sample.

The questionnaire included the following variables: age, sex and country of origin; professional activity; follow-up (ribavirin use, appearance of symptoms); and travel to areas where infected ticks has been identified (endemic countries and some geographic regions in Spain).

To verify if nosocomial transmission had occurred, Ig G antibodies against CCHF virus was determined by immunoenzymatic (Vector Best, Novosibirsk, Russia) and indirect immunofluorescence (EuroImmun, Lübeck, Germany) techniques. Serological tests were performed at the National Centre of Microbiology (Carlos III Institute of Health, Spain).

Results

Fifty-seven high risk contacts were selected out of three hundred eighty-six individuals who met the high-risk contact definition (Fig. 1). The response rate was 86% (49 out of 57). Non-responders were younger (mean age of 33 years vs. 42 years) and had a higher proportion of men (40% vs. 27%), but activities performed were similar in both groups.

Most participants were women (73.5%), physicians (24.4%) or nurses (22.4%), and developed their activity in the intensive care department (53.1%) (Table 1). None of them declared any occupational exposure. During the follow-up, 10 of 49 contacts developed symptoms (20.4%), the most frequent being fever ($n=4$) followed by sore throat ($n=3$) (Fig. 2). Two of them received prophylaxis with ribavirin (4.1%).

One-fifth of the responders ($n=9$) had travelled at least to one country with risk of CCHF virus transmission, the most frequent being Greece ($n=5$) followed by Turkey ($n=4$) (Fig. 3a). One-third ($n=15$) had travelled at least to one geographical region in Spain where infected ticks has been detected (Fig. 3b).

All the serological tests performed gave negative results.

Discussion

The serological results showed that inadvertent transmission to closer high-risk contacts did not happen. We consider that the probability of transmission to the remaining high-risk contacts was even lower. These results are similar to others where IgG antibodies against CCHF virus were not detected [13], highlighting the importance of infection prevention and control measures, especially when infectious agents may not be suspected.

Table 1
Characteristics of the study population. Madrid Autonomous Region, 2017 ($n = 49$ contacts).

Characteristics		N	%
Demographics	Sex (women)	36	73.5
	Age (mean, SD)	42	11.0
Work centre	Infanta Leonor Hospital	22	45.8
	Gregorio Marañón Hospital	26	54.2
	Physician	12	24.4
	Nurse	11	22.4
Profession	Health technician	7	14.3
	Cleaning staff	7	14.3
	Nursing assistant	5	10.2
	Hospital orderly/porter	5	10.2
	Housewife	1	2.1
	Nursing student	1	2.1
	Intensive care	26	53.1
	Anatomical pathology	6	12.1
	General services	5	10.2
	Emergencies	5	10.2
Setting	Medical services	3	6.1
	Laboratory	3	6.1
	Habitual residence	1	2.0
	Ribavirin use	2	4.1
Follow-up	Appearance of symptoms	10	20.4
	CCHFV endemic countries	9	18.4
Travel to CCHF affected areas	Spanish regions with CCHFV positive ticks	15	30.6

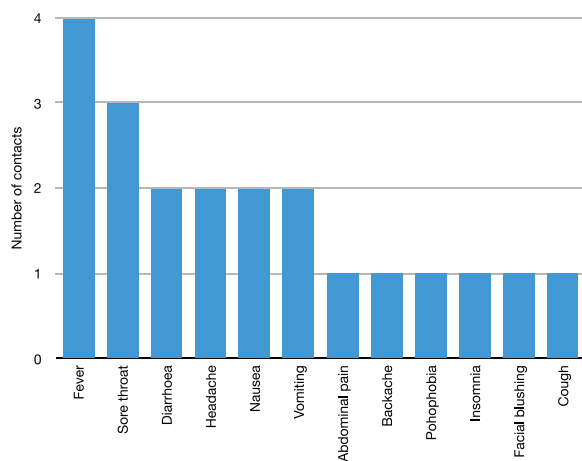


Fig. 2. Distribution of symptoms presented by the study population. Madrid Autonomous Region, 2017 ($n = 10$ contacts).

The identification of the outbreak has made it possible to test the response capacity of the public health services [14]. Half of them worked in the intensive care unit, being a key department where high-risk procedures are undertaken. Approximately half of the exposed personnel were physicians or nurses, as in another study from Turkey [15]. The results stress the importance of training all health care personnel in infection prevention and control measures to reduce the risk of nosocomial spread of emerging diseases.

Many participants had visited areas where CCHF virus has been identified. The current ease of global travel must be considered when assessing the source of infections and it should have been taken into account if any contact had tested positive.

Conclusions

There was no immune evidence of secondary transmission among studied contacts. Adherence to standard precautions may

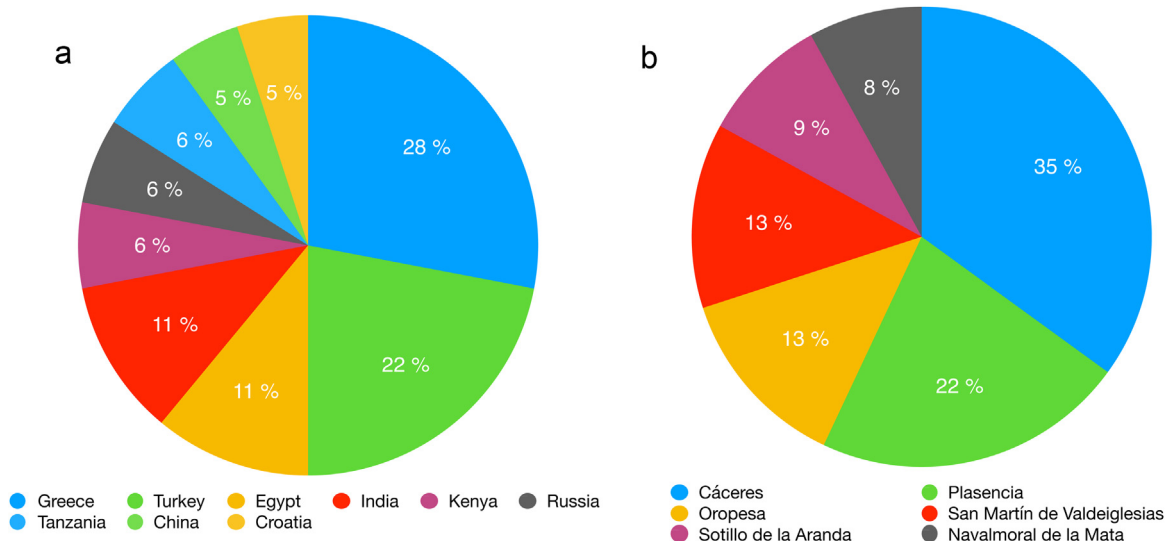


Fig. 3. (a) Travel to CCHFV endemic countries. Madrid Autonomous Region, 2017 ($n = 18$ trips). (b) Travel to Spanish regions with CCHFV positive ticks. Madrid Autonomous Region, 2017 ($n = 24$ trips).

have played an important role in the prevention of inadvertent nosocomial transmission.

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Competing interests

None declared.

Ethics committee approval

The Regional Clinical Research Ethics Committee of the Community of Madrid issues a favourable opinion for carrying out the study (Ref: 07/928301.9/17).

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