Elevated Human Crimean–Congo Hemorrhagic Fever Virus Seroprevalence in Khashm el Girba, Eastern Sudan

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Abstract. Crimean–Congo hemorrhagic fever (CCHF) is a tick-borne disease that can evolve into deadly hemorrhagic fever and that is endemic in many parts of Europe, Middle East, Central Asia, and Africa. Because of several reports about CCHF outbreaks in the south of Sudan during the last years, we examined in this study if unrecognized CCHF-V infections also occurred in the eastern and central parts of the country. The study examined the seroprevalence of CCHF virus infection in 464 sera from three regions of Sudan without previous reports of CCHF infection. The total CCHF virus seroprevalence was 2.6% (12 sera). The percentage was significantly elevated (7.5%) in sera from Khashm el Girba in eastern Sudan. The population in this area should be educated about the risk of disease transmission and how to avoid the infection. Health-care providers should be informed about the disease to identify possible cases and to prevent nosocomial transmission.

Crimean–Congo hemorrhagic fever (CCHF) is a zoonotic viral disease endemic in many countries in Europe, Middle East, Central Asia, and Africa. Natural hosts of the virus are domestic livestock. The CCHF virus (CCHF-V) is transmitted horizontally by ticks primarily of the genus *Hyalomma*. Infections occur through tick bites or crushing of infected ticks during occupational exposure to domestic ruminants. In addition, there is also a risk of human-to-human transmission related to extensive blood exposure or needle stick injury. Hemorrhagic fever begins abruptly with fever and myalgia, followed by increasing prostration, severe headache, dizziness, and various signs of gastrointestinal disturbances. Patients are severely ill and may develop additional signs of bleeding, intravascular coagulation, liver damage, and shock. The CCHF case infection rate is $\geq 1:5$ and the case fatality rate is 15–30%.¹

Crimean–Congo hemorrhagic fever virus is endemic in several countries in Africa. A seroprevalence of up to 23% was previously found in Kenya and Senegal in areas where people practice nomadic pastoralism.^{2,3} Serosurveys in Sudan have shown that CCHF-V is present in Sudan as well.^{4,5} Since 2008, Sudan has experienced several outbreaks of CCHF-V infections in the south of the country including cases of household and nosocomial infections.^{6–9} This prompted us to examine if unrecognized CCHF-V infections also occur in eastern and central Sudan.

Sera were obtained during a routine blood drawing from patients with fever in the towns Port Sudan, Red Sea state; Khashm el Girba, Kassala city, and New Halfa in Kassala state; and El Obeid, North Kordofan, in December 2012 and January 2013 as reported previously.¹⁰ One hundred thirty of 464 sera included in this study were from Port Sudan, 122 from El Obeid, 133 from Khashm el Girba, 41 from Kassala, and 38 from New Halfa (Supplemental Figure 1). Participants were between 1 and 91 years old, with a median age of 35 years. One hundred ninety-seven participants (42.5%) were male and 267 (57.5%) were female. Sixty-five sera (14.0%) were from children and adolescents younger than

20 years (Supplemental Table 1). Patients were informed about the study, and blood was drawn from those who consented to participate. Sera were prepared in the hospital laboratories by centrifugation of the clotted blood specimens and kept at -20°C until they were shipped to Khartoum and later to Leipzig, Germany.

Sera were tested with the VectoCrimea CCHF-IgG ELISA according to the instructions of the manufacturer (Vector Best, Novosibirsk, Russia). Positive sera were retested with the BLACKBOX CCHF-V IgG immune complex ELISA,¹¹ and sera that were positive in both tests were considered CCHF-IgG positive. Frequencies, odds ratios, 95% CIs, and *P*-values were calculated using Microsoft Excel and MedCalc statistical software (https://www.medcalc.org/calc/odds_ratio.php, https://www.medcalc.org/calc/comparison_of_proportions.php).

Twelve of the 464 sera (2.6%) were CCHF-V IgG positive in both tests. The frequency varied between areas. Seropositive sera were found in El Obeid (2 sera, 1.6%) and Khashm el Girba (10 sera, 7.5%) but not in Port Sudan, Kassala city, and New Halfa. Eighty-three percent of CCHF-V IgG positives were found in Khashm el Girba and the odds ratio of seropositives to be from this town was significant ($P = 0.0009$) (Table 1). One of the positive sera was from a 5-year-old girl (Supplemental Table 1).

The study confirms previous reports about the presence of human CCHF-V infections in Sudan and demonstrates that in Khashm el Girba CCHF-V infections occurred unnoticed. The overall seroprevalence found was similar to that previously reported from other parts of Sudan (1.7% and 5%).^{4,5} Compared with that, the seroprevalence was significantly elevated in Khashm el Girba. Thus, people living in the catchment area of Khashm el Girba hospital had a higher risk of acquiring CCHF infection. Most infected individuals were adults, but antibodies against CCHF-V were also found in a 5-year-old child. Crimean–Congo hemorrhagic fever virus infection of children is not unusual and has previously been recorded in Turkey and Iran, and CCHF-V IgG-positive children were found in Kenya.³ It was reported that the disease in children is milder than in adults.^{12–15}

The study was based on a serosurvey for dengue exposure performed previously in which we did not collect information about the residence or the occupation of the

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TABLE 1
Seroprevalence of CCHF virus IgG in outpatients in five towns in eastern and central Sudan

Town	State	No. of sera tested	CCHF-V IgG positive (%)	CCHF-V IgG-positive Khashm el Girba vs. the other four towns	
				Odds ratio	95% CI
Port Sudan	Red Sea	130	0 (0)	22.2*	1.28–382.7
El Obeid	North Kordofan	122	2 (1.6)	4.9*	1.05–22.7
Khashm el Girba	Kassala	133	10 (7.5)	Reference site	–
Kassala	Kassala	41	0 (0)	7.0	0.40–123.1
New Halfa	Kassala	38	0 (0)	6.5	0.37–114.3
Total	–	464	12 (2.6)	13.4*	2.89–61.9

CCHF-V = Crimean–Congo hemorrhagic fever virus.

* Values are significant ($P < 0.05$).

patients. Therefore, no conclusion can be drawn about the occupational risk factors for specific patients or whether the infections were acquired in the towns or in the surrounding areas. A known risk factor for CCHF-V infection is contact with infected livestock. Serological evidence of CCHF-V infection in livestock in Sudan was found in camels and other ruminants exported from the country, in camels in the Khartoum province, and in cattle in North Kordofan and East Darfur, indicating that the CCHF-V infection is endemic in Sudan in domestic animals.^{16–20} Compared with the large towns Port Sudan, Kassala city, and El Obeid, Khashm el Girba is smaller. It was established in the 1960s to relocate people from the Wadi Halfa region in northern Sudan that was flooded when the Assuan Dam was constructed to pond the river Nile. It is a large village-like settlement rather than an urban center. Based on talks with patients and other persons in the hospital, the people living in the surrounding area of Khashm el Girba primarily depend on nomadic pastoralism and agriculture as a source of income. In addition, some people live in the town and work in agriculture and stock farming during the rainy season. Thus, there is an overlap of urban and rural living in the town and livestock in the Khashm el Girba area, including sheep, goats, and cows, and possibly secondary human-to-human transmissions are the probable source of the infections.

In conclusion, a significant percentage of sera from Khashm el Girba in Kassala state showed signs of previous CCHF-V infection. Differential diagnosis of patients from this area with symptoms of hemorrhagic fever should include CCHF virus infection in addition to other causes such as dengue virus and possibly Rift Valley fever virus. It is important to be aware of that virus because different to hemorrhagic fevers caused by dengue or Rift Valley fever virus, infections by CCHF virus can be transmitted nosocomially and from person to person. No information was available about the place of residence and the occupation of the study participants. To obtain a better picture of the population at risk, future epidemiological studies may compare the seroprevalence in rural versus urban neighborhoods and livestock farming versus low exposure with livestock. In addition, comparison of the regional CCHF seroprevalence in livestock animals with the seroprevalence in the human population would be valuable. Further research is also recommended to identify clinical cases. In the meantime, the population should be informed about the risk of disease transmission by ticks and contact with sick family members and how to avoid infection. Health-care providers in Khashm el Girba and the surrounding area should be informed about the prevalence of the infection,

provided with clear case definitions to identify possible cases, and educated about appropriate personal protection measures.

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