



## Letter to the Editor

### Persistence of IgG antibodies in survivors of Crimean Congo hemorrhagic fever virus infection, India



To the Editor,

Crimean Congo hemorrhagic fever (CCHF) represents a serious threat to public health due to its increasing trends, high mortality rate, and no specific therapy. Till now this deadly disease has been reported from approximately 30 countries [1]. In India, it has been reported from three states viz., Gujarat, Rajasthan, and Uttar Pradesh [2,3]. Many outbreaks and sporadic cases of CCHF have been identified from various districts of Gujarat State from 2011 to 2016 [4–7]. During this period, clinical samples of all the suspected cases were referred to ICMR-National Institute of Virology (NIV), Pune, India. A total of 74 cases were tested positive for CCHF using either real-time RT-PCR or IgM-ELISA as described by Mourya et al. [4].

Although CCHF virus is known to cause an asymptomatic infection in animals; it can also cause an asymptomatic infection in humans [8]. This may pose a serious problem in the assessment of actual disease burden of CCHF among human population. Limited information is available on the persistence of IgG antibody in CCHF affected individuals. Hence, the present study was carried out to determine the IgG antibody response among the survivors of CCHF infection in India.

The patients who survived CCHF infection (n = 16) were identified and traced with the help of local health authorities from 5 districts of Gujarat State. Before the specimen collection, the purpose of the study was briefed to each survivor. The written informed consent was obtained from all participants after their approval to participate in the study. Subsequently, the blood sample of each survivor was collected in plain tubes. The samples were further transported to ICMR-NIV, Pune under the cold chain. Serum was separated from the respective tubes by centrifugation and stored at  $-80^{\circ}\text{C}$  until further use.

All the samples were screened for the presence of anti-CCHFV IgG antibodies using indigenously developed anti-CCHFV Human IgG-ELISA [9]. Appropriate controls were included in each test. The sample was considered positive if the O.D > 0.2; P/N (Positive/Negative) ratio > 1.5 and negative if O.D < 0.2; P/N < 1.5.

All the 16 survivors were tested positive for anti-CCHF virus IgG antibodies. The survivors showed the persistence of IgG antibodies ranging from 5 months to 5.5 years (Table 1). Depending on the post onset day (POD) of illness the OD value varied from 1.283 to 0.559. The OD showed a decreasing trend with the increasing POD. IgG antibodies generally become detectable from about 5th POD as earliest and are present in all CCHF survivors as late by 9th POD. A study conducted on 35 CCHF survivors from 1981 to 1987 in South Africa revealed that IgG appeared on 7–9 days of illness and persisted up to 3 years [10,11]. Our study supports the findings of

**Table 1**

Persistence of anti-CCHFV IgG antibodies among patients who survived CCHF infection from India determined by testing anti-CCHF virus IgG antibodies in their follow up samples in 2016.

Case no.	Sporadic case/outbreak location & year	Follow up interval duration	OD of follow up a sample The year 2016
1	Kheda 2011	5 years, 5 months, 20 days	0.559
2	Aravalli 2012	4 years, 10 days	0.567
3	Amreli 2013	3 years, 2 months, 7 days	0.993
4	Amreli 2013	3 years, 2 months, 7 days	1.18
5	Amreli 2013	3 years, 2 months, 6 days	0.579
6	Amreli 2013	3 years, 2 months, 2 days	1.085
7	Amreli 2013	3 years, 2 months, 2 days	1.071
8	Amreli 2013	3 years, 1 month, 27 days	1.318
9	Amreli 2013	3 years, 1 month, 26 days	0.661
10	Amreli 2013	3 years, 1 month, 23 days	1.013
11	Amreli 2013	3 years, 25 days	0.948
12	Amreli 2015	1 year, 5 months, 4 days	1.317
13	Aravalli 2015	1 year, 2 months, 11 days	1.738
14	Amreli 2015	1 year, 2 months, 1 day	1.634
15	Morbi 2015	9 months, 9 days	1.313
16	Kutch 2016	5 months, 2 days	1.283

Burt et al., in 1994 [12] reporting the persistence of IgG antibodies in CCHF survivors for 59 months from South Africa. This is the first study portraying persistence of anti-CCHF IgG antibodies up to 5.5 years from India.

In conclusion, IgG antibodies were found to persist for more than five years in CCHF survivors. This data may be useful for understanding the immune response against live CCHF vaccines for effective protection due to unavailability of specific treatment against CCHF infection.

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#### Competing interests

No competing interests exist among authors.

#### Ethical approval

Institutional Human Ethical Committee of ICMR-National Institute of Virology, Pune, India has approved this study (IHEC No., NIV/IEC/2017/37/42).

#### Author's contribution

Conceived, planned and designed the study: PDY, DTM; data collation and analysis, initial draft: PDY, PGP, DYP, AMS; final draft:

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## References

- [1] Al-Abri SS, Al Abaidani I, Fazlalipour M, Mostafavi E, Leblebicioglu H, Pshenichnaya N, et al. Current status of Crimean-Congo haemorrhagic fever in the World Health Organization Eastern Mediterranean Region: issues, challenges, and future directions. *Int J Infect Dis* 2017;58:82–9.
- [2] Mourya DT, Yadav PD, Patil DY, Bhatia R. Highly infectious tick is borne viral diseases: Kyasanur forest disease and Crimean-Congo hemorrhagic fever in India. *WHO South-East Asia J Public Health* 2014;3(1):8–21.
- [3] Yadav PD, Patil DY, Shete AM, Kokate P, Goyal P, Jadhav S, et al. Nosocomial infection of CCHF among health care workers in Rajasthan, India. *BMC Infect Dis* 2016;16(1):624.
- [4] Mourya DT, Yadav PD, Shete AM, Gurav YK, Raut CG, Jadi RS, et al. Detection, isolation and confirmation of Crimean-Congo hemorrhagic fever virus in human, ticks, and animals in Ahmadabad, India, 2010–2011. *PLoS Negl Trop Dis* 2012;6(5):e1653.
- [5] Yadav PD, Raut CG, Mourya DT. Re-occurrence of Crimean-Congo haemorrhagic fever in Ahmedabad, Gujarat, India (2012): a fatal case report. *Indian J Med Res* 2013;138:1027–8.
- [6] Yadav PD, Gurav YK, Mistry M, Shete AM, Sarkale P, Deoshatwar AR, et al. Emergence of Crimean-Congo hemorrhagic fever in Amreli District of Gujarat State, India, June to July 2013. *Int J Infect Dis* 2014;18:97–100.
- [7] Yadav PD, Patil DY, Mourya DT. Positivity of dengue and chikungunya among Crimean-Congo hemorrhagic fever-negative cases in India: 2013–2016. *J Infect Public Health* 2018;11(6):900–1.
- [8] Mourya DT, Yadav PD, Shete AM, Sathe PS, Sarkale PC, Pattnaik B, et al. Cross-sectional serosurvey of Crimean-Congo hemorrhagic fever virus IgG in livestock, India, 2013–2014. *Emerg Infect Dis* 1837;21(10):2015.
- [9] Mourya DT, Yadav PD, Gurav YK, Pardeshi PG, Shete AM, Jain R, et al. Crimean Congo hemorrhagic fever serosurvey in humans for identifying high-risk populations and high-risk areas in the endemic state of Gujarat, India. *BMC Infect Dis* 2019;19(104).
- [10] Bodur H, Akinci E, Ascioğlu S, Onguru P, Uyar Y. Subclinical infections with Crimean- Congo hemorrhagic fever virus, Turkey. *Emerg Infect Dis* 2012;18(4):640.
- [11] Shepherd AJ, Swanepoel R, Leman PA. Antibody response in Crimean-Congo hemorrhagic fever. *Rev Infect Dis* 1989;11(4):S801–6.
- [12] Burt FJ, Leman PA, Abbott JC, Swanepoel R. Serodiagnosis of Crimean-Congo haemorrhagic fever. *Epidemiol Infect* 1994;113:551–62.

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