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# Crimean-Congo haemorrhagic fever – A ticking bomb: An overview of the current situation in India

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**Abstract**
Crimean-Congo Haemorrhagic Fever (CCHF) is a vector borne zoonotic disease caused by Crimean Congo Haemorrhagic Fever Virus (CCHFV), a member of the genus Orthonairovirus in the family Nairoviridae and order Bunyavirales. CCHFV has been isolated globally from a variety of domesticated and wild mammals. Ixodid ticks of genus *Hyalomma* act both as reservoir and as vector for the CCHF virus. This study was carried out with the data acquired from the web portal of Integrated Disease Surveillance Programme (IDSP). Analysis of the data showed that a total of 34 outbreaks of CCHF had taken place in Gujarat, Rajasthan and Uttar Pradesh during 2010-19. Further the highest incidence rate of 2.01 per one million population was seen in the year 2013. It was found that the highest case fatality rate of 66.67 percent was reported in 2014. In addition to that the mortality rate was found to be in the range of 0-0.78 per one million population. Death to case ratio was found to be 45.33 per 100 people. About 62% of outbreaks took place in monsoon season (Jun-Sept). Laboratory Diagnosis of CCHF was carried out in BSL 3 or BSL 4 laboratories by RT PCR and ELISA/IFA. Treatment mainly consists of supportive therapy along an antiviral drug Ribavirin which has some effect on the virus. Active surveillance with timely diagnosis of the disease in addition with health education to high risk groups and vector control activities may aid to address the future threat of CCHF in India.

**Keywords:** Crimean-congo haemorrhagic fever, ticks, ribavirin

## Introduction
The World Health Organization (WHO)/Food and Agriculture Organization of the United Nations (FAO)/World Organisation for Animal Health (OIE) joint consultation on emerging zoonotic diseases held in Geneva, May 2004, defined an emerging zoonosis as 'a zoonosis that is newly recognised or newly evolved, or that has occurred previously but shows an increase in incidence or expansion in geographical, host or vector range' [1]. Emerging zoonotic diseases have potentially serious human health and economic impacts and their current upwards trends are likely to continue. Many factors lead to the emergence of zoonotic diseases such as ecological changes in man's environment, handling animal by-products and wastes (occupational hazards), increased movements of man, increased trade in animal products, increased density of animal population, transportation of virus infected mosquitoes and cultural anthropological norms. Social and cultural factors such as food habits and religious beliefs play a role too [2]. India is considered as a hotspot for emerging infectious diseases. The emergence of zoonotic diseases in India is being seen as a litmus test for the preparedness of the Indian healthcare system to deal with such challenges. Most of the emerging and re-emerging diseases of humans are zoonotic in nature. Their distribution, lack of effective surveillance, and problems in timely diagnosis pose significant issues to public health. The arboviral and zoonotic diseases are a huge challenge in India leading to increased morbidity and mortality in humans [2]. As these diseases come from animals, prevention and control strategies need to be multi-sectoral and require the coordinated and combined efforts of veterinary, environment, forest, agriculture, climate change, and health sectors. One such emerging zoonotic disease in India is Crimean-Congo Haemorrhagic Fever (CCHF). The disease was first described in the Crimea in 1944 and given the name Crimean haemorrhagic fever. In 1969, it was recognized that the pathogen causing Crimean haemorrhagic fever was the same as that responsible for an illness identified in 1956 in the Congo. The linkage of the two place names resulted in the current name for the disease and the virus [3].

CCHF is a widespread disease caused by a tick-borne virus (Nairovirus) of the Bunya viridae family. The virus is primarily transmitted to people from ticks and livestock animals. Human-to-human transmission can occur resulting from close contact with the blood, secretions, organs or other bodily fluids of infected persons. There is no vaccine available for either people or animals [4]. This paper aims to analyse the severity of CCHF in India, to identify the difficulties in diagnosis of CCHF in India and to elucidate various approaches to face the future threat of CCHF in India.

## Materials and methods

This study was carried out with the data acquired from the web portal of Integrated Disease Surveillance Programme (IDSP). Information such as number of outbreaks, number of people infected and number of people died of CCHF during the period 2011 to 2019 were obtained. Various disease measures such as incidence rate, case fatality rate, mortality rate and death to case ratio were calculated and the data were analyzed using Maxstat. The analysed data were illustrated in the form of tables and graphical representations.


**Fig 1:** Distribution map of CCHF in India

## Results and discussion

The outbreak details of CCHF in India are tabulated below in table 1.

**Table1:** Outbreak details of CCHF in India

| Year | No. Of outbreak | Infected | Deaths | Incidence Rate (Per 1 Million population) | Case Fatality Rate (%) | Mortality Rate (Per 1 Million population) |
|---|---|---|---|---|---|---|
| 2011 | 3 | 15 | 8 | 0.91 | 53.33 | 0.48 |
| 2012 | 0 | - | - | - | - | - |
| 2013 | 9 | 31 | 12 | 2.01 | 38.70 | 0.78 |
| 2014 | 3 | 3 | 2 | 0.60 | 66.67 | 0.39 |
| 2015 | 0 | - | - | - | - | - |
| 2016 | 3 | 4 | 1 | 0.63 | 25.00 | 0.16 |
| 2017 | 1 | 1 | 0 | 0.47 | 0 | 0 |
| 2018 | 0 | - | - | - | - | - |
| 2019 | 15 | 21 | 11 | 0.83 | 52.38 | 0.43 |

Since the first outbreak of CCHF in Ahmedabad (2011), about 34 outbreaks were reported in various districts of Gujarat, Rajasthan and Uttar Pradesh [5]. Despite the high potential of virus transmission by hard ticks that are distributed throughout the country, the incidences of CCHF virus are restricted in these geographic locations. This may be due to the behavior of tick's dropping rhythm that governs the epidemiology of CCHF in India [6]. Hard ticks are two-host ticks and require two hosts to complete their life cycles. The adults lay eggs and emerging larvae of *Hyalomma anatolicum* attach to the vertebrate host mainly cattle. The detachment and dropping rhythms of the species are so adjusted that this occurs only at times when the cattle is resting in the sheds normally at night time. The engorged ticks that drop in the sheds find suitable niche in the cracks and the crevices, where the female ticks oviposit and the larvae and the nymph moult to the next stage. The questing larvae, the unfed nymphs and adults that have moulted from the previous stage can easily find their hosts in the cattle sheds. The humans acquire infection through the tick bite when they come in close contact of this environment. Therefore, only sporadic cases occur for CCHF though the virus is widely prevalent in

various geographical areas.

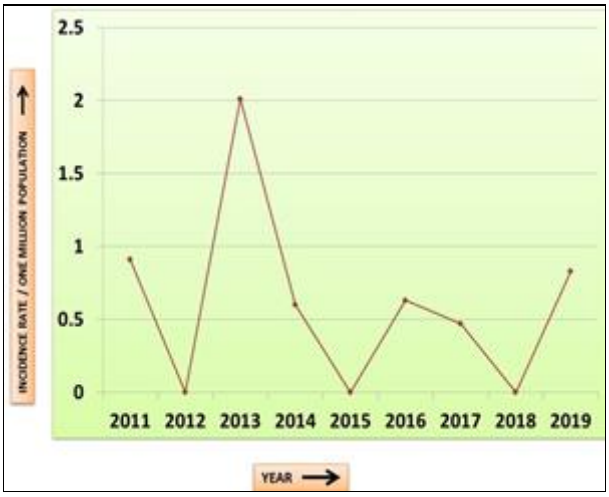


**Fig 2:** Incidence rate of CCHF in India

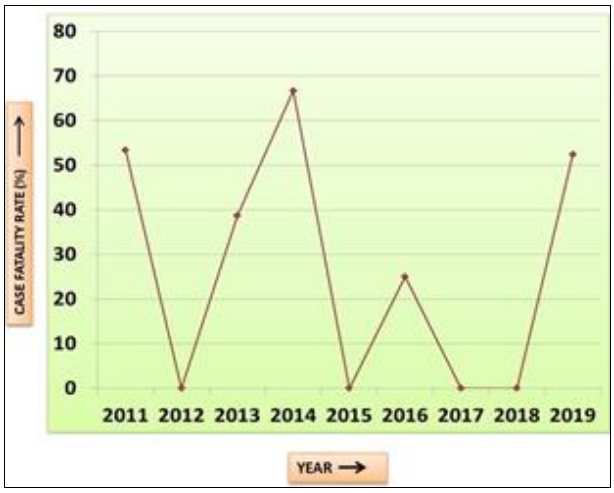


**Fig 3:** Case Fatality Rate of CCHF in India (Per 1 Million population)

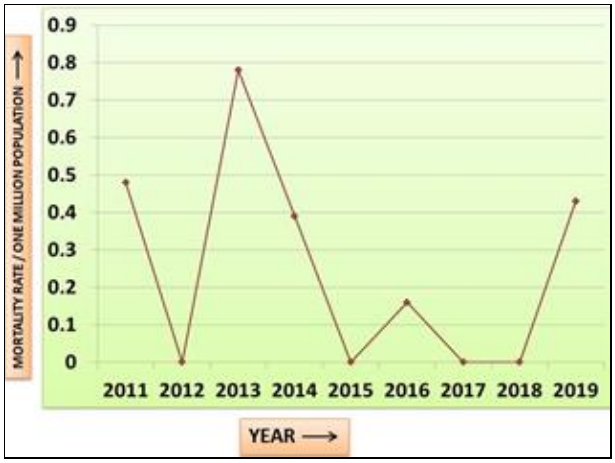


**Fig 4:** Mortality rate of CCHF in India

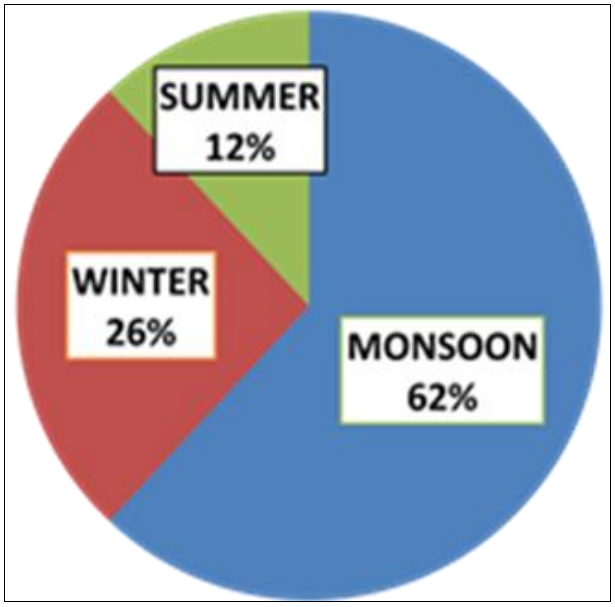


**Fig 5:** Seasonal variation

From figure 2, it is evident that the highest incidence rate of 2.01 per one million population was seen in 2013 and the lowest incidence rate of 0.47 per one million population was seen in 2017. Case fatality rate is used as a measure of disease severity and to assess the prognosis of the disease. Case fatality rate of CCHF in India ranges between 0 - 66.67% (39.3%) which is more when to compared to other countries such as Albania (3.1%), Turkey (5.3%), Russian federation (3.2%), Kosovo (23.4%), Bulgaria (17.9%), Iran (15.1%), Mauritania (17.1%) and Afghanistan (26.2%) [7]. This indicates the severity of CCHF in India and this case fatality rate can be reduced by timely diagnosis and appropriate treatment.

The mortality rate of CCHF in India ranges between 0-0.78 (0.37) per one million population which is less than other viral zoonotic diseases such as Rabies (1.1 per one million population) [8] and Nipah virus infection (0.75 per one million population) [9]. Death to case ratio was found to be 45.33 per 100 people. About 62 per cent of outbreaks occurred during monsoon season (Jun-Sept), 26 per cent during winter (Oct-Feb) and 12 per cent during summer (Mar-May). Occurrence of CCHF in monsoon season was more which may be due to the high prevalence of hard ticks in the monsoon season [10].

The clinical features commonly observed in CCHF patients were high grade fever, headache, body ache, nausea, vomiting, abdominal pain, dizziness, malaise, photophobia, diarrhea, petechiae, ecchymosis and visceral bleeding. Common laboratory findings were thrombocytopenia, raised prothrombin time (PT) and activated partial thromboplastin time (aPTT), raised creatine phosphokinase (CPK) and lactic acid dehydrogenase (LDH) as well as altered liver and renal functions [11].

Laboratory confirmation is done with one of the following assays: (A) Detection by ELISA or IFA of specific IgM antibodies against CCHF virus or a 4-fold increase in specific IgG antibodies against CCHF virus in two specimens collected in the acute and convalescence phases, (B) Detection by RT-PCR of CCHF virus genome in a clinical specimen confirmed by sequencing of the PCR product and (C) CCHF virus isolation [11]. In India, only few Biosafety level-3 and Biosafety level-4 laboratories are available, and out of those only a few are capable to carry out viral diagnosis. This may delay the confirmation of the disease.

Patients are divided into 3 categories:

**Category-A:** Patients having relatively mild disease (fever <38.50 C, No systemic bleeding, Alanine Transaminase (SGPT) levels < 150 IU, Platelet count > 50,000). These

patients improve spontaneously in about day 10 of illness. Patient can be managed with supporting therapy and regular monitoring for worsening of symptoms. These patients do not require Ribavirin.

**Category-B:** Patients who are in the first 5 days of illness and are severely ill with high grade fever (> 38.50C), local and systemic bleeding manifestations, having Alanine Transaminase (SGPT) levels of 150 IU or more, Aspartate Aminotransferase (SGOT) of 200 IU or more, platelets (< 50,000) or Activated Partial Thromboplastin Time (APTT) of 60 seconds or more. Even if the patients still look comparatively well at this stage these clinical path values are markers of poor prognosis if recorded during the first 5 days of illness and persons in this group should be treated as soon as possible with ribavirin. Those who are recognized and treated early enough respond remarkably well to ribavirin.

**Category C:** Patients first seen/recognized as CCHF after day 5 and are in comatose/terminal state with disseminated intravascular coagulation and multi organ failure. Treatment with ribavirin is indicated but the prognosis is very poor.
Category B and C patients, even if they are subsequently tested negative, should receive the full course of ribavirin [12].

## Conclusion

CCHF possess a serious threat to public health services because of its epidemic potential, high CFR and its ability to cause nosocomial outbreaks. The true prevalence of this disease in India is not known. Since we live in a global village, we cannot afford to be complacent about the tremendous economic, social and public health burden of this disease. One health approach is necessary in surveillance and control of the disease for better outcomes. There is a need to develop improved diagnostic facilities, a strong public health structure, effective risk communication, epidemic preparedness and rapid response. Therefore strengthening the nation-wide surveillance and response system, conducting research to develop and evaluate prevention and control strategies, enhancing epidemiologic and laboratory capacity for timely diagnosis of the disease, sero-surveillance of CCHF among domestic animals where the disease become un noticed as they are asymptomatic carriers, vector control activities through integrated vector management with preference to the monsoon, health education for high-risk groups, i.e., veterinarians, farmers, workers in slaughter houses, and other high risk groups, development of safe and effective vaccines may aid to address the future threat of CCHF in India.

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