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CRIMEAN-CONGO HEMORRHAGIC CAUSING VIRUS – AN UNRESOLVED PROBLEM

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ABSTRACT

Crimean Congo Hemorrhagic virus is a 3500-year-old pathogenic virus, capable of spreading through ticks. It causes hemorrhagic fever of fatal nature, resulting in high morbidity and mortality (up to 60%). Being a zoonotic disease, without the privilege of having proper vaccine, treatment and control of the disease in the current decade has become a priority. The CCHFV occurrence is now being reported in the areas that were earlier uninfected, increasing the risk of spreading the disease on a large geographical range. The diverse genetic variation of the virus and its incidence at both, nosocomial and community acquired level. Therefore, it is important to highlight the importance of the disease. This review thus, not only summarizes the general overview of the disease but also give a clear picture about the status of the disease globally and the prophylaxis that can be opted to minimize the occurrence of the disease.

KEYWORDS: Crimean-Congo Hemorrhagic Fever, Worldwide Distribution, Symptoms, Transmission, Precautions.

ABBREVIATION: CCHFV; Crimean-Congo Hemorrhagic Fever Virus, **CCHF;** Crimean-Congo Hemorrhagic Fever.

INTRODUCTION

Crimean Congo Fever (CCHF) is a virulent fever hemorrhagic human disease caused by Crimean Congo hemorrhagic fever virus having relevance worldwide.[37] It causes pathogenic disease of acute severity,[36] classified in the risk group 4, and thus needs to be appropriately catered in BSL-4 Laboratory.[27] The causative agent of CCHF is a virus of family *Buniyaviridae*, genus *Nairovirus.*[29,34,73] CCHF virions are spherical shaped with a diameter of approximately 90-100µm.[93,94] The virus is capable of transmitting via zoonosis.[85] It is a single stranded RNA virus composed of tripartite genome,[71, 72] i.e., has three portions of the genome namely; L, M and S segment. The L segment comprises of large genome, M referring to medium segment while S, the small genome portion containing the conserved genes.[28,46,51,82] The virus is enveloped having lipid bilayer of 5-7 nm thickness[1,50,52,60,61,76,96,117] and is classified into 7 genotypes as follows: Asia-1, Asia-2, Africa-1, Afirca-2, Africa-3, Euro-1, Euro-2.[2,7] Crimean-Congo Hemorrhagic Fever is also known with other synonymic names such asCentral Asian Hemorrhagic Fever, Congo Fever, Crimean Hemorrhagic Fever, Khungribta (Blood taking), Karakhalak (Black death), Khunymuny (Nose bleeding), Viral Tick borne Hemorrhagic Fever Disease and Asian Ebola.[19,52,99] In a massive outbreak in the Crimean Peninsula, during 1944-1945 with case fatality of 10% was reported to have "hemorrhagic fever".[57] The virus was antigenically identical to the Congo virus, isolated from the patient in Belgian Congo in 1956, the link between both the virus resulted in the current name of the disease and virus respectively.[22] The disease has been reported to cause a case fatality rate of up to 50%.[128]

Structure, Nature and Life Cycle of virus

The Crimean Congo Hemorrhagic Virus has an evolutionary history of about 3500 years so it can be considered as one of the oldest viruses.[15] The tripartite genome has 3 segments designated as L, M and S are of 11-14.4, 4.4-6.3 and 1.7-2.1 kilobases respectively.[16] The nucleocapsid protein or NP is a nonstructural protein. 'NS_S' is encoded by the S segment of the genome. The M protein codes for the precursor of 2 envelope glycoproteins known as G_n and G_c, while the RNA dependent RNA polymerases are encoded by the L segment of the genome.[68] The genome contains non-coding regions called as "non-coding complementary", regions that give the genome its genome its characteristic circular appearance. The non-coding complementary regions are found on the 5' and 3' terminal of all the segments of the viral genome.[49] It was earlier considered that each genome was capable of encoding a single protein but it was later found that the S segment

could encode a non-structural protein in the orientation opposite to the Nucleo-capsid protein, making the virus an ambi-sense virus.[128] Protrusions are formed by proteins present on the envelope, about 5-10nm long. The membrane receptors are identified to be G_c and nucleolin.[120] Although the exact mechanism of replication and multiplication is not clear yet however, through studies it has been revealed that the virus binds itself to the cell surface with the help of glycoproteins G_n and G_c, the details however remain identified till date and studies are yet needed to be conducted in this respect.[130] Role of nuceolin in aiding in the entry of cell has been reported but specific receptors have not been identified yet. According to literature and studies conducted, the entry is thought to be followed by Clathrin-mediated endocytosis. The pH and level of cholesterol is also a factor facilitating the entry into the cell.[101,104] The virus is classified into seven genotypes as Asia-1, Asia-2, Africa-1, Africa-2, Africa-3, Euro-1 and Euro-2.[2]

Survival Capacity of the Virus

The virus can thrive under different environmental conditions, depending on variation in the temperature, pH, humidity and the habitat. The virus gets inactivated within 30 minutes at 56^{o}C while at 60^{o}C it is inactivated for 15 minutes. The inactivation by chemical treatment can also be achieved (by using disinfectant or chemical), e.g., 1% hypochlorite and 2% glutaraldehyde. The effect of varying the pH has also been reported, the virus has been observed to get inactivated at a pHless than 6. The virus has tremendous survival capabilities and can withstand humid environment such as at 37^{o}C for 7 hours, 20^{o}C for 11 days, while at 4^{o}C for 15 days. However, its survival in dry conditions is limited to approximately 90 minutes to 24 hours.[82]

Reservoir

Animals that do not depict any visible clinical symptoms are regarded as the reservoir for that disease. The reservoirs for CCHFV include; cattle, livestock, hares, hedgehogs and vertebrates.[5,19] These animals remain asymptomatic and therefore are not noticed until screening is conducted.

Host

The Crimean Congo hemorrhagic virus is capable of invading both wild and domestic animals, including various avian and vertebrate species.[105] The animals that have ticks from Hyalomma are considered as majorly infected from Crimean-Congo virus. The ticks in their premature form i.e., larva and nymph harbor small mammals and birds while, the adults target the cattle and livestock.[118] The livestock includes the cattle, goats, sheep, horses, pigs, hares, ostriches, camels, donkeys, mice and domestic dogs. Sub-clinical and un-apparent infections are observed in contrast to human infection by CCHFV, which is symptomatic and has severity with the course of progression. The distribution of the ticks and its presence in the different regions of the world is majorly involved in the presence of multiple animals to serve as host. As the ticks prefer dry and arid type of vegetative land so the incidence of the disease is considerably high in regions of such climate.[98] The movement of infected livestock, climatic and ecological changes all are important factors in the spread of the virus.

Vectors: The transmission of CCHFV is achieved by both mechanical as well as biological vector.

1. Mechanical Vectors

These include animals that serve as long distance transporters for the disease. Livestock, migratory birds, ungulates etc. are important mechanical vectors. The larvae and nymphs attach themselves to the feathers of the birds and get detached on the stop-site, thus spreading in this way. The presenceof ticks on the livestock is not thought to be unusual if the animal has 100 ticks on its body e.g., *Hyalomma marginatum*.

2. Biological Vectors

The biological vectors for CCHFV vary depending on the geographical region as well as the species of ticks that reside in that area. There are approximately 30 species that have been reported to be involved in the transmission of the virus. The incidence of the CCHF is influenced by the presence of the tick type present in that specific location. *Hyalomma* species are majorly involved along with other tick types such as from genus *Amblyomma, Rhicpicephalus, Dermacentor, Culicoides, Argasidae and Ixodidae etc.*[84]

Risk groups and Risk Factors

Butchers, physicians, health care workers, veterinarians, abattoir workers, farmers, people with occupation that cause interaction with the soil/ agriculture are all at high risk for the diseases. Furthermore, activities like hiking, camping and rural activities that can cause risk of tick exposure are also considered as factors for the disease.[55]

Disease Transmission: The transmission of the virus can be *via*:

1. Vertical transmission

The transmission of virus can occur vertically or trans-placentally, that is from infected mother to child.[53,91] The transmission has been reported in different regions of the world and involve the fatality of mother, child or in some cases, of both.[30,57] Incidents of Crimean-Congo fever in pregnancy have been reported in turkey, Russia and Kazakhstan.[88]

2. Horizontal transmission

Horizontal transmission includes; Person to person, through contact with infectious body fluids. This includes people working in the health care facilities that might experience needle stick injuries or contact with contaminated instrument, body fluids etc. Physicians,

nurses, doctors and lab personnel are ones that might acquire CCHFV via horizontal means.[55]

3. Transmission through migratory birds

Migratory birds act as long distance transporters of ticks e.g., nymphs of *H. marginatum* complex usually attached to the bird in the form of larvae, usually attachment occurs before the migration begins. Thereafter detaching at breeding or stopover sites, establishing new foci in the mammalian hosts.[63,87] E.g., Woodchat shrike (*Lanius senator senator*), an Antikyhira bird has been reported by Lindborg et al.[63] to carry CCHFV during its northward migration. Ticks from birds have been reported to carry CCHFV indicating that the African migratory birds can introduce CCHFV into Europe by the transportation of these infected ticks. Some of the migratory bird species reported include*; Phoenicurus phoenicurus, Erythropygia galactotes, Iduna opaca, Acrpcephalus scirpaceus, Iduna pallida*. The incidence in the cases of CCHFV vary with the seasons and climatic changes, as the reproduction is facilitated by the season and climate. Therefore, it is an important factor to view when the disease transmission is studied.

4. Transmission to humans due to climatic changes

The occurrence of CCHFV and the presence of the global warming as an issue should be considered as well. The global warming may not only introduce CCHFV to newly warmer areas, it might also increase problem in the areas prevalent with the disease. Altering the tick's growth pattern, redirection of the migratory route by birds and earth's altered temperature pattern are some factors that need to ponder on in order to have a clear idea about the seasonal variation in the occurrence of the disease.

5. Transmission by Vectors

The transmission of virus is possible with involved of tick/ or having ticks as mediator of transmission in the following 4 ways[14,69]:

1. **Transtadial Transmission**; that is from larvae to nymphs and then to the adults.
2. **Vertical Transmission**; involves adult females and their eggs.
3. **Venereal Transmission**; in which the transmission is from male ticks to female ticks during reproduction.
4. **Non-Viremic Transmission**; is the transmission from infected to uninfected ticks feeding on the body of the same host.

CCHF is regarded as an infectious emerging zoonotic disease of worldwide importance. It is an arthropod-borne virus with relevance to clinical reporting worldwide. The virus circulates in a tick-vertebrate-tick cycle, in which ticks have the primary role of being reservoirs for the virus or act as vectors e.g. *Hyalomma marginatum* tick are the most common vectors.

6. Nosocomial Infection of CCHF

The occurrence of the disease (nosocomial cases) has been reported in the literature from time to time, occurring in various countries during the course of the history. Nosocomial cases have been reported in Pakistan,[3,9,13] Russia,[89] U.A.E,[106] South Africa,[41,78,113] Iran,[59,70] India,[75] Tajikistan,[111] Kosovo,[40] Sudan[32] and Turkey.[18]

Signs and symptoms

The overall generalized signs and symptoms of the disease have been reported in patients to have sudden onset with fever with chills, malaise, diffuse myalgia, photophobia, irritability, headache, high fever, back pain, joint pain, stomach pain, blood in urine, rectum and gums, vomiting, sputum and abdominal activity.[68] Severe symptoms include: Petechiae (Red spots on skin), Ecchymoisis (Extravastion of blood), Epistasis (Nose bleeding), Gum bleeding, Emesis, Nausea, Diarrhea, Neuro-psychiatric and cardiovascular changes as reported by Mardani and Keshtkar-Jahromi.[68] The symptoms of the disease vary with the severity of the infection. It can be categorized into four phases, namely incubation period, pre-hemorrhagic period, hemorrhagic period and the convalescent period.

1. Incubation period: It is usually of 2-9 days. The route of exposure can vary the incubation period.

2. Pre-hemorrhagic period: It starts with mild symptoms and usually appear a week after the incubation period.

3. Hemorrhagic period: It is of short duration, usually of 2 to 3 days with increased severity and symptoms include; hematuria, mucous membrane and conjunctival hemorrhages, disseminated intravascular coagulation. Circulatory shock, coma and central nervous system dysfunction leading to death of the patient have been reported due to hemorrhages.[12]

4. Convalescent period: It starts 10-20 days after the onset of the disease. It is experienced by survivors; 10 days of hospitalization is further required to ensure maximum recovery of the patient [68]

5. Relapse of Infection: No known relapse of infection has been reported yet.

S. No	Sign and Symptoms	References
1.	Fever (Biphasic pattern)	[1, 117]
2.	Chills	[68]
3.	Malaise	[50, 68]
4.	Diffuse Myalgia	[1, 68]
5.	Photophobia	[50, 117]
6.	Irritability	[50, 68]
7.	Vertigo	[50, 117]
8.	Headache	[1, 50]
9.	Backache	[68]
10.	Limb ache	[1, 68]
11.	Abdominal pain	[60, 128]
12.	Annorexia	[50, 108]
13.	Nausea	[13, 50]
14.	Vomiting (with blood)	[108, 128]
15.	Diarrhoea	[13, 60]
16.	Bradycardia	[50, 108]
17.	Hyperaemia	[13, 60]
18.	Oedema	[108, 60]
19.	Conjuctival Congestion	[50, 76]
20.	Leucopenia	[60,108]
21.	Thrombocytopenia	[13, 76]
22.	Proteinuria	[50,108]
23.	Petechia	[68, 117]
24.	Epitaxis	[1, 76]
25.	Gum hemorrhaging	[13, 60]
26.	Haematuria	[13, 60]
27.	Viginal Bleeding	[50, 108]
28.	Gastric Mucosal Hemorrhaging	[1, 68]
29.	Shock due to blood loss	[50, 68, 108]
30.	Shock due to neurological complications	[68]
31.	Pulmonary hemorrhages	[50, 108]
32.	Incurrent infections	[68]
33.	Poor vision	[128]
34.	Loss of hearing	[13, 50]
35.	Loss of memory	[128]
36.	Sweating	[1,68]
37.	Polyneuritis	[128]
38.	Poor Appetite	[13, 50]
39.	Laboured Breathing	[1, 68]
40.	Melena	[128]

Distribution and status of Disease around the world

The disease was first described in 12th century as hemorrhagic syndrome in Tajikistan.[36,111] The virus has case fatality rate upto 50%.[24,43] First description of this viral infection in humans, was reported in 1944-1955 in Crimea, with 200 cases of the disease, with a case fatality of 10% was recorded.[52,81] The outbreak of this disease has occurred time to time in various continents and regions of the world such as Africa, Asia, Eastern Europe as reported by.[37] The first virus was isolated from a patient in Belgian-Congo having same antigenic relevance with that of Crimean strains hence was given the name Crimean- Congo Hemorrhagic Fever.[5,38,102,128] Since its discovery in 1967, 140 outbreaks have been reported in which approximately 52 countries have been recognized and reported to be endemic or have endemic areas. Following the discovery of the virus, cases related to the disease were reported by areas of former Soviet Union that is Crimea, Astrakhan, Rostov, Uzbekistan, Kazakhstan, Tajikistan, other countries like Bulgaria. After that many out breaks were reported in the years that followed in different countries including continent of Africa (having outbreaks in areas of Uganda, Mauritania and Democratic Republic of Congo), several Middle east countries; Iraq, United Arab Emirates (UAE) and Saudia Arabia and regions of Asia with reported cases in Pakistan, Iran, Iraq, turkey and India.[21]

It is a disease of worldwide distribution and its geographical range is the most extensive of the tick-borne viruses affecting humans,[38,60] the vector responsible for its transmission serves as the main

contributor in the presence of disease on such an extensive range.[22] The countries reported to have cases of Crimean Congo hemorrhagic fever has been summarized in Table 2.

S.No	Continent	Country	References
	Asia		
1.		Syria	[103]
2.		India	[21, 22, 23, 75, 77]
3.		China	[38, 48, 64,66, 86, 107, 109, 115, 119]
4.		Japan	No information available.
5.		Vietnam	No information available.
6.		North Korea	Disease never reported.
7.		Thailand	No information available.
8.		Singapore	Disease never reported.
9.		South Korea	Disease never reported.
10.		Israel	Disease not reported.
11.		Pakistan	[2, 3, 8, 9, 13, 54, 62, 100, 128]
12.		Hong Kong	No information available.
13.		Philippines	Disease never reported.
14.		Iran	[22, 23, 24, 59, 68, 69, 70]
15.		Indonesia	No information available.
16.		Maldives	No information available.
17.		Malaysia	Disease never reported.
18.		Myanmar (Burma)	Disease never reported.
19.		Saudia Arabia	[33, 128]
20.		Srilanka	Disease never reported.
21.		Iraq	[22, 128]
22.		Taiwan	No information available.
23.		Bangladesh	Disease not reported.
24.		Qatar	No information available.
25.		Cambodia	No information available.
26.		Yemen	No information available.
27		United Arab Emirates (U.A.E)	[90, 96, 106, 128,
28.		Afghanistan	[79]
29.		Nepal	Disease never reported.
30.		Lebanon	Disease never reported.
31.		Macau	No information available.
32.		Oman	[38, 95, 97]
33.		Kuwait	[95, 97, 128]
34.		Laos	Disease never reported.
35.		Mongolia	Disease never reported.
36.		Jorden	No information available.
37.		Bahrain	Disease never reported.
38.		Armenia	No information available.
39.		Uzbekistan	[117]
40.		Bhutan	Disease never reported
41.		Krygyzstan	[11]
42.		Brunei	No information available.
43.		States of Palestine	No information available.
44.		Turkmenistan	No information available.
45.		Timor-Leste	No information available.
46.		Tajikistan	[84, 111]
47.		Christmas Islands	No information available.
48.		Cocos Islands	No information available.
49.		British India Ocean Territory	No information available.
1.	Europe		
		Germany	[26]
2.		France	Disease not reported
3.		Italy	No information available.

4.		United kingdom	[11]
5.		Netherlands	[11]
6.		Switzerland	[118]
7.		Poland	No information available
8.		Ukraine	Disease never reported.
9.		Greece	[31, 67]
10.		Sweden	Disease never reported.
11.		Austria	No information available.
12.		Malta	Disease never reported.
13.		Norway	Disease never reported.
14.		Czech Republic	Disease not reported
15.		Denmark	Disease not reported
16.		Belgium	Disease not reported.
17.		Croatia	Disease not reported.
18.		Iceland	Disease never reported.
19.		Finland	Disease not reported.
20.		Romania	[31]
21.		Hungary	Disease never reported
22.		Cyprus	Disease not reported
23.		Bulgaria	[31]
24.		Gibraltar	No information available.
25.		Luxembourg	Disease never reported.
26.		Albania	[86]
27.		Serbia	[31]
28.		Montenegro	Disease not reported
29.		Lithuania	Disease not reported.
30.		Vatican City	No information available.
31.		Republic of Iceland	Disease never reported.
32.		Estona	Disease not reported
33.		Slovenia	[31]
34.		Bosnia and Herzegouina	No information available.
35.		Moldova	No information available.
36.		Kosovo	[40]
37.		Belarus	No information available.
38.		Macedonia	[31]
39.		Andorra	No information available.
40.		Liechtenstein	No information available.
41.		Faroe Islands	No information available.
42.		San Marino	No information available.
43.		Isle of Man	No information available.
44.		Jersey	No information available.
45.		Aland Islands	No information available.
46.		Svalbard and Jan Mayen	No information available.
47.		Kingdom of Hungary	No information available.
48.		Yugoslavia	[114]
	Africa		
1.		Moroco	No information available.
2.		South Africa	[41, 78, 108, 113]
3.		Algeria	No information available.
4.		Nigeria	Disease never reported.
5.		Ethiopia	No information available.
6.		Kenya	[65]
7.		Mauritius	Disease never reported.
8.		Tunisia	Disease never reported.
9.		Democratic Republic of the Congo	[11]
10.		Cape Verde	No information available
11.		Madagascar	Disease never reported.
12.		Tanzania	No information available.

13.		Ghana	No information available.
14.		Seyehelles	No information available
15.		Libya	No information available
16.		Uganda	[83]
17.		Cameroon	No information available
18.		Gambia	No information available.
19.		Senegeal	[21]
20.		Sudan	[6, 32]
21.		Mali	No information available.
22.		Zimbabwe	Disease not reported.
23.		Cote d Ivoire	No information available
24.		Somalia	No information available
25.		Namibia	Disease not reported.
26.		Mozambique	Disease not reported.
27.		Angola	No information available
28.		Rwanda	Disease never reported.
29.		Barkina Faso	No information available.
30.		Eritrea	No information available.
31.		Botswana	Disease never reported.
32.		Zambia	Disease never reported.
33.		Gabon	No information available.
34.		Guinea	No information available.
35.		Sierra Leone	No information available
36.		Chad	No information available
37.		Mauritania	[11, 80]
38.		South Sudan	No information available
39.		Benin	No information available.
40.		Malawi	No information available.
41.		Niger	No information available
42.		Liberia	No information available
43.		Djibouti	No information available.
44.		Togo	No information available.
45.		Burundi	No information available
46.		Reunion	No information available
47.		Lesotho	Disease never reported.
48.		Swaziland	Disease never reported.
49.		Congo	No information available.
50.		Central Africa Republic	No information available
51.		Equatorial Guinea	No information available.
52.		Mauritania	[44]
1.	Americas		
		United states of America	Disease never reported.
2.		Mexico	Disease never reported.
3.		Brazil	Disease never reported.
4.		Canada	Disease never reported.
5.		Venezuela	Disease never reported.
6.		Cuba	Disease never reported.
7.		Colombia	Disease never reported.
8.		Peru	Disease never reported.
9.		Argentina	Disease never reported.
10.		Costa Rica	Disease never reported.
11.		Dominican Republic	Disease never reported.
12.		Puerto Rico	No Information available.
13.		Ecuador	Disease never reported.
14.		Jamaica	No information available.
15.		Bolivia	No Information available.
16.		Bahamas	No Information available.

17.		Guatemala	Disease never reported.
18.		Haiti	No Information available.
19.		Uruguay	Disease never reported.
20.		Nicaragua	Disease never reported.
21.		Aruba	No Information available.
22.		El-Salvador	Disease never reported.
23.		Honduras	Disease never reported.
24.		French Guiana	No information available.
25.		Paraguay	No Information available.
26.		Barbados	No Information available.
27.		Curacao	No Information available.
28.		Turks and Caicos Island	No Information available.
29.		Suriname	No Information available.
30.		Guyana	No Information available.
31.		Saint Lucia	No Information available.
32.		Cayman Islands	No Information available.
33.		Guadeloupe	No Information available.
34.		Martinique	
35.		Trindad and Tobago	No Information available.
36.		Falkland Island	No Information available.
37.		United states Virgin Islands	No Information available.
38.		Grenada	No Information available.
39.		Dominica	No Information available.
40.		British Virgin Islands	No Information available.
	Trans-continental Countries		
1.		Turkey	[10, 35, 39, 47, 58, 112,116, 125, 126]
2.		Russia	[89]
3.		Kazakhstan	[84]
4.		Egypt	[25]
5.		Azerbaijan	Disease never reported
6.		Chile	Disease never reported.
7.		Panama	Disease never reported.
8.		Georgia	No Information available.

Diagnosis and Treatment

Enzyme-linked immunosorbent assay, Quantitative polymerase chain reaction can be used to diagnose the virus while its isolation can be confirmed by cell-culture technique and histochemical staining.[17] There is no vaccine approved for CCHF yet and therefore treatment is mainly relayed on supportive and symptomatic therapies.[56,59,74] For treating the CCFV infected patient administration of oral or intra-venous ribavirin has been reported and proved effected in most of the cases but its effectiveness still varies from patient to patient.[9,105] The effectof "Venin", an immunoglobulin prepared from the plasma pool of boosted donors has been reported to be beneficial, as it is specific for CCHFV, however there might be limitation in the immunotherapy.[42]

Prevention: Prevention can be acquired at both nosocomial as well as community level. By adopting standard precautionary measures, we can decrease the high incidence of the disease. Few precautions that can be adopted are:

The disease can be controlled by controlling its vector that is ticks, tick bite prevention hence can be enabled by use of tick-repellents (such as permethrin or di-ethyltoluamide) and can effectively reduce the tick's population.[62] Special care in the "tick-active season" is needed to avoid from getting ill.[7] The disease spreads over long distances in non-infected regions by bird migration so, monitoring and study on the interaction between CCHFV and birds need to be in the priority list as well. This will help and enable the prevention and disease control. Awareness and health education related to disease transmission and prevention needs to be the priority of the government in areas and regions where annual cases of CCHFV are reported. This will not only help in educating the people in adopting precautions but will also minimize the fatality rate and endemics.

The movement of livestock that carries infected ticks is also one the source for the dissemination of the disease. Thus screening of the livestock for the potential virus before carrying imports and exports may help in declining the incidence of the disease. The interaction of human population with livestock e.g., people working as farmers and livestock handlers are usually more at risk in underdeveloped or developing countries. So, guidance and awareness to livestock handlers might improve their approach to handle livestock.[45] Use of proper clothing, googles and gloves can prove helpful.[128] Avoid use of

unpasteurized milk and consumption of raw meat is also not recommended. It is essential for the lab workers and researchers, dealing with the virus to adopt proper standard precautionary measures which include the use of personnel protective equipment and use of Bio-safety level-4 setup. Autoclaving of the instruments before incineration is recommended in medical facilities. Decontamination of the container's surface and other surfaces should be done with bleach solution. This will help in avoiding an outbreak at nosocomial level/setting. In case of death of a patient, use of bleach solution in the ratio of 1:10 is recommended. The body should be covered and wrapped in a plastic bag and taping is done to avoid the contact of body or its fluids with soil as suggested by CDC.[20]

CONCLUSION

Crimean-Congo Hemorrhagic fever a potentially lethal virus with its diverse genetic variation, is still considered as an "unsolved problem" in the modern world of 21st Century. Even in this era with the modern technology and facility no proper vaccine or treatment is available, while its occurrence has been reported to be round the globe. Therefore, it is suggested that efforts at national and international level are required without the discrimination of border or region to control the disease.

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