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Crimean Congo Hemorrhagic Fever and Its Prevention in Humans through Tick Vectors Control

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Abstract

Crimean-Congo hemorrhagic fever is caused by infection with a tick-borne virus (Nairovirus) in the family Bunyaviridae. Ixodid (hard) ticks, especially those of the genus, *Hyalomma*, are reservoirs and vectors for the Congo virus. Numerous wild and domestic animals, such as cattle, goats, sheep and hares, serve as amplifying hosts for the virus. Transmission of virus to humans occurs through contact with infected ticks or animal blood. Virus can be transmitted from one infected human to another by contact with infectious blood or body fluids. Familiar spread of virus has also been occurred in hospitals due to improper sterilization of medical equipment, reuse of injection needles and contamination of medical supplies. Therefore, the present article deals to learn more about this disease so that persons can stay safe and healthy during or when there is a greater risk of infection spread. The patient may show general symptoms like high fever, headache, joint and muscle aches, nausea, stomach pain and loose motions. The patient be able to suffer from severe bleeding, jaundice, convulsions and coma. Congo fever causes high grade fever with nose and gum bleeding as well as liver and kidney failure. Congo virus is diagnosed using tests like ELISA, isolation of the virus, antigen detection and polymerase chain reaction. Owing to this disease, there is an estimated 10-30% fatality rate in humans and so far no vaccine is available for use. In such a scenario, the only way to prevent peoples from catching this fever is through creating of awareness and adopting precautionary measures. A person cannot be infected by eating well-cooked infected meat since the virus does not survive during cooking. The treatment for fever is primarily supportive and patient is treated with intravenous fluids and an antiviral drug ribavirin with some benefit. Caution should include careful attention to fluid balance and correction of electrolyte abnormalities, oxygenation and hemodynamic support, and appropriate treatment of secondary infections. Health-care workers caring for patients with suspected or confirmed fever or handling specimens from them, should implement standard infection control precautions. These include basic hand hygiene, use of personal protective equipment, safe injection practices and harmless burial practices of waste.

Keywords

Crimean Congo Hemorrhagic Fever, Virus, Tick, Vaccine, Vector Control

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1. Introduction

Crimean-Congo Hemorrhagic fever is a viral disease that spreads through ticks bite. Congo virus is actually not its complete name, this virus has been first found causing deaths in the Crimean Peninsula in Europe where it characterized in 1944 and named as the Crimean virus, and the disease caused by this virus named as the Crimean Hemorrhagic fever. A

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few years later in 1969, this virus has also been found causing illness in the Congo region of Africa and hence from these two regions, the current name of the fever caused by this virus named as the Crimean-Congo hemorrhagic fever. Crimean-Congo hemorrhagic fever is mostly common in the Northern parts of the world including Middle East, Africa and the Asian countries. It is found in Eastern Europe, particularly in the former Soviet Union, throughout the Mediterranean, in north-western China, central Asia, southern Europe, Africa, the Middle East, and the Indian subcontinent (Peters, 1997; Carroll et al., 2010).

Crimean-Congo haemorrhagic fever is a widespread disease caused by a tick-borne virus (Nairovirus) of the Bunyaviridae family. This virus is known as the Nairovirus because of its spread from the ticks or through contact with the blood or other fluids from the infected animals and humans. Hosts of this virus are commonly hares, birds, domestic animals and adult ticks. The genome of this virus is circular, ambisense RNA in three parts - Small (S), Medium (M) and Large (L). The L segment is 11-4.4 kilobases in length, while the M and S segments are 4.4-6.3 and 1.7-2.1 kilobases long, respectively. The L segment encodes the RNA polymerase, the M segment encodes the envelope glycoproteins (Gc and Gn), and the S segment encodes the nucleocapsid protein (Carter et al., 2012). Based on the sequence data, seven genotypes of virus have been recognized, for instance, Africa 1 (Senegal), Africa 2 (Democratic Republic of the Congo and South Africa), Africa 3 (southern and western Africa), Europe (Albania, Bulgaria, Kosovo, Russia and Turkey), Europe 2 (Greece), Asia 1 (the Middle East, Iran and Pakistan) and Asia 2 (China, Kazakhstan, Tajikistan and Uzbekistan). The virons measure 80-120 nanometers (nm) in diameter and are pleomorphic. There are no host ribosomes within the viron and each virion contains three copies of the genome. The envelope is single layered and formed from a lipid bilayer 5 nm thick. It has no protrusions and the envelope proteins form small projections ~5-10 nm long. The nucleocapsids are filamentous and circular with a length of 200-3000 nm (Camicas et al., 1994).

The virus has been isolated from at least 31 different species of ticks within the genera *Haemaphysalis* and *Hyalomma* (Mehravaran et al., 2013). Sporadic infection to humans is usually caused by a *Hyalomma* tick bite. Clusters of illness typically appear after peoples or butchers eat infected livestock, particularly ruminants and ostriches. The main environmental reservoir for the virus are small mammals (particularly European hare, Middle-African hedgehogs and multimammat rats). Tick species that have been identified as infected with this virus include *Argas reflexus*, *Hyalomma anatolicum*, *Hyalomma detritum*, *Hyalomma marginatum marginatum* and *Rhipicephalus sanguineus* (Kayedi et al., 2015).

Some countries being an agricultural states depend on the earning of their livelihoods from the agricultural lands or by selling the products of domestic animals that are reared. This disease is mostly caught by the farmers or the keepers of goats, sheep, cattle etc. Ticks usually live on the skin or in the furs of these animals and the virus usually hosts ticks and gets transmitted to the workers that come in contact with infected animals or their body fluids. This virus also gets transmitted during slaughtering and butchering of animals. The disease has been diagnosed in more than 30 countries in Africa, Middle East, Asia and East Europe, a belt across central Africa, and South Africa and Madagascar. The reason of its widespread occurrence is that the ticks, which belong to genus *Hyalomma* are very common in these areas (Chinikar et al., 2009).

2. Congo Virus Infection

Crimean-Congo hemorrhagic fever, or Congo virus, is a viral infection transmitted by Hyalomma ticks to both animals and humans. The Congo virus is transmitted to peoples either by tick bites or through contact with infected animal blood or tissues during and immediately after slaughtering. The majority of cases have occurred in peoples involved in the livestock industry, such as agricultural workers, slaughterhouse workers and veterinarians. The ticks are found on hairy, small and large animals, and feed on blood to complete their life cycle. Mostly, the virus is transmitted by ticks living in the skins of goats, cows, buffalos and camels, feeding on their blood. The situation needs extra attention as cattle markets are being set up across the states for public to buy sacrificial animals for the religious occasion of Eid-ul-Azha. The disease is rare in infected animals, who mostly act as carriers of the disease which they transmit, but it is severe in infected humans. Though cases have been reported throughout the year, the disease is more common between March to October. So right at these moments, the ticks are very active and can easily spread to other animals, places where livestock are kept and humans too (Okorie, 1991).

Crushing of infected tick could also result in infection of virus. Infection may rarely occur if peoples breathe in the virus passed out in the infected animal's excreta. Thus, peoples who work in close contact with livestock such as those working in agriculture, slaughterhouses and veterinary hospitals are at a higher risk of acquiring the disease. Once a human is affected, the infection spreads to other peoples if they come in contact with the patient's infected blood or body fluids. Infection could also spread in hospitals during injections and surgical procedures of patients. Hospital staff, which treat patients with fever are at a higher risk for

developing the infection (Bell-Sakyi et al., 2012).

The virus can transfer to human beings from animals and can be fatal if not treated immediately. The tick are usually hidden inside and behind the ears, in the lower part of neck and legs. Peoples can get Congo virus by being bitten directly by the tick, humans and animals can transmit the virus to other humans, and through contact with infected animal plasma or tissues during and immediately after slaughtering. Human-to-human transmission can occur by close contact with the blood, secretions, organs or other bodily fluids of infected persons. Hospital-acquired infections can also occur due to improper sterilization of medical equipment, reuse of needles and contamination of medical supplies (Wilson et al., 1991).

3. Symptoms of Congo Fever

The Congo virus exhibits symptoms almost similar to those found in dengue ever. The only difference is that Congo virus is vectored by ticks while dengue is spread by mosquitoes. There are few noticeable symptoms of Congo virus including high fever, headache, pain in joints and muscles, nausea, pain in stomach and loose motions. Sudden fever with the temperature reaching up to 38.5^{o}C or more, muscle ache, dizziness, neck pain, stiffness, backache, headache, sensitivity to light are common. After 2 to 4 days, agitation may be replaced by sleepiness, depression and the abdominal pain gets localized to upper part leading to liver enlargement. The other clinical symptoms include fast heart rate, enlarged lymph nodes, and a rash in the mouth, throat and on the skin. There is a usual evidence of hepatitis and severely ill patients suffer rapid kidney deterioration, and sudden liver failure or pulmonary failure after the fifth day of illness. Through this fever, the death is likely to occur during the 2nd week of illness and death rate is about 30% (Whitehouse, 2004).

After an incubation period of 1 to 3 days following a tick bite or 5 to 6 days after exposure to infected blood or tissues, flu-like symptoms appear, which may resolve after one week. But, in many cases, signs of hemorrhage appear within 3 to 5 days of the onset of the first symptoms. Symptoms include high fever, vomiting, diarrhoea, red eyes, bleeding and severe body pain, especially in the joints, abdominal pain and sore throat, followed by sharp mood swings and confusion. As the condition gets severe, bleeding from gums, skin and large intestine may also occur and red spots appear on the body. The bleeding is due to the shortage of white cells that this disease causes and this can be very dangerous. Anyone who shows these symptoms needs to be immediately taken to the hospital as early diagnosis is important in saving the patient's life. Recovery from illness starts after the tenth day or so (Geisbert and Jahrling, 2004).

3.1. Indication in Animals

Many species of wild and domestic animals can become a host to the virus, such as cattle and pets. Most birds are resistant though they usually have no or few symptoms and survive it, unlike humans who have severe symptoms. The customers while purchasing a sacrificial animal should keep watch for dull or red eyes and animals suffering from a cough or flu. Infected animals show abnormal behaviour and other symptoms, so see a veterinarian swiftly.

3.2. Indication in Peoples

Cattle owners and traders are unaware about their vulnerability to the disease and the threat posed to them and the population at large. Currently and previously times, the disease has claimed several lives including physicians in some states. Symptoms vary from person to person, but some indications of this disease include high fever along with pain in joints and other parts of the body, vomiting, diarrhoea, and some peoples also exhibit signs of hemorrhage signs. Throat pain is also one of the common discomforts experienced as a symptom of this condition. Bleeding from gums, skin and large intestine may also occur and red spots appear on the body. Usually, flu-like symptoms appear first, which may end in a week's time. In nearly 75% of cases, signs of hemorrhagic fever appear in the first week if not treated properly. This means emotional confusion, aggression, mood swings, fever, red eyes, flushed face, joint pain, nosebleeds, vomiting and black stools. The liver gets swollen which causes pain in the upper abdomen. This can be followed by kidney failure, breathing problems, low blood pressure, rapid heart rate and eventually a shock (a serious case of poor blood circulation). In the second week, the condition may start improving, more likely if patients seek treatment (Sanchez et al., 2002).

Onset of symptoms is sudden, with fever, myalgia, (muscle ache), dizziness, neck pain and stiffness, backache, headache, sore eyes and photophobia (sensitivity to light). There may be nausea, vomiting, diarrhea, abdominal pain and sore throat, followed by sharp mood swings and confusion. After two to four days, the agitation may be replaced by sleepiness, depression and lassitude, and the abdominal pain may localize to the upper right quadrant, with detectable hepatomegaly (liver enlargement). Other clinical signs include tachycardia (fast heart rate), lymphadenopathy (enlarged lymph nodes), and a petechial rash (a rash caused by bleeding into the skin) on internal mucosal surfaces, such as in the mouth and throat and on the skin. The petechiae may give way to larger rashes called ecchymosis and other hemorrhagic phenomena. The mortality rate from virus is approximately 30%, with death occurring in the second week of illness. In patients who recover, improvement generally begins on the ninth or tenth day after the onset of illness

(Schwarz et al., 1997).

4. Some Routes of Transmission of Congo Fever

Humans get infected by Congo virus through infected animals, which in turn get it from infected ticks. The health officials commonly fudge or hide facts and the health coverage in poor countries is so low that many deaths go unaccounted. Particularly those in the rural areas, are more exposed to animals and have lesser sanitation than the urban dwellings. Most of agrarian societies thrive on animals or cattle for food and labour. Even in big cities have a lot of donkeys, horses and different kinds of cattle and pets. Therefore, the virus can spread swiftly if not controlled. Generally, there are 4 types of viral transmission, ticks to small or large livestock, ticks to humans, infected livestock to humans, and humans to humans. Transmission in humans is through contact with infected crushed ticks, contact with infected animal tissues, ingestion of unpasteurized milk and contact with infected peoples. The length of the incubation period for the illness appears to depend on the mode of acquisition of the virus. Following infection via tick bite, the incubation period is usually one to three days, with a maximum of nine days. The incubation period following contact with infected blood or tissues is usually five to six days, with a documented maximum of 13 days (Papa et al., 2006).

Transovarial transmission (transmission of the virus from infected female ticks to offspring via eggs) and venereal transmission have been demonstrated amongst some vector species, indicating one mechanism, which may contribute to maintaining the circulation of the virus in nature. The Congo fever virus first enters in these ticks, but it does not do any harm to the ticks, or does not infect the ticks. The virus also has the capability to transfer from one generation to other. However, when the ticks start feeding on small or large animal's blood, the virus infects the animals. Human transmission takes place when these ticks come in contact with the humans, or with the blood or tissue of infected animal. Human to Human transmission is also common during acute phase of this disease. Any effort for crushing of the tick can also result in infection of Congo fever. Peoples working in hospitals are also at great risk, transmission can be occur via injections and surgical instruments if not sterilized, and also the body fluids of affected persons can contribute to further transmission (Hekimoglu et al., 2012).

5. Diagnosis of Congo Hemorrhagic Fever

Patients with fatal disease, as well as in patients in the first few days of illness, do not usually develop a measurable antibody response and so diagnosis in these individuals is achieved by virus or RNA detection in blood or tissue samples. Tests on patient samples present an extreme biohazard risk and should only be conducted under maximum biological containment conditions. However, if samples have been inactivated (e.g., with virucides, gamma rays, formaldehyde, heat, etc.), they can be manipulated in a basic biosafety environment. Samples taken from peoples with suspected persons should be handled by trained staff working in suitably equipped laboratories. Congo virus infection can be diagnosed by several different laboratory tests, for instance, enzyme-linked immunosorbent assay (ELISA), antigen detection, serum neutralization, reverse transcriptase polymerase chain reaction (RT-PCR) assay, and virus isolation by cell culture (Fakoorziba et al., 2012).

6. Prevention and Control of Congo Hemorrhagic Fever

Preventive measures and early diagnosis of Congo virus infection can save lives, so, obviously there is nothing to worry. Less than half of the peoples who contract this virus die and that too are due to improper treatment. According to health experts, the Congo fever could become a grave concern if preventive measures are not taken and stress the need to vaccinate cattle with Ivermectin and use an antiseptic spray preceding the slaughter of cattle. The traders, buyers, butchers and others coming into close contact with sacrificial animals should try to adopt precautionary measures. As, there is no sufficiently effective vaccine available as yet, so creating of awareness is all we can do to control Congo virus infection (Xiao et al., 2011).

6.1. Preventive Measures

Gloves should be used while handling of sacrificial animals, and one should wear full sleeves, long trousers and light colour dresses notably during slaughtering, butchering and culling procedures in slaughterhouses or at homes. The infected blood of cattle can affect human beings and it is suggested to cover the face while culling the animal and especially protection of the eyes and mouth from the animal's blood. When coming in contact with cattle, peoples must wear full outer cover and light-coloured clothes so the ticks can be identified. Avoid physical contact with the infected human and use gloves and other protective equipment while taking care of the infected person. Properly eliminate ticks, use chemical sprays to kill the ticks, use a spray on animals and apply a protective spray on personal clothes and clothing. Unpasteurized milk should not be drunk or boil it before use. In meat, the virus is usually deactivated by post-slaughter

acidification. It is also killed by cooking, for that reason meat should be properly cooked to kill the virus if its infection is present or avoid it if possible. The virus is more common in larger animals than in birds. So, chicken and fish might be safer diets. Parents are advised to check sacrificial animals before allowing children to go near them. The government should spray sacrificial animal markets and diseased animals must be banned from entering in the cities and isolated to avoid contact, and the waste material of sacrificial animals ought to be disposed of properly (Fisher-Hoch et al., 1995; Nabeth et al., 2004).

6.2. Precautionary Measures

Adequate precautions should be taken to avoid being infected with virus in epidemics. Persons must be cautious if are often exposed to any animals or even those are eaten. If persons have any of the previously mentioned symptoms, the obvious stopover should be at clinic or hospital. Timing is the key factor, but sooner steps taken are the better. Peoples exposed to domestic animals or those undergoing activities like hiking should wear protective apparatus to avoid tick bites. Government needs to make isolated wards in every tertiary and secondary care hospitals rather than waiting for a case to emerge. Government should focus on villages to control the virus from spreading, since the primary outbreak location is where cattle are bred and kept. Hospital staff should also take adequate precautions while treating patients suffering with the disease. Ribavirin may be administered to peoples coming in close contact with patients (Sheikh et al., 2004). To avoid tick bites, peoples who go near animals or the cattle market should cover their face, hands and feet and so on. They should avoid to wear dark coloured clothes so that a tick can be easily seen if it sticks on their dresses. Avoid touching or going too close to animals that may have ticks or those that have been bought from markets where they have been in contact with many other animals from all over the state. Contact with infected blood or tissues should also be avoided. Protective clothing and gloves should be used when handling infected animals, particularly when blood and tissues are handled. Stay fully covered, wear bright garments to detect ticks and wear masks when in animal markets for buying the animals or around the animals at home. Avoid areas where there are too many ticks, use long pants tucked into boots and long-sleeved shirts should be worn to minimize tick bites. Isolate patients who have the virus, maintain minimal or protected contact, and wash the body and hands afterwards. The syringes and needles should be carefully disposed. Health practitioners, hunters, agriculturalists and those who handle raw meat during slaughtering, meat-supplying and cooking are also at risk (Crowcroft et al., 2002).

Sanitation is important because the virus is present in all fluids released by the host animals and patients. Do not try to eat or drink around animals whenever possible. The meat can be neutralized by cooking but the disposed organs and leaked blood is risky. So, do not let the leftovers to stay bare and clean everything quickly while remaining covered. Before the arrival of sacrificial animals at sale points, there should be policy requiring for the animals to be vaccinated before being granted entry into the cattle markets. When peoples are careful enough, the community will remain safe and need not to worry about the fever (Chin, 2000). Perform proper burial of dead infected animals to avoid spreading of ticks from the dead animals to other animals and humans. Always tuck the bottom of pants into socks to avoid the ticks entering in the bottom of the pants and bites on toes and legs. Keep houses, medical facilities and other public areas properly cleaned, and use tick killer sprays (Athar et al., 2003).

6.3. Use of Tick Repellents

Acaricides, which are pesticides that kill ticks and mites, can be used on livestock and other domesticated animals to control ticks, particularly where they are kept and before slaughtering. Furthermore, the tick vectors are numerous and widespread, so tick control with acaricides (chemicals intended to kill ticks) is only a realistic option for well-managed livestock production facilities (Sarwar and Sarwar, 2016). For instance, following an outbreak at an ostrich abattoir, measures have been taken to ensure that ostriches remained tick free for 14 days in a quarantine station before slaughter. This decreased the risk for the animal to be infected during its slaughtering and prevented human infection for those in contact with the livestock. Peoples should use approved chemicals intended to kill ticks on clothing, and apply approved repellent on the skin and clothing, regularly. For instance, use tick repellent such as Diethyltoluamide to the skin and Permethrin on clothes (Ergonul et al., 2007).

6.4. Treatment

General supportive care with treatment of symptoms is the main approach to manage Congo virus in people. Although an inactivated, mouse brain-derived vaccine against Congo virus has been developed and used on a small scale in Eastern Europe, there is currently no safe and effective vaccine widely available for human use. Also there is no known vaccine for this virus to use in animals, but in the case of humans, this fever can be treated using Ribavirin, which is an antiviral drug. Ribavirin (tribavirin) can be given both orally and intravenously as prescribed by the physician. This antiviral drug ribavirin has been used in treatment of established fever infection with apparent benefit. It is not a

specific treatment protocol, but this must be started immediately after the virus detection when required by the physician's prescription. Intensive monitoring to guide volume and blood component replacement is required. An appropriate treatment of secondary infections should be instituted. Treatment is primarily symptomatic and supportive, as there is no established protocol. Ribavirin is effective in vitro and has been used during outbreaks, but there is no trial evidence to support its use. Ribavirin inhibits a variety of DNA and RNA viruses. It is active against viral haemorrhagic fevers caused by the Arenaviridae and Bunyaviridae family viruses (Ergonul et al., 2004).

Immunoglobul preparations while used remain unproven. Although recent developments in antibody engineering have raised hopes for novel mAb therapies, this approach remains in its infancy (Keshtkar-Jahromi et al., 2011). The only available and probably somewhat efficacious Crimean-Congo hemorrhagic fever vaccine is an inactivated antigen preparation currently used. Alternatively, many scientists appear to believe that treatment of virus with ribavirin is more practical than prevention, but some recently conducted clinical trials, appear to counter assumptions of drug efficacy. A Turkish research team has successfully developed the first non-toxic preventive vaccine, which passed clinical trials and is pending approval (Ergonul, 2006).

Avoid any contact with the infected persons and animals, but usually avoid fornication and other contacts. Immediately isolate the patient on the observance of fever up to or greater than 38.5^{o}C, and seek physician's advice as soon as possible and hospitalize the patient. A medicine to prevent the virus can be provided to peoples, however, if a person is infected with the virus he or she is incurable. When feverish patients with evidence of bleeding require resuscitation or intensive care, body substance isolation precautions should be taken (Sarwar, 2016).

7. Conclusion

Peoples can get Congo virus by being bitten directly by the ticks, and humans and animals can transmit the virus to other humans, through contact with infected animal's blood or tissues during and immediately after slaughtering. Human-to-human transmission can occur by close contact with the blood, secretions, organs or other bodily fluids of infected persons. Infections in hospitals can occur due to improper sterilization of medical equipment, reuse of needles and contamination of medical supplies. As the illness progresses, large areas of severe bruising, severe nose bleeding, and uncontrolled bleeding at injection sites can be seen, beginning on about the fourth day of illness and lasting for about two weeks. The fever is usually associated with headache and muscle pains, and does not respond to antibiotic or anti-malarial treatment. In documented outbreaks of Crimean-Congo hemorrhagic fever, fatality rates in hospitalized patients have ranged from 9% to as high as 50%. In the absence of a vaccine, the only way to reduce infection in peoples is by raising awareness of the risk factors and educating peoples about the measures they can take to reduce exposure to the virus. Public health advice should focus on several aspects. For reducing the risk of tick-to-human transmission, wear protective clothing (long sleeves, long trousers), wear light coloured clothing to allow easy detection of ticks on the clothes, use approved acaricides (chemicals intended to kill ticks) on clothing, use approved repellent on the skin and clothing, regularly examine clothing and skin for presence of ticks and if found remove them safely, seek to eliminate or control tick infestations on animals or in stables and barns, and avoid areas where ticks are abundant and seasons when they are most active. For decreasing the risk of animal-to-human transmission, wear gloves and other protective clothing while handling animals or their tissues in endemic areas, notably during slaughtering, butchering and culling procedures in slaughterhouses or at home, quarantine the animals before they enter slaughterhouses or routinely treat animals with pesticides about two weeks prior to slaughter. To reduce the risk of human-to-human transmission in the community, avoid close physical contact with Crimean-Congo hemorrhagic fever infected peoples, wear gloves and protective equipment when taking care of ill peoples, and wash hands regularly after caring for or visiting ill peoples.

References

[1] Athar, M. N., H. Z. Baqai, M. Ahmad, M. A. Khalid, N. Bashir, A. M. Ahmad, A. H. Balouch and K. Bashir. 2003. Short Report: Crimean-Congo Hemorrhagic Fever outbreak in Rawalpindi, Pakistan, February 2002. Am. J. Trop. Med. Hyg., 69 (3): 284-287.

[2] Bell-Sakyi, L., A. Kohl, D. A. Bente and J. K. Fazakerley. 2012. Tick cell lines for study of Crimean-Congo hemorrhagic fever virus and other arboviruses. Vector Borne Zoonotic Dis., 12 (9): 769-781.

[3] Camicas, J. L., J. P. Cornet, J. P. Gonzalez, M. L. Wilson, F. Adam and H. G. Zeller. 1994. Crimean-Congo hemorrhagic fever in Senegal. Latest data on the ecology of the CCHF virus. Bull. Soc. Pathol. Exot., 87: 11-16.

[4] Carroll, S. A., B. H. Bird, P. E. Rollin and S. T. Nichol. 2010. Ancient common ancestry of Crimean-Congo hemorrhagic fever virus. Mol. Phylogenet Evol., 55 (3): 1103-1110.

[5] Carter, S. D., S. Rebecca, T. C. Walter, A. Antonio, B. Eric, S. T. Nichol, A. J. Hiscox, A. T. Edwards and N. J. Barr. 2012. Structure, Function, and Evolution of the Crimean-Congo Hemorrhagic Fever Virus Nucleocapsid Protein. Journal of Virology, 86 (20): 10914-10923.

[6] Chin, J. 2000. Control of Communicable Diseases Manual. American Public Health Association, seventh edition, Washington DC. Pp. 54.

[7] Chinikar, S., S. M. Ghiasi, A. Ghalyanchi-Langeroudi, M. M. Goya, M. R. Shirzadi, M. Zeinali and A. Haeri. 2009. An overview of Crimean- Congo Hemorrhagic Fever in Iran. Iran. J. Microbiol., 1 (1): 7-12.

[8] Crowcroft, N. S., D. Morgan and D. Brown. 2002. Viral haemorrhagic fevers in Europe-effective control requires a co-ordinated response. Euro. Surveill., 7 (3): 31-32.

[9] Ergonul, O., A. Celikbas, B. Dokuzoguz, S. Eren, N. Baykam and H. Esener. 2004. The characteristics of Crimean-Congo hemorrhagic fever in a recent outbreak in Turkey and the impact of oral ribavirin therapy. Clin. Infect. Dis., 39 (2): 285-289.

[10] Ergonul, O. 2006. Crimean-Congo haemorrhagic fever. Lancet Infect Dis., 6 (4): 203-214.

[11] Ergonul, O. and A. C. Whitehouse. 2007. Personal Reflections, Jack Woodall, Congo Hemorrhagic Fever: A Global Perspective, Netherlands: Springer. Pp. 23.

[12] Fakoorziba, M. R., P. Golmohammadi, R. Moradzadeh, M. D. Moemenbellah-Fard, K. Azizi, B. Davari, H. Alipour, S. Ahmadnia and S. Chinikar. 2012. Reverse transcription PCR-based detection of Crimean-Congo hemorrhagic fever virus isolated from ticks of domestic ruminants in Kurdistan province of Iran. Vector Borne Zoonotic Dis., 12 (9): 94-39.

[13] Fisher-Hoch, S. P., J. A. Khan, S. Rehman, S. Mirza, M. Khurshid and J. B. McCormick. 1995. Crimean-Congo Haemorrhagic Fever treated with oral Ribavirin. Lancet, 346: 472-475.

[14] Geisbert, T. W. and P. B. Jahrling. 2004. Exotic emerging viral diseases: Progress and challenges. Nat. Med., 10 (S): 110-121.

[15] Hekimoglu, O., N, Ozer, K, Ergunay and A. Ozkul. 2012. Species distribution and detection of Crimean Congo Hemorrhagic Fever Virus (CCHFV) in field-collected ticks in Ankara Province, Central Anatolia, Turkey. Exp. Appl. Acarol., 56 (1): 75-84.

[16] Kayedi, M. H., S. Chinikar, E. Mostafavi, S. Khakifirouz, T. Jalali, A. Hosseini-Chegeni, A. Naghizadeh, M. Niedrig, A. R. Fooks and N. Shahhosseini. 2015. Crimean-Congo Hemorrhagic Fever Virus Clade IV (Asia 1) in Ticks of Western Iran. J. Med. Entomol., 52 (5): 1144-1149.

[17] Keshtkar-Jahromi, M., J. H. Kuhn, I. Christova, S. B. Bradfute, P. B. Jahrling and S. Bavari. 2011. Crimean-Congo hemorrhagic fever: Current and future prospects of vaccines and therapies. Antiviral Res., 90 (2): 85-92.

[18] Mehravaran, A., M. Moradi, Z. Telmadarraiy, E. Mostafavi, A. R. Moradi, S. Khakifirouz, N. Shah-Hosseini, F. S. Varaie, T. Jalali, S. Hekmat, S. M. Ghiasi and S. Chinikar. 2013. Molecular detection of Crimean–Congo haemorrhagic fever (CCHF) virus in ticks from south-eastern Iran. Ticks Tick Borne Dis., 4 (1-2): 35-38.

[19] Nabeth, P., M. Thior, O. Faye and F. Simon. 2004. Human Crimean-Congo hemorrhagic fever, Senegal. Emerg. Infect. Dis., 10: 1881-1882.

[20] Okorie, T. G. 1991. Comparative studies on the vector capacity of the different stages of *Amblyomma variegatum* Fabricius and *Hyalomma rufipes* Koch for Congo virus, after intracoelomic inoculation. Vet. Parasitol., 38 (2-3): 215-223.

[21] Papa, A., S. Bino, E. Velo, A. Harxhi and M. Kota. 2006. Antoniadis A. Cytokine levels in Crimean-congo hemorrhagic fever. J. Clin. Virol., 36: 272-276.

[22] Peters, C. J. 1997. Viral Hemorrhagic Fevers. Viral Pathogenesis. New York: Lippincott-Raven Publishers. p. 779-794.

[23] Sanchez, A. J., M. J. Vincent and S. T. Nichol. 2002. Characterization of the glycoproteins of Crimean-congo hemorrhagic fever virus. J. Virol., 76: 7263-7275.

[24] Sarwar, M. 2016. Ticks (Arachnida: Acari) induced Paralysis in Humans and Control of Incidence in the Current Civilization. International Journal for Research in Social Science and Humanities Research, 1 (7): 27-36.

[25] Sarwar, M. H. and M. Sarwar. 2016. Medical Importance of Ticks Bite and Diseases Transmission by Means of It Affecting Humans. Biomedical and Health Informatics, 1 (2): 44-51.

[26] Schwarz, T. F., H. Nsanze and A. M. Ameen. 1997. Clinical features of Crimean- Congo haemorrhagic fever in the United Arab Emirates. Infection, 25: 364-367.

[27] Sheikh, A. S., A. A. Sheikh, N. S. Sheikh and M. Tariq. 2004. Ribavirin: an effective treatment of Crimean-Congo Haemorrhagic Fever. Pak. J. Med. Sci., 20 (3): 201-206.

[28] Whitehouse, C. A. 2004. Crimean-congo hemorrhagic fever. Antiviral Res., 64: 145-160.

[29] Wilson. M. L., J. P. Gonzalez, J. P. Cornet and L. Camicas. 1991. Transmission of Crimean-Congo haemorrhagic fever virus from experimentally infected sheep to *Hyalomma truncatum* ticks. Res. Virol., 142 (5): 395-404.

[30] Xiao, X., Y. Feng, Z. Zhu and D. S. Dimitrov. 2011. Identification of a putative Crimean–Congo hemorrhagic fever virus entry factor. Biochem. Biophys. Res. Commun., 411 (2): 253-258.