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Original Article

Incidence, Mortality, and Burden of Crimean Congo Hemorrhagic Fever and Its Geographical Distribution in Iran during 2009-2015

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Abstract

Background: This study aimed at estimating the incidence, mortality, burden, and geographical distribution of Crimean Congo Hemorrhagic Fever (CCHF) using Disability Adjusted Life Years (DALYs) in Iran 2009-2015.

Methods: CCHF-related DALYs was calculated using a method developed by WHO for the investigation of Global Burden of Diseases (GBD). DALYs was calculated through adding years of life lost due to premature death (YLLs) to years lived with disability (YLDs). To calculate YLD, the average duration of the disease and its disability weight were set at 25 d and 0.613, respectively. The data on the incidence and mortality were collected from the CCHF surveillance system from the governmental section.

Results: The highest and the lowest incidence rates of CCHF were observed in 2009 (122 cases) and 2010 (254 cases), respectively. Moreover, the lowest and highest mortality rates were reported in 2009 (20 cases) and 2012 (52 cases), respectively. The mean rate of fatality from CCHF observed between 2009 and 2015 was about 21.1%. In addition, the lowest and highest DALYs were observed in 2009 (483 cases) and 2010 (1156 cases), respectively. CCHF incidence, DALYs, and mortality rate over the studied period were higher among males than females. CCHF-related DALYs did not have an equal distribution in all provinces of Iran; some provinces were suffering from a higher burden of the disease.

Conclusion: It is recommended to improve the CCHF surveillance system, identify high-risk areas, practice early diagnosis and intervention, develop vaccines, control, and fight tick, and screen livestock to control and prevent the spread of this disease.

Keywords: Incidence; Mortality; Disability-adjusted life years; Crimean Congo hemorrhagic fever; Iran

Introduction

Crimean Congo Hemorrhagic Fever (CCHF) is a zoonotic disease caused by a virus transmitted by ticks; it can cause severe hemorrhagic fever outbreaks (1, 2). CCHF is an arboviral disease highly

widespread around the world. It is an endemic disease in Africa, Asia, Middle East, and Eastern Europe (3, 4). Iran is also considered as an endemic area for CCHF disease. According to the WHO's 2017 report, Iran, Turkey, Uzbekistan, and Russia are among the countries with the highest rate of reported cases of CCHF (more than 50 cases per year) (5).

Farmers, livestock workers, slaughterhouse staff, health personnel, and people living in endemic areas are at risk of CCHF (1). Currently, there is no safe and effective human vaccine for CCHF and it causes a high rate of mortality among people. Its fatality rate can vary from 10% to 40% (2). Its fatality rate in countries like Kosovo and turkey, which are endemic areas for the disease, is 25.5% and 5%-10%, respectively (6, 7). In recent years, mortality from this disease has also been reported in Sudan, Iraq, Iran, Pakistan, and Afghanistan (2).

CCHF is an important disease that may endanger the lives of many people, therefore, the WHO supports the measures adopted to improve its surveillance system, diagnostic capacities, and responses to the outbreaks in Europe, Asia, Middle East, and Africa so that they would become able to control the disease or combat it (1, 2).

To preserve the international prestige and to control the high mortality rates, surveillance systems of countries pay more attention to some of the infectious diseases. CCHF is one of such diseases that require special attention to be controlled (3, 4).

In order to prevent and control CCHF, to take an appropriate response against CCHF, and to improve policy-making, it is necessary to provide proper and reliable epidemiological information. Burden of disease is one of the important types of information. Estimating the burden of CCHF makes it possible to compare it with the burden of other diseases and provides an opportunity to set it as an agenda for the health policy makers so that they pay more attention to this issue. In addition, estimating the burden of the disease at national and local levels helps to determine its epidemic status as well as its trend over time; it helps to identify areas where the disease may be a danger and threat for the public health. Despite the significance of this issue, no study has been conducted in this field. Moreover, sharing borders with countries such as Iraq, Turkey, Afghanistan, and Pakistan, considered as endemic areas of the disease, doubles the significance of conducting this study.

To depict a comprehensive picture of the disease, we aimed at estimating the burden of CCHF at national and provincial levels as well as its trend between 2009 and 2015.

Methods

The data on Disability-Adjusted Life Years (DALYs) was used for calculating the burden of CCHF. DALYs is calculated through adding Years of Life Lost due to premature death (YLLs) to Years of Life Lost due to disability (YLDs) (8).

DALY= YLL+ YLD Equation [1]

DALYs was calculated using the method developed by the WHO for investigating the GBD (9, 10). We did not consider age weights in the calculations; however, a discount rate of 0.03 was applied for discounting health values in future years (9). YLD is calculated through multiplying annual incidence rate of CCHF by its average period and disability weight. In the present study, after holding an expert panel with infectious diseases specialists, the average period of the disease was set at 25 d. Moreover, the disability weight was set at 0.613 (11).

In addition, disease burden was calculated and reported by age, time, and place for all provinces of Iran. For each age group, the mean age of the group was considered as death age for patients died from CCHF. However, mean age of death for the two age groups of 0-1 and 1-5 was set at 0.1 and 2.6, respectively. The life expectancy remaining for each age group was calculated using life tables of Iranians reported by the WHO. The data on the incidence and mortality from 2009 to 2015 were obtained from the CCHF surveillance system in the Centre for Communicable Diseases Control (CCDC), Ministry of Health and Medical Education (MOHME). We considered both defi-

nite and probable cases of CCHF when calculating DALYs of CCHF. The statistical data on the population of the country and its provinces during the studied years was collected from Statistical Center of Iran (12). Data were analyzed using Excel software (ver. 2010).

Results

Table 1 presents the incidence, mortality, and burden of CCHF by sex from 2009 to 2015. The lowest and the highest incidence of CCHF were observed in 2009 (122 cases) and 2010 (254 cases), respectively. Its incidence among males was higher than that among females. Furthermore, over the studied period, the lowest and the highest mortality were observed in 2009 (20 cases) and 2012 (52 cases), respectively. The mortality was higher among males than females. The lowest and highest DALYs were 483 and 1156, respectively. The trends of CCHF incidence and mortality rate per 100,000 population by sex are presented in Fig. 1. Its fatality was 21.1% (272 deaths out of 1289 cases of CCHF) over the studied period.

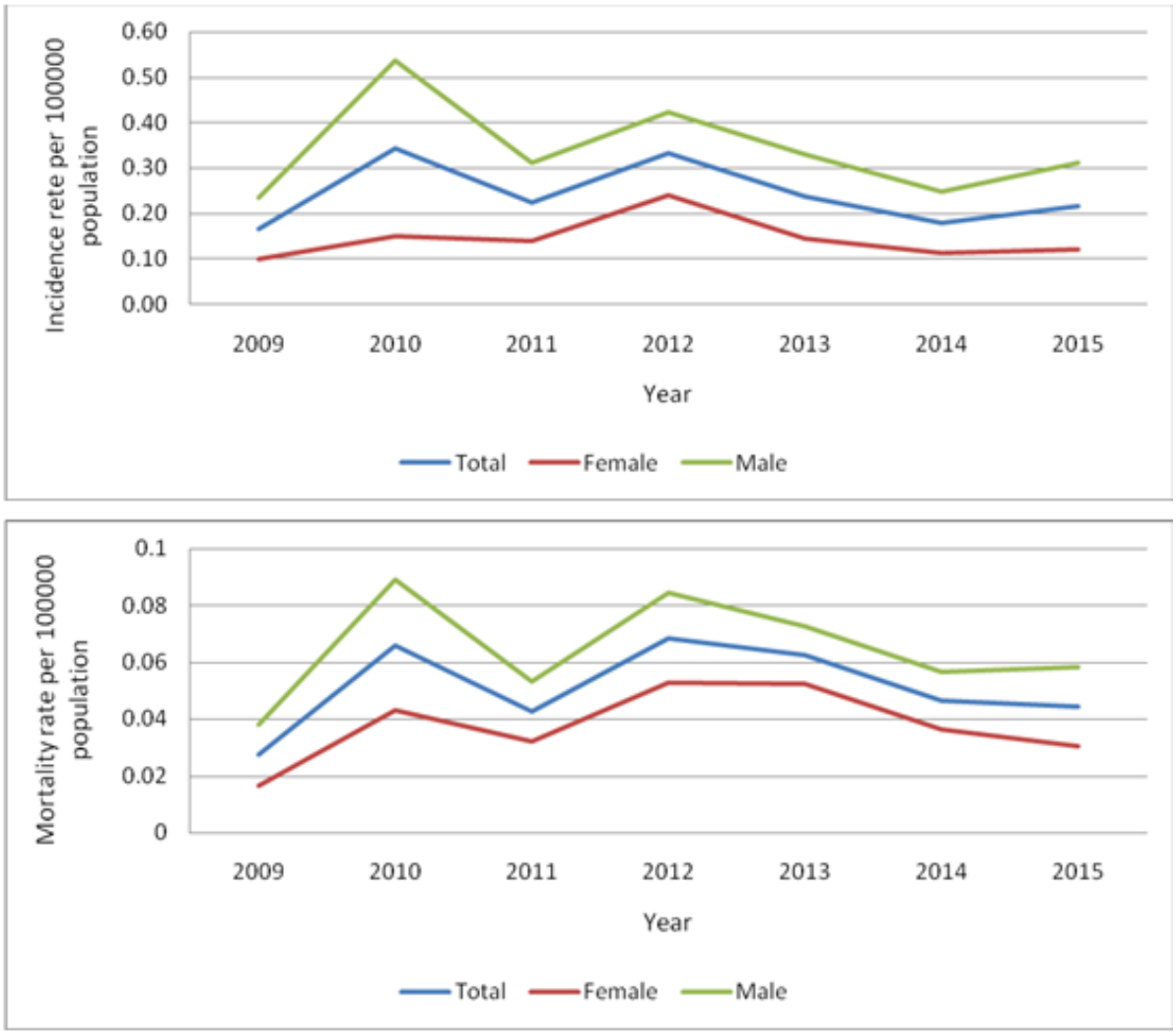

Fig. 1: Time trend of changes in the incidence and mortality of CCHF by sex per 100000 population during 2009-2015

Table 1: Incidence, mortality and burden of CCHF by sex during 2009-2015

Year	*Reported CCHF case in males*	*Reported CCHF case in females*	*Reported incidence rate per 100000 population*	*Reported case leading to death*	*Male DALYs*	*Female DALYs*	*Total DALYs*	*DALY per 100,000 populations*
2015	123	47	0.22	35	498	226	724	0.92
2014	97	43	0.18	36	441	318	759	0.98
2013	127	55	0.24	48	565	450	1015	1.32
2012	161	91	0.33	52	599	362	961	1.26
2011	117	52	0.22	32	400	274	674	0.90
2010	199	55	0.34	49	752	404	1156	1.56
2009	86	36	0.17	20	323	160	483	0.66

Figure 2 presents the trend and variations in CCHF burden per 100,000 population over the studied period. The trend of CCHF-related DALYs had some fluctuations over the studied years. It was 0.66 in 2009 and 0.92 in 2015.

Figure 3 shows the share of YLL and YLD in general burden of CCHF over the studied period. In all the studied years, more than 98% of DALYs were attributed to YLL caused by CCHF, indicating the high fatality rate of the disease.

Figure 4 shows the share of each sex in the burden of CCHF in various age groups in 2015. The highest burden of the disease was observed in people aged 15-44 yr old. In general, disease burden was higher among males than among female.

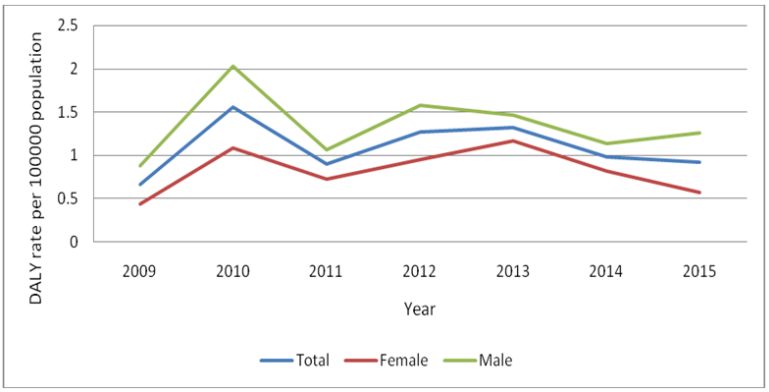

Fig. 2: Time trend of changes in the CCHF-related DALYs by sex during 2009-2015

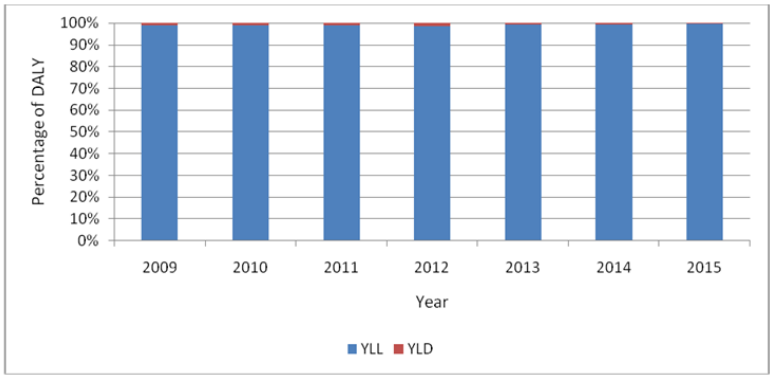

Fig. 3: Share of YLL and YLD in the burden of CCHF (DALYs) during 2009-2015

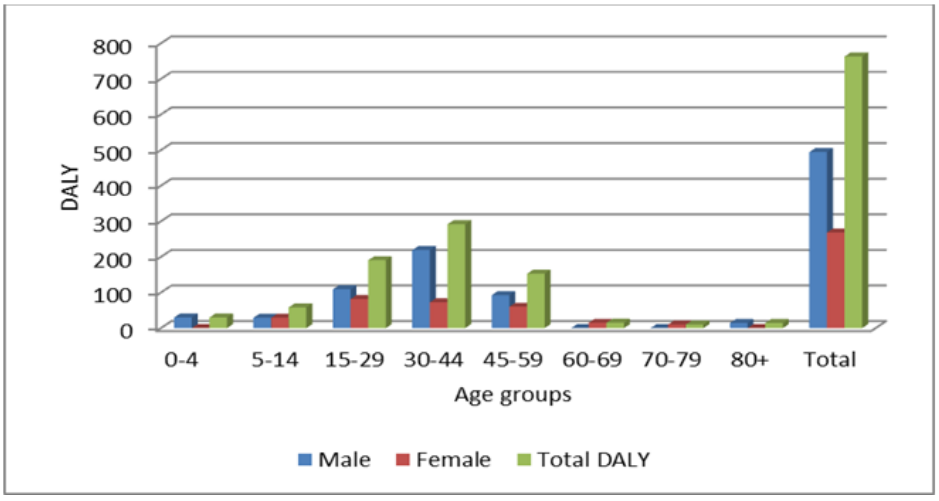

Fig. 4: Share of each sex in the burden of CCHF (DALYs) in different age groups in 2015

The provincial distribution of CCHF in 2010, 2012, and 2015 is presented in Figs. 5-7. In 2010, Sistan and Baluchistan with a DALY of 16.27/100000 population and Yazd with a DALY of 8.01/100000 population had the highest burden of CCHF. In addition, in 2012, the highest CCHF-related DALYs per 100000 population were observed in Golestan (4.65), Yazd (4.23), Sistan and Baluchistan (3.66), and Fars (3.54). Moreover, the highest burden of CCHF was observed in Golestan and Kerman with 4.49 and 3.46 DALYs per 100,000 population in 2015.

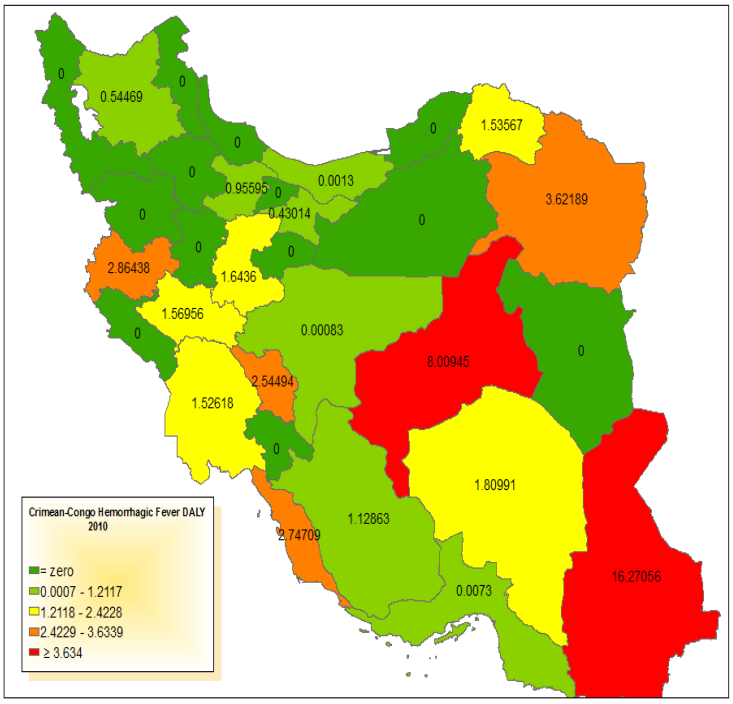

Fig. 5: Geographical distribution of DALYs caused by CCHF per 100000 population in 2010 in Iran

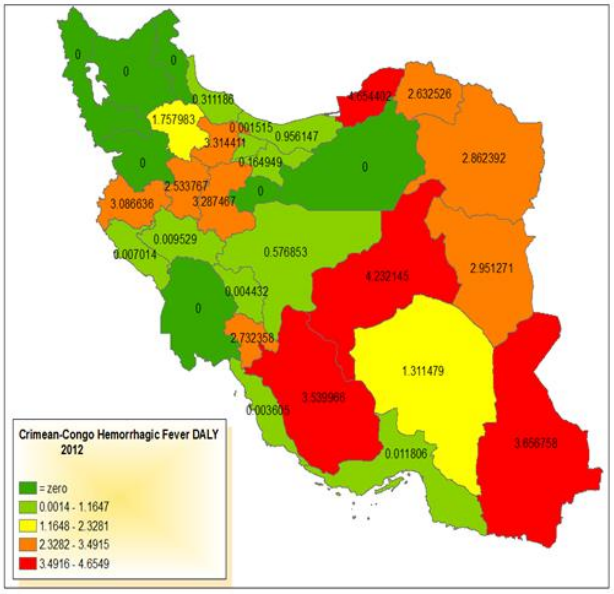

Fig. 6: Geographical distribution of DALYs caused by CCHF per 100000 population in 2012 in Iran

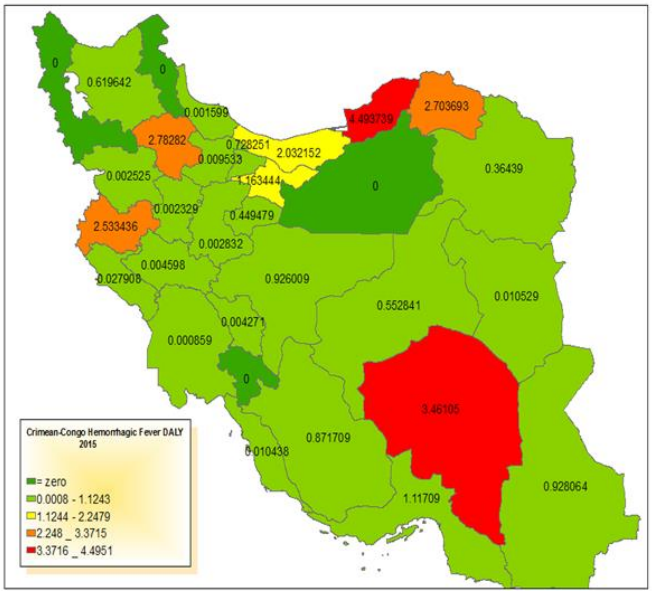

Fig. 7: Geographical distribution of DALYs caused by CCHF per 100000 population in 2015 in Iran

Discussion

Based on the results of our study, CCHF incidence did not have a stable trend between 2009 and 2015. The lowest and highest incidence per 100 000 population were 0.18 in 2009 (122 cases) and 0.52 in 2010 (254 cases), respectively. The absence of suitable human and animal vaccines for CCHF, sharing borders with countries suffering from endemic disease, and unknown aspects that affect the criteria for the outbreak of the disease can be considered as the main causes for the outbreak of the disease and the absence of a specific trend (reduction or increase) in CCHF in the country. According to a study, 534 confirmed cases with CCHF (Confirmed Case) have been

reported in Iran between 2000 and 2008. The lowest and highest number of cases were observed in 2005 (18 cases) and 2008 (120 cases), respectively (13).

In Kosovo, the incidence of CCHF between 1995 and 2013 has not been steady (increasing or decreasing) and varied from zero to 2.2 (46 cases) per 100,000 people (14). According to the Turkish Health Ministry's surveillance system, between 2000 (150 cases) and 2007 (717 cases), the incidence of CCHF was increasing, with a total of 1820 new cases diagnosed with CCHF (15). According to a report by the WHO published in 2017, Turkey, Uzbekistan, Kazakhstan, Russia, and Iran have 50 or more cases of CCHF per year (5).

Over the studied period, the incidence of the disease among males was more than that among females. In Iran, livestock husbandry is a more common job among males than among females, and the disease is more likely to occur in people who live and work near livestock. This finding is in line with the results of other studies in Iran and other countries (13, 15).

Moreover, CCHF mortality rate had a descending trend over the studied period and the disease caused more deaths among males than females. In Iran, between 2000 and 2008, the mortality rate due to CCHF decreased (13). In Kosovo, between 1994 and 2013, the mortality from the disease has fallen from 2.39 to 0.69 per 100,000 people (7, 14).

In our study, the lowest and the highest case fatality rate were 16.4% in 2009 and 26.4% in 2013. Overall, the mean fatality rate was 21.1% (272 deaths per 1289 cases). In Kosovo, CCHF fatality rate changed from zero in 1995 to 50% in 2013 (14). Furthermore, disease fatality rate was 5% (92 deaths per 1820 case) in Turkey between 2000 and 2007 (15), 11.5% in Pakistan in 2010 (16), and 25.5% in Kosovo between 1995 and 2013 (14).

Results of our study indicated that the trend of DALYs caused by CCHF is closely in line with the trend of mortality rate. CCHF DALYs reduced between 2012 and 2015, indicating the high and effective contribution of YLL (more than 98%) to the total DALYs caused by CCHF.

In all the studied years, the burden of disease among males was more than that among females. In addition, in 2015, people aged 15-44 yr old had the highest share in DALYs. In Iran, the DALYs caused by CCHF was 367 (11). Based on our reviews, no similar study has been conducted in other countries.

The high burden of disease, mortality, and incidence rate of CCHF among males than females shows that animal husbandry and farming are a male job. Job is a risk factor for CCHF and those whose jobs are related to livestock are at risk of CCHF (1, 14). In addition, the infection rate of Crimean-Congo Hemorrhagic Fever Virus (CCHFV) in livestock is a strong predictor for determining the incidence of CCHF in countries like Iran (17) and Mauritania (18). However, it is not an important factor for the incidence of CCHF in Bulgaria, because in Bulgaria there is a proper program for the vaccination of population at risk such as ranchers and veterinarians (19).

The two factors of climate and job are the main predictors of CCHF (20, 21). Therefore, the distribution and burden of CCHF may vary in different parts of the country. It is important to understand the geographical distribution of CCHF as well as its real risk in order to increase public awareness, enhance safety programs for health personnel, ranchers, and slaughterhouse workers, and improve protective measures against tick bites (22).

Based on the results of our study, between 2009 and 2015, the presence of patients with CCHF was reported in 29 out of the 31 provinces of the country. The results of our study revealed that the burden of CCHF was different in various provinces of Iran and it did not have an equal distribution; a large share of DALYs is observed in only a few numbers of provinces. Authorities need to pay more attention to provinces such as Sistan and Baluchistan, Fars, Kerman, Yazd, and Golestan if they want to prevent and control CCHF. In similar studies in other countries, there was no equal geographical distribution of CCHF in different parts of a country (7, 23, 24).

According to other studies carried out in Iran (20) and Senegal (25), the incidence rate of

CCHF is high in areas suffering from the shortage of rain and humidity for long periods. Moreover, high temperature has also been reported as a predictor of CCHF in Turkey (23), Bulgaria (19), and Iran (20). In Kosovo, the incidence of CCHF did not have a uniform distribution in all its provinces (14). The high prevalence of livestock farming and agricultural jobs, the suitable weather conditions, and shared borders with countries such as Turkey, Pakistan, Afghanistan, and Iraq have turned Iran into an ideal ecosystem for CCHF. The current status of CCHF disease in Iran indicates the need to seriously focus on different aspects of this disease; for instance, it is necessary to identify high-risk areas, practice early diagnosis and intervention, manage patients, develop vaccines, control, and fight tick, and screen livestock to control and prevent the spread of this disease

Limitations

As one of the limitations of our study, we only used the data collected form CCHF surveillance system to estimate the incidence, mortality, and burden of the disease. CCHF surveillance system, similar to other surveillance systems implemented for other diseases, suffers from under-reporting.

Conclusion

CCHF is an indigenous disease. In recent years, there have been some cases of this disease, especially in some specific areas of Iran. Apparently, there is no effective program in the country to control the spread of this disease in livestock; therefore, it is expected to observe more cases of CCHF in the future. Monitoring the incidence and burden of the disease over time can show the effect of interventions implemented to control the disease. Thus, it is highly recommended to conduct such studies. Given the high CCHF mortality rate and its negative effects on livestock industry, authorities should pay more attention to this disease. Empowering the CCHF surveillance system and implementing effective interventions to prevent virus transmission from livestock to human are the most important measures fully considered by health system managers and policymakers.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors declare that there is no conflict of interests.

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