

Full Length Research Paper

An evaluation of spatial distribution of Crimean-Congo hemorrhagic fever with geographical information systems (GIS), in Samsun and Amasya region

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The widespread geographic distribution of the Crimean-Congo hemorrhagic fever (CCHF) virus and its ability to produce severe human disease with high mortality rates make the virus an important human pathogen. CCHF has a very wide geographic distribution, being endemic in more than 30 countries in Africa, central and southwestern Asia, the Middle East and Eastern Europe. CCHF virus-infected cases were first reported in Turkey in 2002 and a total of 3135 confirmed cases were reported between 2002 and 2008. This increase in Turkey may be attributed to the country lying on the migratory path between Africa and Europe, changes in climatic factors, and environmental factors. This study was intended to provide the risk area and spatial distribution map and, patients diagnosed with CCHF at hospitals in the Turkish province of Samsun and at the Ondokuz Mayıs University Medical Faculty Hospital (OMUMFH) between 01 January, 2004, and 31 December, 2008, by establishing their domicile addresses, and to produce an epidemiological risk map for the disease using Geographical Information Systems.

Key words: Crimean-Congo hemorrhagic fever, geographical information systems, Turkey, epidemiology

INTRODUCTION

The Crimean-Congo hemorrhagic fever (CCHF) virus belongs to the genus Nairovirus, from the family Bunyaviridae, and causes severe disease in humans, with reported mortality rates of 5 to 80% (Ergonul et al., 2004). The widespread geographic distribution of the CCHF virus and its ability to produce severe human disease with high mortality rates make it a significant human pathogen. Humans become infected through tick bites or direct contact with body fluids or tissues from viremic patients or viremic livestock (Tavana et al., 2002; Karti et al., 2004; Yapar et al., 2005; Bakir et al., 2005; Chamberlain et al., 2005; Akyazi et al., 2006; Tanir et al., 2008). Among the risk groups for the disease are those working in agriculture or forestry, people involved with

livestock, farmers, shepherds, butchers, slaughterhouse workers, vets, health personnel, the military, hunters, campers and workers in leather factories (Akyazi et al., 2006; Mardani et al., 2007).

CCHF has a very wide geographic distribution, being endemic in more than 30 countries in Africa, central and southwestern Asia, the Middle East and Eastern Europe (Suleiman et al., 1980; Whitehouse, 2004; Acar, 2006; Ergonul, 2006). Over the last decade, climatic, environmental, and anthropogenic factors have driven the expansion of CCHF endemic foci and the onset of community outbreaks (Uzun et al., 2004; Randolph et al., 2008). In addition, the discovery of the virus in certain birds on the migratory route between Africa and Europe suggests that birds may have facilitated the intercontinental passage of the virus (Fisher-Hoch, 2005; Tanir et al., 2008). CCHF virus-infected cases were first reported in Turkey in 2002, and since then the number of

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cases has gradually increased (Fisher-Hoch, 2005; Ergonul, 2006; The Turkish Ministry of Health, 2009). A total of 3135 confirmed cases were reported to the Turkish Ministry of Health (Turkish Ministry of Health, 2009) in between 2002 and 2008. This increase in Turkey may be attributed to the country lying on the migratory path between Africa and Europe, changes in climatic factors, and environmental factors such as the opening up to agriculture and hunting of areas that had long been closed due to terrorism (Ergonul, 2006; Ergonul, 2008). Turkey's geographical and climatic nature is well suited to ticks (Ergonul, 2006). Ticks enjoy a wide host spectrum in Turkey, from small rodents to wild animals and from birds to household pet mammals, and some 32 species of tick have been reported (Karti et al., 2004; Ergonul, 2006; Mardani et al., 2007). For that reason the disease may be observed everywhere in Turkey, especially in those regions with high levels of animal husbandry, forests and areas with bushy pastures. The genus *Hyalomma* is frequently seen in the Black Sea region, and this is thought to be linked to the fact the region is rainy and densely forested (Fisher-Hoch, 2005). On the other hand, the habitats and migratory paths of wild birds, the two most important of which are found in Samsun, are also significant in terms of the spread and settlement of the disease in the region (Ergonul, 2006; Fisher-Hoch, 2005). Knowledge of the epidemiological characteristics of the disease both permits rapid intervention in epidemics and also provides the information necessary for health policies to be geographically directed. Investigation of such factors as the monitoring of the development and spread of diseases in a health area, the evaluation of risk factors, the development of control strategies regarding health incidents and the management and planning of health services can all be made possible using geographical information systems (GIS). Thanks to modern-day advances in GIS technologies and statistical techniques, health and population data in a geographically defined region can be analyzed simultaneously, the logical investigation of geographical variations in disease risks is possible, and the epidemiological progress of diseases can be better understood. The system's most important characteristics are that it establishes a powerful database, can constantly be updated and can permit rapid coordination among relevant units. It has been used in several studies to date concerning disease status and spread and environmental risk factors and in the preparation of disease control planning (Elliot et al., 1996; Martin et al., 2002; Gupta et al., 2003; Nygard et al., 2004; Dogan et al., 2009). Bearing in mind the increasing number of CCHF cases, which exhibit a broad geographical distribution, mapping the disease using GIS and updating the related information when necessary is important for Turkey in terms of seeing the risk dimensions, taking the requisite precautions and monitoring the sufficiency of those precautions.

MATERIALS AND METHODS

This descriptive study was performed by the necessary legal permission obtained from the Samsun Provincial Health Directorate Department of Infectious Diseases. Cases diagnosed with CCHF at hospitals in the Turkish province of Samsun and at the Ondokuz Mayıs University Medical Faculty Hospital (OMUMFH) between 01 January, 2004, and 31 December, 2008, and recorded by the Samsun Provincial Health Directorate were included.

The research was conducted in two stages. In the first stage, 188 cases diagnosed with CCHF between 01 January 2004 and 31 December 2008 were identified. After analysis of these cases' ages, gender and address data, disease incidences were calculated. Address data for 151 (83.0%) cases was supplied solely in the form of province, district and village name. Of these cases, 135 (89.4%) were from the provinces of Samsun and Amasya then thematic mapping was performed for these two provinces alone. SPSS 12.0 was used for statistical analysis of the data. Qualitative data was expressed as number (%) and quantitative data as median (1st – 3rd quartile). Student's t-test was used in the analysis of data.

Various characteristics of the provinces of Samsun and Amasya were examined in order to produce a thematic map. Samsun is a coastal province in the central Black Sea region. It lies between 41° 44' North and 40° 50' South and between 37° 08' East and 34° 25' West. In terms of the diversity of its migratory bird species and its high population, the province of Samsun contains a Class A watering areas according to international criteria (Republic of Turkey, Samsun Governor's Office, 2003; Yigit, 2003). Samsun possesses a generally moderate climate. However the climate possesses two different features along the coastal strip and in interior regions. The moderate influence of the Black Sea climate can be seen along the coastal strip. Summers are hot and winters warm and rainy. In interior regions, and under the influence of the 2000 m high Akdağ and the 1500 m high Canik Mountains, summers are cool and winters cold, rainy and with heavy snowfall (Republic of Turkey, Samsun Governor's Office, 2009) (Figure 1).

Amasya lies to the south of Samsun in the central Black Sea region, between 34°57' and 36°31' and 41° 04' and 40°16' (Yavuz, 2007). The climate in Amasya is a transitional one between the Black Sea and inland systems. Summers are warm and dry, and winters rainy. Spring is the rainiest season of all (Republic of Turkey, Amasya Governor's Office, 2009).

In the following stage of the study, provincial boundaries, district boundaries, main roads, rivers and lakes in the provinces of Samsun and Amasya were quantified and entered onto the ArcGIS (version 9.2) program. The address coordinates for 134 cases diagnosed with CCHF whose full addresses had been determined were established from standard 1:25000 scale topographical maps and transferred onto the quantified maps.

Various subjects were examined using the spatial and non-spatial data entered into the ArcGIS program (attribute). At the end of this study, the maps below and graphics were produced.

- (i) Total case map.
- (ii) Interpolated map of diagnosed case.
- (iii) Case-altitude correlation graphics.
- (iv) Altitudes map at which cases developed.

RESULTS

One hundred eighty-two cases were diagnosed as CCHF in Samsun provincial state hospitals and the OMUMFH between 2004 and 2008. One hundred six (58.2%) of the patients diagnosed were male and 76 (41.8%) female,

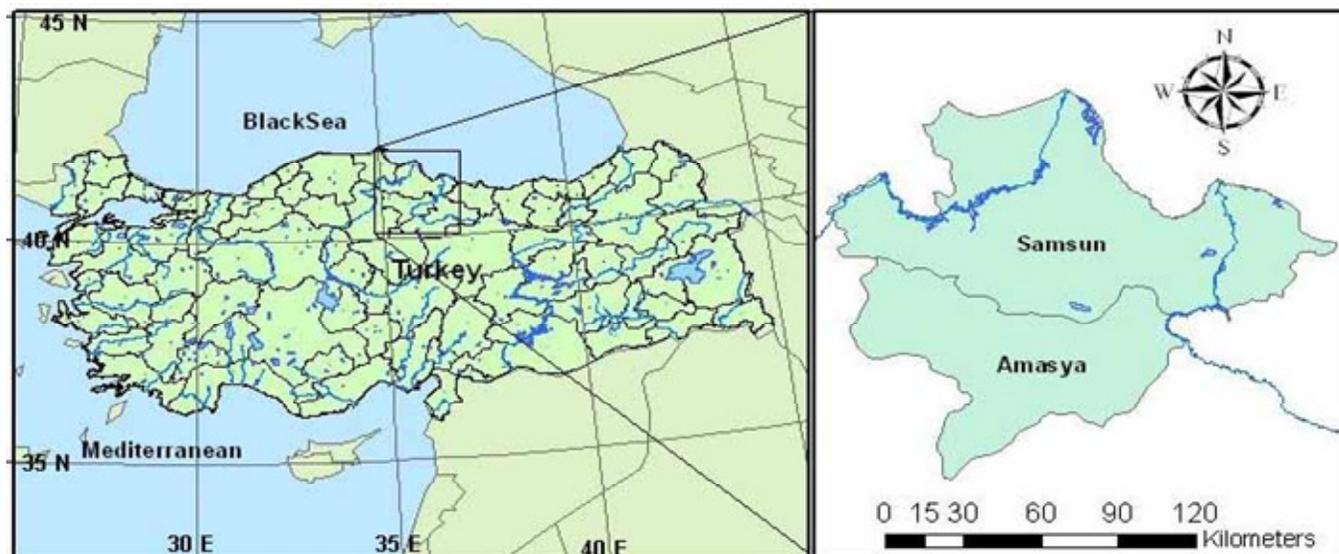


Figure 1. Study area.

with a total mean age of 44.0 (20.5 to 57.0) years. Stratified by gender, male and female mean ages were 45.0 (22.0 to 57.0) and 40.0 (17.0 to 56.5) years, respectively, and no statistical difference was determined between the sexes ($p > 0.05$). Various demographic characteristics of cases by year are shown in Table 1. Detailed address information existed for 151 (83%) of the recorded cases. Distribution of case settlement units by year is given in Table 2.

Month of application to hospital could only be established from the records for the cases reported in 2008 ($n=119$). According to the data obtained, 1 (0.8%) case reported in April, 27 (22.7%) in May, 47 (39.5%) in June, 29 (24.4%) in July, 13 (10.9%) in August, and 1 (0.8%) each in September and October. In terms of CCHF case courses, 170 (93.4%) patients were discharged and 12 (6.6%) died. CCHF patient discharge and fatality rate by year are shown in Table 3. The distribution by district of the 135 cases for which detailed address information could be obtained reported from the provinces of Samsun and Amasya, in which most cases were seen, is shown in Figure 2.

Total population and case distributions for the provinces of Samsun and Amasya were calculated for 2004 to 2008, and CCHF incidence determined using these data. CCHF incidences are shown in Table 4. Investigation of the altitudes at which the cases reported from Samsun and Amasya ($n=135$) residents, 20 (14.8%) lived at "an altitude above 1000 m," 61 (45.2%) at "751 to 1000 m" and 23 (17.0%) at "501 to 750 m" (Figures 3, 4).

DISCUSSION

Cases of CCHF were first seen in Tokat in the spring months of 2002, the disease being identified as CCHF as

the result of work by the Ministry of Health. Following that first report, a total of 3135 cases were identified in Turkey up until 2008, of which 155 (4.9%) resulted in death. The first cases were determined to be concentrated around the Kelkit Valley, though cases were subsequently reported from 27 provinces, including Samsun and Amasya (Gargili et al., 2007; the Turkish Ministry of Health, 2009). This study reported that 8 cases had been reported to the Samsun Provincial Health Directorate in 2004, while the number had risen to 119 in 2008 (Table 1), and the incidence of the disease had risen with the passage of time (Table 4). The Samsun-Amasya region lying on the African-European migratory path for birds, changes in climatic factors and the opening up to agriculture and hunting of areas that had long been closed because of terrorism have all been blamed for this increase in case numbers (Izadi et al., 2004; Tanir et al., 2008; Randolph et al., 2008). The potential roles of migratory birds and the movement of livestock carrying ticks in the spread of the virus over distant geographic areas have been studied (Ergonul, 2006). Birds migrating from the Balkans were suggested to be the cause of the 2002 outbreak in Turkey (Estrada-Pena et al., 2007). On the other hand, Randolph et al. (2008) said,

"By no means may all of this increased incidence be explained away by heightened awareness in Turkey and diagnoses, whose specificity has increased as laboratory capacity has improved in response to the outbreak".

As a result of field studies that began in Turkey in 2005, the area inhabited by *Hyalomma marginatum*, which is linked to CCHF epidemics, was mapped and potential risk areas in terms of the disease identified. A close correlation was revealed between the risk of the disease and a broken-up land structure such as forests, flat

Table 1. Distribution of various demographic characteristics of cases by year (No., %).

| Characteristic | | 2004 (n:8) | 2005 (n:10) | 2006 (n:22) | 2007 (n:23) | 2008 (n:119) |
|-------------------|---------|--------------------|--------------------|-------------------|--------------------|--------------|
| Sex | Male | 6 (75.0) | 6 (60.0) | 14 (63.6) | 15 (65.2) | 65 (54.6) |
| | Female | 2 (25.0) | 4 (40.0) | 8 (36.4) | 8 (35.8) | 54 (45.4) |
| Place of Domicile | Samsun | 1 (12.5) | 4 (40.0) | 7 (31.8) | 6 (26.1) | 42 (35.3) |
| | Amasya | 1 (12.5) | 4 (40.0) | 14 (63.6) | 13 (56.5) | 43 (36.1) |
| | Tokat | 2 (25.0) | 1 (10.0) | 1 (4.5) | 1 (4.3) | 4 (3.4) |
| | Other* | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (4.3) | 30 (25.2) |
| | Unknown | 4 (50.0) | 1 (10.0) | 0 (0.0) | 2 (8.7) | 0 (0.0) |
| Age (years) | ** | 33.5 (13.5 – 53.2) | 32.0 (11.5 – 49.0) | 45.0(30.0 – 48.0) | 46.0(27.0 – 58.0) | |

* Sinop, Ordu, Çorum, Tokat. **No age data available for this year.

Table 2. Distribution of cases by settlement unit.

| Year | Provincial center | | District | | Village | | Unknown | |
|---------------|-------------------|------|----------|------|---------|------|---------|-------|
| | No. | %* | No. | %* | No. | %* | No. | %* |
| 2004 (n:8) | 0 | 0.0 | 1 | 12.5 | 1 | 12.5 | 6 | 75.0 |
| 2005 (n: 10) | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 10 | 100.0 |
| 2006 (n:22) | 3 | 13.6 | 4 | 18.2 | 7 | 31.8 | 8 | 36.4 |
| 2007 (n: 23) | 3 | 13.0 | 7 | 30.4 | 13 | 56.6 | 0 | 0.0 |
| 2008 (n:119) | 8 | 6.7 | 21 | 17.6 | 83 | 69.8 | 7 | 5.9 |
| Total (n:182) | 14 | 7.7 | 33 | 18.1 | 104 | 57.1 | 31 | 17.1 |

*Line percentage.

Table 3. CCHF Death rates by year.

| Year | Discharged (n) | Deaths (n) | Fatality rate (%) |
|---------------|----------------|------------|-------------------|
| 2004 (n:8) | 7 | 1 | 12.5 |
| 2005 (n: 10) | 10 | 0 | 0.0 |
| 2006 (n:22) | 20 | 2 | 9.1 |
| 2007 (n: 23) | 23 | 0 | 0.0 |
| 2008 (n:119) | 110 | 9 | 7.6 |
| Total (n:182) | 170 | 12 | 6.6 |

pasturage, grazing land, pastureland and bush and vector tick density (Estrada-Pena et al., 2007; Gargili et al., 2007; Vatansever et al., 2007). Although these studies permitted the accumulation of a specific knowledge base regarding the epidemiology of CCHF, the epidemiological factors underlying the spread of the disease in Turkey have not yet been fully clarified, and this gave rise to a need for further research on the subject.

We determined that the mean age of the cases was 44.0 and that some 60% were male, with 92% living in villages and minor districts. The majority of adult males in rural parts of Turkey work in agriculture and animal husbandry. The occupations at risk for CCHF are mainly

those involved with animal husbandry and farming, which entail a risk of contact with ticks (Ergonul, 2004; Izadi et al., 2004; Akyazi et al., 2006; Mardani et al., 2007). The fact that the disease is seen more frequently in the middle age group and among males, as also in this study, may be ascribed to the fact that males are more active in the outside environment where the ticks that constitute the disease vector are to be found. On the other hand, epidemiological studies have reported that CCHF is more frequently observed in regions where there is animal husbandry, forests and pasturages, and living in villages or rural areas has been described as a risk factor (Kara, 2006; Mutay et al., 2007; Tanir et al., 2008).

In terms of seasonal distribution, because temperatures

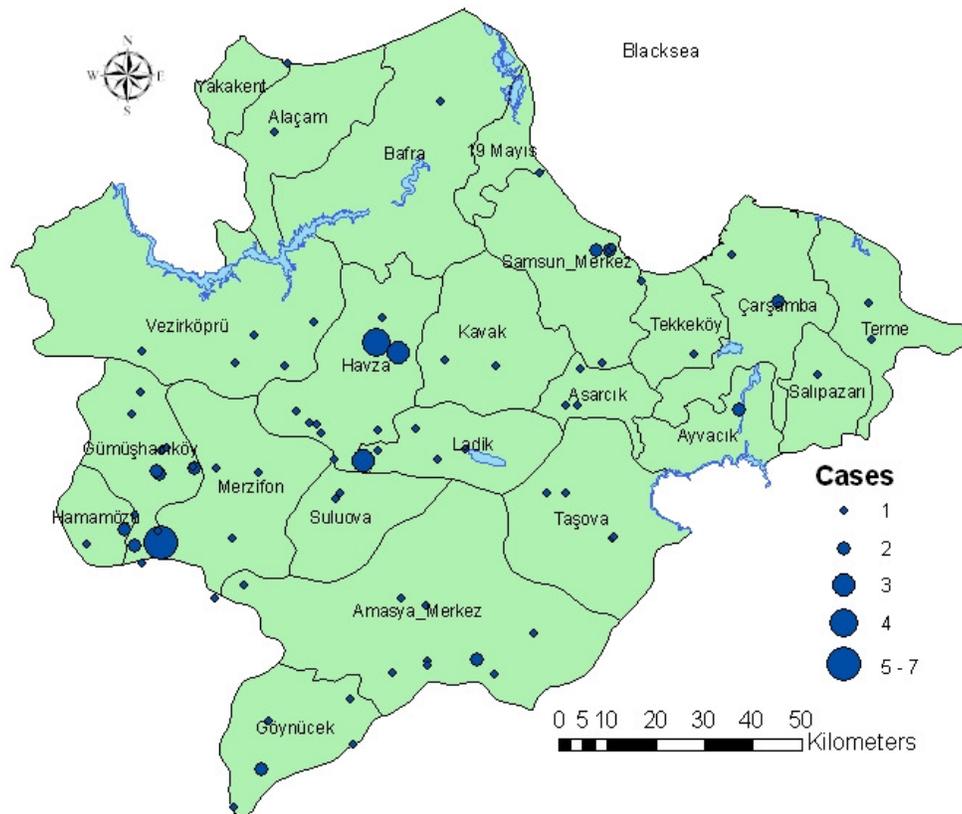


Figure 2. Map of Samsun and Amasya provinces on the basis of total case numbers.

Table 4. CCHF Incidence distribution in the provinces of Samsun and Amasya by year.

| | | 2004 | 2005 | 2006 | 2007 | 2008 |
|--------|------------------------|-----------|-----------|-----------|-----------|-----------|
| Samsun | Mid-year population | 1 243 717 | 1 229 832 | 1 206 928 | 1 228 959 | 1 233 677 |
| | Number of cases | 1 | 4 | 7 | 6 | 42 |
| | Incidence (in 100,000) | 0.08 | 0.32 | 0.58 | 0.48 | 3.40 |
| Amasya | Mid-year population | 335 812 | 329 012 | 324 214 | 328 674 | 323 675 |
| | Number of cases | 1 | 4 | 14 | 13 | 43 |
| | Incidence (in 100,000) | 0.29 | 1.21 | 4.31 | 3.95 | 13.28 |

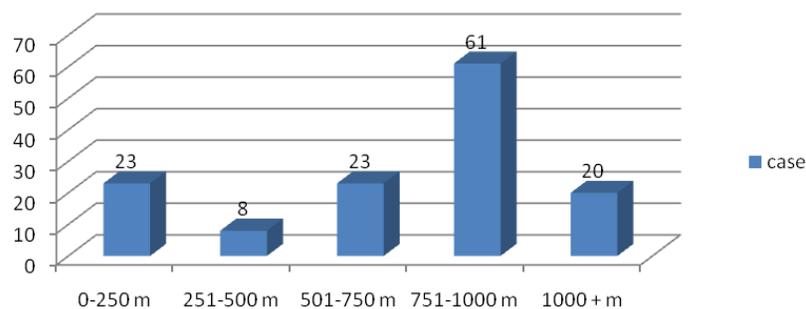


Figure 3. Distribution of CCHF cases by altitude.

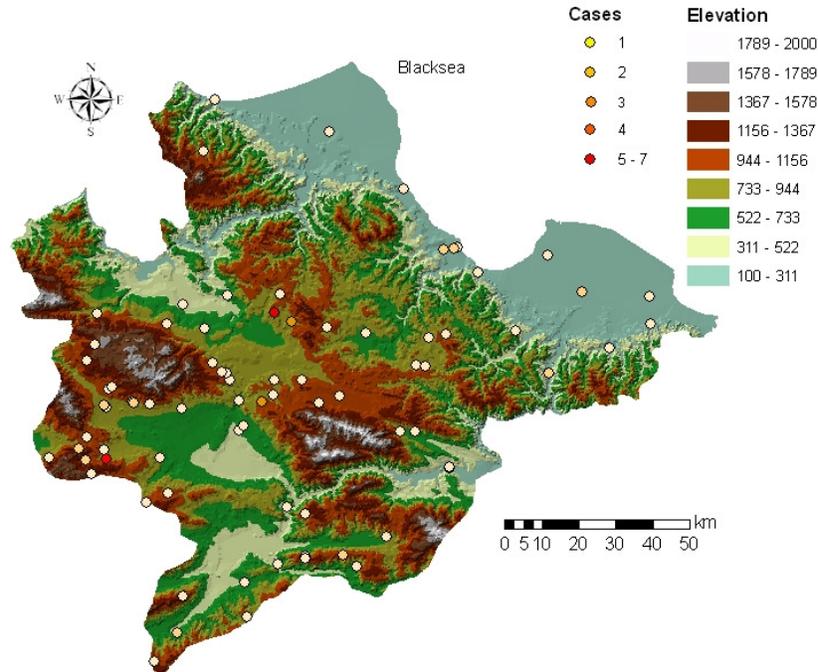


Figure 4. Map of altitudes at which cases developed.

lies, and tick activity increases with temperature, the virus is most active between the months of June and September. This period corresponds to between April and August in the Black Sea region (Bakir et al., 2005; Ergonul, 2008; Randolph 2008, Zivalioglu 2008). Of all the cases, 97.5% were reported between the months of April and August, which are the busiest months for those working in agriculture and the animal husbandry sector. The disease peaks in August-September in Ira, while 2 peaks have been determined in Pakistan, in March to May and August to October (Tavana et al., 2002; Mardani et al., 2003). In the former Soviet Union the number of cases is at its greatest in June to July, while in the Republic of South Africa most cases appear in spring and autumn. The disease may also rarely be seen in January (Bakir et al., 2005). Evaluation of these findings suggests that the disease peaks at different times in different regions and that this is related to the optimal temperature for virus activity. On the other hand, geographical conditions in Turkey are ideally suited to ticks, thus posing a greater danger and indicating that these numbers may rise to very high levels.

This study of 182 diagnosed cases determined that the fatality rate varies between 0 and 12.5%. In terms of cases and fatality distribution by year in Turkey, the case-fatality rate has varied over time between 4.0 and 6.2% (Turkish Ministry of Health, 2009). The only consolation is that Turkey also differs in the virulence of the viral strain, with a lower case-fatality rate compared with an average of 20 to 30% in other countries (Randolph et al., 2008).

On the other hand, geographical location also seems to influence the death rate. Particularly high mortality rates have been reported in some outbreaks from the United Arab Emirates (73%) and China (80%). Geographical differences in viral virulence have been suggested, but are as yet unproven (Iowa State University, 2003).

There are insufficient studies in the literature regarding the altitude above sea level at which patients live, although the data from the provinces of Samsun and Amasya show that 60% live at or above an altitude of 750 m. Zivalioglu et al. (2008) reported that around 74% of cases lived between 600 and 1200 m above sea level, with an average of 800 m. We are of the opinion that, as in other countries in which CCHF is seen, in Turkey, too, and especially in our region, the ticks that carry the disease live more densely at high altitudes and that there is a correlation with animal husbandry that frequently takes place at such elevations (Estrada-Pena et al., 2007; Gargili et al., 2007; Vatansever et al., 2007).

Conclusion and recommendations

In conclusion, this study shows that CCHF causes severe disease and that approximately 74% of cases in Samsun and Amasya live at altitudes of 750 m and above and 86.6% of cases reported in April, May and June when the temperatures rise in spring. Periodic education of high risk groups by people working in the veterinary and public health sectors and regular updating of clinicians also will

play an important role in the early diagnosis of cases and in preventing the virus becoming established in new areas, leading to subsequent outbreaks. This will also contribute to the containment and elimination of the disease in areas where it is already endemic. This is one of the first attempt to use CCHF modeling and GIS in an epidemiological study. The results show that the technique may be useful for CCHV in environmental epidemiologic studies, particularly when detailed biotic (hosts, particularly wild animals) and abiotic (climate, environment, socio-economic levels) are determined.

Limitations

The study has two limitations. One of the most important sources of data for health is information obtained from the reporting and notification of infectious diseases. It is important for the control and prevention of infectious diseases that this information be reliable and accurate. Our study was retrospective and dependent on the case report forms of the Ministry of Health. However, the study determined significant deficiencies in the reporting of data concerning CCHF. Detailed addresses were only available for 83.0% of cases, while seasonal distribution data could only be used for 2008. Awareness of the epidemiological characteristics of patients permits a more rapid intervention in epidemics and also provides the data needed in order to match health policies to specific regions.

A second limitation is that under the prevailing conditions in Turkey we were unable to access data for such factors as vegetation cover, climate, environment and wild animals needed for GIS mapping, and thus to clarify the correlation between CCHF and these factors.

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