Research Article

Determination of Seroprevalence and Risk Factors of Crimean–Congo Haemorrhagic Fever (CCHF) in the Endemic Region in Turkey: A Population-Based Cross-Sectional Study

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Objectives. Turkey is one of the countries that has the most cases of CCHF in recent years among the endemic countries. The disease also poses an important health threat with high mortality rate. The aim of the study was to determine the seroprevalence and risk factors of CCHF in adults aged ≥ 20 years in Tokat in the endemic region, Turkey.

Methods. In this population-based cross-sectional study, a total of 85 Family Medicine Units (FMUs), from over 170 in Tokat, were randomly selected using 50% sampling. The sample size was determined among the subjects aged ≥20 who registered with the FMUs, due to gender, age group, and the urban/rural population size of Tokat using the stratified cluster sampling method. Subjects were invited to the FMUs. A questionnaire was performed face to face. The blood samples were taken, and anti-CCHFV IgG antibodies were measured with ELISA method. Results. 1272 (54.9%) out of 2319 participants were female, and the mean age was 47.3 ± 15.3. Anti-CCHFV IgG seropositivity was 5.6% (n = 130). Seropositivity rates in terms of adjusted odds ratios (AOR) were higher 2.53 times (95% CI: 1.57–4.08; p < 0.001) in males; 4.05 (95% CI: 2.14–7.65; p < 0.001) in age group ≥65; 0.33 (95% CI: 0.14–0.76; p < 0.001) in graduates of high school and above; 0.71 (95% CI: 0.33–1.52; p < 0.001) in ones with good income; 1.84 (95% CI: 1.18–2.86; p < 0.001) in farmers; 1.64 (95% CI: 1.04–2.27; p < 0.001) in people dealing with animal husbandry; and 1.02 (95% CI: 1.03–2.29; p < 0.001) in those with history of tick contact.

Conclusions. CCHF seroprevalence is still a common public health problem in Tokat, Turkey. Male gender, advanced age group, low-educated, low-income, farmers, animal husbandry, and history of tick contact were found to be risk factors for CCHF. The importance of this kind of community-based studies to identify the seroprevalence in regional and national level increases even more.

1. Introduction

Disease transmitted by ticks is Rocky Mountain spotted fever (Rickettsia), Boutonneuse (Rickettsia), Q-fever (Rickettsia), Endemic typhus (Rickettsia), Tularemia (Rickettsia), Lyme (Borrelia), Relapsing fever (Borrelia), Colorado tick-fever (viruses), Arboviruses (viruses), and Crimean–Congo Hemorrhagic Fever (CCHF). CCHF is a tick-borne viral, zoonotic, infectious disease caused by Nairoviruses, transmitted by Ixodidae and Argasidae family ticks, posing a significant health threat as it causes fatal hemorrhagic syndrome in humans [1]. CCHF is currently endemic in about 50 countries in Europe, Africa, and Asia, with seroprevalence ranging within 0.1–14.4% in the general population, 16.5–30.3% in at-risk professionals, and 18.5–85% in patient-related populations [1]. The fatality of the disease
changes from region to region in the world; however, it is reported as 5–30% [2].

Ticks are now accepted as both the vector and the reservoir for the CCHF virus. It is declared that the distribution and reservoirs of the known tick types get common additional globalisation and constantly increasing international animal transportation cause the spread of pathogens and vectors globally [3]. It is stated that more than 30 tick types are capable of living in Turkey’s geographical conditions [4]. The species of Hyalomma genus ticks are the main CCHF vectors in Turkey. It is known that many complex interrelated factors contribute to the emergence and spread of the CCHF, such as environmental and climate changes, and the uncontrolled movement of wild birds and animals [5]. The main modes of transmission of CCHF are tick contact, viraemic animals, and infected body fluids/blood. The most common symptoms are high fever, headache, fatigue, myalgia, and nausea. Later on, haemorrhagic symptoms could show [6]. It is reported that anti-Crimean-Congo haemorrhagic fever virus (anti-CCHFV) immunoglobulin M (IgM) antibodies could be detected in 6–40 days following the entrance of virus to the body and anti-CCHFV immunoglobulin G (IgG) antibodies could be detected between 10th day to 6th year following the infection [7]. Though the local vaccine studies which will play an important role in protection against the disease are ongoing, there has not been a development of a specific antiviral to be used in treatment or a vaccine with world-wide recognised efficacy.

The first CCHF case in Turkey was reported in 2002 in Tokat province [8]. Turkey is one of the endemic countries that has the most cases of CCHF in recent years [9, 10]. The disease is endemic in cities in the region known as “K_PBîkit Basin” (Tokat, Artvin, Bayburt, Erzincan, Erzurum Gümüşhane, Amasya, Çankırı, Çorum, Kastamonu, Sivas, Yozgat) [4, 5, 8] (Figure 1).

Mortality rates change in accordance with the geographical region (4–20%) and with this high mortality rate; CCHF is an important public health problem in Turkey [11, 12]. All CCHF cases are monitored by a strong surveillance system by the Ministry of Health. In Turkey, between the years 2002 and 2018, 11,041 cases of CCHF have been reported and the case-mortality rate was 4.8% [13]. Although it varies from region to region and in the groups studied, the seroprevalence of CCHF in endemic areas is determined to be 0.7% to 19.4% [10, 14–16]. Determining the CCHF seroprevalence is important to understand the epidemiology of the disease better and taking the necessary precautions on time [10]. Regarding CCHF, in literature, apart from the specific groups and few seroprevalence studies in a limited participation, there are not enough studies representing healthy individuals especially in Tokat where the first case in Turkey was detected. In this study, it was aimed at determining seroprevalence and related risk factors of CCHF in adults aged ≥20 years in Tokat in the endemic region, Turkey.

2. Methods

The population-based cross-sectional study was carried out in the city of Tokat, which is in the middle Black Sea region of Turkey. In this study, the population of Tokat province ≥20 years consists of 412,653 individuals. In calculating the sample size, the expected prevalence of the disease to be investigated was found to be 50%, the deviation was taken as 0.05, and the design effect was taken as 2 at 97% confidence level and the population targeted to be reached with the Epi Info version 7 program was found to be 2635.

The sample selection was made by multi-layer proportional cluster sampling method considering the size of the urban and rural settlements of the provincial centres and districts in the Tokat provincial population pyramid, gender,
and age groups. A total of 85 Family Medicine Units (FMU) from over 170 in Tokat were randomly selected using a 50% sampling. Each FMU was considered as a cluster. By using the quota sampling method in the intracluster sample, the number of individuals required to fall to the determined gender and age groups is provided to work. The gender and age groups whose numbers were set for each cluster were randomly selected by systematic sampling method after ranking by Family Medicine Information System. The participants included in the study were invited to the FMUs. All participants signed a voluntary consent form. Those who reported cognitive impairment that would prevent the questionnaire forms from understanding or giving clear answers and those who declared that they were pregnant were excluded from the study.

For the data collection, a questionnaire about the sociodemographic characteristics and CCHF-related risk factors of the participants was completed by face-to-face interviews by physicians in study group and blood samples were taken from the participants for laboratory tests. The sera obtained by centrifuging the samples were stored at +4°C and then transferred to a −70°C unit at the end of the day until further analysis could be performed. Anti-CCHFV IgG were studied by serum in the Public Health Institution of Turkey Microbiology Reference Laboratory. Specific IgG antibody level against CCHFV was measured in serum with the Enzyme-Linked Immuno Sorbent Assay (ELISA) method which is a method that can be used in serosurveillance studies. 92% (2428) of the sample calculated in the study was reached. As a result, the data of 2319 (88%) of Turkey Microbiology Reference Laboratory. Specific IgG were studied by serum in the Public Health Institution of Turkey Microbiology Reference Laboratory. Specific IgG antibody level against CCHFV was measured in serum with the Enzyme-Linked Immuno Sorbent Assay (ELISA)

2.1. Statistical Analysis. The data analysis was performed using SPSS 22.0. Categorical variables were summarized by number, percentage, mean ± standard deviation (min-max), and 95% confidence interval, compared with Pearson Chi-square and Fisher’s exact tests. Logistic regression analysis was used for the descriptive and CCHF-related risk factors for anti-CCHFV IgG seropositivity. The values of \( p < 0.05 \) were considered as statistically significant.

2.2. Ethical Approval. The study was approved by the Ethical Committee of Tokat Gaziosmanpaşa University Faculty of Medicine (approval number: 14-KAEK-142). A written informed consent was obtained from each participant.

3. Results

3.1. Sociodemographic Characteristics. 54.9% (1272) of 2319 participants were female, and the mean age was 47.3 ± 15.3 (20–87 ages). 69.2% of the participants lived in the districts, 58.3% of them were graduates of primary and secondary school, 47.9% of them were housewives, 86.8% were married, and 51.3% had poor level of family income (Table 1).

3.2. CCHF-Related Risk Factors. According to some risk factors for CCHF of the participants, 41.6% of them lived in rural areas, 15.1% were farmers, 33.1% were involved in animal husbandry, and 16% had tick-contact history. 1% of the participants had hospitalization history with suspected CCHF, 7% of those had a relative with history of CCHF treatment, and in the area where 15.5% of participants lived there were people diagnosed with CCHF (Table 2).

3.3. Seroprevalence of CCHF. Anti-CCHFV IgG seropositivity was 5.6% (\( n = 130 \)) (4.2% in females, \( n = 53 \), 7.4% in males, \( n = 77 \)). The mean age of seropositives (57.7 ± 15.2) was higher than those of seronegatives (46.7 ± 15.1) (\( p < 0.001 \)). The highest seropositivity rate was 10.9% in the 60-age group (14.2% in males, 8.1% in females). A statistically significant difference was found for anti-CCHFV IgG seropositivity by age groups in both genders, and the seropositivity increased with advancing age (\( p = 0.001 \) in females; \( p < 0.001 \) in males) (Table 3).

In the logistic regression analysis of the descriptive characteristics of the participants in terms of anti-CCHFV IgG seropositivity (Table 4), gender (\( p = 0.001 \)), age group (\( p < 0.001 \)), education level (\( p < 0.001 \)), marital status (\( p = 0.014 \)), and income level (\( p < 0.001 \)) were found to have significant effects on seropositivity. The rates of seropositivity in terms of adjusted odds ratios (AOR) were higher 2.53 times (95% confidence interval (CI): 1.57–4.08) in males; 4.05 (95% CI: 2.14–7.65) in age group ≥65; 0.33 (95% CI: 0.14–0.76) for those whose education level was high school and above; and 0.71 (95% CI: 0.33–1.52) in those with good income.

In the logistic regression analysis of some CCHF-related risk factors in terms of anti-CCHFV IgG seropositivity of the participants, it was identified that farming, dealing with animal husbandry, history of tick contact, and history of hospitalization with suspected CCHF and being anyone diagnosed with CCHF in place of expected CCHF (AOR: 6.65; 95% CI: 2.70–16.43; \( p < 0.001 \))

4. Discussion

Although the morbidity and mortality of CCHF in Tokat province, where CCHF is endemic, have been reported to be decreasing compared with previous years [13], seroprevalence of the disease is still common in our region. According to the results of our study, the population in the at-risk group that makes a living from agriculture and animal
### Table 1: Distribution of the participants according to some descriptive characteristics.

| Variables                  | Categories                                | n (%)          |
|----------------------------|-------------------------------------------|----------------|
| Gender                     | Female                                    | 1272 (54.9)    |
|                            | Male                                      | 1047 (45.1)    |
| Age groups                 | 20–39 years                               | 925 (39.9)     |
|                            | 40–64 years                               | 1025 (44.2)    |
|                            | ≥65 years                                 | 369 (15.9)     |
| Residential area           | City center                               | 714 (30.8)     |
|                            | Districts                                 | 1605 (69.2)    |
| Education level            | Primary school-secondary school           | 1353 (58.3)    |
|                            | High school-university                    | 554 (23.9)     |
|                            | Housewife                                 | 1110 (47.9)    |
|                            | Farmer                                    | 351 (15.1)     |
| Occupation                 | Worker                                    | 224 (9.7)      |
|                            | Retired                                   | 203 (8.8)      |
|                            | Other (officer, tradesman, others)        | 431 (18.6)     |
| Marital status             | Married                                   | 2012 (86.8)    |
|                            | Single                                    | 142 (6.1)      |
|                            | Divorced                                  | 165 (7.1)      |
|                            | Bad                                       | 1189 (51.3)    |
| Family income status       | Medium                                    | 718 (31)       |
|                            | Good                                      | 412 (17.8)     |
|                            | No                                        | 1087 (46.9)    |
| Chronic disease            | Yes                                       | 1232 (53.1)    |
|                            | No                                        | 1431 (62.6)    |
| Smoking                    | Yes                                       | 868 (37.4)     |
|                            | No                                        | 2104 (90.7)    |
| Alcohol use                | Yes                                       | 215 (9.3)      |
|                            | No                                        | 1416 (61.1)    |
| Obesity (body mass index ≥30 kg/m²) | Yes                                     | 903 (38.9)    |
|                            | No                                        | 2319 (100.0)   |

### Table 2: Distribution of participants according to their characteristics related to some risk factors for CCHF.

| Variables                                      | Categories                   | n (%)          |
|-----------------------------------------------|------------------------------|----------------|
| Location                                      | Urban                        | 1354 (58.4)    |
|                                               | Rural                        | 965 (41.6)     |
| Farming                                       | No                           | 1968 (84.9)    |
|                                               | Yes                          | 351 (15.1)     |
| Animal husbandry                              | No                           | 1551 (66.9)    |
|                                               | Yes                          | 768 (33.1)     |
| Having a pet at home                          | No                           | 1910 (82.4)    |
|                                               | Yes                          | 409 (17.6)     |
| Tick contact history                          | Yes                          | 1949 (84)      |
|                                               | ≤1 year                      | 370 (16)       |
|                                               | ≥1 year                      | 123 (33.2)     |
|                                               | 2–4 years                    | 114 (30.8)     |
|                                               | ≥5 years                     | 133 (35.9)     |
| Hospitalization with suspected CCHF           | Yes                          | 2295 (99)      |
|                                               | No                           | 24 (1)         |
| Is there anyone in your family who was treated for CCHF? | Yes                          | 162 (7)        |
|                                               | No                           | 2157 (93)      |
| If there is anyone in your family who was treated for CCHF, what is the health status? (n = 162) | Is alive                  | 149 (92)       |
|                                               | Is dead                      | 13 (8)         |
| Is there anyone diagnosed with CCHF where you live? | Yes                          | 360 (15.5)     |
|                                               | No                           | 1959 (84.5)    |
| If there is anyone diagnosed with CCHF where you live, what is the health status? (n = 360) | Is alive                  | 242 (67.2)     |
|                                               | Is dead                      | 118 (32.8)     |
| Total                                         |                              | 2319 (100.0)   |
husbandry is considerable. Although the proportion of those living in rural areas is less, those in the city centre often have a history of visit to rural areas. A history of tick contact was detected in 16% of the participants. The main reasons for the high rate are as follows; it is an endemic region, the participants live in rural areas, and they are risky individuals for CCHF as they deal with farming and animal husbandry. Our study reveals that a significant number of participants, either themselves or those around them, have had serious experiences in CCHF, such as history of hospitalization with suspected CCHF (1%), a family member that had been treated for CCHF (7%), and someone with diagnosed CCHF in their circle (15.5%). Similar to our results, in a study comprising healthy people in Turkey, it was determined that 14.4% of the subjects had a history of tick bites [15]. In a seroprevalence study conducted in Turkey, it was found that 11% of the participants had a relative infected with the virus [16].

Table 3: Comparison of anti-CCHF IgG seropositivity frequency in females and males by age groups of the participants.

| Age groups | Female | Male | Total |
|------------|--------|------|-------|
|            | n Seropositivity n (%) | p value* | n Seropositivity n (%) | p value* | n Seropositivity n (%) |
| 20–29      | 169    | 3 (1.8) | 124    | 2 (1.6) | 293    | 5 (1.7) |
| 30–39      | 357    | 7 (2.0) | 275    | 10 (3.6) | 632    | 17 (2.7) |
| 40–49      | 220    | 8 (3.6) | 0.001  | 167    | 10 (6.0) | <0.001  | 387    | 10 (4.7) |
| 50–59      | 228    | 11 (4.8) | 228    | 19 (8.3) | 456    | 30 (6.6) |
| ≥60 years  | 298    | 24 (8.1) | 253    | 36 (14.2) | 551    | 60 (10.9) |
| Total      | 1272   | 53 (4.2) | 1047   | 77 (7.4) | 2319   | 130 (5.6) |

Anti-CCHFV IgG, anti-Crimean–Congo haemorrhagic fever virus immunoglobulin G. *Pearson chi-square tests.

Table 4: Logistic regression analysis of the descriptive characteristics of the participants in terms of anti-CCHFV IgG seropositivity (n = 2319).

| Variables                      | Anti-CCHFV IgG | p value* | COR (95% CI) | AOR (95% CI) |
|--------------------------------|----------------|----------|--------------|--------------|
|                                | Seropositivity n (%) | Seronegativity n (%) |               |              |
| Gender                         | Female 53 (4.2) | 1219 (95.8) | 0.001 Ref. | Ref.         |
|                                | Male 77 (7.4)  | 970 (92.6)  | 1.83 (1.27–2.62)* | 2.53 (1.57–4.08)* |
| Age groups                     | 20–39 years 22 (2.4) | 903 (97.6)  | Ref. | Ref.         |
|                                | 40–64 years 57 (5.6) | 968 (94.4)  | <0.001 Ref. | Ref.         |
|                                | ≥65 years 51 (13.8) | 318 (86.2)  | 2.42 (1.47–3.99)* | 1.84 (1.05–3.20)* |
| Residential area               | City center 43 (6) | 671 (94)   | Ref. | Ref.         |
|                                | Districts 87 (5.4) | 1518 (94.6) | 0.561 Ref. | Ref. |
|                                | Illiterate-literate 46 (11.2) | 366 (88.8) | Ref. | Ref.         |
| Education level                | Primary-secondary 71 (5.2) | 1282 (94.8) | <0.001 Ref. | Ref.         |
|                                | High school-university 13 (2.3) | 541 (97.7) | 0.19 (0.10–0.36)* | (0.30–0.80)* |
|                                | Married 111 (5.5) | 1901 (94.5) | Ref. | Ref.         |
| Marital status                 | Single 3 (2.1) | 139 (97.9) | 0.014 Ref. | Ref.         |
|                                | Divorced 16 (9.7) | 149 (90.3) | 1.84 (1.06–3.19)* | (0.25–3.170) |
|                                | Bad 87 (7.3) | 1102 (92.7) | Ref. | Ref.         |
| Family income level            | Medium 33 (4.6) | 685 (95.4) | <0.001 Ref. | Ref.         |
|                                | Good 10 (2.4) | 402 (97.6) | 0.61 (0.40–0.92)* | (0.33–1.52) |
| Chronic disease                | No 53 (4.9) | 1034 (95.1) | 0.151 Ref. | Ref.         |
|                                | Yes 77 (6.3) | 1155 (93.8) | 1.30 (0.91–1.87) | Ref.         |
| Smoking                        | No 86 (5.9) | 1365 (94.1) | 0.385 Ref. | Ref.         |
|                                | Yes 44 (5.1) | 824 (94.9) | 0.85 (0.58–1.23) | Ref.         |
| Alcohol use                    | No 120 (5.7) | 1984 (94.3) | 0.523 Ref. | Ref.         |
|                                | Yes 10 (4.7) | 205 (95.3) | 0.81 (0.42–1.56) | Ref.         |
| Obesity (BMI ≥ 30 kg/m²)       | No 83 (5.9) | 1333 (94.1) | 0.503 Ref. | Ref.         |
|                                | Yes 47 (5.2) | 856 (94.8) | 0.88 (0.61–1.27) | Ref.         |
| Total                          | 130 (5.6) | 2189 (94.4) |               |              |

Anti-CCHFV IgG, anti-Crimean–Congo haemorrhagic fever virus immunoglobulin G; COR, crude odds ratio; AOR, adjusted odds ratio; CI, confidence interval; Ref, reference; * p value of Yates' corrected X² test for anti-CCHFV IgG serology subgroup comparison.
Anti-CCHFV IgG seropositivity was found as 5.6% (n = 130) in our study. In a meta-analysis in which studies on CCHF seroprevalence in different regions of the world were examined, it was reported that this rate varied between 0.1% and 14.4% in healthy individuals and it is the highest seroprevalence rate in Turkey [1]. In a systematic review conducted in World Health Organization (WHO) European Region, CCHF seroprevalence was found lowest in Spain (0%) and highest in Turkey (19.6%). Although there is low endemicity in Southern and Western European countries like Greece and Spain, the highest seroprevalence was detected in Central and Eastern Europe. In some countries, a neighbor of Turkey, if the anti-CCHFV IgG seropositivity is evaluated, the northeast of Turkey, especially the areas surrounding the Black Sea, are described as highly endemic for CCHFV. The highest rate of CCHFV seroprevalence was determined in Turkey, the Russian Federation, and Kazakhstan. Although Balkan countries are also considered endemic for CCHF, the seroprevalence was reported to be lower than in Turkey [17]. Anti-CCHFV IgG seropositivity was identified as 2.8% in healthy adults in a study with similar sampling method used in Bulgaria and 3.7% in Christova et al.’s study [18, 19]. The seroprevalence in Greece was reported to be between 2.2% and 4.2% [1]. The movement of livestock and ticks plays an important role in the disease transmission. The study conducted in Iran showed a relatively high frequency of the disease in individuals at risk (14.8%). It was reported that most of the cases are from the southeastern regions of Iran and infected livestock imported from the eastern provinces is one of the most common causes of the prevalence of the disease [7].

### Table 5: Logistic regression analysis of some CCHF-related risk factors for anti-CCHFV IgG seropositivity of the participants (n = 2319).

| Variables                        | Anti-CCHFV IgG Seropositivity (%) | Anti-CCHFV IgG Seronegativity (%) | p value* | COR (95% CI) | AOR (95% CI) |
|----------------------------------|----------------------------------|----------------------------------|----------|--------------|--------------|
| **Location**                     |                                  |                                  |          |              |              |
| Urban                            | 70 (5.2)                         | 1284 (94.8)                      | 0.28     | Ref. (1.22)   | (0.85–1.74)  |
| Rural                            | 60 (6.2)                         | 905 (93.8)                       |          |              |              |
| **Farming**                      |                                  |                                  |          |              |              |
| No                               | 93 (4.7)                         | 1875 (95.3)                      | <0.001   | Ref. (2.38)   | (1.59–3.54)* |
| Yes                              | 37 (10.5)                        | 314 (89.5)                       |          | Ref. (1.84)   | (1.18–2.86)* |
| **Animal husbandry**             |                                  |                                  |          |              |              |
| No                               | 66 (4.3)                         | 1485 (95.7)                      | <0.001   | Ref. (2.05)   | (1.43–2.92)* |
| Yes                              | 64 (8.3)                         | 704 (91.7)                       |          | Ref. (1.64)   | (1.04–2.27)* |
| **Having a pet at home**         |                                  |                                  |          |              |              |
| No                               | 104 (5.4)                        | 1806 (94.6)                      | 0.467    | Ref. (1.18)   | (0.76–1.84)  |
| Yes                              | 26 (6.4)                         | 383 (93.6)                       |          |              |              |
| **Tick contact history**         |                                  |                                  |          |              |              |
| ≤1 year                          | 15 (12.2)                        | 108 (87.8)                       |          | Ref. (0.93)   | (0.42–2.04)  |
| 2–4 years                        | 13 (11.4)                        | 101 (88.6)                       | 0.293    | Ref. (0.52)   | (0.22–1.24)  |
| ≥5 years                         | 9 (6.8)                          | 124 (93.2)                       |          |              |              |
| **Hospitalization with suspected CCHF** |                            |                                  |          |              |              |
| No                               | 121 (5.3)                        | 2174 (94.7)                      | <0.001   | Ref. (10.78)  | (4.62–16.43)* |
| Yes                              | 9 (37.5)                         | 15 (62.5)                        |          | Ref. (6.65)   | (2.70–16.43)* |
| **Is there anyone in your family who was treated for CCHF?** | |                                  |          |              |              |
| No                               | 117 (5.4)                        | 2040 (94.6)                      | 0.165    | Ref. (1.52)   | (0.84–2.77)  |
| Yes                              | 13 (8)                           | 149 (92)                         |          |              |              |
| **If there is anyone in your family who was treated for CCHF, what is the health status? (n = 162)** | |                                  |          |              |              |
| Is alive                         | 11 (7.4)                         | 138 (92.6)                       | 0.308    | Ref. (2.28)   | (0.45–11.61) |
| Is dead                          | 2 (15.4)                         | 11 (84.6)                        |          |              |              |
| **Is there anyone diagnosed with CCHF where you live?** | |                                  |          |              |              |
| No                               | 95 (4.8)                         | 1864 (95.2)                      | <0.001   | Ref. (2.11)   | (1.41–3.17)* |
| Yes                              | 35 (9.7)                         | 325 (90.3)                       |          | Ref. (1.66)   | (1.08–2.56)* |
| **If there is anyone diagnosed with CCHF where you live, what is the health status? (n = 360)** | |                                  |          |              |              |
| Is alive                         | 22 (9.1)                         | 220 (90.9)                       | 0.563    | Ref. (1.24)   | (0.60–2.55)  |
| Is dead                          | 13 (11)                          | 105 (89)                         |          |              |              |

Anti-CCHFV IgG, anti-Crimean–Congo haemorrhagic fever virus immunoglobulin G; COR, crude odds ratio; AOR, adjusted odds ratio; CI, confidence interval; *p value of Yates’ corrected X² test for anti-CCHFV IgG serology subgroup comparison.
In a systematic review that examined the seroprevalence studies in Turkey, CCHF seroprevalence was reported as 0.5%–19.6% [17]. In a study conducted in Turkey’s seven provinces representing seven geographical regions and based on layered sample in accordance with the gender and age of adults, in 1066 venous blood samples representing 48.5 million adult anti-CCHFV IgG antibodies were detected with ELISA method, and CCHF seroprevalence was identified as 2.3%. In the same study, seroprevalence rates in Adana, Aydin, Erzurum, Gaziantep, Istanbul, Samsun, and Yozgat provinces were 0.7%–7.5% [10]. In Trabzon, which is endemic region in terms of CCHF, the seroprevalence was 13.6% in people living in the same environment with CCHF cases [20]. In the study performed in Van, CCHF seroprevalence was 14.4% in healthy individuals [15]. In another study performed in three endemic regions in Aydin, the highest rate (19.6%) was found among the CCHF seroprevalence studies in Turkey [16]. The seroprevalence rate found in our study is lower than the results of these studies conducted in Trabzon, Van, and Aydin provinces. With regard to the results of retrospective studies in regions where CCHF is endemic in Turkey, it has been reported that CCHF incidence and mortality rates decreased over the years [11, 21, 22]. When the results in our study area are compared with the results of other areas in terms of endemicity, it is thought that the main reasons for the differences are that the participants are healthy individuals rather than high-risk occupational groups and the study is a community-based study that adequately represents the general population in our province. In addition, as stated in studies conducted in high-risk endemic regions, the increased experience and awareness of both individuals and healthcare professionals in those regions on tick contact and CCHF may have an effect on lower incidence and mortality rates compared to the past [21].

In our study, anti-CCHFV IgG seropositivity was 4.2% in females and 7.4% in males. The mean age was significantly higher in seropositive. Seropositivity was highest in the age group of ≥60 (10.9%) and increased with advancing age. Seropositivity was statistically significantly higher in males and age group ≥65 years. In our study, the male gender was found to be a risk factor for CCHF similar to the study representing the seven geographical regions of Turkey [10]. The reason for this is that it is thought that men spend more time in jobs such as farming and animal husbandry. These activities are mostly performed by men in the countries the most at risk, as in the Middle East. This gender difference varies between countries depending on the participation of women in agricultural work [2, 16]. In opposition to that, in the study conducted in Greece, it is identified that the female gender is risky in terms of CCHF [23]. Also, it is reported that gender does not significantly affect anti-CCHFV IgG seropositivity according to the studies performed in Bulgaria [18], and in Erzurum [4], Van [15], Erzincan [11], and Trabzon [20] in Turkey. Similar to our study, many studies in the literature have shown that increased age was an important risk factor which may be a result of the increased possibilities for transmission [4, 10, 20, 23–25]. The studies have shown that age has no significant effect on seroprevalence contrary to our study [8, 18]. In the study performed in Aydin, the seroprevalence was found to be dramatically higher in the <34 age group, contrary to both our studies and also the ones in the literature [16].

In our study, low education and low-income levels were found to be risk factors for anti-CCHFV IgG seropositivity. Seropositivity was lower in graduated from high school and in those with good income significantly (p < 0.001). In a study, similar to our results, low education level was found to be a risk factor in terms of seropositivity [10]. The main reason for this is that farming and animal husbandry are generally more common among the low-educated and low-income population. In our study, farming, animal husbandry, history of tick contact, and hospitalization with suspected CCHF and being an individual with a CCHF diagnosis in their place of residence significantly affected anti-CCHFV IgG seropositivity (p < 0.001). Seropositivity was higher 1.84 times in farmers, 1.64 in animal husbandry, 1.02 in those with a history of tick contact, 6.65 in those hospitalized with suspected CCHF, and 1.66 in individuals with a diagnosis of CCHF where they lived. It has been reported that the most common risk factors for CCHF seropositivity are animal contact, animal husbandry or farming, history of tick contact, being a housewife, and exposure to secretions risky for CCHF [1]. In the study conducted in an endemic region in Turkey, tick exposure (OR: 9.03; 95%CI: 1.96–41.47; p < 0.005) was found to be an independent indicator for CCHF [26].

In the literature, it has been stated that living in rural areas is a risk factor in terms of exposure to ticks and CCHF [1, 11, 19, 20, 27]. In our study, 41.6% of the participants lived in rural areas; there was not a difference in seropositivity between rural (6.2%) and urban (5.2%) areas (p = 0.28). Similar to our study results, it was found in a study conducted in Van that locality did not have a significant effect on anti-CCHFV IgG seropositivity [15]. In the study conducted in Erzurum, which is endemic in terms of CCHF, the frequency of anti-CCHFV antibodies was found to be significantly higher in those living in rural areas [4]. In a study conducted in Erzincan, which is endemic for CCHF in Turkey, between the years 2011–2017, it was identified that the vast majority of CCHF patients (94.2%) were living in rural areas [11]. Unlike our study, it is thought that the prevalence of CCHF was found to be significantly higher in rural areas, since this study was conducted with CCHF patients. However, our study is a seroepidemiological prevalence study in which healthy individuals were included. Unlike our study results, Yağcı-Çağlayan et al. found that CCHF seroprevalence was 4.1% in rural areas and 1.8% in urban areas; these rates were found to be higher in rural areas compared to urban areas in Aydin (4.1–0%), Istanbul (5.0–1.7%), Samsun (2.6–0%), and Yozgat (16.7–4.8%) [10]. In addition to that in Erzincan anti-CCHFV IgG positivity was found to be significantly higher in individuals who were engaged in animal husbandry in rural areas and had a history of tick exposure compared to individuals who were not exposed to ticks in the urban areas (p < 0.05) [14]. In the
5. Conclusion
In conclusion, in this population-based epidemiological study conducted in adults aged ≥20 years in Tokat in the endemic region, it was found that CCHF seroprevalence is common. Anti-CCHFV IgG seropositivity was significantly high in males, advanced age group, low-educated, low-income, farming and/or animal husbandry, history of tick contact, hospitalization with suspected CCHF, and having individuals with diagnosed CCHF in the place of residence. The results of our study revealed the necessity of increasing measures for public health. It should be kept in mind that CCHF control is not only the duty of healthcare professionals, but multisectoral cooperation is required within the framework of the “One Health” concept. As CCHF is a common and important public health issue, such studies to be realized to identify the seroprevalence in regional and national level with community-based approach gain more importance.

Data Availability
The raw data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest
The authors declare that they have no competing interests.

Authors’ Contributions
This work was carried out in collaboration between all authors. RÇ, ME, and FD designed the study. RÇ, YÖ, YEB, OY, NYÇ, and ŞŞ involved in data collection. RÇ and YÖ conducted the data analysis. RÇ, ME, YÖ, and FD prepared the manuscript draft. All the authors read and approved the final version of the manuscript.
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