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Retrospective Evaluation of Tularemia Cases in Muş Province: 2011-2022

Muş İlinde Görülen Tularemi Olgularının Retrospektif Değerlendirilmesi: 2011-2022

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ABSTRACT

Objective: Tularemia is a bacterial disease of humans, wild and domestic animals. Recently, an increase in human tularemia cases has been observed in many countries worldwide. This study aimed to calculate the incidence of tularemia cases in Muş, determine the seasonal distribution of cases, and describe the socio-demographic and clinical characteristics of tularemia cases detected over a twelve-year period.
Methods: Data from 162 patients diagnosed clinically and serologically with tularemia and admitted to health facilities in Muş province between 2011 and 2022 were retrospectively analysed.
Results: In our study, among 162 tularemia patients with F. tularensis microagglutination test titres of 1/160 and above, the ratio of male and female cases was equal (50%), and the mean age was 24.51 years. In the twelve-year evaluation, there were two major epidemics, and the most cases were seen in 2018 with 37 cases. Most cases were observed in winter (38.3%) and autumn (25.3%). Oropharyngeal tularemia was the most common form (64.2%) among the cases evaluated. Similar disease was found in 33.3% of patients living in the same neighbourhood as the patients, and no mortality was observed in any of the patients.
Conclusion: As the oropharyngeal form is the most common, contact with contaminated water should be questioned, rodent and tick populations should be monitored and detailed epidemiological studies should be conducted. We believe that hygiene and sanitation measures are important with regard to tularemia outbreaks.

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ÖZET

Amaç: Tularemi, insanların, vahşi ve evcil hayvanların bakteriyel bir hastalığıdır. Son zamanlarda, dünya çapında birçok ülkede insan tularemi vakalarının sayısında bir artış fark edilmiştir. Bu çalışma ile Muş ilindeki tularemi vaka sıklığının hesaplanması, vakaların mevsimsel dağılımının belirlenmesi, on iki yıllık süre boyunca saptanan tularemi olgularının sosyodemografik ve klinik özelliklerinin tanımlanması amaçlanmıştır.
Gereç ve Yöntem: 2011-2022 tarihleri arasında Muş ilinde sağlık kurumlarına başvuran, klinik ve serolojik olarak tularemi tanısı konulmuş 162 hastanın verileri retrospektif olarak incelenmiştir.
Bulgular: Çalışmamızda F. tularensis mikroaglütinasyon titresi 1/160 ve üzerinde olan 162 tularemi hastaları arasında kadın ve erkek olgu oranı eşit olup (%50), yaş ortalaması 24,51'di. On iki yıllık değerlendirmede iki önemli salgın yaşanmış bunlar arasında en çok olgu ise 37 vaka ile 2018 yılında görülmüştür. Olgular en çok kış (%38,3) ve sonbahar (%25,3) aylarında görülmüştür. Değerlendirilen olgular arasında en sık (%64,2) orofarengeal tularemi formu görülmüştür. Hastalarla aynı mahallede yaşayanlarda %33,3 oranında benzer hastalık saptanmış, olguların hiçbirinde mortaliteye rastlanmamıştır.
Sonuç: Orofarengeal formun en sık görülmesinden dolayı kontamine sularla temas sorgulanmalı, kemirici ve kene popülasyonunun takibi ve ayrıntılı epidemiyolojik çalışmalar yapılmalıdır. Hijyen ve sanitasyon önlemleri alınmasının tularemi salgınları açısından önemli olduğunu düşünmekteyiz.

1. Introduction

Communities whose economies are based on agriculture and livestock naturally have close contact with rodents, especially domestic animals. It is very difficult for these communities to protect their food and beverages from vectors and animal waste. For this reason, the number of zoonotic diseases to which they are exposed is inevitably high. One of these zoonoses is Tularemia, also known as "rabbit fever" or "hunter's disease," which is a major threat to humans and animals and is caused by *Francisella tularensis* (1). Tularemia infections occur through infected animals (usually rabbits), arthropod vectors (such as ticks or deer flies), inhalation of contaminated dust, and contact with contaminated food and water.

Infections generally occur through the skin (animal contact and arthropod bites), conjunctiva (finger-to-eye transmission), orally (swallowing contaminated food or water), or through the respiratory tract (inhalation of a contaminated aerosol). After a short incubation period (average 3-5 days, up to 2 weeks), flu-like symptoms are usually observed in patients (2,3).

Clinical symptoms of tularemia in humans depend on the mode of transmission. Depending on the route of infection, the disease can develop in one of six classical clinical forms. These include the ulceroglandular and glandular forms (regional lymphadenopathy with or without skin inoculation lesions, respectively), the oculoglandular form (conjunctivitis with cervical or pretragial lymphadenopathy), the oropharyngeal form (pharyngitis with cervical lymphadenopathy), the pneumonic form (acute or subacute pneumonia) and typhoid fever. (severe sepsis) (3). If transmission occurs by inoculation of the bacterium via the arthropod vector, glandular and ulceroglandular forms of the disease occur. Oropharyngeal tularemia develops after ingestion of the bacteria with contaminated food or water. Other forms of the disease include the oculoglandular form and the most severe typhoid form (4). In Turkey, The ulceroglandular form is the most common form worldwide, and the oropharyngeal form (5-7). The Marmara, Black Sea and Central Anatolia regions are known to be epidemic areas (8). Tularemia is a disease with complex epidemiology that is difficult to understand and therefore difficult to control. Tularemia is a disease that can be overlooked, and antibiotics may be given to patients with different diagnoses. This can lead to delays in diagnosis, difficulty in treatment, and surgical procedures in lymphadenopathies (LAP) due to suppuration.

This study calculated the morbidity rates of tularemia cases diagnosed in Muş Province between 2011 and 2022 and aimed to increase awareness of tularemia in the region by showing the demographic, clinical and seasonal characteristics of cases.

2. Materials and Methods

This study was approved by the Scientific Research and Publication Committee of Muş Alparslan University with the permission (Date: 12.10.2022 and Decision No: 41).

All tularemia cases were retrospectively scanned from Tularemia Disease Information System of the Muş Provincial Health Directorate. *F. tularensis* was tested in the serum of suspected patients using the microagglutination test (MAT) at the National Tularemia Reference Laboratory of the Presidency of the Public Health Institution of Turkey. Cases with findings consistent with tularemia such as fever, sore throat, and LAP and *F. tularensis* MAT ≥ 1/160 or a 4-fold increase in antibody titer measured at least two weeks apart were considered definite cases. Positive cases were included in the study. Demographic, epidemiological, clinical and seasonal information on the positive cases and the duration of their diagnosis, were also studied. In this study, patients with fever and/or LAP were considered as glandular form, if the patient with fever and/or sore throat had tonsillitis, pharyngitis, oralulcers and cervical LAP, they were considered as oropharyngeal form.

2.1. Statistical analysis

Socio-demographic data of the patients (age, sex, place of residence, etc.) and clinical data of tularemia (complaints, type of disease, etc.) were used as descriptive data. These data are presented as numbers (n) and percentages (%).

3. Results

In this study, 162 cases of tularemia with F. tularensis MAT 1/160 and above in Muş Province between 2011 and 2022 were investigated Figure (1).

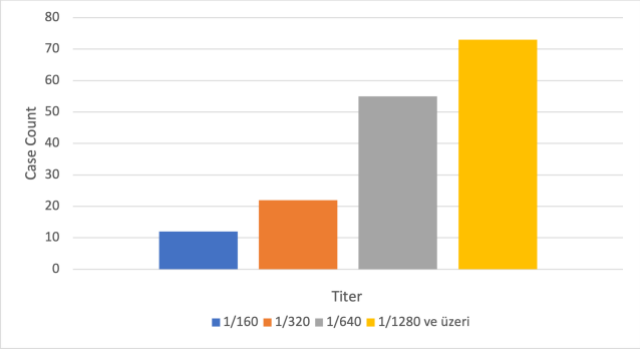

Figure 1. Microagglutination titer distribution detected in tularemia cases, Muş 2011-2022

The distribution of the cases by year is shown in Figure (2). The ratio of male and female tularemia cases was equal (50%), the average age was 24.5 years, and 46.3% of the patients were 18 years or younger Table (1).

Table 1. Demographic characteristics of tularemia cases, Muş 2011-2022

	2011-2016 n (%)	2017-2022 n (%)	Total n
Number of cases	65 (40,1)	97 (59,9)	162
Gender			
Male	29 (45,3)	52 (53,1)	81
Female	35 (54,7)	46 (46,9)	81
Average age	28,6	20,4	24,5

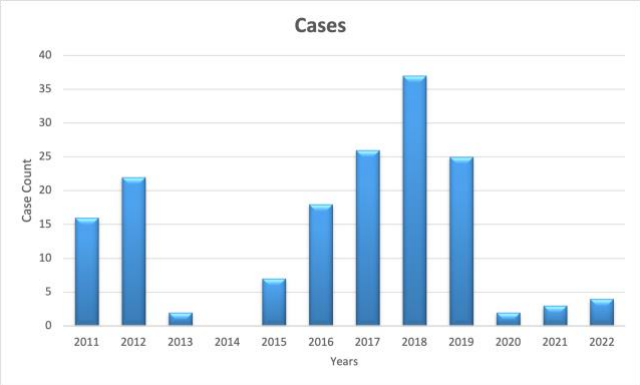

Figure 2. Distribution of tularemia cases by years

The average duration of hospitalisation after on set of the patients' symptoms was 37 days (4-162 days). Of the patients, 56 were housewives, 41 were students, 23 were farmers (6 women), 10 were children aged 0-5 years, 25 were from other occupational groups, 1 was a soldier, and 6 were unemployed. The incidence of tularemia cases in the city by region is shown in Figure (3).

Figure 3. Distribution of tularemia cases according to the districts of residence, Muş 2011-2022

When the distribution of the cases by season was examined, it was found that most cases occurred in the winter and autumn months (38.3% and 25.3%, respectively). This was followed by summer with 19.1% and spring with 17.3% Figure (4).

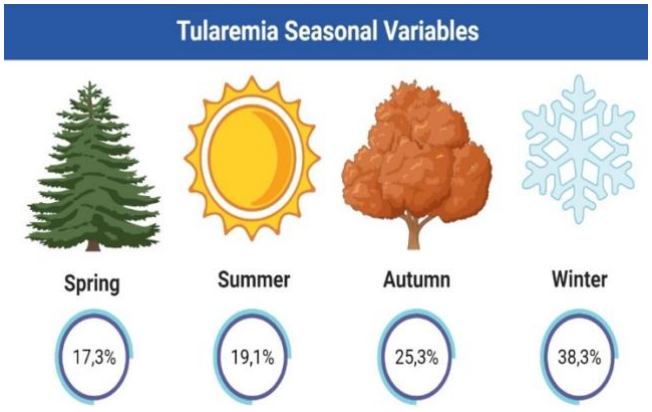

Figure 4. Distribution of tularemia cases according to seasons (%), Muş 2011-2022

The most common clinical findings were lymph node enlargement and/or pain in 96.9% (157), lymphadenopathy 95.1% (154), fatigue 61.7% (100), anorexia 48.1% (78), and Tonsillitis- Pharyngitis was the most common finding in 40.1% (65) Table (2).

Table 2. Symptoms and signs of tularemia cases, Muş 2011-2022

Symptoms	n (%)
Lymph Gland Enlargement	157 (96,9)
Lymphadenopathy	154 (95,1)
Fatigue	100 (61,7)
Anorexia	78 (48,1)
Tonsillitis- Pharyngitis	65 (40,1)
High Fever	62 (38,3)
Muscle-Joint Pain	58 (35,8)
Fever	42 (25,9)
Oral Mucosa Lesion	33 (20,4)
Wound in the Mouth	32 (19,7)
Nausea-Vomiting	23 (14,2)
Redness of the Eye	22 (13,6)
Abdominal Pain - Diarrhea	20 (12,3)
Skin Ulcer-Wound	11 (6,8)
Conjunctivitis	9 (5,5)
Skin Lesion	7 (4,3)
Skin Rash Erythema	6 (3,7)

When the clinical forms of tularemia were examined, the oropharyngeal form was the most common with 104 (64.2%) cases. The glandular form was found in 22 (13.6%), the ulceroglandular form in 11 (6.8%) and the oculoglandular form in 2 (1.2%) cases, and 23 (14.2%) cases could not be differentiated.

92% (149) of the patients lived in districts. The proportion of people using tap water for drinking was 66.7% (108) and reportedly the proportion of chlorination of tap water was 43.5% (47). It was determined that 33.3% (54) of the patients had a tularemia-like disease in their region. Possible risk factors of the cases are listed in Table (3).

Table 3. Possible risk factors of tularemia cases, Muş 2011-2022

Risk Factors of Tularemia	n (%)
Rural Life	143 (88,3)
Engage in Agriculture	95 (58,6)
Animal Nutrition	90 (55,5)
Rodent Presence	64 (39,5)
Activity in Nature	48 (29,6)
Contact with Rodent	19 (11,7)
Contact with Hunting Animal	12 (7,4)
Mosquito	9 (5,5)
Travel	9 (5,5)
Tick Attachment	8 (4,9)

Of the patients, 66.7% (108) were treated as outpatients, 29% (47) were treated as inpatients, 1.8% (3) were referred to a higher health institution and 2.5% (4) were discharged without complete recovery. He was discharged without full recovery.

4. Discussion

In recent years, *F. tularensis* has been identified as a re-emerging pathogen in Europe (9-12). Cases of tularemia cases are still occurring in Turkey as well (13-15).

Since tularemia is listed in group "C" in the list of notifiable infectious diseases (8), tularemia cases have been reported from many cities, especially from the Marmara and Western Black Sea, Central Anatolia and Eastern Anatolia regions. In recent years, with the occurrence of periodic epidemics in different regions of our country and the increasing number of case reports from these regions, tularemia has become popular again (5, 7, 15). When examining the literature of Muş Province, it is noticeable that there are not many studies, but the existing studies are based on small sample groups. In our study, we examined 162 positive cases from the Muş region.

In 2011, one case of oropharyngeal tularemia was reported in a pregnant woman with celiac disease due to drinking water in Muş Province (16). Ozden et al. conducted a study in which they investigated an epidemic of 26 cases in 2011-2015. In this study, 7 (26.9%) of the patients who went to Erzurum from some provinces in the Eastern Anatolia region,6 (23.1%) from Iğdır, 4 (15.4%) from Ağrı, and 4 (26.9%) from Erzurum (15.4%) reported living in Muş, 3 (11.5%) in Erzincan and 2 (7.7%) in Kars (12). Yazgi et al. investigated the seropositivity of tularemia in people who lived in the centre and rural areas of Erzurum in 2011. The *F. tularensis* microagglutination test (MAT) proved positive in 10.4% of the cases (13).

When analyzing the US Centres for Disease Control and Prevention (CDC) tularemia disease data, the highest number of tularemia cases in the United States between 2011 and 2020 was observed in 2015 and 2019. While 314 tularemia cases in the United States were observed in 2015, the number of cases was observed in 2016 (230), 2017 (239), 2018 (229), and 2019 (274) (17). When the epidemic periods and the number of cases in Muş Province were compared by year, epidemics were observed in similar periods, while the highest number of cases in our study was observed between 2017-2019. When evaluating the prevalance rates, it can be seen that the prevalance rates in Muş are higher than in the USA and Turkey. For this reason, it is important to closely monitor and track tularemia outbreaks in Muş Province.

Considering the demographic characteristics of the positive cases in our study, we find that the prevalance rates are the same in males and females. In the tularemia case studies by Çeviker et al., 75% and by Köse et al. 53.9% were found in female patients (7,18). Studies on the epidemiology of tularemia in Turkey have shown that tularemia cases are more frequent in women. This could be because women work intensively both at home and outdoors and are more likely to come into contact with contaminated water and rodent wastes.

While the mean age in our study was 24.5 years, it was reported as 37.7 years in several studies and 47.5 years in another study (7,18). We attribute the lower mean age in our study to the high number of patients in the 0-18 age group. It can be explained by the fact that adults have more contact with contaminated water, food and animals, as they spend more time farming and keeping animals outdoors. In our study, most cases occurred among housewives which is consistent with the existing literature (7). We interpret the frequency in housewives in the same way as the reasons for the frequency in women, and attribute it to the fact that housewives are also involved in livestock and farming.

Tularemia cases occur more frequenly in autumn and winter in our country (19). In our study, most cases were detected in the winter and autumn months. Kose et al. (2021) and Ceviker et al. (2019) reported that in their study they saw most cases in the winter months (7,18,19). This is thought to be due to the increase in rodent populations after the rains.

When the clinical forms of tularemia are examined, the ulceroglandular or glandular form is most common in epidemics in European countries, while the oropharyngeal form is most common in Turkey (7,18,20). In our study, the oropharyngeal form was observed most frequently with 64.2%. Consumption of unchlorinated drinking water contaminated by infected rodents, especially mice, is thought to be the source of the common oropharyngeal form seen in patients in our country.

The most common clinical findings were enlargement and/or pain in the lymph ganglia (96.9%), followed by lymphadenopathy (95.1%) and fatigue (61.7%) which is compatible with the results of other studies conducted in other regions of our country. (5,6,12,21,22).

When the risk factors were examined in the literature, it was reported that the cases used tap water, lived in rural areas, were involved in agriculture and had similar diseases in the neighbourhood/village where the cases lived (6,7,18). The same risk factors were also observed in our study. Kazak et al. (2013) reported a case of ulceroglandular tularemia after an arthropod bite (23). Tick bites were also observed in our study.

In our study, a retrospective evaluation of tularemia cases seen within 12 years is presented. When the distribution of tularemia cases in Muş over the years, we find that it gradually increased between 2015-2019 and peaked in 2018. During these years, it is

known that there were physical inconveniences and inadequacies in the water resources and tanks in Bulanık and Malazgirt districts, healthy drinking and domestic water could not be fully provided, and acute gastroenteritis (diarrhea) epidemics also occurred in the region during the same years due to the accompanying infrastructure works and insufficient chlorination. The lack of a solid structure of the water tanks and the presence of holes up to 30 cm in diameter in some of them may have played a role in the increase in the incidence of tularemia, as they allowed various rodents and animals to access the tanks.

In addition, when investigating the sporadic cases that did not occur in the cluster of tularemia cases, it was found that the patients swam in the Murat River, which flows through the borders of Muş Province, and that women in particular used this source of fresh water for household chores such as washing wool and carpet.

5. Conclusion and Recommendations

As a result, it should be remembered that tularemia occurs in all age groups, and that tularemia can also occur in patients of all ages, especially in autumn and winter, with symptoms such as sore throat and lymphadenopathy in the neck, fever and fatigue. Contact with contaminated water and detailed epidemiological history of such patients should be questioned. Moreover, it takes a long time for patients to apply to a health facility after the onset of their symptoms. However, we believe that early diagnosis, especially in regions where tularemia is endemic, can be achieved through frequent home visits by primary health care services, education about the disease and identification of people complaining of the disease. It is very informative to educate doctors in endemic areas about this issue and to know about the tularemia data of the region where they work. Since data on tularemia in the Eastern Anatolia Region is limited, studies on this topic are needed.

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Authorship Contribution:

YD: Concept, design, supervision, data collection, resource

EA: Literature review, writing, critical reviews

NEŞG: Data collection and/or processing, analysis and/or interpretation

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