

# Evaluation of One Hundred and Fifteen Cases Followed up with the Diagnosis of Leptospirosis

## *Leptospiroz Tanısı ile İzlenen 115 Olgunun Değerlendirilmesi*

Abdullah GÖLBOL<sup>1</sup>, Nuray HEYDAR<sup>2</sup>

<sup>1</sup>Clinic of Infectious Diseases and Clinical Microbiology, University of Health Sciences Turkey, Adana City Training and Research Hospital, Adana, Türkiye

<sup>2</sup>Clinic of Infectious Diseases and Clinical Microbiology, Bayrampaşa State Hospital, İstanbul, Türkiye

### ABSTRACT

**Objective:** This study was conducted to investigate the clinical, laboratory, and epidemiological characteristics of 115 patients who were followed up with the diagnosis of leptospirosis.

**Material and Methods:** The study was conducted retrospectively and descriptively. In total, 115 cases of leptospirosis were analyzed retrospectively. The microagglutination test was used for disease serodiagnosis. The data were analyzed using the SPSS-22 package.

**Results:** The mean age of the patients was 29.4 years (minimum: 10, maximum: 65), and 96 (83.5%) can be deleted were men. 43.6% (n=50) of the patients were hospitalized. Five hospitalized patients were followed up in the intensive care unit. The disease was not fatal. All patients presented with fever. Hepatomegaly was the most common sign 31.3% (n=36). Thrombocytopenia occurs in 73% of patients, and it is the most important laboratory finding. The most important finding of our study was that no deaths were observed in these cases.

**Conclusion:** The coincidence of patient presentation to the epidemic period, consideration of leptospirosis in the differential diagnosis, and early commencement of antibiotic therapy were thought to contribute to the lack of deaths. The younger age of patients in our study may be another reason for the lack of mortality. Leptospirosis remains a common zoonosis in tropical regions, particularly among agricultural irrigation workers. Considering the clinical and serological diagnosis of leptospirosis, initiating antibiotherapy early is of vital importance because it will reduce mortality.

**Keywords:** Leptospirosis, zoonosis, thrombocytopenia, workers, irrigation

### ÖZ

**Amaç:** Çalışma leptospiroz tanısı ile izlenen 115 hastanın klinik, laboratuvar ve epidemiyolojik özelliklerini araştırmak amacıyla yapıldı.

**Gereç ve Yöntemler:** Çalışma retrospektif ve tanımlayıcı bir çalışma olarak planlandı. Toplam 115 leptospiroz hastası retrospektif olarak analiz edildi. Serolojik tanı için mikroagglütinasyon testi kullanıldı. Veriler SPSS-22 paket programı ile analiz edildi.

**Bulgular:** Hastaların yaş ortalaması 29,4 (minimum: 10, maksimum: 65) olup, 96'sı (%83,5) erkekti. Hastaların %43,6'sı (n=50) hastaneye yatırıldı. Hastaneye kaldırılan hastalardan 5'i yoğun bakımda takibe alındı. Ölüm görülmedi. Hastaların tamamı ateş şikayeti ile başvurdu. Hepatomegali %31,3 (n=36) ile en sık görülen bulguydu. En önemli laboratuvar bulgusu hastaların %73'ünde meydana gelen tropositopeni idi. Çalışmamızın en önemli bulgusu, bu olgularda herhangi bir ölümün görülmemesiydi.

**Sonuç:** Hasta prezentasyonunun salgın dönemine denk gelmesi, ayırıcı tanıda leptospirozun düşünülmesi ve antibiyotik tedavisine erken başlanması mortalite görülmemesine katkı sağladığı düşünülmektedir. Çalışmamızda olguların yaşının genç olması mortalite olmamasının bir başka nedeni olabilir. Leptospiroz, tropikal bölgelerde, özellikle tarım sulama işçilerinde yaygın bir zoonoz olmaya devam etmektedir. Leptospiroz akılda tutularak klinik ve serolojik tanısı düşünüldüğünde, erken dönemde antibiyoterapiye başlanması mortaliteyi azaltacağı için hayati önem taşımaktadır.

**Anahtar Kelimeler:** Leptospiroz, zoonoz, tropositopeni, işçiler, sulama

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**Address for Correspondence:** Abdullah Gölbol, Clinic of Infectious Diseases and Clinical Microbiology, University of Health Sciences Turkey, Adana City Training and Research Hospital, Adana, Türkiye  
**Phone:** +90 535 379 09 79 **E-mail:** abgolbol@gmail.com **Received:** 29.05.2024 **Accepted:** 29.07.2024 **Available Online Date:** 15.08.2024  
**ORCID ID:** orcid.org/0000-0003-4999-5259



## INTRODUCTION

Leptospirosis is an acute, febrile, systemic, and zoonotic infectious disease caused by leptospira species. It is characterized by widespread vasculitis (1). Infection is transmitted to humans via the mucosal or percutaneous route after direct contact with infected animals or, more often, with leptospira-contaminated water or soil (2). Leptospirosis is frequently observed in irrigation workers, farmers, soldiers, miners, veterinarians, and sewer workers (1,2). This more common infection, particularly in tropical regions, can also cause epidemics (3). In particular, waterborne outbreaks have been reported in Southeast Asia and America (4,5). In our country, many patients are reported on a case-by-case basis (6-8).

Although the non-icteric form is seen in 90% of patients with leptospirosis, approximately 5-10% of patients have a severe form called Weil's disease, which is characterized by fever, jaundice, bleeding, and fulminant hepatorenal insufficiency. This condition progresses with severe jaundice and hepatorenal failure and has a high mortality rate (9). A definitive diagnosis of the disease is made by the presence of clinical findings and positivity to serological tests or the isolation of leptospira in urine or blood. It is known that serological tests have low sensitivity for the diagnosis of leptospirosis. Some of these patients die without being diagnosed, whereas others remain undiagnosed and recover with non-specific disease treatments (10).

In this study, we aimed to investigate the clinical, laboratory, and epidemiological characteristics of 115 patients who were followed up for the diagnosis of leptospirosis in the Kızıltepe district of Mardin.

## MATERIALS and METHODS

This retrospective and descriptive study was planned. The data on leptospirosis cases observed in Kızıltepe and Derik districts and their villages in Mardin province between 27 May 2019 and 28 July 2019 were retrospectively analyzed. The study was approved by the University of Health Sciences Turkey, Adana City Training and Research Hospital, Clinical Research Ethics Committee (decision number: 1799, date: 24.02.2022). A total of 115 patients who were hospitalized at Kızıltepe State Hospital or followed up for outpatient control were included in the study. The diagnosis of patients is based on either clinical diagnosis or serological test positivity. The clinical diagnosis depends on a history of exposure to infected animals or an environment/water that may be contaminated with animal urine, along with acute febrile illness that may be associated with any of the symptoms expected in leptospirosis like headache, myalgia, and exhaustion. The serodiagnosis of the disease in suspected patients was made

by the leptospira microagglutination test (MAT), and a titer of  $\geq 1/200$  in a single serum sample or  $\geq 4$ - fold increased titer in a double serum sample was considered positive. Accordingly, 62 patients with a clinical diagnosis and 53 patients with confirmed serology were identified. Basic demographic data on patients and characteristics of disease-specific clinical and laboratory findings were obtained from hospital registry records. Complete blood count, routine biochemical tests [aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma glutamil transferase, alkaline phosphatase, etc.] coagulation tests, erythrocyte sedimentation rate, C-reactive protein (CRP) levels, hepatitis indicators (hepatitis A immunoglobulin G, hepatitis B surface antigen, AntiHBs, hepatitis B surface antibody, hepatitis C antibody), and AntiHIV were requested from the patients. Also, 8-10 mL of venous blood was taken into yellow vacutainer tubes and centrifuged at 4000 rpm for 10 min to obtain sera for MAT investigations.

### Statistical Analysis

The data were analyzed using the SPSS-22 package. Descriptive statistics were used in the evaluation of the data, and the data were presented as median [minimum-maximum (min-max) value], number, and percentage distribution.

## RESULTS

The mean age of the patients evaluated in the current study was 29.4 years (min: 10, max: 65), and 96 (83.5%) of them were men. As 58.3% (n=67) of the patients were citizens of the Republic of Turkey, all other patients were Syrian citizens and lived in Turkey. In terms of occupational distribution, 108 (93.9%) patients worked as irrigation workers, and the other 7 (6.1%) were unemployed. When the geographical region where the patients live is studied; all of the patients were from Mardin province; 20 (17.4%) of them reside in Derik, 90 (78.3%) in Kızıltepe, and 5 (4.3%) resided in other districts.

43.6% (n=50) of the patients were hospitalized, whereas the others were followed up with outpatient clinic control. Five hospitalized patients were followed up in the intensive care unit. The disease was not fatal, and all patients were cured.

When the admission symptoms and symptoms developed during the clinical follow-up of the patients were examined, it was observed that all patients presented with fever. The distribution of other symptoms is presented in Table 1.

While hepatomegaly was the most common sign 31.3% (n=36), conjunctivitis, lymphadenopathy, and splenomegaly were other common findings. The distribution of all clinical signs is presented in Table 2.

Thrombocytopenia occurs in 73% of patients, and it is the most important laboratory finding. The mean laboratory findings were; white blood cell count  $100032 \text{ mm}^3$ , of which neutrophils comprised 79%; ALT, 64 International units/

liter (IU)/(L); AST, 72 IU/L; blood urea nitrogen, 17 mg/dL; creatinine, 1.11 mg/dL; total bilirubin, 1.8 mg/dL; creatine kinase, 381 IU/L; erythrocyte sedimentation rate, 32 mm/h; CRP, 99 mg/L, platelet (PLT) 140000 mm<sup>3</sup> at first admission; and lowest PLT 112000 mm<sup>3</sup> at follow-up. The laboratory findings of the patients are summarized in Table 3.

**Table 1. Distribution of patients' symptoms**

Symptoms	Incidence rate (number)
Headache	81.7% (n=94)
Nausea	80% (n=92)
Vomiting	58.3% (n=67)
Fever	100% (n=115)
Rigors	83.4% (n=96)
Diarrhea	56.5% (n=65)
Sore throat	74.8% (n=86)
Cough	21.7% (n=25)
Jaundice	9.6% (n=11)
Burning eye	25.2% (n=29)
Myalgia	94.8% (n=108)

**Table 2. Distribution of patients' signs**

Signs	Incidence rate (number)
Hemoptysis	2.6% (n=3)
Infiltration in lung X-ray	1.7% (n=2)
Hepatomegaly	31.3% (n=36)
Splenomegaly	7.8% (n=9)
Epistaxis	5.6% (n=6)
Conjunctivitis	8.7% (n=10)
Maculopapular skin eruptions	3.5% (n=4)
Petechial rash	9.6% (n=11)
Lymphadenopathy	7.8% (n=9)

**Table 3. Patients' laboratory findings**

WBC	10032 mm <sup>3</sup>
NEU (%)	79
ALT	64 IU/L
AST	72 IU/L
BUN	17 mg/dL
Creatinine	1.11 mg/dL
Total bilirubin	1.8 mg/dL
CK	381 IU/L
Erythrocyte sedimentation rate	32 mm/h
CRP	99 mg/L
Lowest platelet	112000/mm <sup>3</sup>
First admission PLT	140000/mm <sup>3</sup>

WBC: White blood cells, CRP: C-reactive protein, NEU: Neutrophile, CK: Creatine kinase, AST: Aspartate aminotransferase, BUN: Blood urea nitrogen, ALT: Alanine aminotransferase, PLT: Platelet

Two therapeutic agents were used for patient treatment. Ceftriaxone was intravenously administered with a posology of 2x1 g in hospitalized patients, and doxycycline capsules were administered with an oral posology of 2x100 mg in outpatients. In the follow-up of patients in the intensive care unit, broad-spectrum antibiotics were required due to prolonged hospitalization and nosocomial infections. One patient with pulmonary hemorrhage was treated with methylprednisolone 250 mg/day for 3 days.

## DISCUSSION

In our study, fever was the complaint of hospital admission in all of the patients who were agricultural workers. Most of them were of Syrian origin. The fact that no deaths were observed in these cases highlights the most important finding of our study. The coincidence of patient presentation to the epidemic period, consideration of leptospirosis in the differential diagnosis, and early commencement of antibiotic therapy are believed to contribute to this finding. In a retrospective case-control study conducted in New Caledonia, risk factors for the development of severe leptospirosis, in addition to infection due to *Leptospira interrogans* serogroup Icterohaemorrhagiae, were attributed to a delay in antibiotherapy initiation of >2 days following the onset of symptoms (11). The younger age of patients in our study may be another reason for the lack of mortality. Amilasan et al. (12) reported a 51% mortality rate that was also attributed to advanced age and delayed antibiotic therapy.

Rigors, headache, and myalgia follow fever in frequency, and they were commonly observed at similar rates as those reported in the literature. Conjunctival redness is another important but mostly overlooked sign; Vanasco et al. (13) reported that 55% of leptospirosis patients had conjunctival redness. We also found conjunctivitis in 8.7% of our patients; the reason for this inconsistency could be related to the lack of sub-conjunctival hemorrhage as a result of early treatment. Splenomegaly, lymphadenopathy, hepatomegaly, skin rash, and jaundice were observed in our patients at rates comparable to those reported in similar studies in the literature (14,15). In a study conducted by Leblebicioglu et al. (16) from our country, 12 cases were defined in the form of Weil's disease, and they detected jaundice and myalgia in all of these patients. The reason why jaundice was less common in our cases could be that leptospirosis patients were diagnosed at an early stage before the development of Weil's disease, and treatment was initiated at an early stage. The clinical findings of various studies reported from our country and the comparative data of our study are presented in Table 4.

**Table 4. Comparison between the case series reported from our country and the clinical data of our study**

Frequency of symptoms and signs in various leptospirosis studies from Turkey	Current study May 2019 - July 2019 115 cases (%)	Turhan et al. (17) GATA Hospital February-July 2004 22 cases (%)	Ebrahimi (18) Çukurova University 1994-1995 12 cases (%)	Şişli Etfal Hospital 1998-2003 16 cases (%)
Headache	82	81	50	50
Nausea	80	68	92	75
Vomiting	58	68	92	25
Fever	100	90	100	88
Rigors	83	50	100	
Diarrhea	56	40	8	25
Jaundice	10	9	92	100
Burning eye	25			
Myalgia	95	64	58	75
Hepatomegaly	31	16	42	69
Splenomegaly	8	12		25
Epistaxis	6	4	17	
Conjunctivitis	9	22	33	88

GATA: Gülhane Military Medical Academy

Pulmonary manifestation with non-productive cough occurs in 25 to 35% of cases (14,15). Pulmonary hemorrhage is a serious complication of leptospirosis; it may not be diagnosed adequately in highly endemic regions (18). Although cough complaints developed in our patients, pulmonary hemorrhage was seen only in 2 patients. None of them developed acute respiratory distress syndrome (ARDS). This might result from early diagnosis of the infection and early initiation of treatment. Comparable to the literature, we observed leukocytosis, left shift, thrombocytopenia, hepatic transaminase elevation, renal failure, and bilirubin elevation in our patients. Chierakul et al. (19) reported thrombocytopenia as one of the most prominent findings.

The mortality rates in hospitalized patients with leptospirosis ranged from 4% to 52% (12,20). In Peru, 3.7% of 321 patients with serological and clinical evidence of leptospirosis had severe pulmonary manifestations; 71% of these manifestations resulted in death (causes include pulmonary hemorrhage, ARDS, and multiple organ failure) (21). In a retrospective review of 282 cases of leptospirosis during an outbreak in India, pulmonary involvement and central nervous system disease were identified as important predictors of death in logistic regression analysis (12). Although renal failure was present in one-fifth of our cases, the reasons why there was no death in our cases might be the early initiation of antimicrobial therapy, the absence of central nervous system involvement, and the low incidence of pulmonary hemorrhage, and thus the absence of ARDS.

### Study Limitations

The limitations of our study are that the sample was limited to the region where the epidemic occurred and only reflected patients from a limited region. On the other hand, this is a powerful study in which a very high number of patients with leptospirosis were evaluated, and no mortality was observed.

### CONCLUSION

As a result, leptospirosis remains a common zoonosis in tropical regions, especially among agricultural irrigation workers. The differential diagnosis of acute fever in endemic areas should be considered, and the epidemiological history of the area should be investigated. Considering the clinical and serological diagnosis of leptospirosis, initiating antibiotherapy early is of vital importance because it will reduce mortality.

### Ethics

**Ethics Committee Approval:** The study was approved by the University of Health Sciences Turkey, Adana City Training and Research Hospital, Clinical Research Ethics Committee (decision number: 1799, date: 24.02.2022).

**Informed Consent:** Retrospective study.

### Author Contributions

Surgical and Medical Practices: A.G., N.H., Concept: A.G., N.H., Design: A.G., N.H., Data Collection or Processing: A.G., N.H.,

Analysis or Interpretation: A.G., N.H., Literature Search: A.G., N.H., Writing: A.G., NH.

**Conflict of Interest:** All authors declare that they have no conflict of interest.

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