

Clinical hematology of patients with leptospirosis who consult urgently in a hospital in Montería, Colombia

Hematología clínica de pacientes con leptospirosis que consultan de urgencia en un hospital de Montería, Colombia

José María Ortiz Girón^{1a}, Daniel José Ortiz Díaz², Álvaro Bustos González^{3a}, Nohora Díaz Cornejo^{4a}, Luis Carlos Ruiz Garcés^{5a}, Miguel José Sanz De La Rosa⁶

SUMMARY

Introduction: *Leptospirosis is a severe febrile disease transmitted by rodents, generally observed after heavy rains and floods, caused by pathogenic spirochetes of the genus Leptospira spp. It is considered the most frequent zoonosis in the world and recognized as an immunomodulator where innate immunity and immunity acquired in the guest's defense remain unclear. The present work aims to establish the clinical-hematological correlation in patients diagnosed with leptospirosis who consult Emergency in Montería, Colombia. Methodology:* A descriptive and retrospective observational study was conducted; the data were gathered by reviewing the patient's clinical histories. The information obtained from each patient was organized in a database, and the information analysis was subsequently performed to obtain the hematological profiles of the patients. Clinical suspicion was essential for its diagnosis.

Since the culture was not very sensitive, the sensitive polymerase chain reaction was used in blood and urine samples and serological tests. Results: Two hundred five patients who consulted emergency with febrile syndrome were analyzed; 37% of the cases were under 20 years, 51% were male, 64.2% were people from rural zone, 38.5% presented anemia grade III, 89.7% had a fever, and 29% had abdominal pain. **Conclusions:** *Leptospirosis is a re-emerging and important disease in public health since it spreads rapidly, reducing people's quality of life due to little knowledge of this zoonosis in the population; for this reason, it is often underdiagnosed.*

Keywords: *Leptospirosis, Zoonosis, Immune response, Febrile syndrome, Reservoir.*

RESUMEN

Introducción: *La leptospirosis es una enfermedad febril aguda transmitida por roedores, que generalmente se observa después de fuertes lluvias e inundaciones, causada por espiroquetas patógenas del género Leptospira spp. Es considerada como la zoonosis más frecuente en el mundo y, reconocidos como inmunomoduladores, el papel de la inmunidad innata y la inmunidad adquirida en la defensa del*

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ORCID: <https://orcid.org/0000-0001-7663-3777>¹

ORCID: <https://orcid.org/0009-0007-3327-2597>²

ORCID: <https://orcid.org/0009-0002-0356-0073>³

ORCID: <https://orcid.org/0009-0005-4543-3592>⁴

ORCID: <https://orcid.org/0000-0001-8202-381X>⁵

ORCID: <https://orcid.org/0009-0003-2635-9249>⁶

^aUniversidad de Sinú - Elías Bechara Zainum, Faculty of Basic Health Sciences, Medicine Program, Montería, Colombia.

Correspondent author: Luis Carlos Ruiz Garcés. Professor at the University of Sinu

Tel: 300 703 3415, E-mail: luiscarlosg03@gmail.com

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huésped permanecen poco claros. El objetivo del presente trabajo es establecer la correlación clínico-hematológica en pacientes diagnosticados con leptospirosis que consultan a urgencias en Montería, Colombia. Metodología: Se realizó un estudio observacional descriptivo y retrospectivo; los datos se obtuvieron mediante la revisión de las historias clínicas del paciente. La información obtenida de cada paciente se organizó en una base de datos, y posteriormente se realizó el análisis de la información, que permitió conocer el perfil hematológico de los pacientes. La sospecha clínica es fundamental para su diagnóstico. Debido a que el cultivo no es muy sensible, se empleó la prueba más sensible, la reacción en cadena de la polimerasa en muestras sangre y orina, y pruebas serológicas. Resultados: Se analizaron 205 pacientes que consultaron a urgencias con síndrome febril; 37 % de los casos fueron menores de 20 años, 51 % eran de sexo masculino, 64,2 % eran personas procedentes de zona rural, 38,5 % presentaban anemia grado III, 89,7 % presentaban fiebre y 29 % dolor abdominal. Conclusiones: En este estudio se investigaron las características clínicas y hematológicas de los pacientes con diagnóstico confirmado de leptospirosis, que apoyará al personal médico y paramédico en el reconocimiento precoz, confirmación diagnóstica y la detección temprana de la enfermedad.

Palabras clave: *Leptospirosis, Zoonosis, Respuesta inmune, reservorio.*

INTRODUCTION

Leptospirosis is a re-emerging zoonotic disease of global importance caused by *Leptospira*, a Gram-negative spirochete-shaped bacterium belonging to the order Spirochaetales, family Leptospiraceae and genus *Leptospira* (1). They are motile, obligate aerobe microorganisms with an optimal growth temperature of 28°C to 30°C (82.4°F–86°F) (2). The entry doors are microlesions of the skin and mucous membranes (3). The infection can be caused by direct contact with an infected animal or indirect contact through soil or water contaminated with the infected animal's urine. Leptospirosis is present on all continents except Antarctica and is considered the most widespread zoonosis in the world (3). Leptospiral infection has been reported in humans, cattle, pigs, horses, goats, dogs, rodents, and several species of wild animals in Brazil and throughout the world, which can also act as reservoirs; humans and

animals become infected through contact with urine, contaminated soil, and water (4,5). Socioeconomic and environmental factors such as inadequate sanitation and hygiene, lack of potable water, flooding, and close contact with livestock increase the risk of transmission (6,7).

The choice of which diagnostic test to use depends on the stage of evolution of the disease, its prevalence, and the availability of a qualified laboratory; polymerase chain reaction (PCR) has been widely used for diagnosis; culture is rarely used in the clinical setting because it requires prolonged incubation and has low sensitivity; the Microscopic Agglutination Test (MAT) is the most popular serological test, and most reference laboratories perform it (8).

Human leptospirosis has diverse clinical manifestations; the clinical disease in humans can range from a mild and self-limited acute febrile illness to a severe and life-threatening condition with multiple organ dysfunction. Many organ systems can be affected to varying degrees, and also a variety of atypical or unusual manifestations and complications have been described (9); symptoms include headache, chills, nausea and vomiting, myalgia, and, less frequently, skin rash; the most severe form of the disease is Weil syndrome, characterized by multi-organ complications including jaundice, meningitis, pulmonary hemorrhage, liver and kidney dysfunction, and cardiovascular collapse (9,10). The role of innate and acquired immunity in host defense remains unclear; pathogenic species present evasion mechanisms of the humoral response in the bacteremia phase (11). Host responses in leptospirosis are complex but important in the pathogenesis of the disease; contact of the host with the pathogen causes the release of cytokines. The extensive release of cytokines, including interleukin 6 (IL-6), interleukin 1 beta (IL-1 β), and tumor necrosis factor-alpha (TNF- α), are known as cytokine storm, many studies have demonstrated the role of cytokines in the clinical manifestations and pathogenesis of leptospirosis (12). Renal biomarkers, such as neutrophil gelatinase-associated lipocalin (NGAL), could also be involved in the pathogenesis of leptospirosis; a previous study demonstrated that plasma (p) NGAL and urine (u)NGAL correlated with acute kidney injury (AKI) in patients with

leptospirosis (13). Activated neutrophils secrete the NGAL in response to bacterial infections, but the roles of NGAL in the pathogenesis of leptospirosis are still unexplored. IgM and IgG antibodies are detected serologically in patients who have recovered from severe leptospirosis up to six years after initial infection, and the presence of TLR2 and TLR4 is required for effective innate immune defense (10).

Leptospirosis has been designated by the US Centers for Disease Control (CDC) as a neglected tropical disease (NTD), characterized by its impacts on vulnerable populations (14); the disease affects more than one million people annually, causing 59 000 deaths and an estimated loss of 2.9 million disability-adjusted life years per year, reflecting its high socioeconomic impact (15); in the Caribbean and Latin America, the Indian subcontinent, Southeast Asia, Oceania and, to a lesser extent, Eastern Europe are the most important hotspots of the disease, including areas that are popular tourist destinations (16). In Colombia, by the year 2020, according to the National Institute of Health, the incidence of leptospirosis was 0.06 cases per 100 000 inhabitants.

The departments that presented the most cases were Tolima with 29.0 %, Antioquia 19.4 %, Santander 12.9 %, Valle 9.7 %; Bolívar, Boyacá, Cartagena, Casanare, Chocó, Córdoba, Cundinamarca, Huila, Risaralda 3.23 % (17). However, leptospirosis is underreported or misdiagnosed due to limited access to appropriate diagnostic tests, lack of clinical awareness, and because most cases of leptospirosis are mild and usually present as an undifferentiated fever (18)

METHODOLOGY

A descriptive, cross-sectional, retrospective study was carried out, considering the clinical histories of the users treated in the emergency services in a hospital in Montería from January 2016 to December 2018. Clinical suspicion is essential for its diagnosis. The culture is not very sensitive, so it usually requires a sensitive and early polymerase chain reaction in blood and urine and serological tests.

The study population consisted of adults of both sexes with a diagnosis of leptospirosis; the sample size was 205 patients. A data matrix was used in Excel to analyze the collected data, which was processed in the IBM Statistical Package for the Social Sciences program (SPSS 19.0.0).

RESULTS

Between January 2016 and December 2018, 205 patients confirmed with leptospirosis consulted the emergency room, distributed as follows: 38.5 % in 2016, 40 % in 2017, and 21.4 % in 2018. The most significant number of cases occurred at 37 % in those under 20 years of age, and the lowest number of cases occurred at 4.87 % in those over 61 years of age. Regarding the distribution of the population by sex, it was evidenced that 51.21 % of the cases occurred in the male sex and 48.7 % in the female sex. Regarding the origin, 62.4 % of the patients came from the urban population, while 37.5 % came from the rural population.

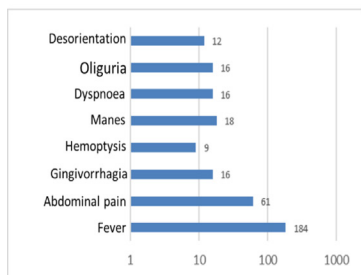
Table 1. Sociodemographic characteristics of the patients with a confirmed case of leptospirosis.

Variables	Categories	Frequency	
		N=	%
Age	≤ 20	76	37
	21-40	59	28.7
	41-60	21	10.24
	61-80	10	4.87
Sex	Female	100	48.7
	Male	105	51.21
Origin	Rural	128	62.4
	Urban	77	37.5

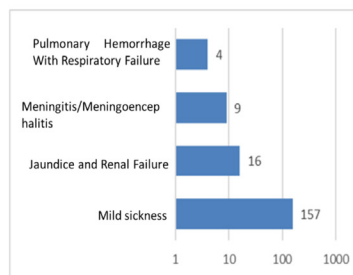
The most frequent clinical manifestation was fever, with 184 cases, and the least frequent was hemoptysis, with nine patients. According to the classification proposed by the WHO, the study population had 157 patients with mild disease,

followed by jaundice and renal failure in 16 patients; 4 presented pulmonary hemorrhage with

respiratory failure (Figure 1A and 1B).



A

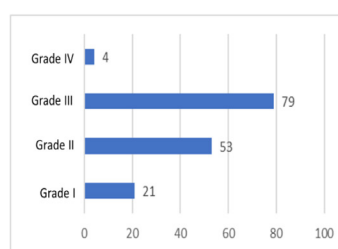
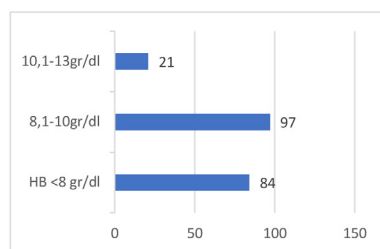


B

Figure 1A. Clinical manifestations of leptospirosis; 1B. Clinical categories of leptospirosis.

47.1 % (97) of the patients presented anemia, with hemoglobin levels between 8.1 and 10 g/dL; 40.9 % (84) had hemoglobin levels below 8 g/dL, followed by 20 % (21) with 10.1 to 13 g/dL.

Regarding the classification of anemia, according to the WHO, 38.5 % (79) presented grade III anemia, 25.8 % (53) grade II anemia, and 10 % (21) Grade I anemia (Figure 2A and 2B).



A

B

Figure 2. A. Hematological alterations (anemia), B. Classification of anemia.

85.8 % (176) presented leukocytosis, 9.26 % (19) a normal leukocyte count, and 4.87 % (10) leukopenia, while 59 % (121)

presented thrombocytopenia, 38.5 % (79) normal platelet count and 2.43 % (5) thrombocytosis (Figure 3A and 3B).

CLINICAL HEMATOLOGY OF PATIENTS WITH LEPTOSPIROSIS

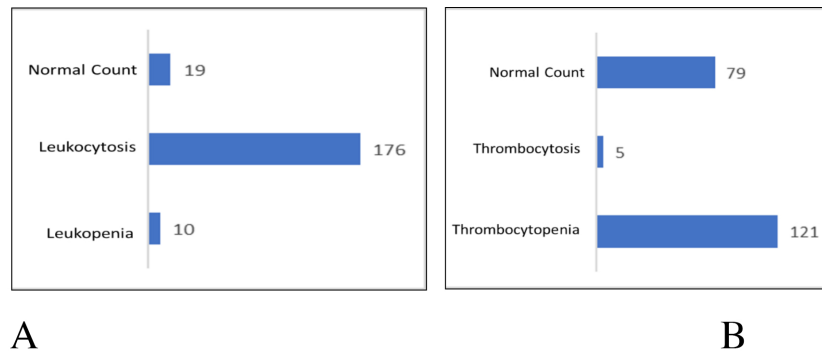


Figure 3. A. WBC count, B. platelet count

DISCUSSION

Leptospira infections generally occur through abrasions or wounds on the skin or contact with the mucosa. Leptospira can be transmitted directly to humans by handling infected animals, making leptospirosis an occupational hazard for people who handle animals regularly, such as livestock producers, slaughterhouses, veterinarians, hunters and game managers, animal control workers, and scientists (19). This requires a multidisciplinary approach to respond to and manage threats from any deadly pathogen. One Health stems from these concerns and is a collaborative, multidisciplinary, cross-sector approach to addressing the risks of interactions between humans, animals, and ecosystems. One health issue would be specifically important in Colombia, a biodiverse country with unique flora and fauna, which appears favorable to many communicable diseases if not adequately controlled (20).

In Colombia, an incidence of leptospirosis of 10.2 cases per 100 000 inhabitants has been reported; in 2015, a total of 634 laboratory-confirmed cases were reported throughout the country (21), and in the department of Córdoba, in 2016, 55 cases were identified; only one of them was confirmed as fatal (16). This hospital-based case series shows a cohort of 205 patients; the most significant number of cases was reported in 2017 with 40 % (82); data coincides with the cases reported by the National Institute of Health that

same year. It is likely that weather patterns mainly increased heavy rainfall and flooding, have led to an increase in severe leptospirosis epidemics. These data demonstrate the importance of studying this disease, particularly in endemic and tropical areas.

Regarding sociodemographic characteristics, the most significant cases in the present work occurred in those under 20 (37 %). Likewise, it is reflected in the data reported by the National Institute of Health, where the most affected age group was 11 to 20 years old with a frequency of 735 (20.1) (17); similar results were reported by Mukadi et al. (22); this is probably because this population is at risk of leptospirosis due to their occupational exposures. Regarding sex, men were more vulnerable, with 51.21 % (105) of cases; a similar result was reported by the National Institute of Health (17) and by Calderón et al. (23), who studied the epidemiological behavior of human leptospirosis in Colombia between 2012 and 2016, concluding that the results are probably due to socioeconomic behavior since men would have a greater exposure during agricultural or occupational activities, making them more susceptible to many infections caused by viruses, bacteria, parasites, and fungi. Regarding the origin, the urban population is more vulnerable, with 62.4 %, compared to the rural population, which is related to several risk factors associated with the development of leptospirosis, including changes in climatic and environmental conditions, occupational and recreational activities of contact with river water

and trips to endemic areas. On the other hand, the expansion of infected animals, especially rodents (rats), is important within the disease's epidemiological chain since they can maintain it and eliminate the bacteria throughout their lives through urine (24).

The clinical characteristics of leptospirosis are like those observed in many other febrile diseases, especially those familiar in our country, such as dengue, rickettsiosis, malaria, and bacterial sepsis (25). In the present study, the most frequent manifestation was fever, with 89.7 % (184) of cases, and the least frequent manifestation was hemoptysis, with 45 % (9). According to the classification proposed by the WHO, the study population presented 76.6 % (157) patients with mild disease, followed by jaundice and renal failure with 7.8 % (16) patients and 1.9 % (4) patients with pulmonary hemorrhage and respiratory failure. Similar symptoms were reported by the National Institute of Health (17) and by Cedano et al. (26). The clinical manifestations in our environment do not differ much from what is reported in the world literature: fever, headache, and jaundice remain the main findings in human symptomatic leptospirosis (27).

Studies by Anandarama et al., 2017 (9) recorded the mean hemoglobin concentration, showing a progressive decrease in mild and severe diseases. Similar results were presented in our study, where (97) of the patients presented anemia with hemoglobin levels between 8.1 and 10 g/dL, 40.9 % (84).

An important laboratory parameter of leptospirosis is thrombocytopenia, which occurs between 40 and 86.6 % of infections (28). This is associated with various complications and a worse prognosis of the disease; mortality rates are higher in patients with thrombocytopenia compared with patients who did not have laboratory-confirmed thrombocytopenia (28); therefore, early recognition of thrombocytopenia and prevention of further complications is important to reduce mortality in leptospirosis (3). Independent risk factors for thrombocytopenia are dehydration, metabolic acidosis, and low potassium levels on admission (23). Low serum potassium was a protective factor against thrombocytopenia; hyperkalemia is associated

with thrombocytopenia (24). The mean total leukocyte counts increased until day 2 in mild disease and until day 5 in severe disease (9). In the present study, leukocytosis occurred in 85.8 % of the patients.

CONCLUSION

Leptospirosis is a re-emerging and important disease in public health since it spreads rapidly, decreasing the quality of life of people due to the little knowledge of this zoonosis in the population; for this reason, it is often underdiagnosed, and patients do not receive the necessary treatment. Necessary care taking lives. This makes it necessary to expand the perception of this disease and raise the alarm to establish programs that collaborate with the prevention and control of leptospirosis from the field of public health.

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