

**SYSTEMATIC REVIEW:**

**EPIDEMIOLOGY of LEPTOSPIROSIS IN INDONESIA**

**Dewi Yuniasih\*, Nuni Ihsana, Dhea Arinda Shalsabila, Novi Wijayanti Sukirto**

Faculty of Medicine, Ahmad Dahlan University, Yogyakarta, Indonesia

\*Corresponding author: [dewi.yuniasih@med.uad.ac.id](mailto:dewi.yuniasih@med.uad.ac.id)

**ABSTRACT**

*The burden of global leptospirosis is very significant; However, inadequate diagnosis has affected disease awareness in the medical community. This systematic review aims to find the leptospirosis rates more accurately and to increase early awareness of leptospirosis with the prevention and control of leptospirosis programs in Indonesia. The method of this paper is a systematic review. This research was carried out by searching information from Medline, Embase, Cochrane library, and Google scholar. Keywords for the search are "Leptospirosis in Indonesia ", "Epidemiology of Leptospirosis in Indonesia "Risk Factors of Leptospirosis in Indonesia "or" Management of Leptospirosis in Indonesia ". The period of the publication is five years, from 2014 to 2018. The results of this study are 447 article titles from Google scholar and Pubmed which be accessed. Leptospirosis cases mostly occur in adults in the age group 20-50 years, male, and working as a farmer. The suggestions put forward are to do a more in-depth analysis to answer the formulation and objectives of the research.*

**Keywords:**

*A systematic review, epidemiology, leptospirosis, Indonesia, characteristic of leptospirosis*

**INTRODUCTION**

Leptospirosis is a zoonotic bacterial disease found mainly in poor populations that inhabit developing countries with tropical climates<sup>1</sup>. The burden of global leptospirosis is very significant; However, inadequate diagnosis has affected disease awareness in the medical community. The incidence of leptospirosis is unfortunately not well documented in many provinces in Indonesia<sup>2</sup>, mainly due to the unavailability of laboratory diagnoses, poor medical awareness, and non-specific symptoms that overlap with many other tropical infectious diseases, especially arbovirus infections. As a result, little is known about the ecological, epidemiological, and clinical characteristics of leptospirosis in the region, and the burden of this disease may be even higher than is known<sup>2</sup>.

Human leptospirosis is caused by bacteria belonging to the genus *Leptospira*. This genus consists of at least 22 species which are grouped into three categories containing pathogenic, moderate, and saprophytic species. At present, there are more than 250 names, of potentially pathogenic serovars<sup>1</sup>. These diseases produce high morbidity and substantial mortality in areas with high prevalence. It is estimated that around 10,000 cases of severe leptospirosis are hospitalized every year worldwide. This disease is usually endemic in areas with a rainy season, humidity, close human contact with livestock, poor sanitation, and workplace exposure to organisms<sup>2</sup>. In recent years, new trends in outbreaks of human leptospirosis have been observed related to

recreational activities among wildlife (a form of tourism that is becoming increasingly popular) and army expeditions, both for training or for purposes related to fighting in the same environment<sup>3</sup>. A systematic literature review of the Leptospirosis Burden Epidemiology Reference Group (LERG) reports estimates of annual global incidents of endemic human leptospirosis and epidemics ranging from 5 to 14 cases per 100,000. Rates of endemic human leptospirosis vary by region from 0.5 / 100,000 in Europe to 95 / 100,000 in Africa. Based on global data collected by the International Leptospirosis Society survey, the incidence is estimated to be 350,000-500,000 cases of severe leptospirosis every year<sup>4</sup>.

The number of cases of leptospirosis in Bantul Regency, Special Region of Yogyakarta Province cannot be said to be low<sup>5</sup>. Leptospirosis is an infectious disease that is transmitted by animals to humans (zoonotic infectious disease) which also has the nickname Weil's disease, swineherd's disease, and Andaman hemorrhagic fever (AHF), rice-field fever, mud fever, and others. This disease is caused by microorganisms that are firm in the genus *Leptospira*. Leptospire are gram-negative spherocytes, pathogenic leptospire are classified into 23 serogroups based on serological cross-activity with 223 subdivision serovars. In the body of animals, especially mammals, *Leptospira* bacteria live in the kidney tubules and can last for several years resulting in chronic infections<sup>5</sup>.

In water, *Leptospira* bacteria can live up to several months. Humid conditions with temperatures ranging between 25°C and neutral environmental pH (+ -7) are the environments that *Spira* needs to live and reproduce. Conversely, dry conditions and exposure to sunlight, water, and soil with a pH of less than 6.2 or more than 8.0 do not support the growth of these microorganisms. Transmission can occur when there is direct contact with urine and body fluids from an infected animal. In addition, leptospirosis can also be transmitted indirectly through water and soil contaminated with *Leptospira* bacteria. Urine can be said to be the main source of infection if the urine of animals that are carriers or carriers of these microorganisms are in the soil and water with the appropriate conditions <sup>6</sup>.

Poor sanitation, population density, poor waste management, poor rodent control, exposure to infected animals, the slaughter of animals, concomitant use of water and toilet, and consumption of contaminated food and water are risk factors for leptospirosis. Post-disaster conditions can also increase the risk of leptospirosis. This refers to conditions where there is an event that makes humans and animals in an environment so that there is an increased risk of leptospirosis. In addition, tropical countries and high rainfall are also often associated with increasing leptospirosis rates <sup>7</sup>.

This disease also has seasonal incidents. Increases during the rainy season whereas in four-season countries the incidence of leptospirosis increases when late summer to early fall. This happens related to the character of the *Leptospira* bacteria that will survive in water, wet soil, vegetation, and mud with temperatures more than 22 degrees Celsius <sup>7</sup>.

#### Epidemiology of Leptospirosis

Indonesia is one of many countries in the Asia-Pacific region with an incidence of mild leptospirosis <sup>8</sup>. The first case of leptospirosis in Indonesia was documented in 1918 by Schaffner on the east coast of the island of Sumatra<sup>9</sup>. In 1922, Vervoort confirmed human leptospirosis among plantation workers on the east coast of Sumatra<sup>9,10</sup>. Since then, most of the main islands in Indonesia such as Java, Bali, Kalimantan, and Sulawesi have identified and reported cases of leptospirosis. The number of cases of human leptospirosis reported annually to the Ministry of Health from 2007 to 2011 was 664, 426, 335, 409, and 857, respectively <sup>9,10</sup>. However, not all provinces report routine leptospirosis annually. Annual death cases for 2007 to 2011 were 8.28%, 5.16%, 6.87%, 10.51%, and 9.57%, respectively<sup>11</sup>. The actual number of leptospirosis cases in Indonesia may be higher than

reported<sup>5</sup>. Less frequent reporting due to infection is not clinically clear, too mild for a definitive diagnosis, wrongly diagnosed as dengue fever or other endemic diseases, and because of the lack of ability of laboratory centers to do confirmations<sup>5</sup>. There is a lack of data available about the risk and incidence of leptospirosis in Indonesia compared to other infectious diseases, such as dengue fever or malaria<sup>2,5</sup>. Peer-reviewed publications on leptospirosis studies conducted in Indonesia have predominantly focused on clinical and laboratory factors rather than determinants of public health. The focus of the study on risk factors for human leptospirosis in Indonesia is mainly available as a report in gray literature. As a result, data sourced from gray literature are important resources for public health planning for the prevention or control of leptospirosis in Indonesia <sup>2</sup>. Gaasem (2020)<sup>2</sup> identified 3.5% of acute infections with *Leptospira* in patients hospitalized with acute febrile illnesses in Indonesia. This number could be the total number of cases less reported in the cohort given that cases of fever confirmed as dengue virus infection were not examined for coinfection with *Leptospira* due to study resource limitations. Unfortunately, there are no recent studies that report the incidence of leptospirosis in seven major cities in Indonesia. The previously published reports originated from Jakarta in 1993-1995, Papua in 1997-2000, Semarang in 1995-1996 and 2005-2009, Tangerang in 2015, and tourists returning from Sumatra and Bali in 2008 and 2013 <sup>11</sup>.

The focus of a leptospirosis prevention or control program is to break the chain of infection by avoiding direct contact or minimizing the risk of indirect contact with the source of infection and by adopting control measures that show benefits in reducing transmission of leptospirosis to humans <sup>3</sup>. Therefore, information about risk factors for leptospirosis or infection is the main requirement for successful prevention of leptospirosis and controlling programs<sup>4</sup>.

So with this systematic review, it can be seen that leptospirosis rates are more accurate, to increase early awareness of leptospirosis with the prevention and control of leptospirosis programs in Indonesia. Furthermore, a better reporting and data collection system are expected for this leptospirosis case.

The purpose of this study is to identify cases of Leptospirosis from the data obtained from this systematic review study and to identify risk factors for the occurrence of Leptospirosis outbreaks in Indonesia.

## METHODS

### a. Searching strategy

This research is a systematic summary (Systematic Review) using the PRISMA (Selected Reporting Item for Systematic Review and Meta-analysis)<sup>12</sup> method which is carried out systematically by following the research or tracing the correct research protocol. Population (P) in this study are all articles published in journals national, international, and gray literature which have topics on the epidemiology of leptospirosis in Indonesia. The sample in this study is the article published in national journals, international literature, and gray topics on the epidemiology of leptospirosis in Indonesia that meets the inclusion criteria. Intervention (I) in this study was not conducted as well as C (Comparison) where there is no specific implementation. While the Outcome (O) expected from this study is the distribution of epidemiological figures, risk factors, and also the management of leptospirosis in Indonesia. In addition, this study was conducted to collect information about animals responsible for leptospirosis cases in Indonesia as well.

The procedure of this Systematic Review consists of several steps, namely 1) compiling the Background and objectives, 2) Research Question, 3) Searching for the literature, 4) Selection Criteria, 5) Screening 6) Quality Checklist and Procedures 6) Data Extraction Strategy, 7) Data Synthesis Strategy. This research was carried out by searching information from Medline, Embase, Cochrane library, and Google scholar. Keywords for inclusion criteria are defined as: "Leptospirosis in Indonesia "," Epidemiology of Leptospirosis in Indonesia "Risk Factors of Leptospirosis in Indonesia "or" Management of Leptospirosis in Indonesia ", Period The publication is for a period of five years, from 2014 to 2018.

**b. Inclusion criteria.**

The inclusion criteria in this research article are as follows: 1) The research article was published in 2014-2018. 2) The language used in the article is English or Indonesian. 3) Research studies discuss the epidemiology, risk factors, or management of leptospirosis in Indonesia. 4) Research studies carried out in Indonesia.

**c. Exclusion Criteria.**

Comments or summaries of articles, editorials, letters to editors, opinions, or comments without original data are issued, as well as publications or lay media broadcasts. We further issue publications that focus on (i) wrong geographical locations, (ii) wrong agents/diseases, (iii) experimental data (in-vitro or in vivo cellular, molecular, biochemical, or other studies

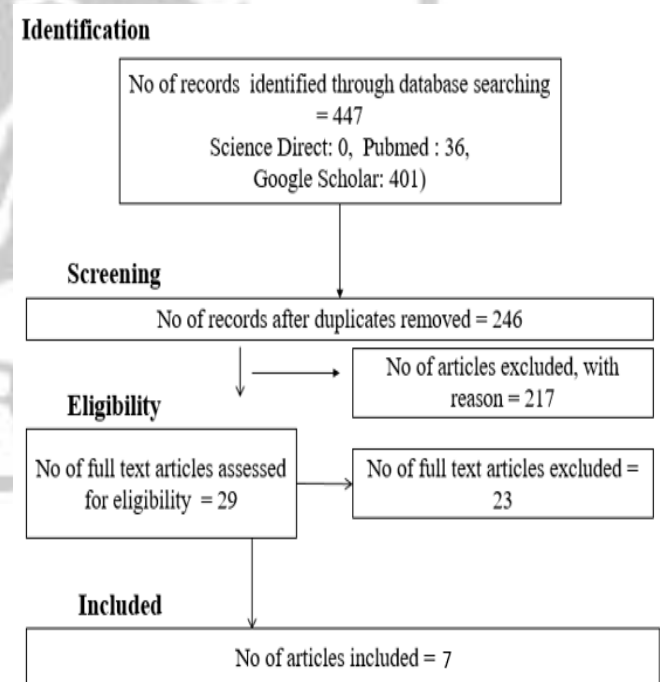
that do not include cases of leptospirosis natural in humans or animals), and (iv) description or study of laboratory methods. Inclusion and exclusion criteria are applied to the title and abstract of all references taken. References that are not available abstracts are included in the later stages of the full-text review. Exclusion criteria during the full-text review. The full text of articles that qualify for inclusion is taken and assessed based on the same exclusion criteria as the abstract review. When more than one reference is taken for the same study, or when the same data is taken in different formats (publications, project reports, conference presentations), only the most comprehensive is retained. Studies, where full text is not available, are excluded unless relevant data (qualitative or quantitative) are available from abstracts or from studies that are published later.

**d. Ethical clearance**

Our study used secondary data, which are freely available on the Internet. Therefore, ethical approval was not necessary for this study.

**RESULTS**

From figure 1, we accessed 447 article titles from Google scholar and Pubmed, unfortunately, there was no article from ScienceDirect. After going through the selection according to the inclusion criteria, 7 published articles were included in the study and further reviewed and analyzed.



Picture 1. Flowchart Searching Process

From picture 1, we see the type of research of the included publication are the case-control method (3/7), case study (2/7), case report (1/7), and cross-sectional (1/7). In the year of publication, 6 out of 7 articles were 2014 reported cases. According to the number of incidences of leptospirosis, 160 cases were successfully obtained from these 7 articles.

The average age of the patients was young, between 20 - 50, male and work-related, and the presence of pets, especially rats, was reported in several studies. In addition, some studies link environmental hygiene and sanitation with the incidence of leptospirosis.

**Tabel 1. The characteristic of the article publication**

Author	Method	Cases (n)	Place	Year	Characteristic of Cases
Ana Erviana <sup>13</sup>	case report	26	Cengkareng	2014	<ul style="list-style-type: none"> <li>• Age group 20-40 years and &gt; 40 years</li> <li>• Male gender</li> <li>• Have a history of injuries</li> <li>• Low education</li> <li>• Poor hygiene and sanitation</li> <li>• There are rats in the house</li> </ul>
Rahma lka Pratiwi <i>et.al</i> <sup>14</sup>	case report	27	Ponorogo	2014	<ul style="list-style-type: none"> <li>• Farm work</li> <li>• Age group 25-50 years</li> <li>• Male gender</li> <li>• Poor physical and social environment</li> <li>• Bad attitude</li> </ul>
YN Wijayanti <sup>15</sup>	Case-control	25	Boyolali	2014	<ul style="list-style-type: none"> <li>• There is no occupational effect on leptospirosis</li> <li>• use of personal protective equipment</li> <li>• Bathing habits in the river</li> <li>• Pet</li> <li>• There is no effect on the habit of washing hands/feet</li> <li>• Storing food has no effect</li> </ul>
S. Pertiwi, O. Setiani, and N. Nurjazuli <sup>16</sup>	Case-control	30	Pati	2014	<ul style="list-style-type: none"> <li>• Stagnant water in the ditch</li> <li>• bad sewer</li> </ul>
Nisa Azza Katulistiwa dan Kusuma S. Lestari <sup>17</sup>	Interview	12	Klaten	2014	<ul style="list-style-type: none"> <li>• Home conditions,</li> <li>• occupant behavior, and</li> <li>• the presence of rats in the house</li> </ul>
Sri Nuraini <i>et.al</i> <sup>18</sup>		39	Boyolali	2014 - 2015	<ul style="list-style-type: none"> <li>• Age group 26 - 45 years</li> <li>• Male gender</li> <li>• Farmer's work</li> </ul>
Rosa De Lima Renita Sanyasi <sup>19</sup>	Case report	1	Magetan	2018	<ul style="list-style-type: none"> <li>• female 40 years</li> </ul>

## DISCUSSION

Leptospirosis usually occurs in groups of farmers and ranchers as well as workers associated with forests and water. This is in line with the results of the study which showed the distribution of leptospirosis cases in the study from Pertiwi<sup>16</sup> and Sri Nuraini<sup>18</sup>.

The results of the study in Boyolali<sup>18</sup> showed that the distribution of leptospirosis cases in Boyolali was mostly among farmers, namely 21 cases (44.7%).

According to gender, the incidence of leptospirosis is more common in men than women, because men often do activities outside the home related to water<sup>18</sup>.

Sri Nuraini et al<sup>18</sup> found men suffer more from leptospirosis in Boyolali, namely 33 cases (70%). This finding is in line with the study of Pertiwi et al<sup>16</sup>, who stated that leptospirosis cases were more dominant in men, namely 52 cases (68.42%) than the female was 16 cases (21.05%).

Leptospirosis bacteria can infect all age groups of humans but most cases of leptospirosis occur in humans adults. This happens because at that age people usually do a lot of related activities outside the home with water and soil<sup>18</sup>. Based on the results of the study, the distribution of leptospirosis cases occurred mostly in the age group of adults. This is in line with the research of Thornley, et al.<sup>20</sup>, Which states that in part Leptospirosis cases (56.9%) in New Zealand occurred at age 25-44 years.

House conditions, occupant behavior, and the presence of rats in the house were statistically associated with the incidence of leptospirosis. Housing and sanitation components were not associated with leptospirosis. Katulistiwa et al<sup>17</sup>, found that unhealthy house conditions are the most influential risk factor for the incidence of leptospirosis in Klaten Regency with a large risk of 2 times more risk than a healthy home condition

## CONCLUSION

From this systematic review research, 7 articles were analyzed. Leptospirosis cases mostly occur in people adults in the age group 20-50 years, male, and working as a farmer. The suggestions put forward are to do a more in-depth analysis to answer the formulation and objectives of the research. In addition, it is hoped that this systematic review research can be expanded from other databases, for example, SCOPUS, CINAHL, and so on. Furthermore, it is necessary to continue with a retrospective study that cannot be carried out in this study because it is hindered by the pandemic.

## ACKNOWLEDGMENT

This work was supported by the LPPM of UAD [grant number PDP-034/SP3/LPPM-UAD/2020]. The author is indebted to Dr.Ing.Suhendra, for editing the pre-submission manuscript and for his invaluable input, and suggestions in improving the quality and contents of this article

## REFERENCES

1. Wang S, Gallagher MAS, Dunn N. Leptospirosis (Weil Disease). In: *StatPearls [Internet]*. StatPearls Publishing; 2022.
2. Gasem MH, Hadi U, Alisjahbana B, et al. Leptospirosis in Indonesia: diagnostic challenges associated with atypical clinical manifestations and limited laboratory capacity. *BMC Infect Dis*. 2020;20(1):1-11.
3. Van Seventer JM, Hochberg NS. Principles of infectious diseases: transmission, diagnosis, prevention, and control. *Int Encycl Public Heal*. Published online 2017:22.
4. Goarant C. Leptospirosis: risk factors and management challenges in developing countries. *Res Rep Trop Med*. 2016;7:49.
5. Sakundarno M, Bertolatti D, Maycock B, Spickett J, Dhaliwal S. Risk factors for leptospirosis infection in humans and implications for public health intervention in Indonesia and the Asia-Pacific region. *Asia Pacific J Public Heal*. 2014;26(1):15-32.
6. Sulistyawati S, Nirmalawati T, Mardenta RN. Spatial analysis of leptospirosis disease in Bantul Regency Yogyakarta. *KEMAS J Kesehat Masy*. 2016;12(1).
7. Sumanta H, Wibawa T, Hadisusanto S, Nuryati A, Kusnanto H. Spatial analysis of leptospira in rats, water and soil in

- bantul district yogyakarta Indonesia. Published online 2015.
8. Hotez PJ, Bottazzi ME, Strych U, et al. Neglected tropical diseases among the Association of Southeast Asian Nations (ASEAN): overview and update. *PLoS Negl Trop Dis*. 2015;9(4):e0003575. <https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0003575>
  9. Van Thiel PH. HISTORY OF THE CONTROL OF ENDEMIIC DISEASES IN THE NETHERLANDS OVERSEAS TERRITORIES. Published online 1971.
  10. Lim VKE. Leptospirosis: a re-emerging infection. *Malays J Pathol*. 2011;33(1):1.
  11. Kementrian Kesehatan Republik Indonesia. Direktorat Jendral Pencegahan dan Pengendalian Penyakit. *Petunjuk Teknis Pengendalian Leptospirosis*; 2017. [https://infeksiemerging.kemkes.go.id/download/Buku\\_Petunjuk\\_Teknis\\_Pengendalian\\_Leptospirosis.pdf](https://infeksiemerging.kemkes.go.id/download/Buku_Petunjuk_Teknis_Pengendalian_Leptospirosis.pdf)
  12. PRISMA. PRISMA Flow Diagram. Published 2020. <https://prisma-statement.org/prismastatement/flowdiagram.aspx>
  13. Erviana A. Studi Epidemiologi Kejadian Leptospirosis Pada Saat Banjir di Kecamatan Cengkareng Periode Januari-Februari 2014. Published online 2014.
  14. Pratiwi RI, Surasri S. FAKTOR RESIKO DAN KEJADIAN LEPTOSPIROSIS DI KABUPATEN PONOROGO (Studi Kasus Di Wilayah Kecamatan Ngrayun Dan Kecamatan Badegan Tahun 2014). *GEMA Lingkungan Kesehat*. 2014;12(2).
  15. Wijayanti YN, Kurniawan TP, SKM MK, Wijayanti AC. Faktor risiko kejadian leptospirosis di wilayah kabupaten boyolali. Published online 2014.
  16. Pertiwi SMB, Setiani O, Nurjazuli N. Faktor Lingkungan Yang Berkaitan Dengan Kejadian Leptospirosis di Kabupaten Pati Jawa Tengah. *J Kesehat Lingkung Indones*. 2014;13(2):51-57.
  17. Katulistiwa NA, Lestari KS. Analyze of House Conditions and The Rat Existence Affected to The Leptospirosis Cases in Klaten District. *J Kesehat Lingkung*. 2015;8(1):1-13.
  18. Nuraini S, Saraswati LD, Adi MS, Susanto HS. Gambaran Epidemiologi Kasus Leptospirosis Di Kabupaten Boyolali, Provinsi Jawa Tengah. *J Kesehat Masy Univ Diponegoro*. 2017;5(1):226-234.
  19. Sanyasi RDLR. Laporan Kasus Kejadian Luar Biasa Leptospirosis di Magetan, Jawa Timur. *Berk Ilm Kedokt Duta Wacana*. 2018;3(1):1.
  20. Thornley CN, Baker MG, Weinstein P, Maas EW. Changing epidemiology of human leptospirosis in New Zealand. *Epidemiol Infect*. 2002;128(1):29-36.