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Meta-analysis

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Meta-Analysis: Effects of Lession and Exposed to Risk Factor on Leptospirosis Infection

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ABSTRACT

Background: Leptospirosis is a zoonotic disease that occurs due to interactions between agents, hosts and the environment. Leptospira bacteria can infect humans through wounds on the skin and mucosa of the body. This study aims to examine the effect of injury history and contact risk factors on the incidence of leptospirosis by using meta-analysis.
Subjects and Method: This was a systematic review and meta-analysis study carried out using PICO model. P: Adults. Intervention: injury and contact. Comparison= no injuries and no contact with risk factors. Outcome: Leptospirosis. The meta-analysis was conducted by systematically reviewing articles from Google Scholar, PubMed, Springer Link, and Science Direct. Search keywords "Wound OR Lession AND Leptospira", "Risk Factor Exposure AND Leptospira", "Risk Factor AND Leptospira AND adjusted odds ratio". The inclusion criteria used were full paper articles from 2002-2022 using Indonesian and English. The study design used was observational and the analysis used multivariate adjusted odds ratio results. Articles were collected using the PRISMA diagram and analyzed using the Review Manager 5.3 application.
Results: Meta-analysis included 22 cross-sectional and case-control studies from Indonesia, India, Iran, Sri Lanka, Malaysia, Thailand, Laos, France, Germany, Kenya, Tanzania, Australia, Fiji, British Virgin Islands, Mexico, Jamaica, Peru, and Argentina. Leptospirosis increased with history of injury (aOR= 3.51; 95% CI= 2.94 to 4.19; p<0.001) and contact with risk factors (aOR=1.82; 95% CI=1.25 to 2.65; p=0.002).
Conclusion: History of injury and contact with risk factors increases the risk of developing Leptospirosis.

Keywords: history of injury, contact risk factors, leptospirosis, meta-analysis

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BACKGROUND

Leptospirosis is a zoonotic disease caused by a spiral-shaped bacterial infection of the pathogenic genus Leptospira, which is transmitted directly and indirectly from animals to humans. The definition of a zoonotic disease is a disease that can naturally be transmitted from vertebrate animals to humans

or vice versa (Kemenkes RI, 2017). Leptospirosis is a neglected infectious disease or Neglected Infectious Diseases (NIDs), namely an infectious disease that is endemic to the poor or the population of farmers and workers associated with water and soil in developing countries (Al-Orry et al., 2016).

Based on WHO reports in recent years, the global incidence of leptospirosis is estimated from 0.1-1 per 100,000 per year in temperate climates and 10-100 per 100,000 per year in the humid tropics. The incidence of this disease can reach more than 100 per 100,000 per year in outbreaks and high exposure in risk groups (WHO, 2009). The number of severe cases is reported to be around 300,000 to 500,000 annually worldwide, with a fatality rate of up to 10% (PAHO, 2023). In 2021, 734 cases of leptospirosis were found in Indonesia. Leptospirosis cases decreased compared to 2020, namely from 1,170 and 921 cases in 2019. Leptospirosis cases in Indonesia were reported by eight provinces, namely DKI Jakarta, West Java, Central Java, DI Yogyakarta, East Java, Banten, North Kalimantan and East Kalimantan (RI Ministry of Health, 2020).

Humans are infected through broken skin or mucous membranes with water or soil containing the urine of animals infected by this bacterium (Gamage et al, 2012). Leptospira bacteria enter the human body through wounds on the skin, mucous membranes (nose, mouth, and eyes), or even through drinking water. After entering the human body, these bacteria are in the blood and attack the tissues and organs of the body (WHO, 2003). Risk factors that play a role in the occurrence of Leptospirosis include people with jobs or activities that involve body contact with a watery environment, wounds on the body and lack of care or protection for injuries, the presence of rats or livestock around the house (Rampengan, 2016).

The results of multivariate statistical analysis showed that having a history of injury had a 12.16 times greater risk of developing severe leptospirosis than no history of injury (OR=12.16; 95% CI=2.99-49.37; p <0.001) (Suratman, 2006). The results of the study, of the 13 variables carried out by Supraptono et al. (2011) stated that contact with meat or body parts of dead animals will experience leptospirosis 77.8 times (95% CI = 5.76-1,050.07), compared to those who do not come into contact with these materials. Contact with standing water will experience Leptospirosis disease increasing 44.3 times (95% CI= 7.36 to 265.99) compared to those who are not in contact with standing water.

Various primary studies have been conducted to see the effect of history of injury and contact risk factors on the incidence of Leptospirosis. Further analysis is needed to reach a convincing conclusion. This study aims to examine the effect of injury history and contact risk factors on the incidence of leptospirosis by using a meta-analysis.

SUBJECTS AND METHOD

1. Study Design

This research was conducted using the method of systematic review and meta-analysis using primary data, namely data from previous research results. Research data was searched from several database using the search keywords "Wound OR Lession AND Leptospira", "Risk Factor Exposure AND Leptospira", "Risk Factor AND Leptospira AND adjusted odds ratio". There were 22 primary studies that met the inclusion criteria of this study.

2. Steps of Meta-Analysis

1) Formulate research questions in PICO.
2) Search primary study research articles from online databases.
3) Conduct screening and quality assessment of primary research articles.

4) Extracting and analyzing data into the RevMan 5.3 application.
5) Interpret the results and draw conclusions.

3. Inclusion Criteria

Full article article with observational study design (cross-sectional, case-control), multivariate analysis with adjusted odds ratio (aOR), intervention given was wound and contact risk factors, and outcome was the incidence of leptospirosis

4. Exclusion Criteria

The exclusion criteria for articles in this study were statistical results reported in the form of bivariate analysis and articles using languages other than English and Indonesian.

5. Variable Operational Definition

Occurrence of Leptospirosis: Patients diagnosed by doctor through clinical examination have clinical symptoms of leptospirosis and confirmed through tests.

History of Wounds: There are scratches, tears, or abrasions on the skin or parts of the patient's body that can allow Leptospira bacteria to enter the body.

Contact risk factors: There are events related directly or indirectly to the body tissues of dead rats, floods, standing water, meat, animal urine blood, and are suspected of being infected with Leptospira bacteria and are at risk as the route of transmission of leptospirosis from animals to humans that occurs within 14 days before illness.

6. Study Instrument

The stages of the research followed the PRISMA flow chart and the quality assessment of article research used the Critical Appraisal Skills Program (CASP) for Case-Control Study, the Critical Appraisal Checklist for Cross-sectional Study (CEBMa, 2014).

7. Data Analysis

The data analysis process in this study was carried out using the Review Manager application (RevMan 5.3), to determine the effect size and heterogeneity of the study. The results of meta-analysis data are presented in the form of forest plots and funnel plots.

RESULTS

The process of searching for articles by searching through the database according to the PRISMA flow diagram can be seen in Figure 1. The research related to the influence of history of injuries and contact risk factors on the incidence of Leptospirosis consisted of 22 articles originating from 5 continents namely Asia, Europe, Africa, Australia and Occeania, as well as America.

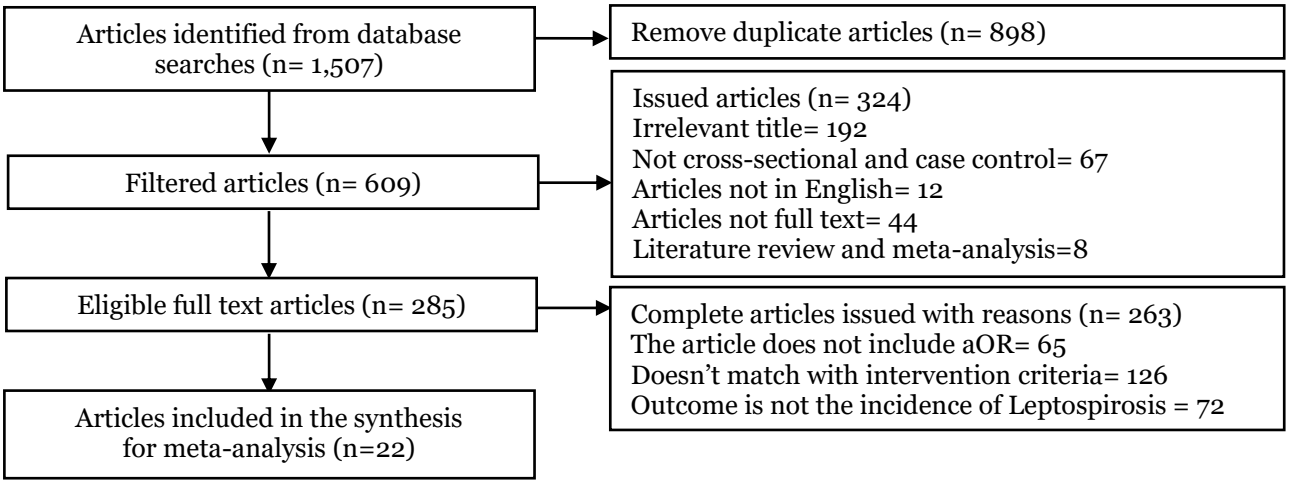

Figure 1. PRISMA Flow Diagram

There were 11 studies originating from the continent of Asia (3 research articles from Indonesia, 2 research articles from India, 1 article from Iran, 1 article from Sri Lanka, 2 research articles from Malaysia, 1 article from Thailand, 1 article from Laos), 2 studies from the European continent (1 article from France and 1 article from Germany), 2 studies from the African continent (2 studies in 1 article from Kenya and 1 article from Tanzania), 2 studies from the continents of Australia and Oceania (1 article from Australia and 1 article from Fiji), 5 studies from the Americas (1 article from Jamaica, 1 article from British Virgin Island and 1 article from Mexico, 1 article from Peru and 1 article from Argentina). The distribution of primary research by continent can be seen in Figure 2.

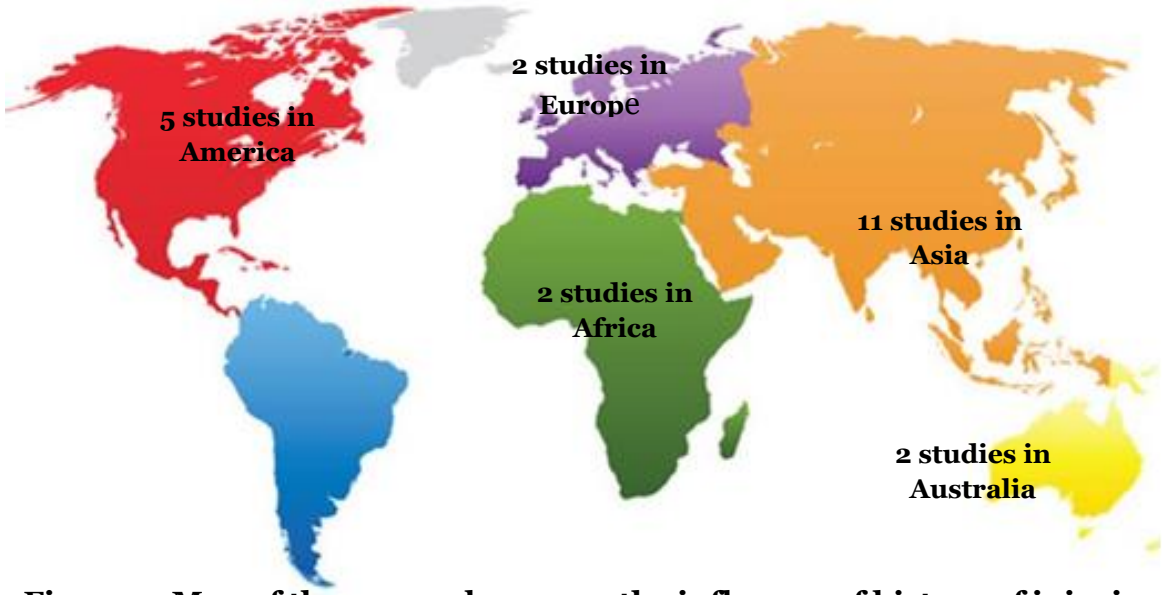

Figure 2. Map of the research area on the influence of history of injuries and contact risk factors on the incidence of leptospirosis

Research quality studies conducted quantitatively. This research was conducted using the Critical Appraisal Checklist for Cross-sectional Study and the Critical Appraisal Checklist for Case-Control Study which originated at the Center for Evidence Based Management which originated at the Center for Evidence Based Management (CEBMa, 2014). The following is a table of the results of the study quality assessment with the variable history of injuries and contact risk factors from a cross-sectional study design presented in Table 1. The following is a table of the results of the study quality assessment with the variable history of injuries and contact risk factors from the case-control study design in Table 2.

Table 1. Assessment of the quality of history of injuries and contact risk factors with a cross-sectional study design

Author (Year)	Criteria												Total
	1	2	3	4	5	6	7	8	9	10	11	12	
Samaraweera et al. (2021)	1	1	1	1	1	0	1	1	1	1	1	1	11
Ridzuan et al. (2016)	1	1	1	1	1	0	1	1	1	1	0	1	10
Castelanos et al. (2003)	1	1	0	0	1	0	1	1	1	1	1	1	9

Author (Year)	Criteria												Total
Phraisuwan et al. (2002)	1	1	1	1	1	0	1	1	1	1	0	1	10
Cook et al. (2017)	1	1	1	1	1	0	1	1	1	1	0	1	10
Schmitz et al.(2022)	1	1	1	0	1	1	1	1	1	1	1	1	11
Lau et al.(2016)	1	1	0	1	1	1	1	1	1	1	1	1	11
Artus et al.(2022)	1	1	1	0	1	0	1	1	1	1	1	1	10
Villaverde et al.(2014)	1	1	1	1	1	0	1	1	1	1	1	1	11
Shafei et al.(2022)	1	1	1	1	1	0	1	1	1	1	0	1	10
Maze et al.(2018)	1	1	1	1	1	1	1	1	1	1	1	1	12
Kawaguchi et al.(2008)	1	1	1	1	1	0	1	1	1	1	1	1	11

Description of the question criteria:

1 = Does the objective clearly address the focus or research problem?
2 = Is the research method (research design) suitable for answering the research questions?
3 = Is the method of selecting research subjects clearly written?
4 = Does the method of sampling cause bias (selection)?
5 = Does the research sample taken represent the designated population?
6 = Is the sample size based on pre-study considerations?
7 = Was a satisfactory response achieved?
8 = Is the research instrument valid and reliable?
9 = Was statistical significance assessed?
10 = Are confidence intervals given for the main results?
11 = Are there any confounding factors that have not been taken into account?
12 = Are the results applicable to your research?

Description of the answer score:

0 = No
1 = Can't tell
2 = Yess

Table 2. Assessment of the quality of history of injuries and contact risk factors with a case-control study design

Primary Study	Criteria												Total
	1	2	3	4	5	6	7	8	9	10	11	12	
Nardone et al. (2004)	1	1	1	1	1	1	1	1	1	1	1	1	12
Kamath et al.(2014)	1	1	1	1	1	1	1	1	1	1	1	1	12
Desai et al.(2016)	1	1	1	1	1	0	1	1	1	1	1	1	11
Maniiah et al.(2016)	1	1	1	1	1	1	1	1	1	1	1	1	12
Andari et al.(2016)	1	1	1	1	1	1	1	1	1	1	1	1	12
Sahneh et al.(2019)	1	1	1	1	1	0	1	1	1	1	1	1	11
Sofiyani et al.(2018)	1	1	1	1	1	1	1	1	1	1	1	1	12
Vanasco et al.(2008)	1	1	1	1	1	0	1	1	1	1	1	1	11
Keenan et al.(2010)	1	1	1	1	1	0	1	1	1	1	1	1	11
Katelaris et al.(2018)	1	1	1	1	1	1	1	1	1	1	1	1	12

Description of the question criteria:

1 = Does the objective clearly address the focus or research problem?
2 = Is the research method suitable for answering the research questions?
3 = Were there enough subjects in the study to establish that the findings did not occur by

chance?
4 = Was the selection of cases and controls based on external, objective and validated criteria?
5 = Were the two groups comparable at the start of the study?
6 = Were objective and unbiased outcome criteria used?
7 = Is there data collection?
8 = Are objective and validated measurement methods used to measure outcomes?
9 = Are effect measures practically relevant?
10 = How precise is the effect estimate? Are confidence intervals given?
11 = Are there any confounding factors that have not been taken into account?
12 = Are the results applicable to your research?

Description of the answer score:
0 = No
1 = Can't tell
2 = Yess

Table 3. Table PICO summary of the article on the influence of injuries and contact risk factors on the incidence of leptospirosis

Author (Year)	Country	Study Design	Sample	P	I	C	O
Nardone et al. (2004)	French	Case control	313	Patients diagnosed with leptospirosis in a hospital in France	There are lesions/abrasions on the skin	No lesions/ abrasions on the skin	Leptospirosis
Kamath et al. (2014)	India	Case control	210	Leptospirosis sufferers in Udupi district	There is an injury/history of injury during work	No injuries/ history of injuries during work	Leptospirosis
Desai et al. (2016)	India	Case control	400	Leptospirosis sufferers in South Gujarat	History of skin diseases/injuries during the endemic season	No history of skin disease/ injury during the endemic season	Leptospirosis
Maniiah et al. (2016)	Indonesia	Case control	64	Leptospirosis sufferers in Semarang City	There is a history of injuries	No history of injuries	Leptospirosis
Andari et al. (2016)	Indonesia	Case control	144	Leptospirosis sufferers in Boyolali District	There is a history of injuries	No history of injuries	Leptospirosis
Sahneh et al. (2019)	Iran	Case control	87	Patients diagnosed with leptospirosis in Golestan province, northern Iran	Skin scratches/ injuries	No scratches/ skin injuries	Leptospirosis
Sofiyani et al. (2018)	Indonesia	Case control	150	Leptospirosis sufferers in Klaten Regency	There is a history of injuries	No injuries	Leptospirosis
Kamath et al. (2014)	India	Case control	210	Leptospirosis sufferers in Udupi district	There is contact with soil that has been contami-nated with rat urine	No contact with soil that has been contaminated with rat urine	Leptospirosis
Vanasco et al. (2008)	Argentina	Case control	182	Leptospirosis sufferers in Argentina	There is contact/ exposure to water contaminated with rat urine	No contact/ exposure to water contami-nated with rat urine	Leptospirosis
Keenan et al. (2010)	Jamaica	Case control	132	Patients diagnosed with leptospirosis at the Jamaica Regional Health Center	There is contact with rats	No contact with mice	Leptospirosis

Author (Year)	Country	Study Design	Sample	P	I	C	O
Katelaris et al. (2018)	Australia	Case control	199	Population in agri-cultural workers and health workers	There is skin contact with rats and mud	No skin contact with rats, mud	Leptospirosis
Ridzuan et al. (2016)	Malaysian	Cross Sectional	350	Oil palm plantation farmers and workers	Working with hand injuries	No injuries	Leptospirosis
Castelanos et al. (2003)	Mexico	Cross Sectional	1,169	Residents of leptospirosis sufferers in Chiapas City	There are sores on the skin of the feet	No toe injuries or abrasions during flooding	Leptospirosis
Phraisuwa et al.(2002)	Thailand	Cross Sectional	315	Population of pool cleaners	There is a history of injuries	No history of injuries	Leptospirosis
Cook et al. (2017)	Kenya	Cross Sectional	738	Slaughterhouse worker population	There are wounds and contact with pets contami-nated with rat urine	No injuries and no contact with pets contami-nated with rat urine	Leptospirosis
Maze et al. (2018)	Tanzania	Cross Sectional	1,396	Population of cattle breeders and farmers in Tanzania	There is contact/ exposure to rat urine	No contact/ exposure to rat urine	Leptospirosis
Schmitz et al. (2022)	Germany	Cross Sectional	450	German population aged 18-85 years	There was contact with a dead rat	No contact with dead mice	Leptospirosis
Lau et al. (2016)	Fiji	Cross Sectional	2,152	Resident population in Fiji	There is contact with rats or mice	No contact with rats or mice	Leptospirosis
Artus et al. (2022)	British Virgin Islands	Cross Sectional	1,161	The household population in St. Croix, St. Thomas, and St. John	Contact with rodents and or their body fluids	No contact with rodents and or their body fluids	Leptospirosis
Villaverde et al. (2014)	Peru	Cross Sectional	254	Leptospirosis sufferers in Peruvian farmers	There is contact with rats	No contact with mice	Leptospirosis
Safei et al. (2022)	Malaysian	Cross Sectional	321	Municipal service workers	There are rats in the workplace and contact with body fluids	No rats in the workplace and in contact with body fluids	Leptospirosis
Kawaguchi et al. (2008)	Laos (Asia)	Cross Sectional	406	Population in a flood-prone village in Khammouane Province	Seeing and contact with mice in the house	No contact with mice in the house	Leptospirosis

Summary of the article on the influence of wound history and contact risk factors on the incidence of leptospirosis There were 22 observational research articles that used a cross-sectional and case-control study design and qualified as sources for a meta-analysis of the influence of wound history and contact risk factors on the incidence of Leptospirosis. The following is an overview of each of the primary studies used, which can be seen in Table 3.

Table 4 presents the Adjusted Odds Ratio (aOR) with 95% Confidence Interval on articles cross-sectional and case-control study design on the effect of injury on the incidence of leptospirosis.

Table 4. Data of adjusted odds ratio (aOR) and confidence interval on the influence of wounds on the incidence of leptospirosis

Author	aOR	CI 95%	
		Upper Limit	Lower Limit
Samaraweera et al. (2021)	2.29	1.58	3.34
Ridzuan et al. (2016)	3.13	1.83	5.36
Phraisuwan et al. (2002)	3.97	1.56	10.1
Castelanos et al.(2003)	4.23	3.12	5.75
Cook et al. (2017)	3.10	1.50	6.10

Author	aOR	CI 95%	
		Upper Limit	Lower Limit
Sahneh et al. (2019)	11.21	3.02	43,06
Kamath et al. (2014)	6.60	2.75	15.86
Desai et al. (2016)	4.2	2.00	8.50
Sofiyani et al. (2018)	1.64	0.40	2.87
Andari et al. (2016)	1.43	0.59	2.26
Maniiah et al. (2016)	8.19	2.31	29.07
Nardone et al. (2004)	7.00	2.70	17.60

Figure 3 shows the results of the sub-group meta-analysis on the influence of history of injury on the risk of leptospirosis. In a cross-sectional study, adults with a history of injury had a risk of developing leptospirosis 3.29 times compared to those without a history of injury (aOR=3.29; 95% CI= 2.69 to 4.03; p<0.001).

The forest plot also shows low heterogeneity of the effect (I^2=38%) so the calculation of the effect estimate using the fixed effect model approach or the distribution of data is said to be homogenous. Forest plot of a case-control study showed that adults with a history of injury had 4.37 times the risk of developing leptospirosis compared with no history of injury (aOR=4.37; 95% CI= 3.01 to 6.35; p<0.001). The forest plot also shows a high heterogeneity of effects (I^2= 53%; p = 0.050) so that the calculation of effect estimates using random effect model approach or data distribution is heterogeneous.

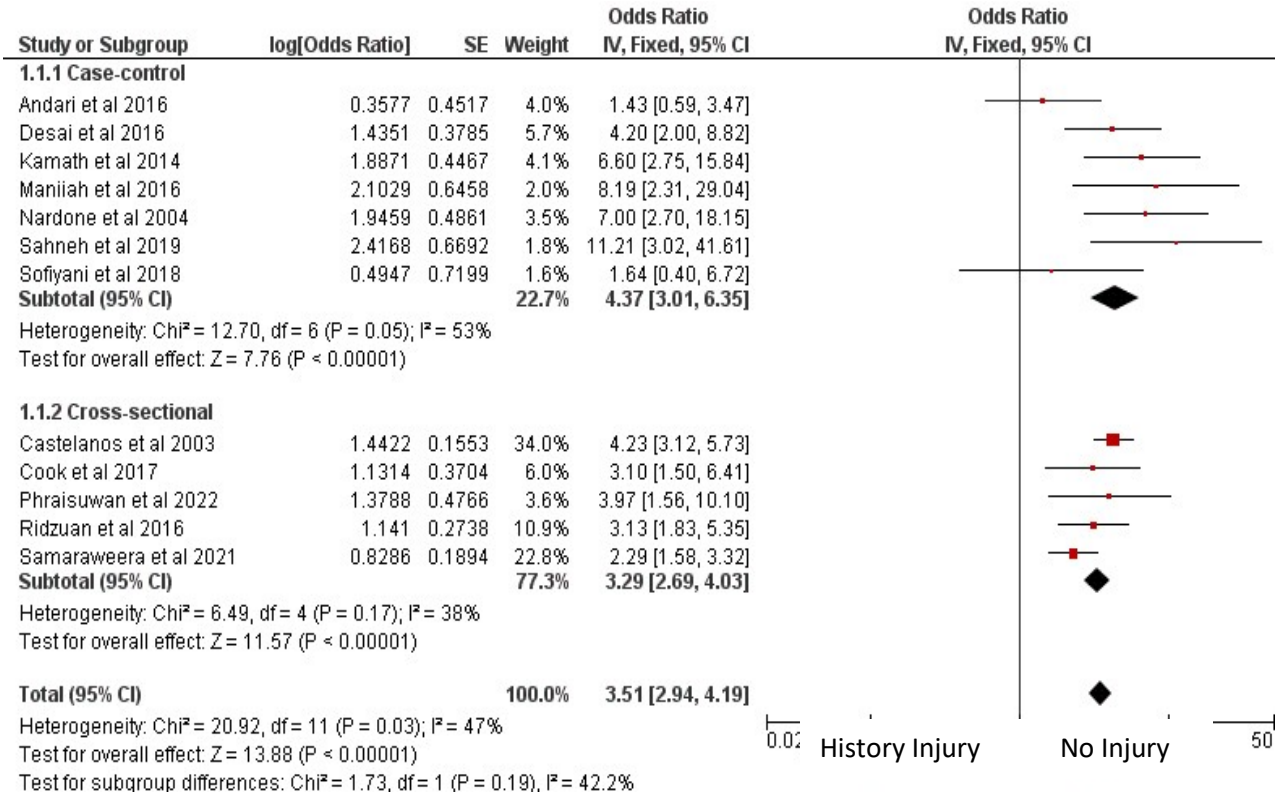

Figure 3. Forest plot of the influence of a history of injury to the incidence of leptospirosis

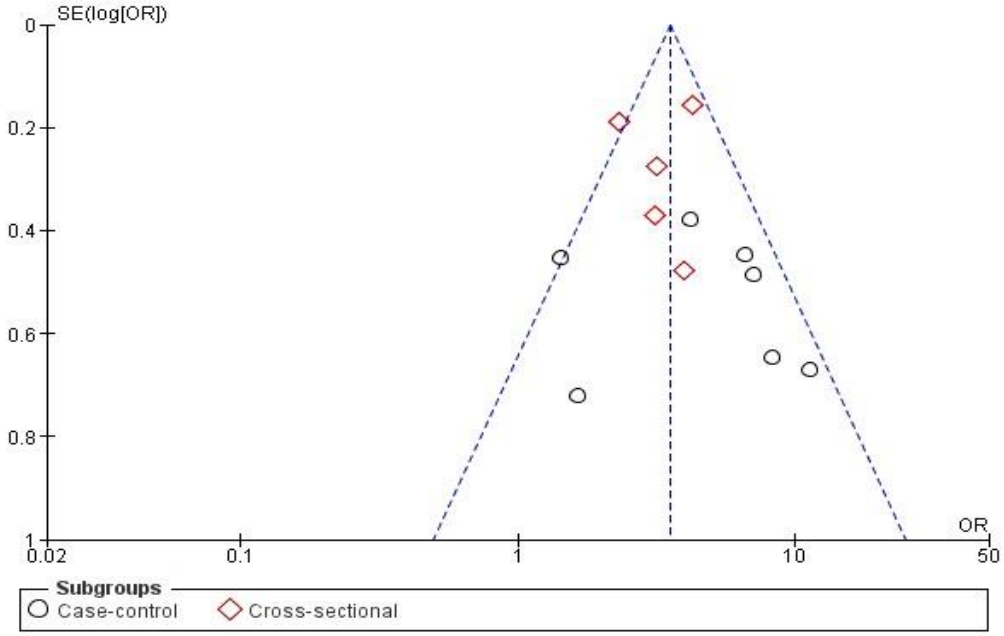

Figure 4. Funnel plot of influence of wound history on the incidence of leptospirosis

In figure 4 presents some of the primary studies used which show that the distribution of effect estimates is more or less symmetrical to the right and left of the mean vertical line, so it does not indicate publication bias in the subgroup analysis of the effect of injury on the incidence of leptospirosis. There are 12 observational research articles using cross-sectional and case-control study designs and qualify as sources for meta-analysis of the effect of contact risk factors on the incidence of leptospirosis.

Table 5 presents data on Adjusted Odds Ratio (aOR) with 95% Confidence Interval (CI95%) in articles cross-sectional and case-control study design on the effect of contact risk factors on the incidence of leptospirosis.

Table 5. Data of adjusted odds ratio (aOR) and confidence interval on the effect of contact risk factors on the incidence of leptospirosis

Author	aOR	CI 95%	
		Upper Limit	Lower Limit
Schmitz et al. (2022)	0.23	0.05	1.04
Lau et al. (2016)	1.58	1.20	2.09
Artus et al. (2022)	2.60	1.10	5.90
Villaverde et al. (2014)	7.90	1.60	37.90
Cook et al. (2017)	3.10	1.50	6.10
Safei et al. (2022)	2.17	1.11	4.25
Kawaguchi et al. (2008)	2.63	0.73	9.44
Maze et al. (2018)	1.20	0.98	1.40
Kamath et al. (2014)	4.45	1.62	12.20
Vanasco et al. (2008)	2.17	1.01	4.68
Keenan et al. (2010)	3.52	1.33	9.36
Katelaris et al. (2018)	7.09	1.29	38.93

Figure 5 presents the results of the sub-group meta-analysis of the effect of contact risk factors on the incidence of Leptospirosis. The results of a meta-analysis of cross-sectional studies showed that adults with contact with risk factors had a risk of developing leptospirosis 1.40 times compared to those without risk factor contact (aOR= 1.40; 95% CI = 0.93 to 2.12; p=0.100). The forest plot also shows high heterogeneity of effects (I^2= 78%) so the calculation of effect estimates using the random effect model approach or the distribution of data is declared heterogeneous.

The bottom section presents the forest plot of the case-control study. Adults with risk factor contact had a risk of developing leptospirosis 3.23 times compared to those without risk factor contact (aOR= 3.23; 95% CI=1.97 to 5.29; p<0.001). The forest plot also shows low heterogeneity of the effect (I^2= 0%) so the calculation of the estimated effect using the fixed effect model approach or the spread of data is stated to be homogeneous.

Based on Figure 6 it can be seen that the Funnel plot shows an asymmetric distribution of estimated effects. The distribution of effect estimates is more to the right than to the left of the average vertical line, thus indicating publication bias, because the distribution of effect estimates is more to the right on the same funnel plot line as the location of the diamond shape in the forest plot which is also on the right, the publication bias tends to overestimate the true effect (overestimate).

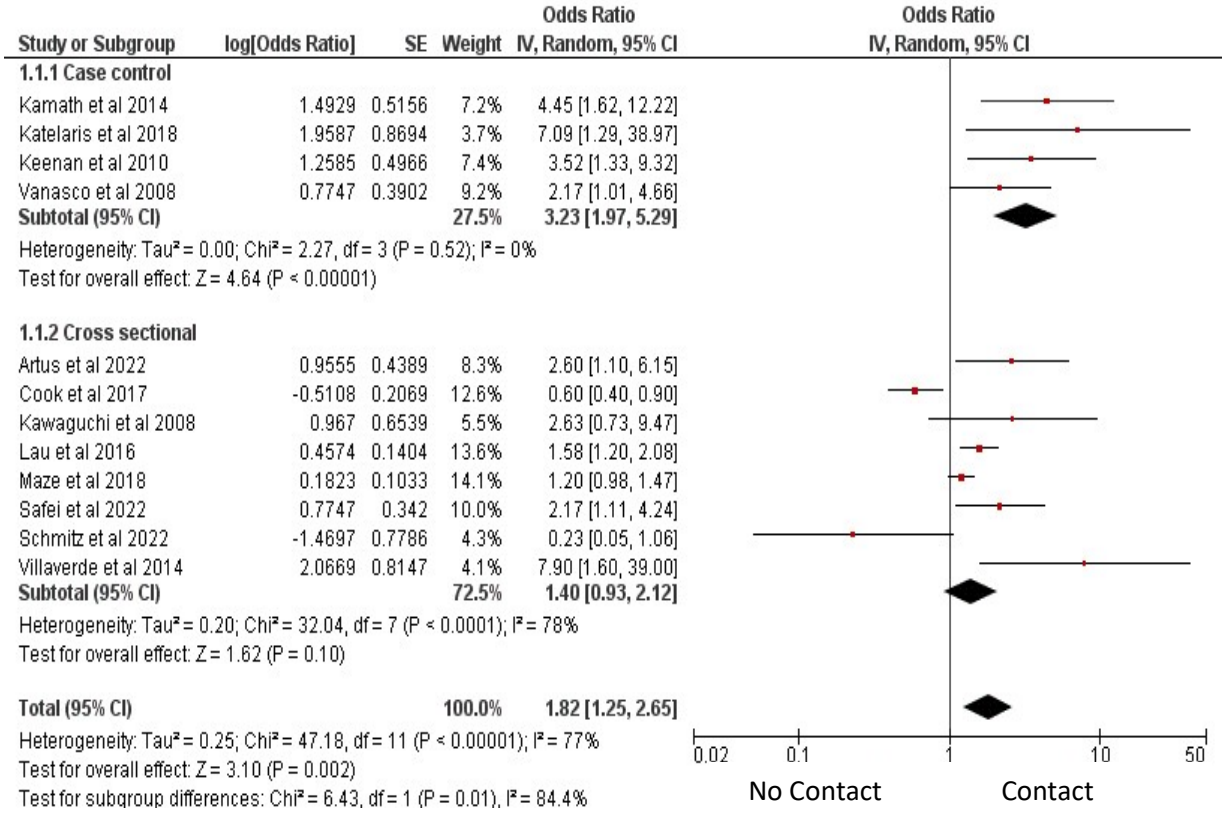

Figure 5. Forest plot of the effect of contact risk factors on the incidence of leptospirosis

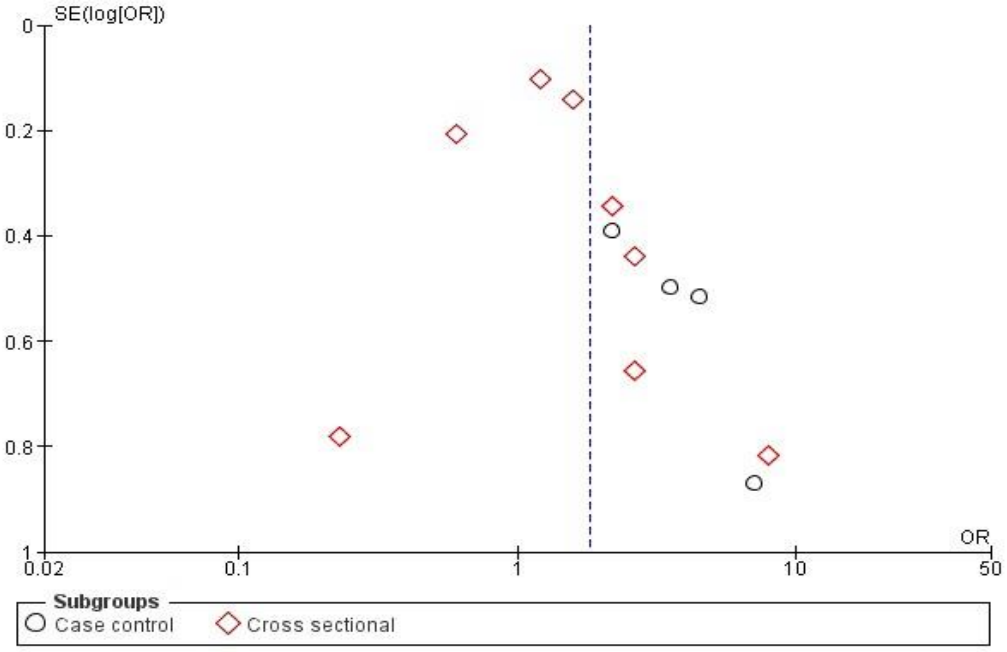

Figure 6. Funnel plot of the effect of contact risk factors on the incidence of leptospirosis

DISCUSSION

This systematic study and meta-analysis research used research that controlled for confounding factors which could be seen from the study inclusion requirements, namely using multivariate analysis and the statistical results reported were the adjusted odds ratio (aOR). A confounding factor is the mixing of estimates of the relationship between exposure and the disease under study, by other factors that are related, both to disease and exposure. Confounding factors affect the relationship or effect of exposure to the occurrence of disease which is estimated (estimated) by the study is not the same as the relationship or effect that actually occurs in the target population (target popularion), or the study results are invalid (incorrect) (Murti, 2018).

Estimates of the combined relationship of the influence of history of injuries and contact risk factors on the incidence of Leptospirosis were processed using the RevMan 5.3 application with the generic inverse variance method. This method is used to analyze data in the form of: rate, time-to-event, hazard ratio, ordinal scale, adjusted estimate, differences average (difference of mean), or average ratio (ratio of mean) (Anulus et al. 2019). The results of the systematic review and meta-analysis of this study are presented in forest plots and funnel plots.

1. The efect of history of injury on the incidence of Leptospirosis

Analysis was carried out with subgroups of each observational study design to determine the estimated influence of the history of injury on the incidence of Leptospirosis. The results of a meta-analysis of cross-sectional studies showed that adults with a history of injury had 3.29 times the risk of developing leptospirosis compared with no history of injury (aOR = 3.29, 95% CI= 2.69 to 4.03; p<0.001). The results of a meta-analysis of case-control studies showed that adults with a history of injury had 4.37 times the risk of developing leptospirosis compared to no history of injury (aOR= 4.37; 95% CI= 3.01 to 6.35; p<0.001).

The entrance of Leptospira bacteria is usually through a wound in the skin or conjunctiva. If a human or animal that has a wound on its body then comes in contact with the urine of a rat or other animal suffering from Leptospirosis, the Leptospira bacteria will infect the human or animal through the wound (Levvet, 2001). Skin that is eroded due to wounds or skin diseases makes it easier for Leptospira to enter the mucous membranes of the human body. The research results are in line with the research conducted by Setyaningsih et al. (2022) in Boyolali District showed that a history of injury had a significant relationship with the incidence of Leptospirosis. This is evidenced by the results of statistical test studies showing an Odds Ratio value of 1.13 which means that people with a history of injuries have a 1.13 times greater chance of being exposed to Leptospirosis than people without a history of injuries.

The results of research by Sofiyani et al. (2018) stated that the risk of Leptospirosis increases with a history of injury (b= 1.64; 95% CI= 0.40 to 2.87; p= 0.009). Another study conducted by Cook (2017) in Kenya states that a history of injury increases the risk factor for Leptospirosis 3.1 times compared to no history of injury. The results of other studies state that there is a relationship between a history of injuries and the incidence of Leptospirosis. History of injury increases the risk of Leptospirosis (OR= 14.63; 95% CI= 2.82 to 75.95; p <0.001). The wound was caused by his work (repairing PDAM pipes), there were also respondents who had been injured by rat bites (Unggul et al., 2016).

2. The effect of contact risk factors on the incidence of Leptospirosis

The results of a meta-analysis of cross-sectional studies showed that adults with exposure to risk factors had a 1.40 times increased risk of developing leptospirosis compared to those without contact with risk factors (aOR=1.40; 95% CI= 0.93 to 2.12; p=0.100). The results of a meta-analysis of case-control studies showed that adults with contact with risk factors had a risk of developing Leptospirosis 3.23 times compared to those without contact with risk factors (aOR=3.23; 95% CI=1.97 to 5.29; p<0.001).

The results of research conducted by Sarkar et al. (2002) stated that contact with sewer water has a 3 times higher risk of getting Leptospirosis (OR=3.63; 95% CI= 1.69 to 7.25), contact with flood water has 3 times the risk of getting Leptospirosis (OR=3.03; 95% CI=1.44 to 6.39), and contact with mud had 3 times the risk of developing leptospirosis (OR=3.08; 95%CI= 1.32 to 5.87). The results of research by Dewi et al. (2020) stated that the risk of Leptospirosis directly increases with contact with rats and flooded areas. The risk of direct leptospirosis increased in the presence of rats (b= 7.34; 95% CI= 4.44 to 10.24; p <0.001) and flooded areas (b= 8.99; 95% CI= 5.02 to 12.96; p<0.001).

Humans are infected with Leptospira through contact with water, soil (mud), and plants that have been contaminated by the urine of animals with Leptospirosis. Transmission of Leptospira to humans occurs due to contact with urine, blood, or organs from infected animals, as well as contact with the environment (soil, water) contaminated with Leptospira (Rampengan, 2016).

A study by Ariani and Wahyono (2020) at the Sentinel Leptospirosis Surveillance Location in Banten Province stated that respondents who had contact with stagnant water had 2 times the risk of getting Leptospirosis compared to respondents who had no contact with stagnant water (OR= 2.87; 95% CI: 1.41 to 5.82; p < 0.001). In the results of this study, there are several confounding factors from several primary studies that are able to reduce the

magnitude of the effect of each of these studies, such as the use of PPE when there is a wound. The use of gloves in the study by Ridzuan et al. (2016), Katelaris et al. (2019) and Sahneh et al, (2019), the use of footwear in a study by Castelanos et al. (2003), Kawaguchi et al. (2008) and Sofiyani et al. (2018), The patient underwent chemo prophylactic treatment for Leptospirosis at the onset of the disease (Samaraweera et al., 2022).

The use of PPE and treatment reduces the risk of Leptospirosis due to injuries to body parts. It can be concluded that the confounding factors that need to be controlled for in the study of the influence of a history of injury to the incidence of Leptospirosis are the use of PPE and treatment, this is necessary to determine the effect that actually occurs in the target population.

AUTHOR CONTRIBUTION

Satriyo Fajar Wicaksono as the researcher who selected topics searched for and collected study data. Setyo Sri Rahardjo and Bhisma Murti analyzed the data and reviewed research documents.

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CONFLICT OF INTEREST

There is no conflict of interest.

REFERENCES

Al-qorry W, Arahou M, Hassikou R, Quasmaoui A, Charof R, Mennane Z (2016). Leptospirosis: transmission, diagnosis and prevention. Int J Innov Appl Stud. 15(3): 457–467.

Andari S, Mudigdo A, Andriani RB. (2016). Path analysis of environmental and behavioral risk factors that influence the incidence of Leptospirosis in Boyolali District. Tesis. Universitas Sebelas Maret, Surakarta.

Anulus A, Murti B, Prasetya H (2019). Risk factors of HIV among male military personnels: A Meta Analysis. J Health Promot Behav, 4(3): 178–188. doi: 10.26911/thejhpb.2019.04.03.03.

Ariania N, Wahyono TYM (2020). Factors affecting the occurrence of Leptospirosis in 2 districts location of the sentinel Leptospirosis surveillance in Banten Province in 2017–2019. J Epid Kes Indonesia. 4(2):57-63. doi: 10.7454/epidkes.v4i2.47063.

Artus A, Schafer IJ, Cossaboom CM, Haberling DL, Galloway R, Sutherland G, Browne S, et al. (2022). Seroprevalence, distribution, and risk factors for human Leptospirosis in the United States Virgin Islands. PLoS Negl Trop Dis 16(11):1-21. doi: 10.1371/journal.pntd.0010880

Castellanos CBL, Suárez RG, Figueroa EG, Allen JLF, de la Peñal JE (2003). Risk factors and the prevalence of leptospirosis infection in a rural community of Chiapas, Mexico. Epidemiol Infect. 131(3):1149-1156. doi: 10.1017/s0950268803001201.

CEBMa (2014). Critical appraisal. Center for Evidence-Based Management.

Cook EAJ, Glanville WAD, Thomas LF, Kariuki SK, Bronsvoort BMC, Fèvre EM (2017). Risk factors for Leptospirosis seropositivity in slaughterhouse workers in western Kenya. Occup Environ Med. 74(1):357–365. doi: 10.1136/oemed-2016-103895.

Dewi PS, Rahardjo SR, Murti B (2020). Analysis of environmental risk factors on the leptospirosis disease in Klaten, Central Java, Indonesia. J Epidemiol Public Health. 05(02): 158-167. doi: 10.26911/jepublichealth.2020.05.02.-04.

Desai KT, Patel F, Patel FB, Nayak S, Patel NB, Bansal RK (2016). A case-control study of epidemiological factors associated with leptospirosis in South Gujarat region. J Postgrad Med. 62 (4): 223-227. doi: 10.4103/0022-38-59.188551.

Gamage CD, Tamashiro H, Ohnishi M, Koizumi N (2012). Epidemiology, surveillance and laboratory diagnosis of Leptospirosis in the WHO South-East Asia Region. In: Lorenzo-Morales J. 213–226. doi: 10.5772/37694.

Kamath R, Swain S, Pattanshetty S, Nair NS (2014). Studying risk factors associated with human Leptospirosis. Global Infect Dis. 6(1): 3-9. doi: 10.41-03/0974-777X.127941.

Katelaris AL, Glasgow K, Lawrence K, Corben P, Zheng A, Sumithra S, Turahui J, et al. (2019). Investigation and response to an outbreak of Leptospirosis among raspberry workers in Australia, 2018. Zoonoses Pub Health. 67(1):35–43. doi: 10.1111/zph.1265.

Kawaguchi L, Sengkeopraseuth B, Tsuyuoka R, Koizumi N, Akashi H, Vongphrachanh P, Watanabe H, et al. (2008). Seroprevalence of Leptospirosis and risk factor analysis in flood-prone rural areasin Lao PDR. Am J Trop Med Hyg. 78(6): 957–961.

Keenan J, Ervin G, Aung M, McGwin G, and Jolly P (2010). Risk factors for clinical Leptospirosis from Western Jamaica. Am J Trop Med Hyg. 83(3): 633–636. doi: 10.4269/ajtmh.2010.09-0609.

Kemenkes RI (2017). Leptospirosis control technical guidelines. Direktorat Jenderal Pencegahan dan Pengendalian Penyakit Kementerian Kesehatan RI. Jakarta: Indonesia.

Kemenkes RI (2020). Profil Kesehatan Indonesia 2020. Pusat Data dan Informasi Kementerian Kesehatan RI.

Lau CL, Watson CH, Lowry JH, David MC, Craig SB, Wynwood SJ, Kama M, et al. (2016). Human Leptospirosis infection in Fiji: An Eco epidemiological approach to identifying risk factors and environmental drivers for transmission. PLoS Negl Trop Dis. 10(1): 1-25. doi: 101371/journalpntd.-0004405.

Levett PN (2001). Leptospirosis. Clin Microbiol Rev. 14(2): 296-326. doi: 10.1128/CMR.14.2.296-326.2001

Maniah G. Raharjo M, Astorina N (2016). Environmental factors associated with the incidence of Leptospirosis in Semarang City. J Kesehat Masy. 4(3): 792-799. doi: 10.14710/jkm.v4i3.13-539.

Maze MJ, Goldwasser SC, Rubach MP, Biggs HM, Galloway RL, Sharples KJ, Allan KJ, et al. (2017). Risk faktors for human acute Leptospirosis in Northern Tanzania. PLoS Negl Trop Dis. 12(6) :1-22. doi: 10.1371/journal.pntd-.0006372

Murti B (2018). Principles and methods of epidemiological research. 5th edn. Surakarta: Program Studi Ilmu Kesehatan Masyarakat, Program Pascasarjana, Universitas Sebelas Maret.

Nardone A, Capek I, Baranton G, Campèse C, Postic D, Vaillant V, Liénard M, Desenclos JC (2004). Risk factors for leptospirosis in metropolitan France:

results of a national case-control study, 1999-2000. Clin Infect Dis. 39(5): 751-3. doi: 10.1086/423272

Pan American Health Organization (2023). Leptospirosis. Regional Office for the Americas of the World Health Organization.

Phraisuwan P, Whitney EAS, Tharmaphornpilas P, Guharat S, Thongkamsamut S, Aresagig S, Liangphongphanthu J, et al. (2002). Leptospirosis: Skin wounds and control strategies, Thailand, 1999. Emerging Infect Dis. 8(12): 1455-1459.

Rampengan NH (2016). Leptospirosis. Fakultas Kedokteran Sam Ratulangi Manado. J Biomedik. 8(3): 143-150.

Ridzuan JM, Aziah BD, Zahiruddin WM (2016). The occupational hazard study for leptospirosis among agriculture workers. Int J Collab Res Intern Med Public Health. 8(3): 284-293.

Sahneh E, Delpisheh A, Sayehmiri K, Khodabakhshi B, Madan MM (2019). Investigation of risk factors associated with leptospirosis in the North of Iran (2011-2017). J Res Health Sci. 19(2).

Samaraweera NY, Karunarathna U, Mediwaka MK, Patabendige D, Jagathpathi J (2022). Cross sectional analysis of factors associated with Leptospirosis cases treated at the district general hospital, Matara Sri Lanka during 2015-2018. Int JAdv Med. 9(3):216-220. doi: 10.18203/23493933.ijam2-0220422.

Sarkar U, Nascimento SF, Barbosa R, Martins R, Nuevo H, Kalafanos I (2002). Population-based case-control investigation of risk factors for Leptospirosis during an urban epidemic. Am J Trop Med Hyg. 66(5): 605-610. doi: 10.4269/ ajtmh.2002.6-6.605.

Schmitz S, Princk C, Schlinkmann KM, Mylius M, Bier NS, Baillot A, Masyar M, et al. (2022). Risk factors for Leptospira seropositivity in rural Northern Germany, 2019. Epid Infect. 151(17): 1–8. doi: 10.1017/S0950268-822001972.

Setyaningsih Y, Bahtiar N, Kartini A, Pradigdo SF, Saraswati LD (2022). The presence of Leptospira sp. and Leptospirosis risk factor analysis in Boyolali district. J Public Health Res. 11(1): 2144. doi: 10.4081/jphr.2021.2144.

Shafei MZ, Sulong MR, Yaacob NA, Hassan H, Mohamad WMZ, Daud A, Ismail Z, et al. (2012). Seroprevalence of Leptospirosis among town service workers in Northeastern State of Malaysia. Int J Collab Res Intern Med Public Health. 4(4): 395-403. doi: 10.51200-/bjms.vi.3139.

Sofiyani M, Dharmawan R, Murti B (2018). Risk faktors of Leptospirosis in Klaten, Central Java. J Epidemiol Public Health. 3(1): 11-24. doi: 10.26-911/jepublichealth.2018.03.01.02.

Supraptono B, Sumiarto B, Pramono D (2011). Interaction of 13 risk factors for Leptospirosis. Berita Kedokteran Masyarakat. 27(2): 55-65.

Suratman (2006). Analysis of environmental and behavioral risk factors that influence the incidence of severe leptospirosis in Semarang City. Universitas Diponegoro.

Unggul PN, Budiyono, Nurjazuli (2016). Environmental factors and behavior of the incidence of leptospirosis in the city of Semarang. J Kesehat Masy. 4(1): 407-416.

Vanasco NB, Schmelinga,MF, Lottersberger J, Costac F, Koc,AI, Tarabla HD (2008). Clinical characteristics and risk factors of human Leptospirosis in

Argentina (1999–2005). Acta Tropica. 107: 255–258. doi: 10.1016/j.actatropica.2008.06.007

Villaverde JOA, Romani FR, Tejada RA, Chero PW, Zambrano MC (2014). Leptospirosis seroprevalence and associated features in rice farmers of tropical region of Peru. Rev Peru Med Exp Salud Publica. 31(2).

WHO (2003). Human Leptospirosis: guidance for diagnosis, surveillance and control, International Leptospirosis Society. Word Health Organization.

WHO (2009). Fact sheet Leptospirosis: World Health Organization Regional Office for South-East Asia. World Health Organization.