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Study of Risk Level Death Based on Clinical Symptoms in Cases of Canine *Leptosprirosis* in Jakarta, Depok and South Tangerang: Data from January - August 2020

Studi Tingkat Risiko Kematian berdasarkan Gejala Klinis pada Kasus Canine *Leptosprirosis* di Jakarta, Depok dan Tangsel: Data dari Januari - Agustus 2020

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Abstrak

Leptospirosis merupakan penyakit zoonosis yang disebabkan oleh bakteri Leptospira sp., yang menyebabkan infeksi pada hewan dan manusia. Anjing yang terinfeksi leptospirosis menunjukkan gejala seperti anoreksia, demam, muntah, lemas, diare dan sering mengalami kekuningan pada area mata dan mukosa sekitar mulut (ikterik) dengan komplikasi sistemik yang fatal dan disfungsi multi organ terutama ginjal dan hati. Leptospirosis merupakan penyakit endemik di Jakarta. Penelitian ini bertujuan untuk mengidentifikasi faktor risiko yang dapat berkontribusi terhadap kematian anjing berdasarkan gejala klinis awal yang ditemukan ketika anjing berada di fasilitas pelayanan kesehatan hewan seperti klinik hewan, rumah sakit hewan, atau dokter hewan yang berpraktek mandiri. Metode yang digunakan dalam penelitian ini adalah manifestasi klinis, pemeriksaan laboratorium, dan rekam medis anjing yang diduga leptospirosis. Pencantuman kriteria didasarkan pada aspek gejala klinis anjing yang berada di wilayah Jakarta, Depok, dan Tangerang Selatan. Analisis data menggunakan uji *chi-square* dengan interval kepercayaan (CI) 95%. Anjing-anjing tersebut dikategorikan berdasarkan usia: 13 atau 32,50%, adalah anak anjing (di bawah usia satu tahun), dan 27 atau 67,50% adalah anjing dewasa di atas satu tahun. Di antara anjing-anjing tersebut, 80% adalah jantan dan 20% adalah betina. Selain itu, 80% gigi taringnya tidak ditampung oleh pemiliknya. Kesimpulannya, Rata-rata angka kematian pada penelitian ini mencapai 46,43%. Tingginya angka kematian terkait leptospirosis pada anjing tahun 2020 dipengaruhi oleh faktor risiko gejala klinis antara lain nyeri perut, conjunctival sufffusion, anoreksia, dan diare, serta sebagai gejala regurgitasi pada daerah paru atau sesak napas.

Kata kunci: anjing; gejala klinik; leptospirosis

Abstract

Leptospirosis is a zoonotic disease caused by *bacteria Leptospira sp*., which causes infection in animals and humans. Dogs infected with leptospirosis showed symptoms such as anorexia, fever, vomiting, weakness, diarrhea and often experience yellowing of the eye area and mucosa around the mouth (icteric) with fatal

systemic complications and multi-organ dysfunction, especially in the kidneys and liver. Leptospirosis is an endemic disease in Jakarta. This study aims to identify risk factors that can contribute to canine mortality based on early clinical symptoms that are found when the dog is in an animal health service facility such as a veterinary clinic, veterinary hospital, or independent practice veterinarian. The method used in this study is clinical manifestations ,laboratory examinations, and medical records of dogs with suspected leptospirosis. Criteria inclusions were based on aspects of the clinical symptoms of dogs in and around Jakarta, Depok and South Tangerang. The data analysis used the chi-square test with a 95% confidence interval (CI). The dogs were categorized by age: 13 or 32.50%, were pups (younger than one-year-old), and 27 or 67.50% were adult dogs over one year old. Among the dogs, 80% were male and 20% were female. Additionally, 80% of the canines were not housed by their owners. In conclusion, case fatality rate in this study reached 46,43% the high mortality rate associated with leptospirosis during the 2020 study in canines was influenced by risk factors for clinical symptoms, including abdominal pain, conjunctival suffusion, anorexia, and diarrhea, as well as symptomatic regurgitation of the pulmonary region or shortness of breath.

Keywords: canine; clinical symptoms; leptospirosis

Introduction

Leptospirosis is a zoonotic disease caused by gram-negative bacteria, which may lead to health problems, particularly in regions with frequent heavy rainfall and flooding. The Ministry of Health published an official report in 2018 detailing 895 cases, which resulted in a case fatality rate of 17.8% and an annual morbidity of 39.2 per 100,000 individuals (Samrot *et al*., 2021). The Jakarta area is one of the endemic areas for leptospirosis (MOH, 2019).

The problem of leptospirosis cases in the field, especially in pet dogs, is not yet fully known by veterinarians when practicing in clinics, resulting in high mortality rates. This study of leptospirosis in dogs aims to provide a standard of understanding for veterinarians who are not familiar with diagnosing leptospirosis in dogs, including the non-specific clinical manifestations of leptospirosis which are sometimes anicteric. Non-specific clinical manifestations such as fever, vomiting, diarrhea, and anorexia sometimes obscure the diagnosis of other diseases. Specific diagnosis when a dog presents with leptospirosis characteristics such as conjunctival suffusion or jaundice for icteric leptospira type may be treated quickly by a veterinarian. Accurate diagnosis of this infection is essential in the case of management concerning the choice of antibiotics for treatment. Cases that are not correctly diagnosed and not treated will increase the risk of severe disease to the organs (Weil disease), which has a mortality rate of >70% of cases (Gasem *et al.,* 2020)14-28 days, and 3 months. Demographic and clinical information were collected during study visits and/or retrieved from medical records and double-entered into clinical report forms. After initially screening for dengue virus and other pathogens, specimens were tested at a central Reference Laboratory for anti-Leptospira IgM using commercial ELISA kits and for Leptospira DNA using an in-house quantitative real-Time PCR assay. Results: of 1464 patients enrolled, 45 (3.1%).

Early diagnosis of leptospirosis in dogs should be made because of the zoonotic nature of the disease and the need to initiate intervention in the early stages of appropriate therapy in infected dogs. A significant barrier to reaching a diagnosis is the often-non-specific clinical signs associated with leptospirosis, ranging in severity from no clinical signs to disease ending in death. Veterinarians should suspect leptospirosis in dogs with significant risk factors, consistent clinical signs, and clinicopathological abnormalities (Taylor 2019; Griebsch *et al.,* 2022). Risk factors that have been associated with leptospirosis include exposure to water, male sex, and shepherds or working dogs in several research studies (Goarant 2016; Retnowati *et al.,* 2022).

Signs of leptospirosis in dogs are often non-specific and may include fever, myalgia, anorexia, vomiting, and diarrhea (Gommeren dan Daminet, 2017). Seven days after the bacterial invasion, signs were mild and limited to lethargy and mild hyperemia. Infected dogs

with severe clinical signs at nine days and worsening until day 13. Other symptoms, such as acute kidney failure and liver disease are also common in dogs (Rahman *et al.,* 2021). Veterinarians should suspect leptospirosis in dogs with signs of kidney or liver failure, uveitis, pulmonary hemorrhage, acute febrile illness, or abortion (Klaasen *et al.,* 2014).

This study aimed to identify and determine the risk factors that significantly influence the general and specific clinical symptoms of leptospirosis cases in dogs that contributed significantly to dog mortality during the study 2020.

Materials and Methods

Sampel collection

This study is an observational analysis involving 40 dogs suspected of having leptospirosis during Januari until august 2020 . The data for this study was collected from 22 cases and 18 control dogs. All cases refer to the fatalities of individuals that may have had leptospirosis. Simultaneously, measures were implemented to monitor leptospirosis patients who survived throughout January-August 2020 at the following healthcare facilities: Ragunan Animal Hospital in Jakarta, Piara Pet Depok, Veterina Satwa Bintaro, South Tangerang, and Drh Made Clinic in West Jakarta.

Data Criteria

The inclusion criteria in this study included having at least 2 of the following clinical symptoms or signs: fever, anorexia, myalgia, vomiting, shortness of breath, jaundice, conjunctival suffusion, a history of exposure to a contaminated environment, living in a flooded area, contact with rats or other activities which is a risk factor for leptospirosis in the previous three to seven days, a positive result on the Microscopic Agglutination Test (MAT) serology examination which is gold standart for testing from leptospirosis case , and the dog is domiciled and settled in the Jakarta, Depok, South Tangerang area.

Data Analysis

Research data analysis consisted of bivariate analysis to see the relationship between the dependent and independent variables, in the analysis of the results of this test using the Chi-square test to see the magnitude of the risk using the odds ratio (OR). The independent variables in this study were clinical symptoms that accompany general symptoms such as fever, anorexia, vomiting, diarrhea, and specific symptoms such as myalgia, conjunctival suffusion, and jaundice. In contrast, the dependent variable was recovery from dogs treated in veterinary hospitals in the form of death status

Results and Discussions

This study is the first to be conducted in Indonesia to identify risk factors for clinical manifestations and symptoms of dogs affected by leptospirosis in animal health care facilities such as veterinary hospitals and independent clinics that have additional facilities for blood chemistry examinations as a screening selection for sampling. From January to August 2020, it was found that 40 dogs had suspected leptospirosis that met the criteria, 22 of which died while being treated at a veterinary service facility. A total of 32 dogs were male (80%) and eight female dogs, with the presentation of dogs in the puppy category (under one year) was 13 dogs (32.50%) and 27 adult dogs in the age category above one year - 18 years old (67.5%). Leptospirosis research conducted in the United Kingdom during 2016 showed that sex has been recognized as a risk factor for leptospirosis, but no statistical associations between sex in leptospirosis diagnosis (Taylor 2021). Dogs with maintenance management were not caged. As many as 32 (80%) were used to guard the barn and yard, and the rest (20%) were caged. Data on the identification of dog characteristics can be seen in (Table 1).

Risk factors from clinical manifestations when the patient first came in. Bivariate analysis was carried out to determine the effect of each risk factor (independent variable) on the incidence of mortality from Leptospirosis (dependent variable) using the Chi-square test to determine the difference in the percentage proportions between several groups of data (association relationship). The independent variable is the variable that explains or affects

Table 1. Identification of characteristics of dogs suspected of leptospirosis (n = 40)

No.	Variable and Category	Description	Quantity	Percentage (%)
1	Sex	Male	32	25,00
		Female	8	75,00
2	Age	Adult	27	67,50
		Puppy	13	32,50
3	History of vaccination	Have	18	45,00
		Does not have	22	55,30
4	Maintenance system	Caged	8	25,00
		Not caged	32	75,00
5	Mouse contact history (3 – 7 days)	No contact	18	45,00
		Have contact	22	54,20
6	Flood affected area	Not flooded	5	12,50
		Flooded	35	87,50
7	Source of drinking water	Boiled water	17	42,50
		Raw water	23	57,50
8	Recovery	Life	18	45,00
		Dead	22	55,00

other variables, while the dependent variable is the variable influenced by the independent variable. The strength of the association can be measured using RR and OR in a 2x2 table (Budiharta, 2002). The data from the Chi-square analysis are presented in Table 2**.**

Table 2. The bivariate analysis of clinical symptoms on *leptospira* mortality in dogs (n = 40)

No.	Variable and Category	Description	Life	Death	OR	*p*-value	95% CI
1	Fever	Male	12	20	5.00	0.057	0,866-28,661
		Female	6	2			
2	Age	Adult	12	15	1.071	0.919	0,284-4,046
		Puppy	6	7			
3	History of vaccination	Have	7	11	1.571	0.482	0,444-5,559
		Does not have	11	11			
4	Maintenance system	Caged	3	5	0.680	0.638	0,139-3,337
		Not caged	15	17			
Based on clinical manifestation							
5	Fever		18	22	-	-	-
6	Icteric	No	5	4	1.731	0.470	0388-7.725
		Yes	13	18			
7	Myalgia	No	0	5	2.059	0.031*)	1.464-2.985
		Yes	18	17			
8	Vomit	No	0	1	1.857	0.360	1.389-2.483
		Yes	18	21			
9	Anorexia	No	0	5	2.059	0.031*)	1.464-2.958
		Yes	18	17			
10	Abdominal pain	No	18	17	0.486	0.031*)	0.345-0.683
		Yes	0	5			
11	Conjunctiva suffusion	No	0	4	2.000	0.057	1.443-2.773
		Yes	18	18			
12	diarrhea	No	15	14	2.857	0.167	0.629-12.981
		Yes	3	8			

Significant $p < 0{,}05$*)

The bivariate analysis results in the study of leptospirosis in dogs showed five clinical symptoms that influenced the death of dogs, including myalgia, anorexia, shortness of breath, or symptoms of abdominal pain, conjunctival suffusion, and diarrhea. Fever was a common symptom found in cases of leptospirosis in dogs (100%). Clinical manifestations of anorexia, myalgia, and conjunctival suffusion are commonly found in deceased patients. Dogs infected with leptospires cause diseases of varying severity, depending on the infecting strain, geographic location, and immune response. Some dogs show mild or no disease symptoms, while others experience severe illness or death, often with impaired kidney function or acute nephritis (Sykes *et al.,* 2022) management, surveillance, and control of leptospirosis relies on accessible and accurate diagnostics that can be applied to humans and companion animals and livestock. Diagnosis should be multifaceted and take into account exposure risk, clinical presentation, and multiple direct and/or indirect diagnostic approaches. Methods of direct detection of Leptospira spp. include culture, histopathology and immunostaining of tissues or clinical specimens, and nucleic acid amplification tests (NAATs.

The results of observations of clinical manifestations were analyzed using the Chi-square test. Odds Ratio was used to determine the strength of the association, namely the ratio of dogs experiencing death due to leptospirosis from several clinical symptom factors found during the study. OR > 1 positively affects factors and disease (Budiharta 2002)

The chi-Square analysis illustrates that the independent variables associated with the dependent variable at a significance level of 95% (P <0.05) in this study are myalgia with OR (2.059), anorexia with OR (2.059), and shortness of breath or symptoms in abdominal pain with OR value (0.468). Other clinical symptoms that can cause death in dogs are conjunctival suffusion, diarrhea, and vomiting. If these factors are identified, diagnostic tests for leptospirosis and treatment should be instituted (Reagan & Sykes, 2019). Early identification and appropriate therapy by a clinician or veterinarian can result in an approximate 80% survival rate (Goldstein, 2006).

The independent factor associated with death in this study was jaundice. During the study period, 67.4% (31) dogs showed jaundice in table 2 have an OR value = 1.731 with a p-value of 0.407. The presence of organ dysfunction was significantly associated with mortality in the group of dogs with an icteric form of leptospirosis. The presence of jaundice is the factor that has the most substantial effect on poor prognosis. Of the 22 cases that died, 18 were patients characterized by jaundice. Jaundice is a common symptom in patients with severe leptospirosis, and death occurs in cases with icterus. Myalgia can occur due to the direct invasion of leptospira bacteria with changes in the form of local necrosis and vacuolization (Haake dan Levett, 2015)

The case fatality rate in this study reached 46.43% (Table 3). Therefore, the selection of treatment must be carried out appropriately in administering antibiotics. Ampicillin 500 mg every 6 hours or doxycycline 100 mg twice daily can be used to treat mild leptospirosis, while for severe cases, Penicillin G 1.5 million unit (MU) can be used intravenously every 6 hours (Charan *et al.,* 2013) fever days, numbers of patients presenting with oliguria, and number of patients undergoing need-based dialysis. Analysis was done by comprehensive meta-analysis software 2. Qualitative outcomes are summarized as odds ratio and quantitative outcomes are summarized as standard mean difference with 95% confidence interval. Random and fixed models are used for analysis. There was no significant difference between penicillin group and controlled group

Table 3. Case Fatality Rate (CFR) for the period January – August 2020

	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Total	Mean of CFR
MAT (+)	7	4	3	2	1	3	3	2	25	-
Infausta	5	2	0	1	1	0	3	0	12	46.43
% CFR	71	50	0	50	100	0	100	0		

for mortality (Odds ratio 1.59 (95% CI 0.59-4.29.

Conclusions

The study's mortality rate of leptospirosis cases in dogs period of January – August 2020 was 46.43%. This study found clinical symptom factors related to the mortality rate of dogs affected by leptospirosis, including myalgia, anorexia, and shortness of breath or symptoms in the abdominal pain area with p-value < 0.05, conjunctival suffusion with p-value < 0.10 and other accompanying symptoms such as diarrhea, anorexia, and icteric symptoms. Correct diagnosis of non-specific and specific symptoms in cases of leptospira in dogs will reduce mortality and achieve a cure. Mild and severe cases of leptospirosis need to be treated with antibiotics. Intravenouse antibiotics can be required for dogs with severe leptopsirosis and support management of electrolytes is often necessary under the supervision of a veterinarian.

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