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Epidemiology and Characteristics of Leptospirosis Inpatients in Demak Regency in 2018-2023

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Abstract. Demak Regency is an endemic area of leptospirosis. Cases of death due to leptospirosis in humans in Demak Regency in 2018-2023 with a CFR of >11%. Many deaths are found in leptospirosis patients who are hospitalized due to their poor prognosis. This study aimed to describe the characteristics of leptospirosis patients who are hospitalized in Demak Regency. This study used a quantitative descriptive design. Patients' data were taken from medical records at Sunan Kalijaga, Sultan Fatah, and NU Islamic Hospital in Demak Regency. The results of the study showed that of the 73 confirmed cases, 58.9% were male patients, and 69.9% were >40 years old. Of the 22 deaths, women exceeded men with 54.5%, and >40 years old at 81.8%. Based on laboratory examinations, the average platelet level was 110.18 cells/mm, creatinine level was 3.66 mg/dL, and urea level was 131.54 mg/dL. In the case of death, the patients' platelet level <100.000 cells/mm was 86.3%, creatinine level >3 mg/dL was 77.2%, and urea level >90 mg/dL was 86.3%. Symptoms that often appeared were myalgia. In this study, icteric and oliguria were not always symptoms in leptospirosis patients who died. Yet dyspnea and icteric symptoms have the potential to be predictors of death in leptospirosis patients. As many as 64.38% of patients did not have comorbidities. As many as 69.86% of leptospirosis patients were given a single type of antibiotic and 30.14% with a combination of antibiotics. Overall, 100% of the patients received antibiotics based on the severity of the disease. Detailed case description reports and

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patient prognosis need to be carried out to improve the handling of patients with leptospirosis.

1 Introduction

Leptospirosis is a zoonotic disease that has the potential to become an outbreak [1,2]. Leptospirosis is categorized as a priority zoonotic in Indonesia (Permenkes RI Nomor 1501/MENKES/PER/X/2010) [3]. Leptospirosis causes a variety of symptoms, ranging from mild infection to severe potentially fatal illness. In general, the mortality rate of leptospirosis cases ranges from 5-20%.[4] The main organs infected with Leptospira germs are the kidneys, liver, and lungs [5,6].

Humans can become infected with leptospirosis due to direct or indirect contact with the urine of animals infected with Leptospira [7, 8 ,9]. Leptospirosis transmission factors are influenced by agent factors related to the cause (number, virulence, pathogenicity of Leptospira germs); host factors (type of work, socioeconomic); and environment (standing water, rat population) [7, 10, 11, 12].

Demak Regency is one of the areas with a high risk of leptospirosis in Central Java Province and is an endemic area of leptospirosis. Based on preliminary study data at the Demak Regency Health Office, the number of leptospirosis cases in humans is found every year from 2008 to 2023 with a CFR value of >11% [13].

Based on the results of epidemiological investigations, the distribution of leptospirosis cases in Demak Regency in 2023 is known to be higher in men (75%) than in women (25%). When viewed by age, leptospirosis patients in Demak Regency range from 19 to >45 years old, with details of the age of >45 years old at 53%, 30-44 years old at 28%, and <30 years at 19%. Based on occupations, 25% of patients of leptospirosis are farmers/farm laborers, 9.4% are itinerant traders, and 6.3% are factory workers, while others have various kinds of jobs. Environmental risk factors also contribute to the spread of leptospirosis in Demak Regency, such as waterlogging/flooding/rob, the presence of rats, and the state of sewers/drainage.

To improve the prediction and management of mortality risk in leptospirosis patients, various clinical and biochemical factors have been analyzed as potential predictors. Predictors of leptospirosis mortality include socio-demographic conditions, laboratory test results, symptoms and signs, treatment management, and complication conditions or comorbidities [4, 14, 15, 16, 17]. According to studies that have been conducted at various levels, laboratory test variables such as thrombocytopenia (<100.000/ µL), total bilirubin more than 300 mcmol/L, creatinine more than 200 mcmol/L, and urea are predictors of leptospirosis mortality [16].

Based on a preliminary study, the database of characteristics of leptospirosis patients in hospitals is still limited and not continuously studied. This study aims to find out the epidemiological data and characteristics of leptospirosis patients in hospitals in Demak Regency. The results of this study can be used as a case overview and basis for improving the treatment of leptospirosis patients in hospitals.

2 Method

This study is a quantitative descriptive observational study using a cross-sectional design based on laboratory results on leptospirosis patients in Demak Regency. The study used medical record data and laboratory examination results of hospitals in Demak Regency. The samples used in this study are all leptospirosis patients who are confirmed and recorded in medical records at Sunan Kalijaga Hospital, Sultan Fatah Demak Hospital, or NU Islamic Hospital in 2018-2023 whose final evaluation results are known (dead/ recovered). The sample method used was a total sampling of 73 leptospirosis patients. Medical record data in the form of demographic data (gender and age), laboratory results (platelet level, creatinine level, urea level), and clinical profile (icteric, oliguria, dyspnea, myalgia, comorbid, antibiotic status).

3 Results

3.1 Distribution of leptospirosis cases by sub-district in Demak Regency

Based on data from the hospitals, there were a total of 73 cases of leptospirosis with a total of 22 deaths or around 30% of deaths in Demak Regency, with a distribution that varied in each sub-district. The sub-district with the highest number of cases was Demak (16 cases, 22%), followed by Bonang (12 cases, 16%) and Karangtengah (8 cases, 11%). The sub-district with the highest number of deaths is Demak (6 deaths, 27%), followed by Karangtengah, Wedung, Guntur, and Mijen (3 deaths each, 14%). This might indicate a higher level of risk in the sub-district or there might be other factors such as agent malignancy, access to health services, and less effective prevention. The complete data are presented in Table 1.

Table 1. Distribution of leptospirosis cases by sub-districts in Demak Regency

Sub-Districts	Died	Recovered	Total Cases	Case Percentage (%)	Death Percentage (%)
Demak	6	10	16	22	27
Bonang	2	10	12	16	9
Karangtengah	3	5	8	11	14
Wedung	3	3	6	8	14
Guntur	3	2	5	7	14
Mranggen	1	4	5	7	5
Wonosalam	0	5	5	7	0
Karangawen	1	3	4	5	5
Mijen	1	3	4	5	5
Sayung	2	2	4	5	9
Gajah	0	2	2	3	0
Karanganyar	0	1	1	1	0
Kebonagung	0	1	1	1	0
Total	22	51	73	100	100

3.2 Demographic and Clinical Profile of Leptospirosis Inpatients in Demak Regency

Table 2 showed that in this study there were 30.1% of leptospirosis inpatients who died, while 69.9% of them were recovered. As many as 82.8% were leptospirosis patients with severe clinical symptoms. The majority of leptospirosis patients were >40 years old (69.9%). The distribution of leptospirosis patients was relatively unchanged in male (58.9%) and female (41.1%) sexes.

Judging from the results of laboratory examinations, leptospirosis patients had more thrombocytopenia (<100.000 cells/mm), which was 54.8%. Examination of creatinine levels in 73 leptospirosis patients showed that 46.6% of them had creatinine levels of >3 mg/dL in the blood. Furthermore, the examination of urea levels, which was also a predictor of mortality in leptospirosis patients, showed that 50.7% of the leptospirosis patients had urea levels of >90 mg/dL.

In the univariate analysis, results were also obtained based on the symptoms felt by leptospirosis patients that the majority of leptospirosis patients who were hospitalized had no icteric symptoms (80.8%), no oliguria (56.2%), and had symptoms of myalgia/muscle pain (87.7%). Meanwhile, symptoms of dyspnea/shortness of breath were found in 46.6% of the leptospirosis patients. Based on the ownership of comorbid diseases, only 35.6% of the patients had comorbid diseases. The types of antibiotics given also varied. Most leptospirosis patients (69.9%) took 1 type of antibiotic during the treatment period.

Table 2. Characteristics of Leptospirosis Inpatients in Demak Regency

Variables	Frequency (f)	Percentage (%)
Survival		
Died	22	30.1
Recovered	51	69.9
Clinical Symptoms		
Severe	60	82.2
Mild	13	17.8
Age		
>40 years	51	69.9
=>40 years	22	30.1
Gender		
Male	43	58.9
Female	30	41.1
Platelet Level		
<100.000 sel/mm	40	54.8
=>100.000 sel/mm	33	45.2
Creatinine Level		
>3 mg/dL	34	46.6
<=3 mg/dL	39	53.4
Urea Level		
>90 mg/dL	37	50.7
=<90 mg/dL	36	49.3
Icteric		
Icteric (+)	14	19.2
Icteric (-)	59	80.8
Dyspnea/Shortness of breath		
Dyspnea (+)	34	46.6
Dyspnea (-)	39	53.4
Myalgia		

Variables	Frequency (f)	Percentage (%)
Myalgia (+)	64	87.7
Myalgia (-)	9	12.3
Oliguria		
Oliguria (+)	32	43.8
Oliguria (-)	41	56.2
Comorbid		
Comorbid (+)	26	35.6
Comorbid (-)	47	64.4
Antibiotic Status		
1 Type of Antibiotics	51	69.9
>1 Types of Antibiotics	22	30.1

The range of time it took for leptospirosis inpatients to experience death was 1 to 18 days, a median of 5 days, and an average of 5.26 days from 73 leptospirosis patients admitted to Demak Regency Hospital in 2018-2023. Leptospirosis patients who were the study sample had an age range of 10 to 77 years, with an average age of 49 years. In the results of laboratory examinations, platelet levels in leptospirosis patients ranged from 11-570 cells/mm with an average of 110.18 cells/mm. The average creatinine level in 73 leptospirosis inpatients was 3.66 mg/dL with a range of 0.5-14 mg/dL. Urea levels based on examination results in leptospirosis patients showed a range of 14.1-480 mg/dL, with a median of 93 mg/dL and an average of 131.54 mg/dL. The complete data is presented in Table 3.

Table 3. The mean hospital stay ± SD for the patients

Variables	n	Range	Median	Mean ± SD
Person -Time	73	1-18	5.00	5.26 ± 2.421
Age	73	10-77	49.00	47.96 ± 15.753
Platelet Level	73	11-570	85.00	110.18 ± 100.529
Creatinine Level	73	0.5-14	2.80	3.66 ± 2.936
Urea Level	73	14.1-480	93.00	131.54 ± 115.320

3.3 Leptospirosis inpatient status based on clinical profiles in Demak Regency

We studied 73 leptospirosis patients in the development data set. Patients with leptospirosis infection were categorized as dead (n = 22) and recovered groups (n = 51). Table 4 showed that the percentage of mortality was higher in women than in men (40.00% vs 23.26%), but it was insignificantly different. Of the 53 patients over 40 years old, 18 died (35.29%) and 33 recovered (64.70%). People over the age of 40 had a higher risk of death than those aged 40 years or less.

Based on platelet level, the mortality rate of patients with platelet level was higher in patients with platelet level <100.000 cells/mm compared to =>100.000 cells/mm (47.50% vs 9.09%). Patients with creatinine >3 mg/dL had a higher percentage of deaths than patients with creatinine <=3 mg/dL (50.00% vs 12.82%). Meanwhile, in patients with urea ≥90 mg/dL, out of 39 patients with urea of 90 mg/dL or more, 19 died (51.35%) and 20 recovered (48.65%). Mortality was higher in patients with urea ≥90 mg/dL compared to <90 mg/dL (51.35% vs 8.33%).

Based on symptoms, the majority of patients who died experienced epilepsy and dyspnea, but not all patients who died experienced these symptoms. In dead patients, more people had icteric symptoms compared to those who did not experience icteric symptoms (64.29% vs 22.03%). Of the 36 patients with dyspnea, 20 died (58.82%) and 14 recovered (41.18%). Of the 32 patients with oliguria, 10 died (31.25%) and 22 recovered (68.75%). The average patient experienced symptoms of myalgia. When observed, both myalgia (+) and myalgia (-) patients had a low percentage of deaths, compared to the recovered cases. Judging from the comorbid variables, both patients with and without comorbidities had a low percentage of deaths, compared to recovered cases. In the variable of antibiotic status, in the case of more patients who died, they were given one type of antibiotic compared to >one type of antibiotic (39.22% vs 9.09%).

Table 4. Clinical Profiles of Leptospirosis Inpatients in Demak Regency

Variables		**Leptospirosis Survival**	
		Died	**Recovered**
Gender	Male	10 (23.26%)	33 (76.74)
	Female	12 (40.00%)	18 (60.00%)
Age	>40 years	18 (35.29%)	33 (64.70%)
	=<40 years	4 (18.18%)	18 (81.82%)
Platelet Level	<100.000 sel/mm	19 (47.50%)	21 (52.50%)
	=>100.000 sel/mm	3 (9.09%)	30 (90.91%)
Creatinine Level	> 3 mg/dL	17 (50.00%)	17 (50.00%)
	<=3 mg/dL	5 (12.82%)	34 (87.18%)
Urea Level	>90 mg/dL	19 (51.35%)	18 (48.65%)
	<=90 mg/dL	3 (8.33%)	33 (91.67%)
Icteric	Icteric (+)	9 (64.29%)	5 (35.71%)
	Icteric (-)	13 (22.03%)	46 (77.97%)
Oliguria	Oliguria (+)	10 (31.25%)	22 (68.75%)
	Oliguria (-)	12 (29.27%)	29 (70.73%)
Dyspnea	Dyspnea (+)	20 (58.82%)	14 (41.18%)
	Dyspnea (-)	2 (5.13%)	37 (94.87%)
Myalgia	Myalgia (+)	19 (29.69%)	45 (70.31%)
	Myalgia (-)	3 (33.33%)	6 (66.67%)
Comorbid	Comorbid (+)	9 (34.62%)	17 (65.38%)
	Comorbid (-)	13 (27.66%)	34 (72.34%)
Antibiotic Status	1 Type of Antibiotics	20 (39.22%)	31 (60.78%)
	>1 Types of Antibiotics	2 (9.09%)	20 (90.91%)

4 Discussion

The initial condition of leptospirosis inpatients at Demak Hospitals showed that most patients came to the hospitals in severe condition, which impacted the need for intensive care and increased the risk of complications and mortality. The results of the study showed that of the 73 confirmed cases, 58.9% were male patients and 69.9% >40 years old. Of the 22 deaths, women were higher with 54.5%. Or it can be analyzed that the percentage of deaths was higher in women than in men (40.00% vs 23.26%), but it was insignificantly different. According to Depo (2018), the high risk of occupational exposure affects this. Most studies have found that although gender is not the main determinant of leptospirosis deaths, the number of deaths is higher in men than in women [18]. This is influenced by the high risk of occupational exposure and the influence of low socioeconomic classes with various professions such as sugarcane farmers, sewer workers, rice farmers, and construction workers [19]. In this study, mortality was higher in women. This is related to age, occupations that are at high risk in the amount of exposure such as farmers, and ownership of comorbidities. In terms of response to treatment, appropriate and timely treatment, especially with the appropriate use of antibiotics, is a key factor in improving patient survival, and response to this treatment is not affected by gender.

Of the 53 patients over 40 years old, 18 died (35.29%) and 33 recovered (64.70%). People over the age of 40 had a higher risk of death than those aged 40 years or less. The results of this study are in line with previous studies such as a study by Pavlo (2022) in Ukraine where the incidence rate of death of leptospirosis patients was higher in the age group of >40 years compared to =<40 years, which was 56% vs. 35% per 100 person-days [18]. In addition, research conducted in Sri Lanka showed an incidence mortality rate of 90% in the age group of >40 years and 56% of age = <40 years [20]. Based on demographic factors, the age of patients with leptospirosis is between 46-65 years old. This happens because the elderly are usually physically weak, and can easily contract infectious diseases [21].

The mortality rate of patients with platelet levels was higher in patients with platelet levels <100.000 cells/mm compared to =>100.000 cells/mm (47.50% vs 9.09%). Low platelet levels can be a poor indicator of the prognosis of leptospirosis patients. Prolonged disease and acute kidney injury are the risk factors for thrombocytopenia [22]. Patients with severe thrombocytopenia tend to have a higher risk of death [23]. The results of this study are in line with previous studies such as a study conducted by Tantitanawat (2003) in Thailand where the average platelet value in death cases was around 48,560 cells/mm [24]. According to Sucipto's research results, a low platelet level is a risk factor for death in leptospirosis [15].

In the case of death, the patients' creatinine level >3 mg/dL was 77.2%, or it can be analyzed that patients with creatinine >3 mg/dL had more possibility of death than patients with creatinine <=3 mg/dL (50.00% vs 12.82%). Leptospirosis can cause varying degrees of damage to the kidneys. As a result, kidney function can be impaired. This can be reflected in increased levels of creatinine in the blood [25]. The results of this study are in line with previous studies such as a study conducted by Pavlo (2022) in Ukraine where the value of patients' creatinine levels was much higher in patients who died [16].

Mortality was higher in patients with urea ≥90 mg/dL compared to <90 mg/dL (51.35% vs 8.33%). Urea levels in the blood are also a biomarker to evaluate kidney function in cases of leptospirosis. Urea levels in the blood can increase in response to kidney disorders that occur during infection [26]. According to previous studies, there is a relationship between mortality rates in patients with leptospirosis and urea levels in the body [27, 28].

Based on symptoms, the majority of patients who died experienced epilepsy and dyspnea, but not all patients who died experienced these symptoms. In patients who died, more people had icteric symptoms compared to those who did not experience icteric symptoms (64.29% vs 22.03%). Icteric is often a sign of disease severity in leptospirosis patients [29]. The severity of the icteric can provide clues concerning the seriousness of the liver damage and the disease overall [30,29]. The results of this study are in line with previous studies such as the study conducted in Bantul revealing that that the strongest risk factor in the occurrence of death in the Bantul Regency is caused by the presence of icteric [14].

Mortality was higher in patients with dyspnea than in non-dyspnea (58.82% vs 5.13%). Dyspnea or shortness of breath can occur in leptospirosis patients as a result of impaired lung function being the most common [31]. The results of this study are in line with previous studies such as a study conducted in France where 58% of the total leptospirosis deaths were shortness of breath [32]. Shortness of breath is the dominant predictor associated with leptospirosis death. Dysparnea is often an indicator of disease severity in leptospirosis patients. Patients with severe dyspnea may have more severe disease and a higher risk of death. Shortness of breath is the initial symptom of serious complications such as acute respiratory distress syndrome (ARDS). ADRS is a lung problem caused by fluid that builds up in the lungs, causing respiratory failure and low oxygen levels in the blood. Najafi's research concluded that ADRS is the main cause of death in patients with leptospirosis [33].

Of the 32 patients with oliguria, 10 died (31.25%) and 22 recovered (68.75%). Evidence of the absence of a link between oliguria and leptospirosis mortality can be explained by several studies based on the results of meta-analyses examining organ dysfunction in cases of leptospirosis death. Only 6 of the 23 studies found a link between oliguria as a predictor of leptospirosis death [34]. This is due to the severity of infection, response to treatment, variability of symptoms, or different prognosis conditions in each leptospirosis patient. Oliguria can occur in patients with leptospirosis who have severe complications, such as acute kidney failure. However, not all patients with oliguria experience severe complications, and oliguria is not always a direct predictor of survival.

The average patients experience symptoms of myalgia. When observed, both myalgia (+) and myalgia (-) patients have a low percentage of death, compared to recovered cases. This is because myalgia is a sign in the early phase of leptospirosis. This is followed by an immune phase that shows signs of severity that affect the death of leptospirosis patients [35].

Judging from the comorbid variables, both patients with and without comorbidities have a low percentage of deaths, compared to recovered cases. The comorbid studies found most of them such as hypertension, and diabetes mellitus. The existence of comorbidities in themselves does not necessarily determine the prognosis of the patients since the importance of comorbidities depends on the type and severity of those comorbidities. Evidence of no comorbid association with leptospirosis death can be explained by several studies such as the results of a study conducted by Dupont in the French West Indies which explained the absence of a history of diabetes mellitus, hypertension, and kidney disease [32].

In the antibiotic status variable, in the case of more patients who died, they were given 1 type of antibiotic compared to >1 types of antibiotic (39.22% vs 9.09%). This study may result in the discovery that the administration of more than one antibiotic is a factor that can reduce the possibility of death in leptospirosis patients. This may be related to its effectiveness in targeting Leptospira bacteria and its spectrum of activity. However, further research must be carried out.

5 Conclusions

This study concludes that there are variations in the characteristics of leptospirosis inpatients in Demak Regency. The mortality rate is higher in female patients, >40 years old, platelet levels <100.000 cells/mm, creatinine levels >3 mg/dL, and urea levels >90 mg/dL. Symptoms that often appear are myalgia. In this study, icteric and oliguria are not always symptoms in leptospirosis patients who died. Yet dyspnea and icteric symptoms have the potential to be predictors of death in leptospirosis patients. The administration of >1 types of antibiotics in the treatment process may potentially reduce the chance of death of leptospirosis patients. Further research is needed to understand the risk factors for death and the spread of leptospirosis in Demak Regency, especially in sub-districts with high cases and deaths.

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