INTRODUCTION

Climate change is an ongoing global threat. In 2020, the global average surface temperature was 1.2 ± 0.1°C warmer than 1850-1900. Moreover, the global sea level has been rising an average of 3.29 ± 0.3 mm per year, but it has slightly decreased at the end of 2020 due to the La Niña phenomenon in the tropical pacific. Nevertheless, the rise of sea level average in Asia is faster than globally because of coastal area loss and shoreline retreat. Meanwhile, over 23.1 million migrants and refugees were triggered by weather-related events in 2010-2019, 42% due to hydrometeorological disasters such as flooding, hurricane, or typhoon season. Global warming has caused higher and prolonged flood levels in the Mekong delta in Southeast Asia and affected extreme tropical cyclones (1-2).

The correlation between climate change and a tropical cyclone’s characteristics has been widely discussed. Future projections of tropical cyclone behavior are highlighted in decreasing tropical cyclone occurrence but increasing in maximum intensities, and cyclones were related to rainfall. It was predicted that climate change on the sea-level rise would impact storm surges in all coastal areas (3). This is especially so in Indonesia as it is a large archipelago and is located at the equator. The average radius of tropical cyclones is nearly 150 to 200 km, with powerful winds of up to 63 km/h, and mostly occur in the Indian Ocean and the South China Sea (4).

From 26 November to 1 December 2017, the Cempaka Tropical Cyclone occurred in the southern sea of Java Island and surrounding areas. The peak of this cyclone was on 27 November. It hit the southern coast of Yogyakarta Province, causing extreme rainfall of up to 175 - 250 mm/day and severe flooding in Bantul, Gunung Kidul, Wonogiri, and Pacitan districts (5). The cyclone was formed by a combination of small-scale clouds and low-pressure centers on the south coast of East Java, as well as the presence of low-level jets that moved towards the southern coast of Java Island (6).

Changes in climate variability and extreme weather events might shift human infectious diseases’ geographic and seasonal patterns and can be observed from outbreak frequency and severity. This is
because climate variables spatiotemporally affect the development, survival, or reproduction of disease hosts and pathogens, including the process of transmitting vector-borne diseases, such as leptospirosis (7).

Leptospirosis is a zoonotic disease caused by the pathogenic bacteria called *Leptospira*. Overall, it is estimated that there are 1.03 million cases with 58,900 deaths each year due to leptospirosis worldwide. The highest leptospirosis morbidity and mortality estimates were observed in Oceania, the Caribbean, Andes, Latin America, East Sub-Saharan Africa, South Asia, and Southeast Asia (8).

The risk factors for leptospirosis include the dense population of reservoirs of infection such as cattle, pigs, dogs, goats, and rats; environmental factors such as weather, flooding, and poor sanitation; recreational factors such as outdoor water activities and water sports; occupational factors such as fishermen, oil-palm plantation workers, cattle rearing (9), urban sanitation workers, (10) and farmers. Farmers who work in wet and muddy rice paddies during harvest season could also lead to a major outbreak of leptospirosis. Personal protective equipment will prevent farmers from contaminated water puddles (11).

WHO classified leptospirosis as a neglected tropical disease. Clinical manifestations range from the common cold to acute kidney failure, pneumonia, jaundice, pulmonary hemorrhages, to death. In Asia, the most positive reported rat species were *Rattus norvegicus, Rattus rattus, Rattus exulans, Rattus argiventer, Rattus tanezumi, and Rattus losea*. The common pathogenic *Leptospira* are *L. interrogans, L. borgpetersenii, L. kirschneri, L. noguchii, L. weilii*, etc. Furthermore, frequently reported serovars included *Icterohaemorrhagiae, Autumnalis, Javanica, Canicola,* and *Pyrogens* (12-13).

In Fiji, two consecutive cyclones and severe flooding in 2012 resulted in 576 cases and 40 deaths from leptospirosis outbreaks. The risk factor for human leptospirosis infection in Fiji is high maximum rainfall during rainy months (OR = 1,003 per mm) (14). The three human leptospirosis cases firstly were reported in the US Virgin Island, 2.5 months post- Irma and Maria hurricane in 2017. A potential source for *Leptospira* transmission was found in contaminated well water (15).

According to the monthly cases data report from the Bantul District Health Office 2010 - 2016, Bantul District has the highest human leptospirosis endemic cases in Yogyakarta Province and has revealed a pattern of repeated increases after four years. The incidence rate of human leptospirosis cases in 2011 was 15 per 100,000 population, but it increased gradually from 4 per 100,000 population in 2012 to 8 per 100,000 population in 2015. Therefore, this study aims to analyse the Spatio-temporal pattern between flooding, weather, and leptospirosis cases after the Cempaka Tropical Cyclone.

**METHODS**

**Study Area**

Bantul District is part of Yogyakarta Province and is located in the southernmost region of Java, Indonesia (14° 04’ 50” - 27° 50’ 50” South latitude and 110° 10’ 41” - 110° 34’ 40” East longitude). The district’s eastern boundary is the Gunung Kidul, while the western boundary is the Kulon Progo. The district’s northern boundary is Yogyakarta and Sleman, while the southern boundary is the Indian Ocean.

Bantul has 17 administrative sub-districts, 75 villages and covers around 506.85 km². Its population in 2017 was around 995,264 residents with a population density of 1,964/km². The majority of the population’s livelihood relies on agriculture, trade, industry, and services. Bantul was an area of highlands and valleys crossed by main rivers such as the Oyo River, Opak River, Progo River, Winongo River, Code River, and Bedog River. In 2012-2016, the average flood occurrences were 13 times per year which majority occurred in Kretek, Bambanglipuro, and Kasihan sub-districts. Bantul has a tropical monsoon climate with the dry season from June to October, and the wet season occurs from November to May. The temperatures were relatively consistent throughout the year, with mean temperatures of 22° - 31°C.

**Data Collection and Spatio-temporal Analysis**

This study was an ecological time-series study design, with a Spatio-temporal distribution in the entire Bantul district, Yogyakarta, Indonesia. The average monthly temperature, relative humidity, and cumulative rainfall data were obtained from the national database reported from three weather stations of the Meteorology, Climatology, and Geophysical Agency of Yogyakarta. The monthly flooding data per village was obtained from the Bantul Disaster Management Agency. Flooding occurrence was defined as village areas affected by flooding, either by inundation or flash floods. The monthly per village human leptospirosis data was defined as probable positive cases reported in the surveillance
form within 24 hours and obtained from the Bantul District Health Office. The monthly data were collected for 12 months after the Cempaka Tropical Cyclone from November 2017 to October 2018.

Spatial distribution analysis was used to analyse the distribution of flooding occurrence, inverse distance weighting (IDW) interpolation of rainfall, and incidence rate (IR) of human leptospirosis cases per village within Bantul District. In the IDW interpolation method, cumulative rainfall data from 3 weather stations were weighted during interpolation, so that influence of one point relative to another declines with distance from the unknown point to be created. The incidence rate is new human leptospirosis cases per village divided by population in 2017 multiplied by 100,000. Therefore, the free software QGIS 3.16 was chosen to create a map in the study area. Pearson’s correlation was used to analyse the correlation between monthly weather data and human leptospirosis cases whose data were normally distributed in the time lag of that month (lag 0) and previous 1-3 months (lag 1-3). The statistic correlations were conducted by Stata 13. Temporal analysis was used to analyse the time-series graph mean temperature, relative humidity, cumulative rainfall, and human leptospirosis cases. Time-series were done using Tableau Public.

RESULTS
Spatial Analysis of Flooding, Rainfall, and Human Leptospirosis Cases

According to Figure 1, the number of villages affected by flooding (dark brown) for a year was 33 (44%), including 12 sub-districts. During the Cempaka Tropical Cyclone, two bottom flooding points occurred in Sriharjo and Selopamioro, part of the Imogiri sub-district. There was an increase in river water discharge of the Winongo River, Opak River, and its surroundings, such that the flood submerged hundreds of houses for days. Flooding villages tend to be in the upstream area from the north and central to the downstream area in the south, which is a boundary to the Indian Ocean. In addition to flooding, landslides and fallen trees occurred at several points, causing damage to houses, infrastructure, and fatalities.
Statistical Analysis of Weather Data and Human Leptospirosis Cases

The descriptive statistics of weather data and human leptospirosis cases in Bantul a year after the cyclone are shown in Table 1. It can be concluded that weather data fluctuates every month. Mean temperature (25.89 ± 0.89), relative humidity (84.41 ± 3.08), and human leptospirosis cases (8.25 ± 7.41) have a relatively low variation, while rainfall (195.83 ± 251.32) values are spread over a wide range. The highest difference in cumulative rainfall follows the wet and dry seasons.

Table 1. Distribution of Weather Data and Human Leptospirosis Cases

| Variable                      | Mean  | SD   | Min  | Max  |
|-------------------------------|-------|------|------|------|
| Mean Temperature              | 25.89 | 0.89 | 24.2 | 27.1 |
| Relative Humidity             | 84.41 | 3.08 | 79   | 90   |
| Cumulative Rainfall           | 195.83| 251.32| 0    | 744  |
| Human Leptospirosis Cases     | 8.25  | 7.41 | 0    | 26   |

Table 2. Pearson Correlation Test Results for Weather Data and Human Leptospirosis Cases

| Time-lag | Mean Temperature | Relative Humidity | Cumulative Rainfall |
|----------|------------------|-------------------|---------------------|
|          | r     | p-value | r     | p-value | r     | p-value |
| 0        | 0.3379 | 0.2827 | 0.3763 | 0.2280 | 0.1102 | 0.7332 |
| 1        | 0.1574 | 0.6252 | 0.6849* | 0.0140 | 0.7451* | 0.0054 |
| 2        | 0.3813 | 0.2213 | 0.5173 | 0.0850 | 0.4760 | 0.1178 |
| 3        | 0.1073 | 0.7400 | 0.6666* | 0.0179 | 0.8561* | 0.0004 |

*) significant correlation (p<0.05)

The Pearson’s correlation between weather and leptospirosis cases can be seen in Table 2, and there was no significant correlation (p > 0.05) in the overall time-lag. A significant correlation (p < 0.05) was found in the remaining variables. A 1-month lag of relative humidity (r = 0.6849) and a 3-months lag of rainfall (r = 0.6666) had a strong positive correlation with human leptospirosis cases. It means that the increase of human leptospirosis cases follows the increase previous 1 and 3 months of relative humidity. The 1-month lag of rainfall (r = 0.7451) and 3-months lag of relative humidity (r = 0.8561) also had a strong positive correlation with human leptospirosis cases that means the increase of human leptospirosis cases follows the increase previous 1 and 3 months of rainfall.

Temporal Analysis of Weather Data and Human Leptospirosis Cases

The Cempaka Tropical Cyclone occurred for six days from 26 November to 1 December 2017. Figure 2 exhibits that during November 2017, the district had a mean temperature of 25.8°C, 90% relative humidity, and 744 mm of cumulative rainfall. There were no leptospirosis case findings around the district in the critical week. New cases were found to rise sharply 1-5 months after the tropical cyclone in December 2017 to April 2018, and case reports were around 12-26 cases per month. Relative humidity and rainfall seem to fit the seasonal pattern, except for mean temperature. The dry season started in May 2018, with 26.3°C of mean temperature, 83% relative humidity, and 5 mm of cumulative rainfall. The decrease in the number of cases seen during the dry season was around 2-5 cases per month. Overall, the total number of human leptospirosis cases a year after the cyclone reached 99 cases.

Figure 2. Time-series Graph of Human Leptospirosis Cases and Mean Temperature, Relative Humidity and Cumulative Rainfall

DISCUSSION

A Spatio-temporal analysis in leptospirosis research contributed to understanding the disease transmission and support leptospirosis control interventions. Spatial approaches are often used to describe the distribution of incidence/prevalence geographically or detect clustering and hotspots in the mapping (16). Our study examined the Spatio-temporal distribution of flooding occurrence, temperature, relative humidity, rainfall and, human leptospirosis cases.

Flooding hit during the cyclone made human leptospirosis outbreaks rise in those villages. Most leptospirosis cases were confirmed within the first month after major flooding, even in Thailand. Flooding enhanced the bacteria’s potential to disperse and survive longer in the water flushes and moist soil. Moreover, sharing and consuming more than two water sources, including environmental water surrounding households, ponds, groundwater, tap water, rivers/canals, was likely a risk factor. Therefore, reducing contact between humans, animals, the leptospira bacteria, and contaminated environment might help disease control transmission (17–20).
Based on the geographical study area, rivers might have an important role in causing flooding and leptospirosis outbreaks. The river level was very influential on the risk of disease transmission for those who live close to bodies of water. Living <100 m to the river and having 1 meter of river water level increase the risk of infecting leptospirosis. Another problem due to flooding was the relocation of residents in refugee areas, leading to overcrowding conditions and poor sanitation practices so that leptospirosis was more difficult to overcome (21-22). Besides that, sand mining activities by residents at the Opak River estuary were also at high risk. *L. interrogans Pyrogenes* was found in 58% of 4 riverbank soil samples in New Caledonia. These pathogenic bacteria could survive > 9 weeks and were carried away during floods (23).

The highest spatial IDW interpolation of rainfall was revealed in the southern region bordering the Indian Ocean. High annual precipitation was detected around the southern coast of South Korea due to typhoon-induced changes and convective systems within air mass (24). The IDW interpolation method was a better choice and easy to use for calculating time-series rainfall data in geographic information compared to ANUDEM, Spline, and Kriging (25).

As global burden diseases, 318 leptospirosis outbreaks were identified worldwide in 1970-2012, mainly in tropical and subtropical regions such as Latin America, the Caribbean, Southern Asia, and North America (26). Due to the Cempaka Tropical Cyclone, our study findings revealed a 1-year leptospirosis outbreak reported in 51 out of 75 villages in Bantul. The Philippines has typhoon-related leptospirosis cases across the regions due to topography, sanitary conditions, and human-animal contact patterns (27). Heavy rainfall typhoon Ketsana also caused an outbreak that resulted in patients ranging from severe symptoms to death. A majority had waded in floodwater and suffered complications after *leptospira* infection (28). Moreover, typhoons Nesat, Nalgae and Washi resulted in widespread flooding and leptospirosis in the productive age group (29).

These are several risk factors for post-flood leptospirosis as the most frequently reported outbreak after a natural disaster. First, poor access to clean water, sanitation, and hygiene (WASH) was the common issue encountered in a post-hydrological disaster. Second, exposure to livestock encouraged the presence of rats because they were attracted to animal feed and waste. Third, people who helped with post-flood cleaning activities were prone to lacerated wounds, increasing their chances of contracting pathogenic *Leptospira* inside the body (30-31). Additionally, from a socio-economic point of view, Bantul is included in the category of rural districts. Similar to China, high-risk counties are predominantly in larger rural and economically less-developed areas. It might affect the public awareness and limitations of health facilities in dealing with the disease (32).

Our study findings revealed that relative humidity’s 1-month lag and 3-month lag positively correlated with human leptospirosis cases. In South Korea, a 1% increase in daily minimum relative humidity was associated with 4% increases in leptospirosis cases at 11 weeks. Higher relative humidity had an impact on the viability, infectivity, and stability of rodents. *L. interrogans* requires warm and humid conditions for survival outside the host for 1 - 2 months (33). Even during the disaster emergency response (lag 0), it was also associated with leptospirosis cases (34). Conversely, a 1% increase in weekly humidity would be reduced by a 1% number of cases due to the robust role of rainfall and major flooding in Malaysia (21).

Most modeling studies used Pearson’s correlation and examined the correlation between flood risk or precipitation as climatic factors and human leptospirosis risk of infection (16). Our study findings also revealed that a 1-month lag and 3-month lag of rainfall had a strong correlation with human leptospirosis cases. This is similar to the number of cases that peaked after heavy rains that occurred one month earlier in India (34). However, in French Polynesia, leptospirosis seems to be delayed by two months after peak rainfall. Most of the rainfall peaks in January, then followed by cases peaks in March. It depends on the duration of soil soaking after heavy rains as it supports the survival of leptospires in the environment (35).

Previous studies have shown that heavy rainfall and leptospirosis cases had a shorter time-lag, 1-week lag in Colombia, 2-weeks lag in Manila, and 3-weeks lag in Sri Lanka. A lag of 1-3 weeks indicates the incubation period of leptospirosis, duration of onset symptoms until severe, or misdiagnosis of another disease as leptospirosis cases (36–38). In South Korea, a 1 mm increase in daily rainfall was associated with 2% increases in leptospirosis cases at six weeks. Heavy rains that cause flooding triggered the wider spread of *Leptospira* into the environment. Especially in high rodent density areas, *L. interrogans* would be carried to contaminate rivers or lakes (33).

Our study findings revealed that new cases of leptospirosis were found 1 - 5 months after Cempaka Tropical Cyclone. 2-6 weeks post-natural hazard extreme flooding in Western Fiji was reported to cause
the largest leptospirosis outbreak in the South Pacific (39). Leptospirosis outbreaks generally increase within 2 weeks, 6 weeks, and 2 months after hurricane storms. The indirect transmission of infectious diseases, high-speed storms, and floods could destroy houses, infrastructure, lead to overcrowding, more exposure to animals, malnutrition, and physiological stress (17).

In our temporal study, our findings revealed that an increasing number of leptospirosis cases fit the seasonal pattern in the high intensity of rainfall from November to March. Like Brazil, leptospirosis rates had a positive temporal correlation to rainfall levels in the rainy season ($r = 0.68$) from January to December, with the average rainfall was 158.68 mm. From 2005 - 2015, the mean rate of cases was 7.03 per 100,000 habitants from October to March (40). In Colombia, most spatiotemporal clusters were detected less than 8 months before outbreaks and correlated to rainfall anomalies induced by La Niña episodes (41). However, in general, high incidences of leptospirosis related to El Niño events on December - May, were related to the wet season with intense precipitation and severe river flooding. A low number of confirmed cases occurred in the La Niña events during the dry season. Understanding the Oceanic Niño Index (ONI) would predict leptospirosis outbreaks early (42). On the other hand, the high number of cases was also due to occupational exposure to agricultural and livestock activities during the rainy season, even when flooding occurs (43).

In order to improve the public awareness and quality of tourism in Bantul, travel-related leptospirosis needs to be considered. Several positive cases of leptospirosis were found among returning travelers from South-East Asia to the Netherlands (44). This study’s limitations were that monthly temperature and relative humidity data were only taken from 1 weather station due to limited proper tools, and missing weather data must be processed using the Amelia II package by RStudio. Lastly, there is the high under-reporting of complex leptospirosis cases in Indonesia. Finally, these findings support numerous studies that leptospirosis is a climate-sensitive disease and is predicted to increase in the future. Implementing the One Health approach should be better in predicting zoonotic outbreaks and intervention planning (45).

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CONCLUSION

In summary, our Spatio-temporal study suggested that flooding occurrence, relative humidity, and rainfall after the Cempaka Tropical Cyclone contributes to the human leptospirosis outbreak at 1 and 3 months later. It is recommended that cross-sectoral cooperation of public health authorities be conducted to integrate climatic information as an early warning for disaster-prone areas and community groups at risk. Further studies should develop any disaster-related diseases surveillance, prevention, and control strategies.

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