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A descriptive analysis of the spatiotemporal distribution of hepatitis A virus outbreak in Pacitan, East Java, Indonesia

Un análisis descriptivo de la distribución espacio-temporal del brote del virus de la hepatitis A en Pacitan, Java Oriental, Indonesia

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SUMMARY

Background: *Hepatitis A virus (HAV) is one of the most serious notifiable viral hepatitis and causing public health problems in Indonesia. The outbreaks of HAV in Indonesia have been reported in several sites from 1998-2018, however systematic epidemiological data regarding Spatio-temporal distribution of HAV outbreak are lacking. Aims: To explore, visualize, and report systematically the recent HAV outbreak and identify the socioeconomic determinants associated with the risk of HAV outbreak.*

Methods: *The study design was a retrospective cross-sectional study. Data on the incidence and distribution of HAV outbreak 2019 were collected from the database of CDC District Level Health Office of Pacitan. Maps were constructed using qGIS software to visualize the Spatio-temporal distribution of HAV outbreaks.*

Results: *Out of a total of 1 326 case records, 399 (30.1 %) were classified as probable cases of HAV, and 125 (9.4 %) as confirmed cases based on positive IgM Anti-HAV. Majorly the diagnosis was based on symptoms and exposures only, a limited number of tests was performed because testing capacity is insufficient. Majorly the cases occurred in sub-district that are*

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passed with the same river as source water in the community. The pattern of outbreak transmission is a common source. Linear regression analysis showed that proportion of low-level education (r= 1.34; p-value= 0.012), number of household (r= -1.08; p-value= 0.003), and population density (r= 1.87; p-value= 0.005) for each sub-district were significantly correlated with number of cases.

Keywords: *Geographic information system, hepatitis, epidemiological mapping.*

RESUMEN

Antecedentes: *El virus de la hepatitis A (VHA) es una de las hepatitis virales de declaración obligatoria más graves y causa problemas de salud pública en Indonesia. Se han notificado brotes de VHA en Indonesia en varios sitios entre 1998 y 2018; sin embargo, faltan datos epidemiológicos sistemáticos sobre la distribución espaciotemporal del brote de VHA.*

Objetivos: *Explorar, visualizar y notificar sistemáticamente el reciente brote de VHA e identificar los determinantes socioeconómicos asociados con el riesgo de brote de VHA.*

Métodos: *El diseño del estudio fue un estudio transversal retrospectivo. Los datos sobre la incidencia y distribución del brote de VHA 2019 se recopilaron de la base de datos de la Oficina de Salud de Pacitan a nivel de distrito de los CDC. Los mapas se construyeron utilizando el software qGIS para visualizar la distribución espaciotemporal de los brotes de VHA.*

Resultados: *De un total de 1326 expedientes de casos, 399 (30,1 %) se clasificaron como casos probables de VHA y 125 (9,4 %) como casos confirmados con base en IgM anti-VHA positivo. En su mayoría, el diagnóstico se basó únicamente en síntomas y exposiciones, se realizó un número limitado de pruebas porque la capacidad de prueba es insuficiente. La mayoría de los casos ocurrieron en sub-distritos que son atravesados por el mismo río como fuente de agua en la comunidad. El patrón de transmisión de los brotes es una fuente común. El análisis de regresión lineal mostró que la proporción de educación de bajo nivel (r= 1,34; valor de p= 0,012), el número de hogares (r= -1,08; valor de p= 0,003) y la densidad de población (r= 1,87; valor de p= 0,005) para cada subdistrito se correlacionaron significativamente con el número de casos.*

Palabras clave*: Sistema de información geográfica, hepatitis, mapeo epidemiológico.*

INTRODUCTION

Hepatitis A virus (HAV) is the most common widespread viral hepatitis and growing worldwide public health problems (1). WHO has reported nearly 1.4 million cases of hepatitis A worldwide every year, with approximately half of the cases occurring in the Asian region and endemic throughout most of South-East Asia. The viral hepatitis challenge is monumental and ironic, as the seventh leading cause of death (5.416 per year) in the world although HAV is completely preventable (2). HAV is a major public health issue globally that has not been prioritized until now (2,3). It was controlled by improvements in water, sanitation, and hygiene. However, multiple outbreaks of such preventable diseases are often reported throughout the region. The lack of consistent and credible data on the incidence of hepatitis and spread of HAV across subpopulations in South-East Asia hinders the development and monitoring of effective national policies to fight viral hepatitis (2).

The rate of infection is closely related to access to unsafe food or drinking water, inadequate sanitation, poor personal hygiene, and socio-economic factors such as population density, economic variables, and educational background (3,4). It has been shown that improvement of socio-economic status reduces the incidence of all types of viral hepatitis (3). In Indonesia, as a middle-income country, hepatitis A endemicity remains moderate-to-high and is connected to socio-economic disparities that contribute to different hygiene and sanitation standards being found in close proximity (Table 1) (5).

In 2010 there were 6 outbreaks with 279 cases, while in 2011 there were 9 outbreaks with 550 cases. In June 2012, there were 4 outbreaks with 204 cases. In 2018 there were 88 cases in Lamongan and Bangkalan, it has been assumed that poor hygiene and sanitation in canteens (no washbasins accessible) and the proximity of septic tanks to wells may have lead to the spread of HAV (4,6,8). Ministry of Health reported there were outbreaks in Pacitan (1 326 cases), and Depok (306 cases, 87 % is students) caused by contaminated food in the school canteen in 2019. The outbreak of HAV in Pacitan, East

Table 1

Outbreak hepatitis A virus in Indonesia

No.	Province	Districts	Total Case	Year	Ref (s)
1	West Java	Bogor	74	1998	(6)
2	East Java	Bondowoso	47	2004	(6)
3	East Java	Bondowoso	65	2006	(6)
4	Banten	Tangerang	17	2007	(6)
5	DI Yogyakarta	Yogyakarta	1 160	2008	(6)
6	East Java	Ngawi	146	2009	(6)
7	Riau	Bintan	87	2013	(7)
8	Lampung	Lampung Timur	11	2013	(7)
9	West Sumatera	Padang	15	2013	(7)
		Darmasraya	43	2013	(7)
10	Jambi	Jambi	26	2013	(7)
11	Central Java	Sukoharjo	26	2013	(7)
12	East Java	Pasuruan	110	2013	(7)
		Ponorogo	25	2013	(7)
		Lamongan	72	2013	(7)
		Jombang	14	2013	(7)
		Pacitan	66	2013	(7)
13	Bengkulu	Bengkulu	19	2014	(7)
14	West Sumatera	Sijunjung	159	2014	(7)
15	East Kalimantan	Paser	282	2014	(7)

Java Province (2019) which the highest number of HAV cases (1 326 cases) during the 1998-2019 period. The prevalence of hepatitis in East Java increased to 1 percent in 2013. Data from the Ministry of Health's Pusdatin recorded that there were 287 cases of HAV in East Java. Meanwhile, in 2013 there were 66 incidents in the Ngadirojo sub-district of Pacitan district mostly students were infected (7). The prevalence in the population in Pacitan as small towns (1 342.42 Km^2) is much higher than in the big cities (6). In low-income areas, the prevalence of infection is generally high, but the burden of disease is low, and HAV is not perceived to be a major public health issue (8). Pacitan had experienced an HAV outbreak in 2013, it is certainly a problem and challenge for the government. The transmission is direct contact with an infected person, thus, the population density in the region needs to be studied through mapping to prevent repeated outbreaks in the future.

Even though several incidences of HAV outbreaks in Indonesia had been reported in the last decade, according to our knowledge there are no available maps of HAV outbreak mapping to show their spatial distribution and attack rate/incidence proportion. Mapping the epidemiological distribution and incidence of HAV outbreaks will help to identify vulnerable communities and socioeconomic determinants where outbreaks pose significant threats and allocate the resources for their disease control and prevention. Since Pacitan had experienced an HAV outbreak twice in 2013 and 2019, it is important to analyze and explore the

variation of outbreak geographical locations and socioeconomic determinants. Moreover, this study is vital to provide an informed decision-making process for the local government leading to better control and prevention of HAV outbreaks in the study area.

Maps are valuable instruments for epidemiological research analysis and are especially effective in transmitting important public health messages to a wide range of audiences (8). The importance of creating an epidemic distribution map is to study the variables that have an impact on the agent, host, environment, and geography that are very helpful in trying to execute the strategy accordingly (4). A geographic information system (GIS) was used to analyzing and studying the epidemiological spread of a number of infectious diseases or outbreaks. GIS also has been used to assess the spatial and temporal patterns of outbreaks and to classify risk areas or areas of concern for the outbreak in a specific area (4). The present study aimed to report the recent HAV outbreak in the study area (Pacitan, East Java Province) and identify the socioeconomic factors associated with the risk of HAV infection in the study area using GIS-based approach analysis.

MATERIALS AND METHODS

Study population / Sample

This study was a retrospective cross-sectional observational study during hepatitis A outbreak in Pacitan, East Java, Indonesia occurred between May and October 2019. HAV outbreak data were collected from the database of CDC District Level Health Office of Pacitan. The outbreak investigation was conducted one day after the outbreak by the District Level Health Office (Dinas Kesehatan) of Pacitan. A clinically suspected case was defined as any individuals with acute symptoms including those with clinical manifestation of hepatitis were recruited and recorded. An acute clinical manifestation was defined by the onset of acute illness with a minimum of two of the following clinical symptoms: fever, malaise, flatulence, anorexia, nausea, vomiting, dark or tea-colored urine, and jaundice between May and October 2019.

A probable case was defined in the presence of jaundice/or elevated serum alanine aminotransferase (ALT/AST) more than twice the upper limit of normal or 80 IU/L in a suspected case. A confirmed case was defined as a suspected or probable case that was shown a positive result for anti-HAV IgM. The human population of the study districts, population density, household units, education categories, toilet ownership, and disparity economy value was collected from the District Central Bureau of Statistics in 2016 based on the census conducted in 2015.

Data Collection

The trained public health officers from the hospital and PHCs dedicated to the outbreak data collection and compilation input the data to the electronic case report form. The baseline characteristics of patients were collected comprising demographic, clinical, and laboratory data. Demographic data including gender, age, and address were collected. Clinical data including the status of admission (outpatient or inpatient) and clinical symptoms were recorded. Laboratory data were also compiled.

The Ethics Committee of the Faculty of Medicine, Universitas Airlangga, Surabaya had approved the research protocol. Patient consent was not required to review their medical records because the research has no more than minimal risk to the subjects. Research and data access protocol was also approved by the Center for Disease Control and Prevention (CDC) – District Level Health Office (Pengendalian dan Pemberantasan Penyakit / P2 Dinas Kesehatan) of Pacitan.

Statistical analysis and geographical mapping

We performed the descriptive analysis of the data. The comparison between two groups was conducted using the Student T-test or Mann Whitney for continuous data, and Chi-square or Fisher Exact test for categorical data. The demographic and socioeconomic data for each sub-district was collected from the Central Bureau of Statistics in 2019. Statistical analysis was conducted using SPSS v.19 (IBM Corp., NY, USA) and statistical analysis was significant if p-value < 0.05.

To demonstrate geographical variability and hepatitis A incidence, we also mapped sub-district-specific incidence using QGIS 2.18.10 (GNU General Public License, OSGeo Foundation).

Risk factor analysis

HAV outbreak is a multi-factorial viral infectious disease that is strongly associated with socioeconomic determinants. HAV cases have been reported in several varieties of settings from urban to remote rural areas with low socioeconomic status. HAV outbreaks are also considered a disease of poverty in middle and low-income areas with several determinants including high population density, lack of flushed toilets, low education level, high regional disparity index, and a number of household units in a certain area (9-11). The probability of HAV occurrence can be calculated from 5 socioeconomic variables using the Pearson correlation coefficients and their associations obtained in SPSS version 19.0 (IBM Corp, NY, US).

RESULTS

Epidemiologic Characteristics of the HAV Outbreak

In this study, we collected surveillance data of HAV infections in Pacitan, East Java Province during the outbreak from May to October 2019, and collected a number of socioeconomic variables to determine the geographic distribution of HAV outbreaks.

Among a total of 1 326 case records (Table 2), 399 (30.1 %) were classified as probable cases of HAV, and 125 (9.4 %) as confirmed cases

Table 2

Key findings from CDC – District Level Health Office of Pacitan, East Java, Indonesia

No.	Parameters (n= 1 326)	Total (%)	Percentage
1.	Age [mean±SD (years)]	34.5 ± 15.2	
	Age group, y.o [n(%)]		
	0 - 5	6	0.5
	6 - 18	232	18.8
	19 - 60	936	75.7
	> 60	62	5.0
2.	Gender [n (%)]		
	Male	716	54.0
	Female	610	46.0
3.	Symptoms [n (%)]		
	Fever	1236	93.2
	Nausea	1261	95.1
	Tea-colored urine	1257	94.8
	Jaundice	1170	88.2
4.	Laboratory parameters [median± IQR (U/L)]		
	AST	402 ± 515	-
	ALT	488 ± 343	-
5.	Status of cases [n (%)]		
	Clinically-suspected	927	69.9
	Probable	274	20.7
	Confirmed	125	9.4
6.	Patient Outcomes [n (%)]		
	Inpatient	514	38.8
	Outpatient	810	61.1

based on positive IgM Anti-HAV. Majorly the diagnosis is based on symptoms and exposures only, a limited number of the test was performed because testing capacity is insufficient to meet current needs.

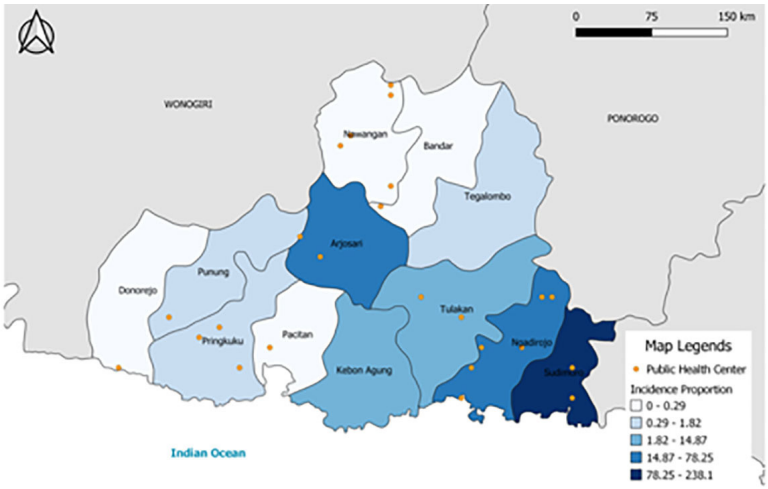

Figure 1. Clinically-reported HAV outbreak cases in Pacitan, East Java, Indonesia 2019.

The majority of cases were male, which accounted for 54.0 % of all clinically suspected cases. Most case-patients were 19 to 59 years of age (75.7 %), 0.5 % were aged 5 years or younger, 18.8 % were aged 6 to 18 years, and 5 % were aged 60 years or older. Most of the cases were managed in an outpatient setting (61.1 %). The laboratory results from the probable cases showed median serum AST level 402 U/L and ALT level 483 U/L. Almost 90 % of cases, reported classical symptoms of HAV infection.

Table 3

Clinically-suspected HAV cases based on reported sub-district in Pacitan, East Java, Indonesia

No.	Sub-districts	Total [n (%)]	Hospitalizations [n (%)]	Attack rate (%)
1.	Sudimoro	734 (55.3)	149 (20.2)	2.381
2.	Ngadirojo	362 (27.3)	269 (74.3)	0.782
3.	Tulakan	116 (8.7)	33 (28.4)	0.148
4.	Arjosari	86 (6.5)	34 (39.5)	0.218
5.	Kebonagung	13 (1.0)	4 (30.7)	0.030
6.	Tegalombo	9 (0.7)	7 (77.7)	0.018
7.	Punung	2 (0.2)	2 (100)	0.005
8.	Pacitan	2 (0.2)	1 (50)	0.001
9.	Donorojo	1 (0.1)	1 (100)	0.003
10.	Pringkuku	1 (0.1)	0	0.006
	Total	1 326 (100)	500 (37.7)	0.240

According to sub-districts that reported the HAV outbreak (Figure 1, Table 3), majorly the cases were reported in Sudimoro sub-districts, followed by Ngadirojo, and Sukorejo. However, hospitalized cases were reported mostly by Ngadirojo sub-districts. Based on the interview, Sudimoro has poor hygiene and a healthy lifestyle compared to other sub-districts. There have been 171 ODF villages in Pacitan, the most recent being the Sudimoro sub-districts.

Temporal distribution of HAV outbreak

We found a person-to-person spread as the main apparent transmission route of the HAV infection. HAV outbreak in Pacitan rapidly spread from a single sub-district to others in just 60 days. Based on the interview, the first case with clinically fever, icteric, and abdominal pain occurred in the Sudimoro sub-district on May 8th, 2019. The surveillance team found 60 cases with the same sign and symptom in other sub-district (Ngadirojo, Sukorejo, Tulakan). Geographically, the Kaligoro river in Sukorejo as source water in the community passes through the HAV outbreak area. Based on water sample inspection this river was containing an increase of E. coli that contaminated household waste. In the dry season, the area had difficulty accessing clean water.

Based on the epidemiological curve (Figure 2), the pattern of outbreak transmission is a "common source" that occurs in the Ramadhan period (May 2019), people usually buy food or water for iftar that may be contaminated. The sudden increase in the number of cases is reported after the Islamic Id Al-Fitr holiday (June 2019). In the Arjosari public health center, 71 cases (82 %) occurred in Pondok Pesantren Tremas that infected children aged 11-19 years. Arjosari has the longest duration of incidence it is around 4 months. The incidence of the outbreak was decreasing in the rainy season in November 2019.

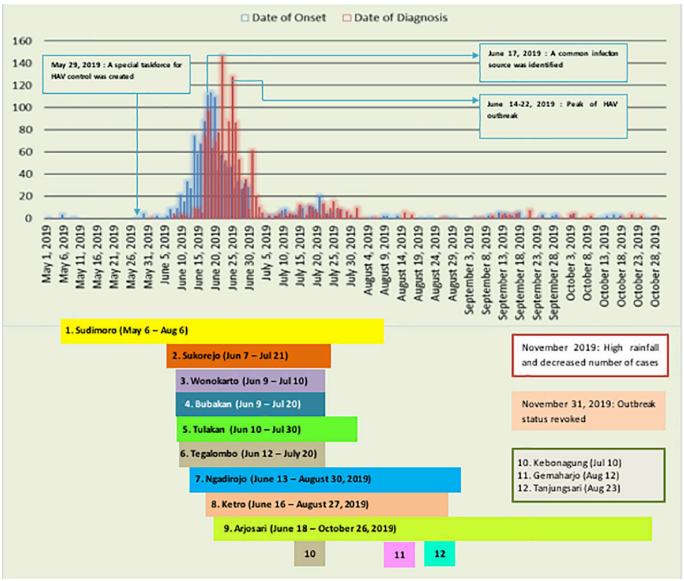

Figure 2. Outbreak curve of HAV cases in Pacitan, East Java, Indonesia

Pearson correlation matrix of socioeconomic determinants and modeling approach in HAV outbreak

The final set of socioeconomic determinants are the number of households, the proportion of household toilet ownership, the proportion of low-level education, regional disparity index, population density. We conducted Pearson correlation matrix analysis for all variables. The highest correlation coefficient is between numbers of households and regional disparity

index (0.958) followed by proportion of low-level education and population density (-0.874). However, we found significant multicollinearity among variables.

Linear regression analysis is often used to determine the probability and significance of a dependent variable based on one or several independent variables. The dependent variable represents the attack rate of HAV outbreak in a sub-district. The independent variables are a set of socioeconomic factors thought to associate with the distribution of HAV cases. Our results showed that proportion of low level education (r= 1.34; p-value= 0.012), number of household (r= -1.08; p-value: 0.003), and high population density (r= 1.87; p-value= 0.005) for each sub-district were significantly correlated with number of cases.

DISCUSSION

The incidence of HAV cases varies geographically within the study area (Pacitan District, East Java Province, Indonesia). The overall incidence of diagnosed HAV cases was 0.24 % and mainly occurred in the Sudimoro sub-district with an attack rate of 2.38 % (734 cases in 30 825 total populations) then followed by Ngadirojo with an attack rate of 0.78 %. It had already been recognized that hepatitis A is strongly related to the socio-economic and environmental factors of a country or region (12). In developing countries, such as Indonesia and several parts of Asia, hepatitis A is categorized as high endemicity (8). Several studies reported the relationship among socioeconomic variables with hepatitis A risk, including the education level, the gross domestic bruto, population density, toilet ownerships, and environmental hygiene (5,9,12,13).

Socio-economics determinants associated with HAV outbreak risk included in this study were a number of households, the proportion of household toilet ownership, the proportion of low-level education, regional disparity index, population density. The associations between these determinants and HAV risk showed significant results. The results of the analysis in this study show that the lower the educational level of the population and the higher the population density, the greater the attack rate of hepatitis A. The result means that the lower the socioeconomic level of a region, the more susceptible the adults will be infected by Hepatitis A. This finding is consistent with other studies (9,10,12,14). In Assis Brazil, for example, the poorer socioeconomic conditions (i.e. low education level) the higher the hepatitis A infection risk and this connection were statistically significant (9).

Based on surveillance data of the HAV outbreak in Pacitan, the majority of cases were male. It is a similarity to previous studies of Hepatitis A cases in Jember (2013) and Bondowoso (2016). Men have a lower awareness of their healthy lifestyle and more often consume food outside the home (4). Most cases in Pacitan were young adults, related with studies in Kerala, India at 2017 were 81 % in adults/young adults (15). In the Arjosari sub-district, most young adult cases occurred in boarding schools. Studies in Cirebon (2018), there were risk factors of hepatitis that occur in boarding school, such as the habit of washing cutlery without soap, using cutlery, and drinking together (16). From the cutlery used together were likely transmission of the disease occurs. The most dominant variables are eating together in one place and snack habits (17). Young adults have a high level of mobility and habit of snack outside the home, are lack in behaving in a clean and healthy life. They also in overseas areas where they live with their friends, and the level of interaction with each other is also high (18).

Majorly the cases were reported by the Sudimoro sub-district, this area was the eastern boundary of Pacitan, and far from urban development (19). The inaccessible health facilities and slow information in rural areas also tend to make people hard to come to health facilities, people are constrained by access, such as geographical access, length of travel, and transportation (20). From geological factors, it is considered much more difficult to get clean water sources (21). In Southern Sumatra (2000), there is a water-borne hepatitis A outbreak that infected individuals were more likely to have consumed water from a public well, and more likely to have used a dry pit outside their house for human waste disposal (5).

In a rural area like Pacitan, community outbreaks owing by poor hygiene and sanitary

practices (5). HAV virus spreads through food or water contaminated with the feces of infected people (4). Soil and water are places where the HAV virus can remain stable for a long time, especially during the rainy season, which probably helps the virus to percolate along with water to contaminate wells (15). Another case in Central Java shows a significant correlation between hepatitis A and water source because the transmission is through contaminated food or drink, that contain the virus from water with poor environmental conditions (14). Studies in an economically disadvantaged area in southern China, Yujia village reports in developing areas with poor living conditions such as an inadequate water supply, poor sewage facilities, and substandard sanitary conditions, the level of HAV transmission within the community is high (13).

Based on data, HAV outbreak Pacitan rapidly increase during Ramadhan (May 2019) and after Eid al-Fitr (June 2019) public holiday (Figure 2). The sudden increase in numbers of hepatitis A cases can be associated with socioeconomic status, sanitation, and lack of access to safe drinking water (22). Culturally, Ramadhan's largest and one of the most important holidays of the year, which usually followed with returning people to their family/hometown and cultural visitation to the neighborhoods for celebrating Id Al-Fitr by eating together. People tend to share the food without considering the hand and food hygiene, and also the source of food material that is used. The practice of poor hand washing is also a risk factor because it results in a risk of HAV entering the body when eating becomes large (4). Studies show that people who frequently purchased outside food have a higher risk (5).

The epidemiology of Hepatitis A outbreaks in Indonesia as developed countries remain moderate-to-high and is linked to socioeconomic differences (23) that lead to different standards of hygiene and sanitation is found (5). Based on East Java Regional Development and Planning Agency (BAPPEDA JATIM) data 2018. The number of people with poor economic levels in 2017 in Pacitan was recorded at 85 260 people (24). East Java was dominated by the elderly who had low education like primary school and under (25). The average education level of age 15 and over as much as 67.97 percent have graduated from primary or secondary school (24). People with a lower level of education have the possibility of morbidity caused by an unhealthy lifestyle and poor prevention action (25).

CONCLUSION

Based on our analysis of the HAV outbreak, we identified the distribution and incidence of HAV outbreak in the study area. The importance of socioeconomic determinants and values of Geographic Information System in the mapping the epidemiological distribution and incidence of HAV outbreak.

Conflict of Interest

The authors have no conflicts of interest in this study.

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