Spatiotemporal proximity of rubella cases to the occurrence of congenital rubella syndrome in Yogyakarta, Indonesia

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ABSTRACT

Introduction: Rubella infection during early pregnancy may cause fatal consequences such as congenital rubella syndrome (CRS). The incidence rate (IR) of CRS confirmed cases in Yogyakarta, Indonesia between July 2008 and June 2013 was high at 0.05 per 1,000 live births. This study aimed to discover the spatiotemporal pattern of rubella and CRS and also identify whether the proximity of rubella cases was associated with the occurrence of CRS cases.

Methods: This observational research used a spatiotemporal approach. We obtained CRS and rubella surveillance data from Dr. Sardjito Hospital, Provincial, and District Health Offices in Yogyakarta, Indonesia during January-April 2019. The home addresses of rubella and CRS cases were geocoded using the Global Positioning System. Average of the nearest neighbour and space-time permutation analyses were conducted to discover the spatiotemporal patterns and clusters of rubella and CRS cases.

Results: The peak of rubella cases occurred in 2017 (IR: 22.3 per 100,000 population). Twelve confirmed cases of CRS were found in the 2016-2018 period (IR: 0.05 per 1,000 live births). The occurrence of CRS in Yogyakarta was detected 6-8 months after the increase and peak of rubella cases. The spatiotemporal analysis showed that rubella cases were mostly clustered, while CRS cases were distributed in a dispersed pattern. Rubella cases were found within a buffer zone of 2.5 km from any CRS case.

Conclusions: Rubella cases were spatiotemporally associated with the occurrence of CRS in Yogyakarta. We recommend strengthening the surveillance system of CRS and rubella cases in order to contain any further spreading of the disease.

KEY WORDS:
Congenital rubella syndrome, rubella, spatial-temporal analysis, Yogyakarta, Indonesia

INTRODUCTION

In Indonesia, rubella is one of the significant public health problems that require effective prevention. Typically, in 77% of cases, it is young children under 15 years of age who suffer from rubella. Data from the Ministry of Health recorded the number of rubella cases in Indonesia in a five-year period between 2014 and July 2018 identifying 5,737 positive rubella patients.[1]

In the year 2015 and 2016, 13 CRS sentinel hospitals reported 226 CRS cases consisting of 83 confirmed cases and 143 clinical cases. From the 83 laboratory confirmed cases reported, the three main clinical manifestations were heart abnormalities (77%), cataracts (67.5%), and deafness (47%).[2]

Yogyakarta, situated in the middle part of southern Java, is one of the 34 provinces in Indonesia. Yogyakarta is bordered by the Indian Ocean to the south, East Java Province to the northeast, and southeast, and Central Java Province to the West and Northwest. Based on the geographical conditions, Yogyakarta is located on several different physiographic stretches between the slopes of the Merapi mountain, low land areas, Menoreh mountains, and Seribu mountains. Different geographical conditions can be distinguished in the demographic profiles of these areas.[3]

The number of laboratory-confirmed CRS cases among Indonesian infants is high. Among the symptoms of rubella, hearing impairment is the most common clinical feature found in infants with CRS. Recent research findings have indicated the importance of the implementation of rubella vaccination in the national immunisation program in Indonesia. Research also recommended that a CRS hospital-

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based surveillance program should be conducted in all hospitals in Indonesia.[4]

In order to achieve the global targets for measles elimination and rubella / CRS control by 2020, Indonesia began introducing rubella immunisation into the national routine immunisation program starting with the campaign launching and implementation of measles rubella (MR) immunisation in August-September 2017 with the target age of between nine months to <15 years.[5]

Research conducted by Asriati in 2017 showed that the burden of rubella in Yogyakarta was high, with an incidence rate (IR) in 2015 of IR: 20.68 per 100,000 population. There were clusters of rubella cases in three sub-districts of three districts in Yogyakarta which indicated the existence of herd immunity, while most districts in Yogyakarta did not have herd immunity.[6]

This study aimed to discover the spatiotemporal patterns of rubella and CRS cases and to identify whether the proximity of rubella cases was associated with the occurrence of CRS cases.

MATERIALS AND METHODS

Study design, site and data collection

This study was an observational research using a spatiotemporal approach. We obtained CRS data from Dr. Sardjito Hospital (DSH) as a sentinel hospital of CRS, and rubella cases data from case-based measles surveillance from the Yogyakarta Provincial Health Office, and five District Health Offices in Yogyakarta during January-April 2019. Home addresses of rubella and CRS cases were visited and geocoded using the Global Positioning System (GPS). Some locations of unknown cases were estimated using Google Maps.

Criteria of case enrolment

Rubella cases were patients with positive laboratory results as rubella, and CRS cases were those with final diagnoses confirmed as CRS. Distribution of rubella, CRS and risk factors of CRS cases data were obtained between January 2016 and December 2018, whereas data from spatial distribution for CRS cases were obtained from CRS cases born between September 2016 and June 2018, and rubella cases which occurred between January 2016 and December 2017.

Data management and analysis

Average nearest neighbour and space-time permutation analyses were done to discover the spatiotemporal pattern and clusters of rubella and CRS cases. Distributions of rubella and CRS cases with the characteristics of risk factors of CRS were analysed descriptively.

Ethical considerations

The research was conducted after obtaining approval from the Medical and Health Research Ethics Commission of the Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada with Ref: KE/FK/0070/EC/2019 and recommendations from the licensing services.

RESULTS

Congenital Rubella Syndrome case distribution

There were 40 CRS cases reported during January 2016 to December 2018 in DSH. From those, only 12 cases came from the Yogyakarta Region (IR: 0.05 per 1,000 live births). Most cases were boys (42%), aged under six months (66.7%), and located in Bantul District (50%). Clinical manifestations of CRS were congenital heart disease (75%), hearing impairment (75%), microcephaly (67%) and congenital cataracts (50%). Risk factors of CRS were the appearance of clinical symptoms such as fever and rash (58%) during pregnancy. About half of the cases reported fever and rash in the first trimester of pregnancy. All the mothers did not have a history of rubella immunisation (Table I).

Rubella case distribution

During January 2016 to December 2018, incidence rate (IR) of rubella in Yogyakarta was high. The peak of rubella cases occurred in 2017 (IR: 22.3 per 100,000 population). Following the introduction of the measles rubella vaccination in all Java Provinces which began between August and September 2017, then the number of rubella cases in Yogyakarta dropped significantly in 2018. Most of the rubella cases involved children aged 5-14 years (48.15%) and women (56.37%), with the highest number of cases in the Gunungkidul District (25.82%) (Table I).

Temporal distribution of CRS and rubella cases

There was a peak of CRS cases based on the month of birth in June 2016, and this was suspected to be due to a peak of rubella cases in November 2015 (not illustrated in the graph). The range between the peak rubella cases and the occurrence of CRS cases was around 6 to 8 months. After that period, a small peak of rubella cases reappeared in October 2016, and around eight months later, in June 2017, there was only one case of CRS. The highest peak of cases of rubella occurred in April 2017, but enigmatically, 6-8 months later no cases of CRS were found. The CRS cases then appeared in January 2018 six months after the increase in the rubella cases in July 2017. The peak of the rubella cases reappeared in August 2017 after which six to eight months later, a single CRS case occurred between February - April 2018 (Figure I).

Spatial-temporal analysis of CRS and rubella cases

We managed to collect Global Positioning System (GPS) coordinates data of many of the CRS and rubella cases. There were 404 coordinate points from cases in 2016 and 687 coordinate points from cases in 2017 of the rubella cases. Whereas only five coordinate points of CRS cases fulfilled the inclusion criteria.

a. *Distribution pattern of rubella and CRS cases using average nearest neighbour analysis*
   The results of the average nearest neighbour analysis using Quantum GIS 3.6 software found z-score of -27.1236 and a p-value of <0.001 which indicates that rubella cases in the Yogyakarta Province between January 2016 to December 2017 have a clustered distribution pattern, whereas CRS cases showed a dispersed pattern with p-value<0.001 and z-score of 4.908627.
b. *Cluster analysis of rubella cases using space time permutation analysis*
   Space time permutation analysis used SaTScan v9.6 and

Table I: Characteristics of CRS and rubella cases during January 2016-December 2018

Characteristics	n(%)
CRS cases (N=12)	
Age	
<6 months	8(67)
>6 months	4(33)
Gender	
Boys	7(58)
Girls	5(42)
Residences	
Bantul District	6(50)
Gunungkidul District	1(8)
Kulon Progo District	2(17)
Sleman District	2(17)
Yogyakarta Municipality	1(8)
Clinical manifestation	
Congenital heart disease	9(75)
Hearing impairment	9(75)
Microcephaly	8(67)
Congenital cataract(s)	6(50)
Developmental delay	5(42)
Splenomegaly	3(25)
Icteric 24 hours postpartum	2(17)
Meningoencephalitis	1(8)
Fever and rash history of the mother during pregnancy	
Yes	7 (58)
No	5(42)
Gestational age at the mother's history of fever and rash	
First trimester	6(50)
Second trimester	1(8)
Unknown	5(42)
History of mother's rubella immunization	
Yes	0(0)
No	12(100)
Rubella cases (N=1437)	
Age	
<1	47(3.28)
1-4	123(8.58)
5-9	361(25.19)
10-14	329(22.96)
>15	573(33.99)
Gender	
Men	627(43.63)
Women	810(56.37)
Residences	
Bantul District	225 (15.66)
Gunungkidul District	371(25.82)
Kulon Progo District	279(19.42)
Sleman District	339(23.59)
Yogya Municipality	223(15.52)

the visualisation in GPS mapping used Quantum GIS 3.6 software. The distribution of rubella cases from January 2016 to December 2017 obtained 12 clusters, including a most likely cluster and 11 secondary clusters. The most likely cluster (cluster 1) occurred in the period 1 between May 2016 and 31 December 2016 with a radius of 6.87 km (p-value<0.001). Secondary clusters included 11 clusters, with p-value <0.05 in six clusters (clusters 2-7) and p-value >0.05 in five clusters (clusters 8-12). The results of the analysis are shown in Table II, while cluster visualisation is shown in Figure 2. Next, the rubella clusters were layered with CRS cases which fulfilled the inclusion criteria indicating that there were three occurrences of CRS in the rubella cluster circle, and two CRS cases outside of the rubella cluster circle. Of the 12 clusters that existed, there were nine other clusters that were not identified as having CRS cases in them (Figure II). Geographically viewed, six clusters were in the border areas. This spatiotemporal pattern is interesting considering that the clusters were only in the border areas, whereas Gunungkidul borders with the Indian Ocean, Klaten and Sukorejo Districts, the slopes of Mount Merapi in Sleman, while the area of Kulon Progo borders with Purworejo and Magelang which have quite difficult and limited access.

c. *Proximity of rubella cases to the occurrence of CRS cases*

A buffer analysis was conducted to ensure the CRS cases were not in the cluster circle. Correlation analysis was done between rubella exposure and the occurrence of CRS to obtain more detailed information regarding the possibility of rubella infection due to exposure to rubella cases which occurred in the first trimester of pregnancy in

Table II: Cluster analysis of rubella cases

Cluster	Location	Radius (km)	Observed/ Expected	Test statistics	Time frame	p-value
1	Samigaluh, Girimulyo, Kalibawang	6.87	3.97	21.105587	2016/5/1-2016/12/31	0.000
2	Saptosari, Paliyan, Panggang	5.14	3.18	18.226380	2017/1/1-2017/4/30	0.000
3	Pakem, Cangkringan	5.22	3	14.459460	2016/1/1-2016/8/31	0.000
4	Wates, Pengasih, Sentolo, Sedayu, Nanggulan, Lendah	6.77	2.86	14.245271	2016/1/1-2016/4/30	0.000
5	Karangmojo, Ponjong, Semanu	5.66	4.91	13.603599	2016/9/1-2016/12/31	0.000
6	Nglipar, Ngawen, Gedangsari	5.49	2.11	11.828534	2017/5/1-2017/8/31	0.000
7	Banguntapan, Kota Gede	1.43	3.86	8.572765	2017/5/1-2017/8/31	0.020
8	Kretek, Pundong, Bambanglipuro, Pandak, Jetis, Imogiri, Dlingo, Pleret, Banguntapan, Sewon, Bantul, Pajangan, Piyungan	10.75	2.09	7.488076	2016/1/1-2016/4/30	0.083
9	Ngaglik, Ngemplak, Pakem	2.85	4.44	6.463667	2017/9/1-2017/12/31	0.325
10	Gondokusuman, Umbulharjo, Mergangsan, Gondomanan, Depok, Banguntapan	2.02	2.66	5.357924	2017/1/1-2017/4/30	0.768
11	Gamping, Godean	2.19	2.83	4.753307	2016/5/1-2016/12/31	0.940
12	Gedongtengen, Wirobrajan	1.09	9.77	4.148380	2016/5/1-2016/8/31	0.996

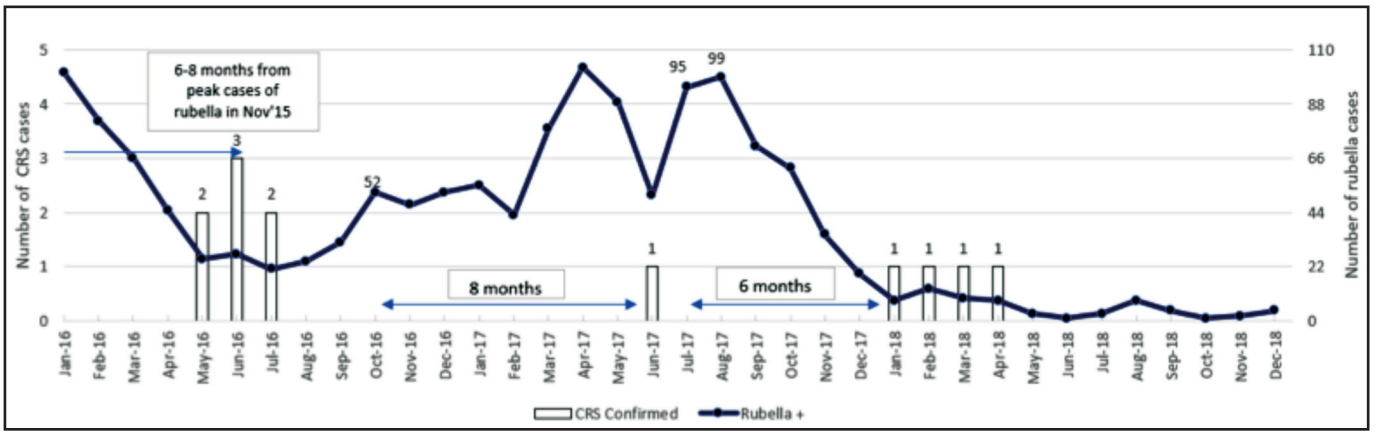

Fig. 1: Distribution of rubella cases to the occurrence of CRS by time.

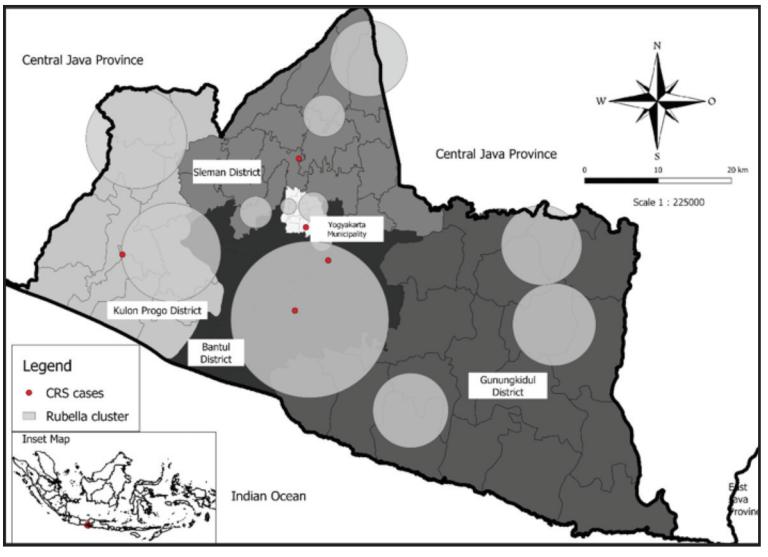

Fig. 2: CRS cases located within the radius of rubella cluster.

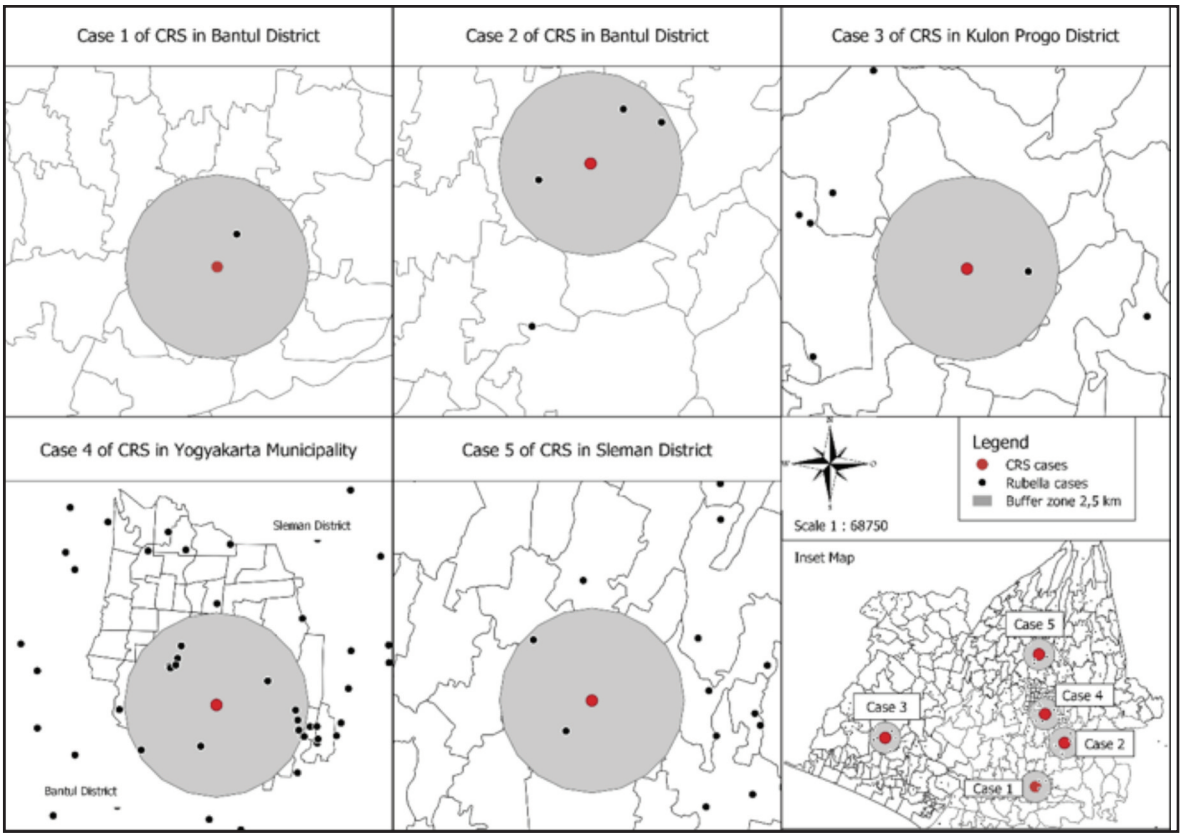

Fig. 3: Spatiotemporal distribution of occurrence of CRS by rubella case in the first trimester of pregnancy.

mothers who give birth to CRS cases using buffer analysis in Quantum GIS 3 software. The results of the analysis showed that in all the first trimester of pregnancy of mothers who gave birth to CRS cases, there was a case of rubella positively confirmed within a radius of 2.5km (Figure 3).

DISCUSSION

CRS was identified in DSH in as many as 12 confirmed CRS cases, with clinical symptoms of congenital heart disease (75%), hearing impairment (75%), microcephaly (67%) and congenital cataracts (50%) (Table I). Robertson et al., documented the following symptoms among infants with CRS, finding hearing impairment (60%), congenital heart disease (45%), microcephaly (27%), cataracts (25%), purpura (17%), hepatosplenomegaly (19%), mental retardation (13%), and meningoencephalitis (10%).[7] The study conducted by Herini et al., in 2018 in the same site studied between 2008-2013 also found that clinical manifestations in CRS cases were congenital heart disease (83.3%), hearing loss (75%), congenital cataracts (66.7%) and microcephaly (50%) (8). A prospective study conducted by Herini et al., in 2017 indicated CRS clinical manifestations included hearing loss (100%), congenital cataracts (72.7%), microcephaly (72.7%) and congenital heart disease (45.5 %).[4] There were eight cases found (66.7%) of CRS in infants aged under six months (Table I). This finding is in line with the research of Herini et al., that found that 90% of cases showed positive IgM results at <6 months of age.[4] The results were also similar with a study conducted by Toda et al., in 2015 that found in most CRS cases, positive IgM was detected at less than seven months of age.[9]

The incidence of CRS identified in Yogyakarta occurred about 6 to 8 months after the increase and peak of the cases of rubella (Figure 1). This finding is in line with the research conducted by Toda et al., which identified the peak of CRS cases was between 6-8 months after the peak of the rubella outbreak).[9] Lanzieri et al., in 2003 also stated that the peak incidence of CRS occurred seven months after the peak of the rubella outbreak in Brazil in 2000.[10] Similar with the results of a study in Japan, the peak CRS cases occurred 33 weeks after the peak of rubella cases in 2013.[11] These results also support the premise that rubella exposure in the first trimester of pregnancy leads to the incidence of babies born with CRS (Figure 3). Counterintuitively, the peak of rubella cases was found in April 2017 but after 6-8 months there were no CRS cases. CRS cases in this study were only obtained from Dr. Sardjito Hospital as a sentinel hospital of CRS, because only this hospital could confirm CRS cases in Yogyakarta. There were possible cases of CRS in other hospitals in Yogyakarta, but the confirmed CRS cases could only could be diagnosed in DSH as a CRS sentinel hospital in Yogyakarta becoming a limitation of this study.

Rubella infection during pregnancy is known to cause defects in the foetus. CRS occurs in 90% of babies born to women infected during the first trimester of pregnancy.[12] In this study, of the seven cases that had the onset of symptoms of

fever and rash during pregnancy, six cases occurred in the first trimester of pregnancy. Moreover, there were five cases (41.7%) that did not have a history of fever and rash. All of the mothers did not have a history of rubella immunisation. Research conducted by Zanga et al., in 2017 among pregnant women in the Congo showed high seropositivity, while they had no history of rubella vaccination. Symptoms of fever were only found in about 2.5% of cases, and non-specific symptoms of rubella were found in 10.26%.[13]

In children, rubella infection is usually asymptomatic or with mild symptoms accompanied by a rash that quickly disappears, which is often overlooked. In adults, infections are generally accompanied by more pronounced symptoms of the disease, although they also tend to be mild.[14] Interestingly, about 20-50% of infected patients show no symptoms.[15]

Primary subclinical rubella is considered a significant risk for the foetus. This suspicion, based on occasional observations of individual cases, has been strengthened by a retrospective survey. A summary of the first four years of the National (of Indonesia) CRS surveillance program found that 42% of mothers with confirmation or suspected CRS could not remember having experienced a rash during pregnancy, although many of them remembered having had the disease. In a survey in America, 19-50% of mothers of confirmed CRS cases were unaware of a rash.[16-18] In this study, we also found that 41.6% of mothers did not have a history of the rash during pregnancy (Table I). Research in the Philippines showed only four cases (22.2%) had a history of rashes during maternal pregnancy.[19]

CRS surveillance is suitable for countries that want to assess whether to add the rubella vaccine to the national immunisation program. Surveillance is usually limited to children aged 0-11 months because it is difficult to ascertain rubella as a specific cause of congenital defects in older children. Parents of infants with CRS tend to look for special health facilities that are usually not involved in routine infectious disease surveillance systems, for example, eye hospitals and hospitals that specialise in cardiac surgery. For comprehensive CRS surveillance, these facilities must be included in CRS detection, investigation, and reporting activities.[7] Our results showed that CRS cases detected in the CRS Sentinel Hospital in Yogyakarta, Dr. Sardjito Hospital were not found to be from border areas in Yogyakarta (Figure 2). Gunungkidul with the highest number of rubella incidents in 2017 did not show any cases of CRS included in the inclusion criteria. Data showed that there was one case of CRS that was not included in the inclusion criteria. The case came from Wonosari, but the pregnant woman was confirmed to be rubella positive in the Ngawen Public Health Center. Gunungkidul is located about 100km from the city centre of Yogyakarta. The possibility of under reported cases can occur, but this gap in reporting requires further study, especially related to geographic conditions and social cultural aspects in the community related to health seeking behaviours.

Rubella cases were found at a distance of 2.5km from the CRS cases. The results of this study were obtained from buffer trials starting at a distance of 1km, and extended out until a distance of 2.5km was obtained from all cases of CRS and we found the coordinate points of a rubella case. Researchers have not found the optimal distance of rubella cases that can increase the risk of the occurrence of CRS case. One possible assumption is the existence of the mobility of the pregnant women because they were looking for health care facilities to check the status of their child's development in the womb. They also possibly came into contact or were exposed to the rubella virus in the health care facility. However, this possibility requires further research considering the data taken related to these risk factors used secondary data. Subsequent research is recommended to conduct in-depth interviews with mothers who gave birth to CRS cases, especially related to the history of contact with rubella cases, history of obstetric examinations, mobility especially in the first and second trimesters and information about whether there were cases of rubella around their location of house or workplace or recreation.

Our study has some limitations, such as our reporting was only including one province in Indonesia, i.e., Yogyakarta. The results might not reflect the current distribution pattern of rubella and CRS cases in whole country. Furthermore, our study should focus on females in the reproductive age group instead of the whole population of rubella cases. Unfortunately, we do not have access to data on females in the reproductive age group, therefore, we are unable to reanalyse the data to only include the population at risk, becoming another weakness of our study. The use of whole population in our study might cause the bias in the estimated ages.[11] Moreover, this study has discovered that the incidences of CRS occurred within 6-8 months after the community outbreak of rubella. As a communicable disease, pregnant woman is susceptible for getting infected from individuals with rubella cases. This finding is the first evidence in the current study site of Yogyakarta province. This temporal phenomenon is also similar with the findings in Vietnam, Brazil and Japan[9-11] that utilised number of rubella cases in the whole population, not the specific group of women in reproductive ages.

CONCLUSION

Rubella cases were spatiotemporally associated with the occurrence of CRS in Yogyakarta. We recommend strengthening the CRS surveillance system by enlarging the target population of pregnant women to include a baby born until one year old in an area with rubella cases/or CRS outbreak. Further study is needed to investigate the under reporting of CRS cases, especially after the implementation of rubella vaccination in the national immunisation program.

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REFERENCES

1. Biro Komunikasi dan Pelayanan Masyarakat Kementerian Kesehatan Republik Indonesia. Fatwa MUI Bolehkan Imunisasi Campak dan Rubella, Kemenkes Fokus Turunkan Beban dan Dampak Penyakit Tersebut. 2018 [cited 2018 Nov 30]. Available from: http://www.depkes.go.id/article/view/18082400002/fatwa-mui-bolehkan-imunisasi-campak-dan-rubella-kemenkes-fokus-turunkan-beban-dan-dampak-penyakit-te.html.
2. Kementerian Kesehatan, WHO SEARO, UNICEF. Status Campak dan Rubella Saat Ini di Indonesia 2017 [cited 2018 Sep 27]. Available from: http://www.searo.who.int/indonesia/topics/immunization/mr_measles_status.pdf?ua=1.
3. Biro Tata Pemerintahan Setda DIY. Profil Perkembangan Kependudukan Daerah Istimewa Yogyakarta Tahun 2017. Yogyakarta: Setda Daerah Istimewa Yogyakarta; 2018.
4. Herini ES, Gunadi, Triono A, Mulyadi AW, Mardin N, Rusipah, et al. Hospital-based surveillance of congenital rubella syndrome in Indonesia. Eur J Pediatr 2017; 176(3): 387-93.
5. Kementerian Kesehatan Republik Indonesia. Pedoman Surveilans Congenital Rubella Syndrome (CRS). Jakarta: Kementerian Kesehatan; 2018.
6. Asriati. Epidemiologi Rubella di Daerah Istimewa Yogyakarta: Universitas Gadjah Mada; 2017.
7. World Health Organization. Rubella and Congenital Rubella Syndrome (CRS). Western Pacific Region: World Health Organization 2017 [cited 2018 Sep 27]. Available from: http://www.wpro.who.int/mediacentre/factsheets/fs_20120228/en/.
8. Herini ES, Gunadi, Triono A, Wirastuti F, Iskandar K, Mardin N, et al. Clinical profile of congenital rubella syndrome in Yogyakarta, Indonesia. Pediatr Int 2018; 60(2): 168-72.
9. Toda K, Reef S, Tsuruoka M, Iijima M, Dang TH, Duong TH, et al. Congenital rubella syndrome (CRS) in Vietnam 2011–2012—CRS epidemic after rubella epidemic in 2010–2011. Vaccine 2015; 33(31): 3673-7.
10. Lanzieri TM, Segatto TC, Siqueira MM, de Oliviera Santos EC, Jin L, Prevots DR. Burden of congenital rubella syndrome after a community-wide rubella outbreak, Rio Branco, Acre, Brazil, 2000 to 2001. Pediatr Infect Dis J 2003; 22(4): 323-9.
11. Kinoshita R, Nishiura H. Assessing herd immunity against rubella in Japan: a retrospective seroepidemiological analysis of age-dependent transmission dynamics. BMJ open 2016; 6(1): e009928.
12. Heymann DL, editor. Control of Communicable Diseases Manual. 18th ed. Washington: American Public Health Association; 2008.
13. Zanga J, Mbanzulu MK, Kabasele AF, Ngatu NR, Wumba DR. Rubella Seroprevalence and real-time PCR detection of RUBV among Congolese pregnant women. BMC Infect Dis 2017; 17(1): 250.
14. Martin D, Schoub B. Rubella infection in pregnancy. In: Newell M-L, McIntyre J, editors. Congenital and Perinatal Infections. Cambridge: Cambridge University Press; 2000.
15. Marino T. Viral Infections and Pregnancy: Background, Clinical Presentation, Workup [cited 2019 May 7]. Available from: https://emedicine.medscape.com/article/235213-overview#a2 .
16. Smithells RW, Sheppard S, Holzen H, Dickson A. National Congenital Rubella Surveillance Programme 1 July 1971-30 June 1985. Br Med J (Clin Res Ed) 1985; 291(6487): 40-1.
17. Avery GB, Monif GG, Sever JL, Leikin SL. Rubella syndrome after inapparent maternal illness. Am J Dis Child 1965; 110(4): 444-6.
18. Cradock-Watson JE, Ridehalgh MK, Anderson MJ, Pattison JR. Outcome of asymptomatic infection with rubella virus during pregnancy. J Hyg (Lond) 1981; 87(2): 147-54.
19. Lopez AL, Raguindin PF, Jonas Del Rosario J, Najarro RV, Du E, Aldaba J, et al. The burden of congenital rubella syndrome in the Philippines: results from a retrospective assessment. Western Pac Surveill Response J 2017; 8(2): 17-24.