Diphtheria Outbreaks in Indonesia 2017 Prevention for Asian Games and Asian Para Games Events

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Abstract. Asian Games and Asian Para Games 2018 were held consecutively in August and October 2018 in Indonesia. Unfortunately, national diphtheria outbreak in Indonesia occurs from December 2017 to February 2018. The Outbreak Response Immunization (ORI) commenced on 11 December 2017 for the affected regions. The aim of this study is to describe the issues with diphtheria case notifications and ORI uptake rate for the Asian Games and Asian Para Games Venues. Data were collected from the National surveillance dataset and Provincial Health Offices of the four provinces via the surveillance district officers. Routine immunization coverage, diphtheria cases and ORI coverage from four respective provinces from January 2017 to 31 October 2018. All notifications and reference laboratory data were used. The variables were analyzed descriptively in tables, graph, and map. A total of 260 cases were reported in 11 districts in South Sumatra, West Java, Jakarta, and Banten. One case was excluded because of missing data. There were 129 case notifications within the target age group of interest. The first round of immunization uptake rate was poor during the outbreak immunization response (ORI). However, for the second round improved in most of the districts. The decline in cases in most districts can be attributed to the quick response of the health authorities to contain the outbreak. They implemented measures including active case finding, contact tracing and an active increase in risk communication and public health education, especially focused on vulnerable groups for the target age groups between the ages of 1 to 18 years old. Highly dense urban areas in the affected provinces with the highest incident rates were also targeted in areas of mass gathering (e.g. shopping centers). Neighboring areas around the venues of the Asian Games 2018 were also targeted as areas to improve immunization rates.

Keywords: Diphtheria · Outbreak · Asian Games · Asian Para Games

I. Nurlaila et al. (Eds.): ICHR 2022, AHSR 56, pp. 683–696, 2023.
https://doi.org/10.2991/978-94-6463-112-8_62

1 Introduction

Diphtheria is a vaccine preventable disease (VPD), caused by a gram-positive bacteria *Corynebacterium diphtheriae* strain. Surveillance definitions may vary between countries on whether to include toxigenic and non-toxigenic forms of *C. diphtheriae* [1]. In 2018, the World Health Organization (WHO) recommended surveillance standards only include the toxigenic form. However, there are non-toxigenic strains which are not vaccine preventable [2, 3]. Humans are a known reservoir of *C. diphtheriae* and the infection occurs from human-to-human droplet transmission Untreated cases usually result in up to 50% mortality rate. Even with antimicrobial treatment. Common presentation of diphtheria often involve the upper respiratory mucosa, tonsils, and even the skin with an incubation period of two to five days[4–7]. The classic symptom is the formation of a pseudo-membrane that typically develops in the tonsils. Non-toxigenic strains can also cause disease; respiratory symptoms are milder and do not present with a pseudo-membrane. Additionally, both toxigenic and nontoxigenic *C. diphtheria* strains can also be invasive and cause complications such as sepsis and endocarditis [2, 4, 6–8].

In the non-immunized groups, children under the age of 5 are commonly affected. Although the vaccine-induced immunity is only directed at the toxin produced by *C. diphtheriae*, some European countries have shown a near elimination of diphtheria cases by achieving the necessary herd immunity levels as a result of mass immunization.

In 2017, a total of 954 case-notifications of suspected, probable, and confirmed diphtheria in the 30 provinces of Indonesia with 44 deaths (Country CFR: 4.61%) [9]. Most notifications were from the provinces of East Java, 331; West Java, 170; Banten, 127 and Aceh, 109. The annual 2017 CFR by province is 3.63% in East Java, 12/331; 8.24% in West Java, 14/170; 6.3% Banten, 8/127; 3.67% in Aceh, 4/109. In Bangka Belitung Islands, the CFR rate was 50%, 2/4; 9.09% in Riau, 1/11; 10% in Kalimantan Barat, 1/10; and 3.64% in DKI Jakarta, 2/55. The notifications started increasing in November 2017, which indicated a possible nation-wide diphtheria outbreak [9].

Diphtheria outbreaks are an ongoing problem in Indonesia, which has one of the highest incidences globally [4, 10–15]. Indonesia had a mean DTP3 vaccination rate of 82% between 2011 to 2015 [1, 2]. The vaccination schedule is three doses with four boosters which is supposed to be completed by 8 years old [2]. Immediate countermeasures for a diphtheria outbreak in Indonesia taken included active case finding; contact tracing; an increased risk communication through preventative public health education especially focused on the target vulnerable groups for Outbreak Response Immunization (ORI), initiate on 11 December 2017 in close coordination with the South-East Asia Region office (SEARO) of the WHO [9]. The original aim is to achieve a coverage of $>$ 90% in the target age groups, those aged between 1 to 18 years old, within the districts and neighboring areas around the Asian Game venues [2]. Furthermore, the urgency for ORI commencement stems from the August 2018 Asian Games and Asian Para Games.

Since August 2018, vaccination priority has been carried out on at-risk populations, with a target age range of 1 to 19 years, located in 11 districts. Jakarta [5 districts], West Java [4 districts], Banten (1 district), South Sumatra (1 districts). The 2018 Asian Games were held simultaneously in two cities, namely DKI Jakarta and Palembang. The Asian Games and Asian Para Games venues are located in 11 regencies/cities. Some of the athletes and visitors came from participating countries, such as India and Nepal, where these areas have the highest incidence of diphtheria in Asia [2, 16, 17].

The aim of the study is to identify the issues with diphtheria case notifications and the immunization uptake rate, in response to the outbreak, for the Asian Games and Asian Para Games venue. Eleven districts within three provinces will be analyzed for cases before and after the ORI was initiated. The ORI uptake rates will be reported for the first and second round using census 2010 data for each district. Those not within the target age range are included to evaluate if a need to vaccinate adults beyond the target age groups.

2 Materials and Methods

2.1 Study Area

The study areas were located in DKI Jakarta which are consist with Jakarta Selatan, Jakarta Utara, Jakarta Timur, Jakarta Barat and Jakarta Pusat. Within West Java, the targeted city districts are Kota Bekasi and Kota Depok while the regencies are Bogor and Bekasi. In Banten and South Sumatra, the city districts are Kota Tangerang and Palembang respectively (Fig. 1).

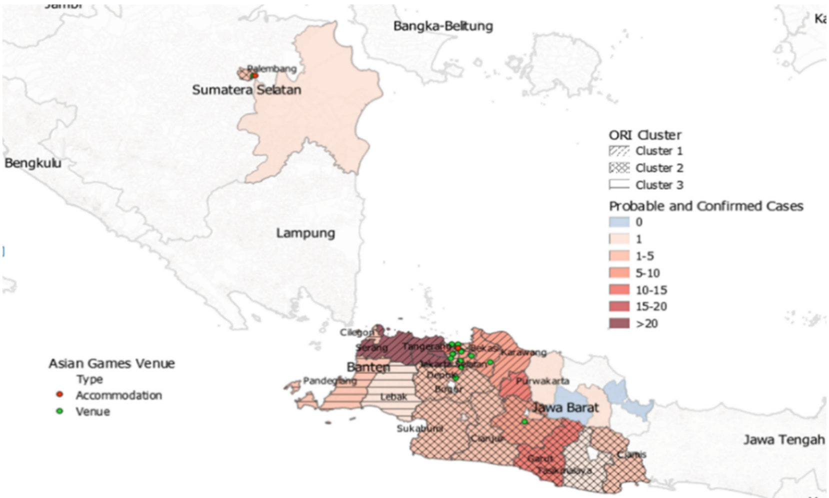

Fig. 1. Map of Diphtheria cases (probable and confirmed not inclusive of suspected) and ORI cluster areas with Asian Games/Para Games 2018 venues for 2017 only.

2.2 Case Definitions

The standard 2014 WHO guidelines recommend that only probable and confirmed cases are included as part of the surveillance standard. A probable case of diphtheria was defined as any Indonesian resident in the month of December 2017, who has seen a doctor and developed the following symptoms:

- a sore throat with difficulty in swallowing, difficulty in breathing, inflammation of either the larynx, pharynx or tonsils.
- and an adherent whitish or grayish pseudo-membrane on the tongue, palate, throat or nose [1, 13, 14, 16].

A confirmed diphtheria case was a probable case confirmed by isolation of C. diphtheriae from the nose or throat; OR Histopathologic diagnosis; OR epidemiologic linkage to a laboratory-confirmed case of diphtheria [2, 18]. Countries with high incidence of diphtheria are reliant on symptoms to diagnose likely genuine cases [4]. In Indonesia's case, all suspected, probable and confirmed cases are reported and entered into the surveillance system.

2.3 The Outbreak Response Immunization (ORI) Clusters

The Outbreak Response Immunization (ORI) commenced on 11 December 2017 in the affected regions of West Java, Banten and the capital region of DKI Jakarta (under the category of province). DKI Jakarta is the most populated city in Southeast Asia with an approximated 10.15 million while surrounded by West Java, the most populated province, with 46.66 million. East Java's ORI commenced in February 2018 as the fourth cluster. The first initial Outbreak Response Immunization (ORI) concentrated on DKI Jakarta, West Java and South Sumatra because of the upcoming Asian Games and Asian Para Games 2018. The main international airport, Jakarta International Airport (Soekarno-Hatta), is situated in the city of Tangerang, Banten province. The ORI was carried out based on three clustered phases for the target group (aged one to below 19 years old) in West Java, Banten, DKI Jakarta and South Sumatra (see Table 1).

2.4 Data Collection

Data were collected from the National surveillance dataset and Provincial Health Offices of the four provinces via the surveillance district officers. Variables in the datasets consisted of health care facilities (hospital/primary health settings/clinics or any of the two) which admitted or saw the notified cases; demographic characteristics (age, sex, and region); antimicrobial and anti-diphtheria toxin administration; immunization status; number of deaths; and laboratory confirmation. Routine immunization coverage, diphtheria cases and ORI coverage from four respective provinces were collected from January 2017 to 31 October 2018. All notifications and reference laboratory data were used, regardless of whether it has missing data, suspected, probable and laboratory confirmed cases in the 11 districts.

Table 1. Table of Outbreak Response Immunization (ORI) concentration area (*Excluding fourth cluster which only includes East Java*)

Cluster	Immunization Rounds	Date	Regencies/City	Province/Capital
1	1	December 2017	12	**DKI Jakarta**, **West Java**, Banten
1	2	February 2018		
1	3	August 2018		
2	1	February 2018	24	**West Java**, **South Sumatra**, West Sumatra, Aceh, Lampung, West Kalimantan Barat, South Kalimantan, East Kalimantan.
2	2	June 2018		
2	3	December 2018		
3	1	February 2018	6	**DKI Jakarta**, Banten,
3	2	April 2018		
3	3	October 2018		

2.5 Data Analysis

All variables were analyzed descriptively in tables. Each district ORI coverage and cases, occurring before and after the ORI initiation, were grouped into the target ORI age group (one to below 19 years old) and non-target age group (below one and above or equals to 19 years old). Post-ORI grouping refers to total number of cases occurring a month after ORI was initiated and up to end of October 2018. Microsoft Excel was used for data cleaning and visualization.

The ethical approval was obtained from The City University of Hongkong, Hong Kong, China (ethical reference: 2-3-201809_02).

3 Results

For January 2017 to 31 October 2018, there were 260 cases reported in the 11 districts (See Fig. 2). There was missing data on the age of one case. There were 259 reported cases, classified into the non-target and target group in Table 2. There were 129 case notifications within the target age group of interest. A month after ORI initiation in August to October 2018), there are 76 case notifications. For cases in the non-target age group, there were 35 case notifications prior to the ORI intervention, and after, 25 notifications. Only 9 reference laboratory results could be definitively linked to the surveillance data.

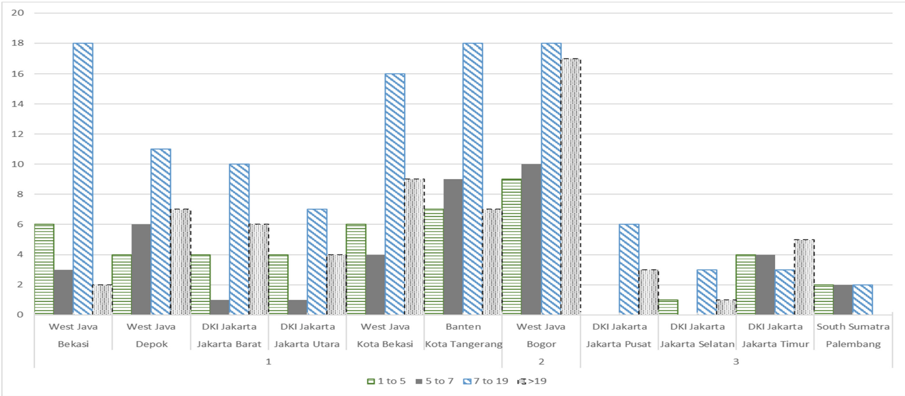

Fig. 2. Diphtheria case notifications by age groups from January 2017 to October 2018 per City/Regency, Province and Clusters

For the first round of ORI, Jakarta Pusat reaching 561.58% and Jakarta Utara reaching a target of 100.45% while the remaining three districts reported below 4% (range: 0.07% to 3.67%). After recalculating against the population of the capital region of DKI Jakarta, the overall ORI coverage for the target group was actually at 65.31%. Jakarta Pusat and Jakarta Timur had no cases occurring in the target group post-ORI while Jakarta Selatan, Jakarta Barat and Jakarta Utara reported a decline for the same group. In the non-target group, Jakarta Pusat and Jakarta Utara had reported one case and three cases respectively post-ORI.

The city district of Kota Bekasi and the regency of Bekasi reported 15 cases and 18 cases in the target group post-ORI respectively while the regency of Bekasi also had two cases in the non-target group post ORI. However, their ORI uptake rate in the first round is low: 6.75% for Kota Bekasi and 5.80% for Bekasi.

For the ORI, there were a subsequent increase in the second uptake for the target group in all selected districts except for DKI Jakarta Pusat which initially registered 561.58% and Jakarta Utara at 100.45 (see Table 2) compared to the other districts in DKI Jakarta which ranged between 0.08 to 3.67 in the first round. After the ORI commenced, there was still an increase seen in the non-target group in Bekasi, Bogor, Jakarta Utara and Kota Depok while Kota Bekasi reported an increase in the target group. The vaccination coverage in Kota Bekasi was estimated to be at 6.75% for the first round and 65.69% for the second round. We also found that there is significant different number of diphtheria cases at pre and post ORI responds in DKI Jakarta province (P value = 0.007).

Table 2. Table of *ORI coverage and cases reported in 2017 to October 2018*

Cluster	Province	City district/Regency	Age Groups*	Number of sub population*	% of population	First Round (R1)	R1%	Second Round (R2)	R2%	*Number of Pre-ORI Cases (including ORI month)*	*New Cases counted up to Oct 2018*	*Pvalue*
1	West Java1	Bekasi	1 to < 19 (Target)	1,145,059	43.53	**66444**	**5.80**	**1004784**	**87.75**	9	18	0.205
1	West Java	Bekasi	Non Target (<1 and ≥ 19)	1,485,342	56.47					0	2	
2	West Java	Bogor	1 to < 19 (Target)	2,031,439	42.57	**417425**	**20.55**	**863936**	**42.53**	20	17	
2	West Java	Bogor	Non Target (<1 and ≥ 19)	2,740,493	57.43					6	10	
1	West Java	Kota Bekasi	1 to < 19 (Target)	836,139	35.81	**56,444**	**6.75**	**549250**	**65.69**	11	15	
1	West Java	Kota Bekasi	Non Target (<1 and ≥ 19)	1,498,732	64.19					5	4	
1	West Java	Kota Depok	1 to < 19 (Target)	661,444	38.05	**158179**	**23.91**	**500744**	**75.70**	11	10	

(*continued*)

Table 2. (*continued*)

Cluster	Province	City district/Regency	Age Groups*	Number of sub population*	% of population	First Round (R1)	R1%	Second Round (R2)	R2%	*Number of Pre-ORI Cases (including ORI month)*	*New Cases counted up to Oct 2018*	*Pvalue*
1	West Java	Kota Depok	Non Target (<1 and ≥ 19)	1,077,126	61.95					3	4	
1	DKI Jakarta*	Jakarta Barat	1 to < 19 (Target)	758,310	33.23	**27820**	**3.67**	**200278**	**26.41**	13	2	0.007
1	DKI Jakarta*	Jakarta Barat	Non Target (<1 and ≥ 19)	1,523,635	66.77					6	0	
3	DKI Jakarta*	Jakarta Pusat*	1 to < 19 (Target)	263,236	29.15	**1478271**	**561.58***	**200278**	**76.08**	6	0	
3	DKI Jakarta*	Jakarta Pusat	Non Target (<1 and ≥ 19)	639,737	70.85					2	1	
3	DKI Jakarta*	Jakarta Selatan	1 to < 19 (Target)	663,716	32.18	**511**	**0.08**	**541314**	**81.56**	3	1	
3	DKI Jakarta*	Jakarta Selatan	Non Target (<1 and ≥ 19)	1,398,516	67.82					1	0	
3	DKI Jakarta*	Jakarta Timur	1 to < 19 (Target)	914,156	33.93	**1567**	**0.17**	**649119**	**71.01**	11	0	

(*continued*)

Table 2. *(continued)*

Cluster	Province	City district/Regency	Age Groups*	Number of sub population*	% of population	First Round (R1)	R1%	Second Round (R2)	R2%	*Number of Pre-ORI Cases (including ORI month)*	*New Cases counted up to Oct 2018*	*Pvalue*
3	DKI Jakarta*	Jakarta Timur	Non Target (<1 and ≥ 19)	1,779,740	66.07					5	0	
1	DKI Jakarta*	Jakarta Utara	1 to < 19 (Target)	539,506	32.78	**541918**	**100.45**	**471314**	**87.36**	11	1	
1	DKI Jakarta*	Jakarta Utara	Non Target (<1 and ≥ 19)	1,106,153	67.22					1	3	
1	Banten	Kota Tangerang	1 to < 19 (Target)	641,176	35.65	**65411**	**10.20**	**529049**	**82.51**	25	9	0.180
1	Banten	Kota Tangerang	Non Target (<1 and ≥ 19)	1,157,425	64.35					6	1	
3	South Sumatra	Palembang	1 to < 19 (Target)	506,518	34.81	**20376**	**4.02**	**344156**	**67.95**	3	3	1.000
3	South Sumatra	Palembang	Non Target (<1 and ≥ 19)	948,766	65.19					0	0	

4 Discussion

For the December outbreak, West Java had the highest number of reported cases. These provinces have highly dense populations in their urban area. The reported ages of the cases suggest that routine immunization coverage in infants and boosters (18 months of age) has not reached the program targets and is not evenly distributed in each region. The next largest distribution of cases was in the 19–40-year age group. Diphtheria can affect adults; hence it is necessary to consider boosters [19, 20]. There is also another concern is that diphtheria may be underreported in other provinces due to poor healthcare access, less active case finding and lower vaccination rates in the remote areas [9, 10, 17, 21]. Diphtheria cases are underreported, and diagnostic testing is still limited. Not all cases will have samples sent to the laboratory for culture. Albert staining [22] and other microscopy tests are still used in Indonesia. Even then, there was a difficulty in linking reference laboratory confirmations with the reported surveillance systems due to a difference in identification. It was not known if antimicrobials (for 2017 and 2018) and the anti-diphtheria toxin (for 2018) were dispensed prior or before the sample was taken.

The current decline seen in December outbreak in 2017 is most likely due to the implementation of countermeasures in view of an upcoming mass gathering. Indonesia had hosted the 2018 Asian Games that involves participants from all over Asia. With the varying vaccination uptake rates in Asia, this mass gathering presents a high risk for regional and local dissemination of diseases including diphtheria [15, 16, 23]. The recommendations were to initiate immunization around resident areas near the venue of the Asian Games in Palembang (capital city of South Sumatra) and Jakarta (in the island of Java). It is recommended that all countries should advise those travelling to Indonesia to have their booster (for the vaccinated) or complete the full vaccination schedule against Diphtheria and other VPDs.

Sero-epidemiology should be studied in high prevalence districts to determine the immunity levels after the primary vaccination schedule has been completed and to time the booster [24]. Furthermore, the data quality on vaccination status in Indonesia needs to be further improved to incorporate both public and private health facilities, as well as overseas vaccination in neighboring countries like Singapore. This will determine any variation in coverage and herd immunity [25]. There are limitations to our data. Positive isolation of the C. diphtheriae could be done through either microscopy (i.e.Albert Staining) or culture via the main reference centers and remains low compared to the probable cases. This is an ongoing issue as another Indonesian study on the six year surveillance of diphtheria, had reported [10]. While laboratory confirmation is ideal, Indonesia has limited control over that aspect due to its decentralized healthcare system in which most provinces hold autonomy; the standardization of tests nationally; and the vast geographical spread of cases. These are not the only hurdles. Other than the general epidemiological investigations, Indonesia should be engaged in a multidisciplinary approach to ultimately reduce and prevent diphtheria as well as other VPD outbreaks from happening.

There is the continuing multi-faceted issue of vaccination hesitancy and refusal that can be attributed to socio-cultural factors. Socio-cultural factors include religious objection to vaccination or suspicion of locally manufactured vaccines. Sociodemographic studies on uptake rate should be expanded further to include the religious aspect and the influence of religious leaders, rather than the socio-economic focus [26–29]. Vaccine rumors in neighboring Islamic countries (i.e. Malaysia) have contributed to the religious objection and an increase in anti-vaccine group. Such vaccine rumors are related to what is religiously permitted in Islam ('halal') and that will pertain to the vaccine ingredient. Differing opinions between religious leaders can lead to further confusion and ultimately the rejection of vaccination [27, 30].

There is a distrust and hesitancy to use locally produced vaccine due to previous scandals [31]. In 2016, a re-vaccination of children had to take place in Java because of a fake/counterfeit vaccine syndicate for approximately more than a decade [32]. Public health programs, which could have effectively reduced the occurrence of vaccine preventable diseases, were affected and under public suspicion. Additionally hoax and rumors were circulating in the internet could have added to the vaccine hesitancy and possibly the rate of vaccine refusal as well as negative impression of the public health system and its programs [23, 33, 34].

The data quality for ORI and diphtheria are particularly of importance given that two DKI Jakarta districts (Jakarta Pusat and Utara) were above 100% of the target population for the first round which could be due to the two districts covering for the target population of the three others (Jakarta Timur, Barat and Selatan). We were unable to trace or link the data to the laboratory reports. This is a limitation as we cannot ascertain the actual coverage of the five districts in DKI Jakarta and a follow up study will review the data collection methods.

Therefore in the lessons learnt from this outbreak, the long term recommended measures should include a review of data linkages between the surveillance and laboratory reporting systems; the use of social media and expansion of health education to areas where the ORI uptake was identified as low; cluster sero-prevalence in areas identified as high risk; improving linkages and data quality between the laboratory and national surveillance datasets for future risk identification; by collaborating with available resources on a provincial, and city level [23, 27–29]; improve cross sector coordination with relevant ministries (e.g. education) and vaccine producers [35, 36]; further strengthening routine immunization and conduct regional risk mapping by the second administrative level (i.e. city and regency level); and reviewing immunization policies including school immunization delivery.

Acknowledgement. This paper was supported by Sub Directorate of Surveillance, Directorate of Surveillance and Health Quarantine, Directorate General of Prevention and Disease Control, Ministry of Health. We are thankful to our colleagues in Public Health Emergency Operational Centre who provided the data which we need for this paper.

We have to express out appreciation to the RSPI SS for sharing their data pearls of wisdom with us during the course of this research. We are also immensely grateful to drg. Vensya Sitohang, M.Epid, Director of Directorate of Surveillance and Health Quarantine for comments on an earlier versions of the manuscript.

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