ORIGINAL ARTICLE: CLINICAL PROFILE AND EPIDEMIOLOGICAL ASPECTS OF DIPHTHERIA CASES IN RUANG ISOLASI KHUSUS RSUD DR SOETOMO FROM JANUARY UNTIL DECEMBER 2015

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Abstract. Background Diphtheria is a vaccine-preventable disease and is eradicated mostly in developed countries. But the prevalence of diphtheria cases still remains endemic in developing countries such as Indonesia, mainly in East Java. Purpose: To study the clinical profile and epidemiological aspects of diphtheria cases admitted in Ruang Isolasi Khusus RSUD Dr. Soetomo in 2015. Method: This research is a hospital-based, cross-sectional study. The samples are all patients admitted in Ruang Isolasi Khusus RSUD Dr Soetomo with the diagnosis of diphtheria in 2015. Results: There were 23 diphtheria cases reported in Ruang Isolasi Khusus RSUD Dr Soetomo in 2015. The most prevalent age group was 6 until 10 years old (56.52%) and the most common gender was male (57%). Most of the patients came from a non-endemic area (82.61%) and most of them are not fully vaccinated (73.91%). There are more unknowledgeable mothers (91%) about DPT immunization. The most prevalent clinical manifestations are fever, dysphagia and pseudomembrane (100%). Tonsillar diphtheria (86.96%) was the most prevalent type of diphtheria presented. There were no complications and mortality reported and the main managements used were isolation (100%), antibiotics (100%) and anti diphtheria serum (82.61%). Conclusion: There is an age shift in the occurrence of diphtheria to 6 until 10 years of age. The immunization coverage especially the booster dose is still low among the patients. Less knowledge about DPT immunization contributes to low childhood immunization coverage. No complications and mortality reported.

Keywords: diphtheria, re-emerging, anti diphtheria serum, DPT immunization

Summary
Diphtheria is a vaccine-preventable disease and is eradicated mostly in developed countries. The prevalence of diphtheria cases still remains endemic in developing countries such as Indonesia, mainly in East Java. The resurgence of diphtheria started around 2003 in Bangkalan. In 2011, there were 333 diphtheria cases in East Java with 11 deaths and declared an outbreak. This study aims to evaluate the clinical profile and epidemiological aspects of diphtheria cases in RSUD Dr. Soetomo Surabaya. It is a cross sectional study that observes the number of cases, age, sex, address, parent’s occupation, ethnic backgrounds, religion, immunization status, maternal education about DPT immunization, clinical manifestations, diagnosis, complications, mortality and managements. There were 23 cases reported. The most prevalent age group was 6 until 10 years old and predominate in male. Most of the patients came from a non-endemic area and are not fully vaccinated. There were more unknowledgeable mothers about DPT immunization. The most prevalent clinical manifestations were fever, dysphagia and pseudomembrane. Tonsillar diphtheria was the most common type of diphtheria. The managements were isolation, antibiotics and anti diphtheria serum. It concludes that there is an age shift from 6 until 10 years old. Booster dose is still low among patients.

Intro Resurgence of diphtheria cases has been seen in both developed and developing countries in the last decade, especially in Indonesia. Due to the growing numbers of diphtheria cases in East Java, it is crucial to do a periodic evaluation every year. This study aims to analyze the clinical profile and epidemiological aspects of diphtheria cases in Ruang Isolasi Khusus RSUD Dr Soetomo from January until December 2015 as there is no evaluation has been done for the year 2015. In Indonesia, the resurgence of diphtheria started around 2003 in Bangkalan,
East Java and spread throughout the whole districts in East Java. In 2011, due to the fact that there were 333 diphtheria cases in East Java with 11 deaths, East Java Provincial Government has declared an outbreak. Padang has also reported an outbreak of diphtheria in 2014 and has spread to the districts of Padang Pariaman and Solok. (Ministry of Health Republic of Indonesia, 2016).

According to the data from Profil Dinas Kesehatan Surabaya (2015), there are 27 cases of diphtheria reported, with 19 males and 8 females. The Case Fatality Rate (CFR) is 0%. There is a decrease in the number of cases when compared to 2014 with 47 cases. In 2015, the pediatrics ward in RSUD Dr Soetomo has recorded 20 patients and 2 patients are put into the isolation room while in 2016, 44 patients are clinically diagnosed with diphtheria and 9 patients are suspected to have diphtheria. This numbers show that diphtheria is still endemic in East Java and increasing year by year.

The incidence of diphtheria in Indonesia is the second highest after India (WHO, 2015), especially in East Java. Apart from clinical profile, epidemiological aspects are also analyzed to know what variables are contributing to the increase of diphtheria cases and finding out ways to stop the outbreaks from happening again in the future. The epidemiological data may be different from country to country, for example, when the outbreaks happened in Russia, the group that has the highest numbers of severe disease and death is from adults 40-49 years compared to children who only suffered mild symptoms (Misgard et al. 2000) while in Indonesia, the prevalence of diphtheria patients in children is higher compared to adults. Although diphtheria vaccine is already under the National Immunization Program Schedule, the cases still remain high in RSUD Dr. Soetomo in 2015. It is important to know the clinical profile and epidemiological aspects to stop the re-emerging of diphtheria cases and to eradicate the infection comprehensively.

**Materials And Methods**

This research was a hospital-based descriptive cross sectional study. It was performed by collecting secondary data from medical records of all clinically diagnosed patients with diphtheria infection based on WHO 2011 criteria in Ruang Isolasi Khusus RSUD Dr. Soetomo, Surabaya within the period of one year, January - December 2015. Data taken from the medical records were number of cases, age, sex, address, parent’s occupation, parent’s ethnic background, parent’s religion, immunization status, maternal knowledge about DPT immunization, clinical manifestation, diagnosis, complications, mortality causes and management.

**Results**

There were a total of 23 patients admitted in Ruang Isolasi Khusus RSUD Dr. Soetomo in 2015. Age distributions of the patients are from 2 months old until 16 years old with sex distributions of 13 males (57%) and 10 females (43%).

**Table 1. Address distribution**

| No | Address     | Frequency | Percentage (%) |
|----|-------------|-----------|----------------|
| 1. | Endemic     | 4         | 17.39          |
| 2. | Non-endemic | 19        | 82.61          |
|    | **Total**   | **23**    | **100**        |

There are no obtainable data for parent’s occupation, ethnic backgrounds and religions.

**Table 2. Immunization status of patients with the diagnosis of diphtheria**

| No | Immunization status | Frequency | Percentage (%) |
|----|---------------------|-----------|----------------|
| 1. | Fully vaccinated    | 3         | 13.04          |
| 2. | Not fully vaccinated| 17        | 73.91          |
| 3. | Unimmunized         | 3         | 13.04          |
The immunization status is categorized as fully vaccinated, not fully vaccinated and unimmunized based on the patient’s age and the past vaccination history of primary series vaccination and boosters.

**Figure 1.** Maternal knowledge about DPT immunization of diphtheria cases

A mother is considered knowledgeable when the patient has complete immunization history and whether she knows about measles immunization.

**Figure 2.** Clinical manifestations of diphtheria cases

| Clinical Manifestations |
|-------------------------|
| Fever                  |
| Stridor                |
| Dysphagia              |
| Bullneck               |
| Pseudomembranes        |
| Submucosal             |

| No  | Diagnosis             | Frequency | Percentage (%) |
|-----|-----------------------|-----------|----------------|
| 1.  | Tonsillar diphtheria  | 20        | 86.96          |
| 2.  | Tonsilopharyngeal diphtheria | 2  | 8.70          |
| 3.  | Laryngotracheal diphtheria | 1  | 4.35          |
There were no complications such as myocarditis, acute renal failure, neuropathy, palatal palsy and tracheostomy fistula reported (0%) among diphtheria patients in 2015.

**Mortality**

There were no mortality (0%) among diphtheria patients in 2015.

### Table 4. Managements of diphtheria cases

| No | Managements           | Frequency, \( n = 23 \) | Percentage (%) |
|----|-----------------------|---------------------------|----------------|
| 1. | Anti-diphtheria serum | 19                        | 82.61          |
| 2. | Antibiotics           | 23                        | 100            |
| 3. | Isolation             | 23                        | 100            |

**Discussion**

There are a total of 23 patients diagnosed with diphtheria in Ruang Isolasi Khusus of RSUD Dr Soetomo in 2015. Furthermore, also in East Java, a total of 296 diphtheria cases are reported with 16 deaths and a Case Fatality Rate (CFR) of 4.0% during 2014. Out of 22 districts, the highest number of cases from East Java contributes to as high as 74%. (Indonesian Health Ministry, 2014). This shows that diphtheria cases have not been absent in East Java since 2000 – 2009 and the cases still remain endemic. (Health Department Republic of Indonesia, 2009b; Dinas Kesehatan Provinsi Jawa Timur, 2009)

The age shift phenomenon shows that the primary immunisation rates have improved significantly in these past years making children have higher immunity towards diphtheria infection. Other than that, reduced circulating wild organisms also making it possible for natural immunity boosting to occur during subclinical infections in children. Hence, leading to more susceptible adolescents than children. Adults become more susceptible due to the lack of periodic administration of booster doses of diphtheria toxin or repeated toxin exposure throughout the years. (Phalkey et al, 2013; Galazka, 2000). This is supported by the study conducted by Phalkey et al (2013) in Maharashtra, India shows increasing attack rates with age and age group 10 – 15 years old were the highest recorded. A recent study in Indira Gandhi Institute of Child Health by G. V. et al showing 23 (74.1% ) out of 31 cases are from patients above the age of 5 years old.

According to Dittman et al (2010), women are more susceptible to diphtheria infections and have higher incidence rates compared to men. However, this is not supported by the data obtained from this study as the result shows a predominance of male patients and the study sample is only consists of children under 18 years old of age. According to Patel (2006), boys have more susceptibility towards infections because they always spend their time playing outside of the house and are exposed more to the transmission of many type of diseases. A study conducted by Maheriya et al (2014) in Civil Hospital Ahmedabad shows 23 (61%) male patients out of 38 were admitted.

There is an increase of diphtheria cases reported in 2010 – 2011 that mainly predominates in the Tapal Kuda districts which consists of Kabupaten Lumajang, Kabupaten Bondowoso, Kabupaten Situbondo, Kabupaten Bangkalan and Madura Island. (Izza, 2015). The
immunization coverage from these districts are reported as relatively low with only 8.5% - 22.9%. (Indriasih and Ariningrum, 2011). However, the result obtained in this study does not show any significant correlation between endemic and non endemic area as all of the district hospitals are able to treat diphtheria patients and only severe patients are referred to RSUD Dr. Soetomo Surabaya.

Parent’s occupation is closely related to the level of education and the family’s socioeconomic status. Recent outbreaks in Europe and the United States mainly include low socioeconomic groups living in a crowded places and this may associate to the transmission and increasing diphtheria infections. (Galazka, 2000).

A study by Husada (2016) reveals that majority of carrier and diphtheria patients came from Madurese people. They believe that vaccination is *haram*, have low awareness on visiting health facilities in addition to the geographic and climate barriers that they faced making it harder to have better immunization coverage. (Indriasih and Ariningrum, 2011). There were 19 out of 25 Polish people who were diagnosed with diphtheria and all of them have traveling history from countries such as Russia, Ukraine and Belarus during 1992 – 1995. (Galazka, 2000). During the diphtheria outbreaks in East Java, diphtheria cases significantly increased in Madura, and cities that are focused on migrations such as Surabaya and Tapal Kuda districts. This may indicates a correlation between migrants and the transmission of diphtheria infections during the outbreak. (Primayani, 2016)

There are evidence of opposition towards immunization programs among some Muslim populations in polio virus immunization programs in Nigeria, Pakistan and Afghanistan. Some allegedly claimed that vaccines spread HIV virus, some are related to political power and are related to some controversional clinical trial on investigational antibiotics. Furthermore, some Jews and Muslims communities have expressed concerns about porcine-origin components in the vaccines as they follow a faith-based beliefs about pork consumptions in their diet. (Grabenstein, 2013). According to a study conducted by Shrivastwa et al (2015), children from Hindus and Muslim families have a 2.2 times greater odds of being non-vaccinated and a 1.42 times higher of being undervaccinated.

The main contributor of diphtheria cases in the world since 2000 is India while Indonesia is second with 3203 diphtheria cases reported from 2011 until 2015. Immunization coverage is still low in this study. The parents mainly have lack of knowledge and also due to lack of information, some of them are afraid of the side effects of the immunization. A study conducted by Arifin and Prasasti (2017) in Bangkalan shows 34 (70.8%) out of 48 diphtheria cases are from undervaccinated children.

According to the study by Kamau and Esamai (2001), maternal education is strongly associated with the completedness of the immunizations given. The result obtained from this study shows a strong correlation between maternal education and immunization status. A study conducted by Luthfi (2014) in Posyandu Mardi Rahayu, based on the mother’s knowledge level, results shows 9 (45%) out of 20 mothers have good knowledge level, while 7 (35%) mothers have an average knowledge level and 4 (20%) mothers have low knowledge level. This contributes to 15 (75%) of children gets fully immunized.

The result of this study is in line with the study conducted in 2014 by Meera and Rajarao in Hyberabad, India, showing all 2925 cases (100%) presented with fever, sore throat and a pseudomembrane is present during examination. While Maheriya et al (2014) showed 35 out of 38 patients were diagnosed with tonsilopharyngeal diphtheria, followed by 2 cases of laryngotracheal diphtheria and 1 case of nasal diphtheria.

G.V. et al (2016) presented 13 (41.9%) out of 31 children developed myocarditis, and 10 (76.9%) out of those 13 children with myocarditis died. However, there are no complications reported in this study.

There are no incidence of mortality reported. This may due to the early detection and admission of patients. Furthermore, anti
diphtheria serum, antibiotics and isolation are available in RSUD Dr Soetomo as it is a tertiary referral hospital. A study conducted in 2014 by Meera and Rajarao in Hyderabad, India, shows 2844 out of 2925 patients who were presented early and received early interventions have a better prognosis and obtained full recovery from the illness. The main managements of diphtheria patients in RSUD Dr Soetomo is with isolation, giving anti-diphtheria serum and antibiotics (Procaine Penicillin). Diphtheria antitoxin and antibiotics should be given to patients suspected with diphtheria, while respiratory support and airway management should also be administered when needed. (CDC, 2015)

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