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Research Article

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The Effect of Diphtheria AntiToxin (DAT) to Decrease Degrees of Diphtheria Severity

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Abstract

Background: *Diphtheria incidence and mortality in Indonesia continue to increase from 2014-2017. DAT is critical to reduce the severity of diphtheria. The study aimed to determine the effect of DAT on reducing severity in diphtheria patients.*

Method: *Analytical research with a case-control design. The research was conducted at RSPI Prof. Dr. Sulianti Saroso. The sample in this study was patients diagnosed with suspected diphtheria and diphtheria who received inpatient care at RSPI SS within a period of four years from 2014 to 2017. The cases in this study were 86 diphtheria-treated patients who were treated for 86 days, controls were 86 diphtheria-treated patients who were treated for <10 days. Data were collected from medical records.*

Results: *the variable associated with a decrease in severity of diphtheria sufferers was DAT (OR = 4,063; 95% CI: 1,354-12,195, p = 0.012), corticosteroid administration (OR = 3,653, 95% CI 1.568-8,513, p = 0.003) and culture (OR = 0.170; 95% CI: 0.054-0,547), myocarditis is a confounding variable (OR = 1,690; 95% CI: 0.565-5,052, p = 0.348).*

Conclusion: *Provision of DAT has been shown to affect decreasing the severity of diphtheria.*

Keywords: Degree of Severity, Anti Diphtheria Serum (DAT)

Introduction

Diphtheria is an acute infectious disease caused by the *Corynebacterium diphtheria* bacteria. Signs and symptoms include upper respiratory tract infection (URTI), sore throat, swallowing pain, not high fever (less than 38, 50C), and white/greyish/blackish pseudomembranes that are not easily released and bleed when removed in the tonsils, pharynx or larynx [1].

Based on data from the World Health Organization (WHO), in 2014 to 2016, the number of diphtheria cases in the world in 2014 was 7774 cases; in 2015 the number of diphtheria cases in the world was reported to decline to 4086 cases and increasing in 2016 back to 7097 cases. Diphtheria cases that occurred in Southeast Asia (SEARO / South-East Asia Region) in 2014 amounted to 7666, then decreased in 2015 to 2504 and increased again in 2016 to 4016 cases [2, 3].

The Indonesian Health Profile in 2014 reported that diphtheria cases in Indonesia amounted to 396 cases died as many as 16 cases (CFR 4.04%) with the highest cases coming from East Java Province. In 2015 Diphtheria cases amounted to 252 cases, with the number of cases died as many as 5 cases (CFR 1.98%) with the highest cases occurring in West Sumatra and East Java. Whereas in 2016, diphtheria cases increased to 415 cases with 24 cases died (CFR 5.78%) [4-7].

RSPI Prof. Dr. Sulianti Saroso (Dir PPI & PM RSPI SS), in 2014, treated 3 cases of diphtheria, then in 2015 hospitalization of diphtheria cases increased to 16 cases, in 2016 it rose to 37 cases with 2 cases died (CFR 5.40 %). In 2017, the incidence of diphtheria outbreaks in the Jabodetabek area made RSPI SS treat up to 260 diphtheria cases, with deaths of 3 cases (CFR 1.15%) [8].

The success of the management of diphtheria cases is inseparable from the administration of DAT, where the role of DAT serves as a treatment to neutralize diphtheria toxins circulating in the blood. Diphtheria antitoxin is used to prevent the severity and complications of the disease, in moderate and severe cases diphtheria toxin will cause swelling in the neck, forming a membrane in the trachea, causing inflammation of the heart muscle wall, accompanied by a heart condition in which the electrical impulses do not occur from the atrium to the ventricles (heart block) and congestive heart failure that is very fast, thus giving DAT as early as possible is very

necessary [9].

Significant increases in diphtheria cases in both the RSPI SS and in Indonesia in the last three years (2015-2017) turned out to be accompanied by a national scarcity of DATs. As a result of 267 cases of diphtheria treated at RSPI SS in 2017, there were 175 patients with a final clinical diagnosis of diphtheria, 35 (20%) of whom did not get DAT with one person (2.9%) dead. While 140 other patients, who received DAT, there were two people (1.4%) who died.

The purpose of the study to prove the administration of DAT affects the decrease in severity of diphtheria patients treated at RSPI Prof. Dr. Sulianti Saroso 2014-2017 [10].

Method

This study was an observational analytic study using a case-control design. The study was conducted at the RSPI Prof. Dr. Sulianti Saroso. The sample in this study were patients with a diagnosis of suspected diphtheria and diphtheria who received inpatient care at the RSPI Prof. Dr. Sulianti Saroso in a period of four years from 2014 to 2017. The total sample of 172 people with sampling techniques was the total sample. The comparison of cases and controls is 1: 1. The cases in this study were 86 diphtheria-treated patients who were treated for 86 days, controls were 86 diphtheria-treated patients who were treated for <10 days. The dependent variable was a decrease in severity, the independent variables included DAT administration, DAT dose, time of administration of DAT, administration of antibiotics, corticosteroid administration, age, sex, the area of residence, immunization status, pseudomembrane, bull neck, myocarditis and culture results. The research data is secondary data from the patient's medical record file. Data analysis in univariate, bivariate and multivariate.

Results

Table 1: Factors Associated With Decreasing Severity Degrees in Diphtheria

Independent variables	Decreasing Severity Degrees in Diphtheria		P value	OR (CI 95%)
	Cases (%)	Control (%)		
DAT Administration				
Not Given	5 (5.8)	19 (22.1)	0.004	0.218
Given	81 (94.2)	67 (77.9)		(0.077-0.614)
Dosage of DAT Administration				
Inappropriate	34 (39.5)	41 (47.7)	0.356	0.718
Appropriate	52 (60.5)	45 (52.3)		(0.392-1.314)
Time of DAT Administration				
Late > 72 jam	40 (46.5)	38 (44.2)	0.878	1.098
On-time ≤ 72 jam	46 (53.5)	48 (55.8)		(0.602-2.003)
Antibacteria Administration				
Not Given (PP)	4 (4.7)	6 (7.0)	0.745	0.650
Given (PP)	82 (95.3)	80 (93.0)		(0.177-2.392)
Corticosteroid Administration				
Not Given	47 (54.7)	67 (77.9)	0.002	0.342
Given	39 (45.3)	19 (22.1)		(0.176-0.663)
Age				
Toddler (0-5 years)	19 (22.1)	25 (29.1)	0.351	-
Children > 5-14 years	41 (47.7)	32 (37.2)		
Adolescents and adults (>14 years)	26 (30.2)	29 (33.7)		
Sex				
Male	46 (53.5)	41 (47.7)	0.542	0.262
Female	40 (46.5)	45 (52.3)		(0.694-2.297)
Domicile				
Outside DKI	49 (57.0)	46 (53.5)	0.759	1.152
DKI	37 (43.0)	40 (46.5)		(0.632-2.101)
Immunization Status				
Not Completed	45 (52.3)	44 (51.2)	0.745	1.000
Completed	41 (47.7)	42 (48.8)		(0.576-1.906)
Pseudomembrane				
Exist	82 (95.3)	79 (91.9)	0.533	1.816

Not Exist	4 (4.7)	7 (8.1)		(0.512-6.447)
Bullneck				
Exist	27 (31.4)	22 (25.6)	0.499	1.331
Not Exist	59 (68.6)	64 (74.4)		(0.685-2.588)
Miocarditis				
Exist	17 (19.8)	10 (11.6)	0.209	1,872
Not Exist	69 (80.2)	76 (88.4)		(0.803-4.365)
Culture Results				
Positive	19 (22.1)	4 (4.7)	0.002	5.813
Negative	67 (77.9)	82 (95.3)		(1.866-17.915)

Based on [Table 1], the treatment factor for DAT was a group of cases that were not given DAT of 5.8%, whereas in the control group that was not given DAT it was 22.1%. The treatment factor at the dose of DAT was seen from the suitability of the dose provided by DAT to the severity suffered by the patient, then in the case group stated an inappropriate dose of 39.5%, so did the control group which reported an inadequate dose of 47.7%. Treatment factors at the time of DAT administration were in the case group late in obtaining DAT> 72 hours by 46.5%, whereas in the control group late in obtaining DAT> 72 hours at 44.2%. Treatment factors for the administration of Penicillin Procaine (PP) antibiotics were in the case group not given PP antibiotics of 4.7% and in the control group at 7.0%. The treatment factor for corticosteroids was in the case group not given corticosteroids at 54.7%, whereas in the control group no corticosteroids were given at 77.9%.

Sociodemographic factors at age were in the case group, the most significant age suffered from diphtheria in children aged more than 5 years to age 14 years (47.7%) similar to that in the control group the most considerable age suffered from diphtheria also in children with more age from 5 years to 14 years old (37.2%). Sociodemographic factors in sex, among others; in the group of cases of male sex having greater diphtheria was 53.5%, whereas in the Control group the group of women suffered from diphtheria which was 52.3%. Sociodemographic factors in the area of residence, among others, in the case group, it was seen that most who received treatment for diphtheria at RSPI Prof. Dr. Sulianti Saroso came from an area outside DKI Jakarta by 57%, as well as the control group with 53.5% of patients from outside the DKI Jakarta area. In the immunization status factor, in the case group, incomplete immunization status was 52.3%, while the deficient immunization status control group was 51.2%.

Pseudomembranous clinical factors are one of the typical symptoms suffered by diphtheria patients, in the case group, there were 95.3% with pseudomembranes, as well as in the control group, there were 91.9% of patients with pseudomembranes. Bullneck clinical symptoms are one of the typical signs and symptoms experienced by patients with diphtheria in moderate degrees of diphtheria. In the case group, there were 31.4% who suffered a bullneck, while in the control group there were 25.6% of patients who experienced a bullneck.

The clinical symptom of myocarditis is a complication that occurs in patients with diphtheria that attacks the heart nerve. In the case group, there were 19.8% who had myocarditis, whereas in the control group 11.6% had myocarditis. Factors in the presence or absence of bacteria through the results of diphtheria culture examination, among others, in the case group there were 22.1% with positive results of *Corynebacterium diphtheria* bacteria and in the control group found 4.7% positive results of *Corynebacterium diphtheria* bacteria.

Variables that have a significant relationship ($p < 0.05$) with a decrease in severity are DAT (OR 0.218, 95% CI 0.077-0.614, $p = 0.004$), corticosteroid administration (OR 0.342, 95% CI 0.176-0.663, $p = 0.002$), and culture results (OR 5.813, 95% CI 1.866-17,915, $p = 0.002$). Variables not related to a decrease in severity were the dose of DAT ($p = 0.356$), time of administration of DAT, administration of antibiotics ($p = 0.878$), age ($p = 0.745$), gender ($p = 0.351$), area of residence ($p = 0.542$), immunization status ($p = 0.759$), pseudomembrane ($p = 0.533$), bullneck ($p = 0.499$) and myocarditis ($p = 0.209$). However, because the variable myocarditis is $p < 0.25$, the variable myocarditis is included in the multivariate analysis.

Multivariate modelling uses the logistic regression test with the Enter method. The variables included in the multivariate analysis are variables which in the bivariate test have a value <0.25. After a series of analyzes, the final results of the study (multiple logistic regression models) are as follows:

Table 2: Final Model of Multivariate Analysis Factors that Influenced The Decreasing Severity Degrees in Diphtheria (n = 172)

Variables	B	P value	OR (Exp B)	95% CI	R^2
DAT Administration	1.402	0.012	4.063	1.354-12.195	26.3
Corticosteroid Administration	1.296	0.003	3.653	1.568-8.513	
Miocarditis*	0.525	0.348	1.690	0.565-5.052	
Culture	-1.769	0.003	0.170	0.054-0.547	

The final multivariate results showed that the variables associated significantly with severity decreasing of patients with diphtheria were DAT, corticosteroid administration and culture, whereas myocarditis was a confounding variable. The overall R2 is 26.3%, which means that the above variables can explain the decrease in the severity of diphtheria by 26.3% and the other factors explained.

The most dominant variable associated with a decrease in severity is the administration of DAT with an OR of 4,063 (95% CI: 1,354-12,195), meaning that patients with diphtheria who get DAT are 4 (four) times more likely to experience the decreasing of diphtheria severity.

Discussion

There is a difference in the proportion between cases and controls for the variable DAT in the non-given category compared to 32.6%. Giving DAT with a decrease in the severity of P-value = 0.016 means that there is a significant relationship between the administration of DAT to decrease the severity of diphtheria. The OR = 3,728 (95% CI: 1,274-10,913) means that in diphtheria patients who were not given DAT they had a 3,728 times greater risk of decreased severity compared with diphtheria patients given DAT. DAT is considered a protective factor.

Relevant to the article written by both, 2014 Access to Diphtheria Antitoxin for Therapy and Diagnostics, in 1980 Behring and Kitasato discovered diphtheria antisera as the forerunner of the therapeutic serum. The antisera were later developed by the Pasteur Institute through a large-scale experiment in 1894 in Paris where there was a mortality rate of 24.5% in 448 children given diphtheria antitoxin therapy, and mortality reached 60% in 520 children who were not given diphtheria antitoxin therapy [11].

This is consistent with Himashree (2016) study in Meghalaya India, a significant cause of severity in 7 diphtheria patients in the region was the absence of diphtheria antitoxin, and the severity was exacerbated by low immunization status, socioeconomic status and community awareness and behaviour towards health and search for treatment [12].

The study conducted by NC Sharma in Delhi, India (2007), diphtheria CFR in North India 32-56.3%, 13.2% in South India, 16% in the Northeast and 42.9% in West India. The most significant cause of death is the unavailability of diphtheria antitoxin, followed by misdiagnosis and poor handling of specimens [13].

In this study there were some patients who were not given DAT, this was due to clinical considerations such as diphtheria in pregnant women and allergies to DAT, and another factor was the availability of the DAT stock itself.

For DAT stock availability, there are limitations in the availability of DAT in 2016 until 2017, and this caused diphtheria patients who do not get DAT or get DAT less than their needs.

Because administration of DAT is significant to reduce the severity in diphtheria patients, the availability of DAT in RSPI SS as a referral hospital must receive more attention from the government and the government as well as providing adequate and sufficient DAT throughout the health facilities in Indonesia.

There is a difference in proportion between incompatibility and dose suitability for DAT to decrease the severity of 6.2%. The results of the statistical test obtained a value of P-value = 0.356, meaning that there was no relationship between the dose of DAT to decrease the severity of diphtheria.

Given that DAT aims to inactivate toxins that have not been bound as soon as possible and to prevent the progression of the disease, even though the results of the analysis show statistically insignificant results (P-value = 0.356), dose mismatches should be associated with a decrease in diphtheria severity.

The absence of a relationship between the suitability of the dose of DAT administration and the reduction in the severity of diphtheria is likely due to DAT being given as quickly as possible to patients based on the enforcement of clinical diagnoses without waiting for laboratory confirmation results.

The factors that influence the dosage mismatch of DAT administration in this study are the availability of DAT itself. Some cases of diphtheria in this study have DAT less than instructions, and some have not received DAT at all because of the vacancy in the provider DAT. Because the dose of DAT is essential in reducing the severity of diphtheria, it is expected to establish an accurate diagnosis, as well as the availability of sufficient DAT.

The results of the study stated that there were differences in the proportion between cases and controls for the variable time of administration of DAT in the category of late administration > 72 hours compared to on-time administration ≤ 72 hours by 4.6%. The results of the statistical test obtained a value of P-value = 0.878 which means there is no relationship between the time of administration of DAT to the decrease in the severity of diphtheria.

Although the results of the analysis statistically showed no significant effects (P-value = 0.878), the delay in the time of administration of DAT should be related to the decrease in the severity of diphtheria. The possibility of the absence of a relationship between the time of administration of DAT and a decrease in severity can be caused in some cases of DAT diphtheria has been given in referral hospitals, limited availability of DAT and source of research data based on what is recorded in the patient's medical record so that the data cannot be controlled.

In the Puspitasari study, a study in India stated that the delay in diagnosis and administration of DAT for 48-72 hours would cause severe complications for patients [14].

Likewise, a study conducted in Georgia (2000), a time interval of more than three days from the onset of symptoms or pain until given antitoxin had a significant relationship with fatal outcomes [15].Therefore, even though the time of administration of DAT in this study was not considerable, the time of administration of DAT is significant in reducing the severity of diphtheria, so that an accurate diagnosis is needed, public awareness to seek treatment and adequate DAT availability in each facility.

The results showed that there was a difference in proportion between not given and given PP antibiotics to a decrease in severity of 4.6%. The results of the statistical test obtained a value of P-value = 0.745, meaning that there is no relationship between giving PP

antibiotics to a decrease in the severity of diphtheria. In this study, the administration of antibiotics did not have significant value because most cases and controls received antibiotics.

Based on the data obtained, patients who were not given PP were due to patients who were allergic to PP, parents who refused their children were given injections of PP and provided other antibiotic alternatives to PP, namely *erythromycin*, *azithromycin*, *cefotaxime* or *ceftriaxone*.

Based on research by Puspitasari (2012), in the medical principle of diphtheria the most important is the administration of DAT according to its severity and administration of antibiotics to eliminate germs by 95% [14]. Likewise with the case report by James (2017), on the case of a girl who has never immunized symptoms of diphtheria with bullneck complications. Through the administration of DAT and administration of Penicillin Procaine antibiotics, in 14 days the patient experienced clinical improvement, as well as pseudomembranes, disappeared within one month [17]. Therefore, even though the results of the analysis statistically showed results were not significant (P value = 0.745), PP antibiotic administration should be associated with a decrease in the severity of diphtheria.

Based on the results of the study that there was a difference in proportion between not given and given corticosteroids to a decrease in severity of 46.4%. The results of statistical tests obtained a value of P-value = 0.002, which means that there is a relationship between corticosteroid administration and a significant decrease in the severity of diphtheria. The amount of OR = 0.342 (95% CI: 0.176-0.663) means that in diphtheria patients who are not given corticosteroids have a risk of 0.342 times greater experiencing a decrease in severity compared to diphtheria patients given corticosteroids.

In this study, the assessed corticosteroids were prednisone. At RSPI Prof. Dr. Sulianti Saroso, prednisone is a corticosteroid given to diphtheria patients with an indication of myocarditis. The significance of the relationship between corticosteroid administration and a decrease in severity in this study can be caused because prednisone given to patients is following the indication of the seriousness of the patient. In this case, RSPI Prof. Dr. Sulianti Saroso has provided optimal case management to reduce the severity of diphtheria in patients treated.

Based on the results of the research on the statistical test of the relationship between age and a decrease in severity, a P value = 0.351 means that there is no relationship between age and a decrease in the severity of diphtheria. The results of this study are not in accordance with the research conducted by Pracoyo (2015) in the Riskesdas survey, the results of the analysis showed that the age variable had a significant relationship with antibody titers (OR = 0.78, p = 0.001; 95% CI (0.69-0.88) and from the age variable, the age group 1-4 years is the most protected age group from diphtheria infection by 78% and protection against diphtheria decreases with increasing age while in this study shows the highest age of suffering from diphtheria is children aged> 5 to 14 years (42.4%, teenagers and adults> 14 years and over (32%) and ages 0 - 5 years (25.6%) [18].

The theory of Nuzirwan Acang in the Internal Medicine Faculty textbook at the University of Indonesia (2006) states that the most common age for diphtheria is 2-10 years, rarely at the age of 6 months and the age of 15 years [19]. Results of the Husada study (2017), in diphtheria outbreaks that occurred in East Java, the largest age group infected with diphtheria was at the age of 15 years and under (69.4%) but the trend showed an increase in the proportion of adolescents and adults [20].

Increased cases of diphtheria in the past three years in Indonesia can be caused by an increase in antivaccine groups in parents who have the effect of not bringing their children immunized, low or doubtful immunization coverage, low cold chain management, and possible long-term effects of diphtheria vaccines in some regions in Indonesia, especially Jabodetabek.

Increased cases of diphtheria in adulthood are probably due to a lack of awareness and knowledge to booster diphtheria vaccine in adulthood, an increase in diphtheria carriers and adult age to and from infected areas or endemic areas of diphtheria. Given diphtheria has attacked all age groups, it is hoped that the community will be aware this disease, increases awareness of the importance of healthy and clean life and includes carrying out immunization in children and diphtheria booster in adults.

Based on the results of the study that there is a difference in proportion between male and female sex to a decrease in severity of 2.4%. From the results of the statistical test obtained a value of P-value = 0.542 means that there is no relationship between the sexes to decrease the severity of diphtheria. The absence of a relationship between sex and a decrease in severity in this study is consistent with the research conducted by Lestari (2012) in Sidoarjo, where sex did not have a significant relationship with the incidence of diphtheria (p = 0.113, OR = 0.482).

Sociodemographic description based on the sex of diphtheria patients treated at RSPI Prof. Dr. Sulianti Saroso in 2014-2017 was almost balanced, judging from the overall sample the number of men was 50.6% and women were 49.4%. The higher number of male patients in the case group can be due to higher activity and mobility of men than women so that men come with more severe severity than women, while the number of female patients is higher in the control group can be attributed to women more sensitive in feeling pain so that the search for treatment in women is earlier than men.

In the Husada (2017) study, in 2011-2016 outbreaks in East Java, the proportion of men suffering from diphtheria was 53.4%, a slight difference with women [20]. In the Bottiger study (1998), sex diphtheria immunity showed diphtheria immunity in men based on age were higher than female immunity (CI = 95%, p-value <0.005). Those (men and women) who were younger had diphtheria protection better than the older age group. Groups that did not receive an immunization program when children showed significant antibody differences, namely the older age group [21].

Based on the results of the study there were differences in the proportion between incomplete immunization status and complete immunization status to a decrease in severity of 2.2%. From the results of statistical tests obtained P-value = 1,000 means that there is no relationship between immunization status and a reduction in the severity of diphtheria. Even though in this study the results of the analysis were not significant (P-value = 0.745), immunization status should be related to a decrease in the severity of diphtheria.

In contrast to the results of a case-control study by Arifin (2016)

in Bangkalan Health Center, the DPT immunization status was associated with high cases of pediatric diphtheria in the region (P-value = 0.0037; OR = 4.667) [22]. Likewise with the study of Ramadhani (2016), the results of DPT immunization status, maternal education and occupancy density were associated with diphtheria (p = 0.041; OR = 2.42), (p = 0.025; OR = 0.333) and (p = 0.0163; OR = 3.2) [23]. While the study conducted by Puspitasari (2012) at RSUD Soetomo in 2004-2009, diphtheria patients with incomplete and never immunized immunizations all come with severe severity [14].

Based on the results of the study there are differences in the proportion between the outer area of DKI and the DKI area towards a decrease in severity of 7%. The results of the statistical test obtained a value of P-value = 0.759, meaning that there was no relationship between the area of residence and the decrease in the severity of diphtheria.

As a national referral hospital for infectious diseases, RSPI Prof. Dr. Sulianti Saroso has the role in receiving referrals for patients with potential outbreaks from both the DKI and outside DKI areas. In the Mapping of Diphtheria Outbreak released by PHEOC Ministry of Health in December 2017, it was mentioned that diphtheria outbreaks in some of the capital's buffer zones, including in Banten Province, were 81 cases with three deaths and diphtheria outbreaks in West Java Province, 95 cases with ten deaths. And RSPI Prof. Dr. Sulianti Saroso herself in previous years has treated positive diphtheria confirmation patients from Tangerang (Banten Province) and Bekasi and Bogor (West Java Province) [16].

In a serosurvey conducted by Pracoyo and Roselinda (2013), it was stated that respondents living in the case area were at risk of being infected with diphtheria 2.3 times greater than respondents who lived in non-case areas [24].

The research conducted by Sari (2014) in Bangkalan District stated that there were epidemiological interactions between cases of diphtheria with other cases among sub-districts in Bangkalan Regency with cluster-shaped distribution patterns and the most dominant factor in influencing diphtheria incidence in this region was individual mobility from one area to another (p = 0.000; OR = 9,344) [25]. Therefore further research is needed in the capital's buffer zones which contribute to cases of diphtheria to prevent widespread transmission between regions.

According to the results of the study, there were differences in the proportion between cases and controls for pseudomembrane variables in the existing category compared to none at 6.8%. In the results of statistical tests obtained P-value = 0.533 using alpha 5% (0.05) then H0 is accepted which means there is no relationship between pseudomembrane with a decrease in the severity of diphtheria.

The absence of a relationship between pseudomembranes and a decrease in the severity of diphtheria in this study can be caused because in general diphtheria patients treated by RSPI Prof. Dr. Sulianti Saroso came with a complaint of finding a pseudomembrane in the upper respiratory tract (93.6%).

Based on medical record file records, the location of the pseudomembranes is generally located on the tonsils both bilaterally and unilaterally, the remainder is found in the pharynx, uvula and larynx, and in this study did not specify the location of the membrane but the only pseudomembrane was present or not.

Based on the results of the study, there are differences in the proportion between cases and controls for the bull neck variable in the existing category compared to none at 11.6%. According to the statistical test results obtained P-value = 0.499 by using alpha 5% (0.05) then H0 is accepted which means there is no relationship between bull neck with a decrease in the severity of diphtheria, bull neck value does not indicate possible reduction in severity due to the number of patients with bull neck 28.5% of the whole sample and bull neck itself still have confusion with enlarged lymph nodes (LN).

In some diphtheria patients who were referred to by the bullneck when getting a follow-up examination at RSPI Prof. Dr. Sulianti Saroso, then the bull neck in question is not bullneck diphtheria but LN enlargement. The bullneck data in the case group and the control group was taken based on the data contained in the medical record file so that valid data cannot be controlled.

Based on the results of the study, there were differences in the proportion between cases and controls for the variables of myocarditis in the existing category compared to none at 16.4%. According to the results of statistical tests obtained P-value = 0.209 using alpha 5% (0.05) then H0 is accepted which means there is no relationship between myocarditis and decreasing in the severity of diphtheria.

In a study conducted by Puspitasari (2012), the most common complication in diphtheria patients who received treatment at Soetomo General Hospital was myocarditis (11.5%), and the most significant cause of death of diphtheria was myocarditis (81.8%) [14].

Mortality due to diphtheria usually occurs in the initial four weeks of illness due to heart failure and respiration, so to detect myocarditis, an electrocardiogram (ECG) must be carried out at the beginning of treatment and every two days after a week of illness to identify myocarditis earlier. Therefore, patient awareness is needed to keep checking their health after returning home and collaborating with regional surveillance officers in monitoring cases that have returned home, because RSPI Prof. Dr. Sulianti Saroso was unable to capture the incidence of myocarditis after the hospital treatment was completed.

Based on the results of the study, there were differences in the proportion between cases and controls for the culture outcome variables in the positive category compared to the negative of 34.8%. According to the statistical test results obtained P-value = 0.002 using alpha 5% (0.05) then H0 is rejected which means there is a relationship between the results of culture with a decrease in the severity of diphtheria. OR value = 0.170 (95% CI: 0.054-0,547) means that in diphtheria patients whose positive bacterial culture has a risk of 0.170 times greater decreased severity compared with diphtheria patients with negative diphtheria culture results.

The limitation of this study is that it cannot provide data on the type of diphtheria germs completely because examination of diphtheria specimens was not carried out in the RSPI laboratory Prof. Dr. Sulianti Saroso, but sent to a reference laboratory that takes a long time and the results given depend on the results issued by the reference laboratory. Therefore, it is expected that RSPI Prof. Dr. Sulianti Saroso can have Toxigenic PCR Culture laboratory to enforce accurate diagnoses, prevent laboratory data from not being recorded or scattered and for the benefit of research and RSPI Prof.

Dr. Sulianti Saroso as an infectious national referral hospital.

Conclusion

Based on the analysis results of the study on the Effect of Diphtheria AntiToxin (DAT) to Decrease Degrees of Diphtheria Severity in RSPI Prof. Dr. Sulianti Saroso Year 2014-2017, it can be concluded that the administration of DAT proved to be influential and most dominant towards the decrease in the severity of diphtheria in diphtheria patients treated at RSPI Prof. Dr. Sulianti Saroso. Significant factors associated with a reduction in the severity of diphtheria are DAT, corticosteroid administration and culture results while myocarditis is a confounding variable.

Suggestion

1. Maximizing the management of diphtheria incidence by strengthening the coverage of vaccine cold chain immunization and strict supervision throughout Indonesia; strengthening cross-sector cooperation and involving religious leaders, community leaders and public figures in receiving immunizations to reduce resistance to vaccination (antivaccine); monitoring the availability of DPT vaccines to prevent the circulation of fake DPT vaccines, providing halal and independent vaccines and serums to avoid scarcity of vaccines and serums (DAT), rejection of vaccinations and dependence on vaccine imports to other countries.
2. Developing further research with a prospective cohort method to provide valid results, examining other factors not included in this study to obtain results with a broader perspective.

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