The Effectiveness of BCG (*Bacillus-Calmette Guerin*) Immunization to the Tuberculosis Incidence on Children at Banyuasin Regency

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Abstract. Bacillus Calmette Guerin (BCG) vaccine is still the only licensed vaccine against Tuberculosis (TB), with an estimated global coverage of 85%. However, although the vaccine has been established, discussions about its benefits and shortcomings continue.The coverage of immunization is appropriate with the target, but still the occurrence of child TB cases raises a problem of its own. This studywas a non-experimental study with study design was Case Control Study by retrospective. The effectiveness of BCG immunization in this study is 85%, meaning that children are given BCG 85% immunization will be protected from Tuberculocis (TB) disease. If the child does not get BCG immunization will increase the chances for the child, with OR = 6.87 (95% CI; 2.2 – 21.1) with p value = 0.000. It is suggested to Banyuasin regency Health Office to conduct the contact examination of house of children who are around TB positive patients periodically (monthly / at posyandu).

1 Introduction

Bacillus Calmette Guerin (BCG) vaccine is still the only licensed vaccine against Tuberculosis (TB), with an estimated global coverage of 85% [1.2]. WHO recommends that infants be immunized immediately after birth with a single intradermal BCG dose in all countries with a high risk of TB infection. Even Indonesia, since 1956, has implemented an immunization program, one of which is BCG vaccination. The Ministry of Health is implementing the Immunization Development Program (PPI) for children in efforts to reduce the incidence of diseases that can be prevented by immunization (PD3I) [3].

However, the presence of different BCG strains and immunization policies that took place several decades prior to the release of such global recommendations have made it difficult to assess the efficacy of BCG vaccine. Currently, more than 3 billion people have received BCG vaccination and make BCG vaccine as the most widely used vaccine worldwide. However, although the vaccine has been established, discussions about its benefits and shortcomings continue.The issues discussed include vaccine safety aspects, loss of sensitivity to tuberculin as a diagnostic reagent, and the fact that although it has been shown to help end the TB Epidemic in Europe, the efficacy of this vaccine is generally disappointing in trials conducted in developing countries [4].

Despite the growing consensus that BCG vaccination protects children effectively against early manifestation of TB, but estimates of its protection against adult pulmonary TB range from 0-80% based on large and controlled field trials [5-7]. A meta-analysis study examining more than 1200 articles from international publications has concluded that the overall value of BCG protection against all forms of TB is only 50%, but protection against more serious infections is greater, such as tuberculosis meningitis, ie 64% - 78% [8].

Until now, tuberculosis is still the main cause of morbidity and mortality in children, but not a priority in the handling. TB is the ninth cause of death worldwide, above HIV / AIDS. By 2016, there are an estimated 1.3 million deaths due to TB among HIV negative people and an additional 374.000 deaths among HIV-positive people. Indonesia is second only to India [9].

An estimated 10.4 million people suffer from TB by 2016, 65% are male, 10% are living with HIV, and 90% are adults, and 10% of children [9]. This high TB child rate indicates tuberculosis in children is an important component in TB control because the number of children aged less than 15 years is 40-50% of the total population and there are about 500.000 children in the world suffer from TB every year. In Indonesia the proportion of Child TB cases among all TB cases that were notified in the TB program was 9% of the estimated 10-15% [10].

Children infected with TB are mostly from adult TB patients, so it is important to understand the epidemiological description of TB in adults in tackling child TB. TB infection in children and children with tuberculosis is caused by contact with adults with active TB disease. Enforcing diagnoses of TB in adults is obtained from positive sputum examination. Confirmation of difficult childhood tuberculosis diagnosis resulted in the neglected treatment of tuberculosis, resulting in several years of TB child excluding public health priorities in many countries, including Indonesia [11].

Research on tuberculosis, especially on TB in adults has been widely practiced, but research on child tuberculosis, especially on the effectiveness of BCG immunization against child TB has not been done especially in Banyuasin Regency, South Sumatera. Immunization coverage is appropriate with the target, but still the occurrence of child TB cases raises a problem in itself.

2 Materials and Methods

This studywas a non experimental research with case control study design as retrospective. Case groups include children diagnosed with Tuberculosis (TB) by doctors based on a scoring system established by the Ministry of Health (data from the Banyuasin regency Health Office), amounting to 76 children. While the control group includes children who do not suffer from Tuberculosis (TB) which is the nearest neighbor of the case or are in the neighborhood around the case, also amounted to 76 children.

The study was approved by the Ethics Committee Public Health Faculty of Sriwijaya University. All children TB patients who were registered in the Health Office of Banyuasin Regency and were not more than 15 years of age and have been living at the same address were eligible for the study. As for control was a healthy child or not being sick any, aged less than 15 years, and have lived at the same address. Informed consent was obtained before the interview. Households of children suffering from TB were kept, and consent is requested from the head of the household to conduct research. Information was collected using standard questionnaires.

Bivariate analysis was conducted to see the significance relationship between variables such as the main independent variables (BCG immunization status). The statistical test used

was the Chi Square test. At this stage an association size is generated in the form of Odd Ratio (OR).

3 Results and Discussions

Data were collected from 152 respondents in Banyuasin Regency, South Sumatera, Indonesia. The data were collected from February - April 2018. The analysis was conducted to see the relationship between independent variables (BCG immunization)and dependent variable(Child TB incidence). The test used in this study was Chi square test with $\alpha = 0.05$.

Table 1. Bivariate analysis of the relationship among BCG Immunization and Child TB Incidence and its covariate variables

Variabel		Child TB Incidence				*P value*	OR
		Positive		Negative			95% CI
		n	%	N	%		
BCG Imunization Status							
	No	21	84	4	16	0.000	6.87
	Yes	55	43.3	72	56.7		2.2 – 21.1

In Table 1, it was found that 21 (84%) of children diagnosed with TB were not given BCG immunization, and for BCG immunized children 55 (43.3%) of children diagnosed with TB. From the statistical test, p = 0,000, it can be concluded that there was a difference of proportion in TB incidence between BCG immunized child and BCG immunization (there wass a significant relationship between BCG Immunization and Child TB Incidence). From the analysis results also obtained the value OR = 6.87 (95% CI 2.23 - 21.17) which meant that children who were not given BCG immunization at risk 6.87 times to get tuberculosis compared with children who were given BCG immunization.

As is commonly known, one third of the world's population is already infected with mycobacterium tuberculosis (TB). The most effective TB control is combined with OAT and vaccination. To date, vaccination of Bacillus Calmette-Guerin (BCG) has been mandatory in 64 countries and recommended in several other countries[12]. Recently, the World Health Organization expanded the coverage of the immunization program by recommending BCG at 3 months of age, while in some countries there were those who recommended vaccinations at birth, at school entry, and in adolescence [13].

The effectiveness of BCG vaccine in reducing TB disease has been estimated in several studies [14], and has resulted in great variations in its effectiveness. Although the efficacy of BCG vaccine in the prevention of miliary and meningeal tuberculosis among children has been shown to be consistent, the efficacy of BCG vaccine variables to the pulmonary disease results in many differences [15].

A meta-analysis study showed that BCG vaccination was effective in reducing the risk of severe TB manifestation, and reducing the risk of contracting TB in newborns with an average of 50% protection [16, 17]. On the other hand, many other published case-control studies have also discussed the effectiveness of BCG vaccines, ranging from no protection at all [18] to yielding an 83% reduction in TB incidence [19].

A large follow-up study, conducted over a period of 1948-1998 (60 years), examined Native American and Alaska Indigenous populations who participated in a controlled BCG vaccine trial trial, found the estimated success of BCG vaccine was 52% (95% CI, 27% -

69%)[20]. The researchers added, BCG has a good protective effectiveness to the tuberculosis up to 60 years after vaccination.

Clinical studies and case-control studies conducted in various countries to measure the protective effect of the first dose of BCG vaccine to the death clinical and miliary tuberculosis form showed a protection rate above 80% for different types of vaccines(Copenhagen, Moreau, Glaxo) [21]. Meta-analysis also showed the average protective effect of the first dose of BCG vaccine ranging from 73% to 86% [15]. In Brazil, three case-control studies in various cities also reported high levels of protection from the first dose of BCG vaccine, respectively 84.5%, 93.3% and 99.5% [21].

Meanwhile, the protective effects of BCG vaccine for pulmonary tuberculosis are found to range from zero to 80%, in clinical studies and case controls conducted in various countries since the 1940s [21]. The protective effect observed in the meta-analysis is also quite heterogeneous, ranging from -88% to 79%. [17] argues that the number is due to the heterogeneity of the observed effects.

Two things need to be considered in addressing the differences in the effectiveness of BCG vaccine. First, the position of latitude. Latitude correlates with many ecological characteristics, such as temperature, humidity, soil type, and vegetation, each of which affects the environmental microflora [8]. A study that summarizes the effectiveness of BCG vaccine against pulmonary tuberculosis by latitude shows a very significant trend ($p < 0.001$). An overview also concluded that latitude can account for 41% of the variance between published studies [22]..

A meta-analysis aimed at studying the relationship between the geographical location (latitude) of the study evaluating the protective effect of BCG vaccine and its effectiveness / effectiveness on tuberculosis, also acknowledged the association between the geographical location of the study and the reported protective effect of BCG vaccine against tuberculosis [6].

Secondly, there are many different species of environmental mycobacteria present in the environment, all of which adapt to different conditions. There may be some species that are relatively, not even absolute, more frequent in some parts of the earth[8].

4 Conclusion

In immunized children as many as 72 children (56.7%) did not suffer child TB, whereas in non-immunized children 21 (84%) children suffered child TB. The effectiveness of BCG immunization in this study was 85%, whereas if BCG immunized children were 6.87 times more likely to suffer TB compared with BCG immunized children. In this study was obtained that 33% of child TB incidence in population, donated by BCG immunization status, so BCG immunization can suppress the decrease of child TB incidence by 33.5% (50% to 16,5%).

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