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Profile of Serious Adverse Effect Following Immunization (AEFI) of Measles Rubella Vaccine in East Java Province, Indonesia

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ABSTRACT

The measles rubella immunization campaign conducted in 2017 on the island of Java has replaced the previous measles immunization, and its administration is carried out at 9-12 months of age and 18 months of age. As a new vaccine, the administration of MR vaccine cannot be separated from AEFI. We aimed to study the AEFI profile of MR vaccine administration by passive surveillance from the first campaign of MR vaccine in East Java Province. Our study was a retrospective observational study. The research was conducted from January - April 2021. Children who received the MR vaccine in the MR campaign at all age were enrolled in the study. Total samples were collected. A questionnaire was used to collect the data. The total sample is 43 children with serious AEFI, consisted of 22 (51.2%) males and 21 (48.8%) females. The most common AEFI reported was fever (76.7%), followed by gastrointestinal symptoms (60%), local reactions (25%), respiratory tract symptoms (23.2%), central nervous system symptoms (11.6%), and rash (6.9%). Fever is the most frequently reported symptom. Most of the AEFI symptoms didn't had causal relationship with MR vaccine. Thrombocytopenia is known to have a causal relationship as a reaction to the MR vaccine.

Keywords: AEFI, Measles, Rubella, MR vaccination

INTRODUCTION

Measles, also known as morbili, is an acute infectious disease that affects the respiratory system, immune system, and skin. This infection is caused by the morbili virus – single-stranded RNA morbili virus – which belongs to the paramyxovirus group. While Rubella (German measles) is an infectious disease caused by togavirus, through the RNA chain. Measles has a high rate of morbidity and mortality. On the other hand, rubella has relatively mild symptoms, but is clinically significant when it occurs during pregnancy and puts children at risk for congenital rubella syndrome.[1,2] There is no specific treatment for measles nor rubella, but both can be prevented by vaccination. Since the discovery of the MMR vaccine (measles, mumps, rubella) in October 1988, the transmission of measles has decreased dramatically, and the incidence of measles is very low.[3] The measles mortality rate which decreased significantly after vaccination shows evidence that the coverage of measles vaccine is very important because it can reduce mortality and morbidity due to measles, especially in low-income countries. This disease is highly contagious in immunocompromised communities.[4]

Until mid-2017, Indonesia was still providing measles single immunization, but due to the increasing incidence of CRS in the last decade, the single measles vaccination was replaced with the MR combination vaccine. MR immunization campaign is carried out with the aim of achieving measles elimination and CRS control in 2020. The target of MR immunization is all Indonesian children aged 9 months to <15 years. During the campaign period, MR immunization was given regardless of immunization status or previous history of measles and rubella. Then the MR immunization will be included in the routine immunization schedule given at the age of 9 months, 18 months, and in first grade of elementary school.[5] Along with the higher immunization coverage, the use of vaccines also increases, the unwanted reactions after immunization also increase. WHO has defined adverse effect following immunization (AEFI) as an unwanted medical event that follows immunization and does not necessarily have a causal relationship with vaccine use. Based on the symptoms, AEFIs are broadly classified into three categories: common minor AEFI, which includes fever, rash, and local reactions; Serious AEFI, which results in hospitalization, life threatening, death, or significant disability; and severe AEFI, which includes any adverse event of increased severity.[6]

The MR vaccine used in the immunization campaign program is a live-attenuated vaccine containing the Edmonston-B strain of measles and the RA 27/3 strain of rubella. The administration of the Edmonston B vaccine was associated with a high rate of fever (temperature of 39.4°C or higher in 20% to 40% of vaccinees) and rash (approximately 50%), but the general condition remained well.[7] A study conducted in India about AEFI in MR vaccines reported that the most common symptoms was fever (38%), followed by upper respiratory tract infection (30.9%), local swelling at injection site (26.1%), and skin rash (4%).[8]
Reported AEFI following the use of combined vaccines (MR and MMR) are similar to those described with single antigens. The type and rate of serious adverse events does not differ significantly for MMR or MR combinations compared with the individual antigens. The MR vaccine is highly safe and well tolerated.[9]

AEFI reporting in Indonesia is a passive reporting process. As only a few Indonesian studies on adverse reactions of vaccines could be traced, we wished to collect bigger data on AEFI in pediatric population of Indonesia through the present study.

METHOD

We did a retrospective observational study, with cross-sectional design, among the children whom attended the MR vaccination campaign in year 2017 in Blitar region, East Java province, Indonesia. The research was conducted from January - April 2021. Total samples from all population who had experienced serious AEFI in MR vaccination campaign were collected. We did passive surveillance based on data in East Java provincial health office. The parents were given questionnaire to fill out regarding the child's basic data, the MR immunization procedure that had been carried out, and the symptoms of AEFI. The exclusion criteria for this study were if the parents were not willing to fill out the questionnaire or the parents were not present. Confidentiality of the data collected was ensured. Data was entered in a Microsoft Excel sheet and subsequently analyzed in an Excel sheet. The ethical clearance was approved by the Health Research Ethics Committee Faculty of Medicine, Airlangga University (No. 283/EC/KEPK/FKUA/2020).

RESULT

A total of 50 children had experienced serious AEFI in MR vaccination campaign in Blitar region, but among them there were 5 parents/guardians who were not present at the time of the survey, and 2 parents who refused to fill out the questionnaire. Out of the 43 children for whom survey could be completed, 22 (51.2%) were males and 21 (48.8%) were females. Ages 1 – 5 years are the largest group who had experienced AEFI MR. There were 27 (62.8%) children with poor nutrition, and 8 (18.6%) children with history of allergy. More of the basic characteristic of research subjects are presented in Table 1.

Table 1. Basic characteristic of research subject

Characteristics	Frequency (N = 43)	Percentage
Sex:		
- Male	22	51.2%
- Female	21	48,8%
Age:		
- < 1 year	2	4,6%
- 1 – 5 years	38	88,4%
- > 5 years	3	7%
Nutritional status:		
- Good nutritional status	27	62,8%
- Poor nutritional status	16	37,2%
History of allergies:		
- Present	8	18,6
- Not present	35	81,4%
Parents education level:		
- Low	15	34,9%
- Medium	22	51,1%
- High	6	14%
Parents knowledge about immunization		
- Good	35	81,4%
- Poor	8	18,6%

Based from the onset of symptoms, 70 (79.5%) were in the initial 7 days and 18 (20.45%) were appear more than 7 days after vaccination. (Table 2) Of the AEFI's recorded, the most common was fever (76.7%), followed by gastrointestinal symptoms (60%), local reactions (25%), respiratory tract symptoms (23.2%), central nervous system symptoms (11.6%), and rash (6.9%). Thirty-five children experienced more than one AEFI. The most common combination was fever and gastrointestinal symptoms (n=20).

Table 2. Symptoms and onset of adverse effect following immunization

AEFI reported	Number of AEFI		Total n
	Within 7 days after vaccination	More than 7 days after vaccination	
Local reactions (Pain, Swelling, Reddish)	11	-	11 (25%)
Fever	25	8	33 (76.7%)
Rash	2	1	3 (6.9%)
Respiratory tract symptoms (cough, runny nose, dyspnea)	8	2	10 (23.2%)
Central nervous symptoms (seizure, encephalopathy)	4	1	5 (11.6%)
Gastrointestinal symptoms (nausea-vomiting, diarrhea)	20	6	26 (60%)

DISCUSSION

The incidence of serious and non-serious AEFIs during the 2017 MR campaign period in Blitar district was 502 children out of a total of 256,138 immunization coverage (0.19%), consisting of 50 serious AEFI cases and 452 non-serious AEFI cases, and there was 1 report of death. Not many study centers have reported AEFIs using the MR. A study in India [8] reported AEFI of MR in 9-12 months children as many 42 out of 271 children, but the study still cannot describe the AEFI of MR in population. Meng et al [10] reported AEFI of MMR in Anhui province in China as many as 1893 children out of 9.9 million dose of vaccine (0.019%). Meanwhile in selected province in Iran, Esteghamati et al [11] reported 792 cases out of 43447 of AEFI in MMR vaccination.

In this study, all subjects were hospitalized, with fever became the most common symptoms. Fever is the most frequently reported symptom of AEFI in various study centers. [8,11–13] Vaccine Adverse Effects Reporting system (VAERS) in the USA reports that the incidence of fever can be found in the serious and non-serious AEFI groups. Experts who are members of VAERS found several explanations for the occurrence of this fever. Fever may just be one of many signs and symptoms that are actually coincidental at the same time, for example a fever associated with sore throat and cough after immunization is much more likely to be caused by the common cold than a vaccine. The lack of data also makes it impossible to infer the level or relative risk of fever after immunization, compared with the unvaccinated population.[14] Children experience an average of 2-6 episodes of acute fever in the first 2 years of life, with two-thirds of cases requiring medical treatment, so the assessment of fever as an AEFI must take into account the background factors of the disease, and the infectious process that occurs at the time of immunization the most common cause of fever. [15,16] Poland et al [17] defined that fever reported as AEFI is a manifestation of acute viral infection and trauma due to injection that causes an immune reaction and causes the release of cytokines in the body.

Other symptoms involving organ systems have been tested for causality by AEFI's regional commission in East Java province and none of them meet the causal relationship as AEFI MR. Systemic reactions that have been proven as AEFI vaccines containing measles are febrile seizures, thrombocytopenia, and anaphylactic reactions.[6] This study found 2 cases of AEFI that had a consistent causal relationship as a reaction to the MR vaccine, which is thrombocytopenia, that manifested as ITP. The risk of ITP after MMR immunization was investigated by France et al [18] who found 259 cases of ITP in 1,036,689 children who received MMR vaccine (0.02%). The greatest incidence of ITP occurs in children aged 12-23 months and 76% of cases have been shown to

be consistent with MMR AEFI reactions with the number of cases being 1 per 40,000 doses of vaccine. ITP in children over the age of 5 years was only found in 5 out of 259 cases. A systematic review of 12 studies found the incidence of ITP as an MMR AEFI of 0.087 – 4 cases per 100,000 doses of vaccine. ITP as a vaccine reaction is very rare, and is generally not life threatening and self-limited.[19]

Limitation of the study

The weakness of this study is the bias in the data recall process.

Conflict of interest statement

The authors declare that there is no conflict of interest

CONCLUSION

Among all serious AEFI reports, fever is the most frequently reported symptom. Most of the AEFI symptoms that had been reported didn't had causal relationship with MR vaccine. Thrombocytopenia is known to have a causal relationship as a reaction to the MR vaccine.

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