Factors associated with measles antibody titers in children aged 12-36 months in Indonesia: an analysis of National Health Research 2013

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Abstract

Background: The immunization program in Indonesia has been implemented since 1956 started to eradicate smallpox and expanded until 1980, including Measles. The timely and complete implementation of basic immunization is the main strategy to protect the population, including outbreak prevention. The purpose of this study is to determine the level immunity of Measles antibody as the outcome of completed basic immunization and its contributors in children aged 12-36 months.

Methods: This study is a secondary data analysis of the Indonesia Basic Health Survey (RISKESDAS) 2013. The analysis was carried out on a serological sample of the antibody titer of children aged 12-36 months, totaling 229 samples. The sample inclusion criteria were children who had complete sociodemographics data, basic immunization records and Measles antibody titer data. Measles examination was carried out using the Enzyme-Linked Immunosorbent Assay (ELISA) method.

Results: Incomplete immunization, being a boy, and lack of cleanliness in the family room were significantly associated with lower measles antibody levels in children. Having each variable controlled, completeness of immunization (OR=1,99; p=0.018; 95% CI=1.124-3.544) and gender of boy (OR=2.0; p=0.016; 95% CI=1.137-3.515) remain as significant variables for antibody's titer.

Conclusion: The completeness of immunization has a significant association towards titer antibody of Measles in children. Immunization completeness is an actual effort to reach herd immunity in children and to prevent measles outbreak in the community. Adequate health promotion is needed to change people's behavior to believe in the safety and importance of implementing complete basic immunization for children even in pandemic conditions. ***(Health Science Journal of Indonesia 2021;12(2):97-103)***

Keywords: antibody titer, immunization, children aged 12-36 months, Indonesia, measles

Abstrak

Latar belakang: *Program imunisasi di Indonesia telah dilaksanakan sejak tahun 1956 yang dimulai dengan pemberantasan cacar yang diperluas hingga tahun 1980, termasuk campak. Pelaksanaan imunisasi dasar yang tepat waktu dan lengkap merupakan strategi utama untuk perlindungan penduduk, termasuk pencegahan Kejadian Luar Biasa (KLB). Tujuan dari penelitian ini untuk mengetahui tingkatan kekebalan antibodi Campak sebagai hasil dari kelengkapan imunisasi dasar dan faktor yang berkontribusi pada anak usia 12-36 bulan.*

Metode: *Penelitian ini merupakan analisis data sekunder Riset Kesehatan Dasar Indonesia (RISKESDAS) 2013. Analisis dilakukan pada sampel serologi titer antibodi anak usia 12-36 bulan yang berjumlah 229 sampel. Kriteria inklusi sampel adalah anak yang memiliki data sosiodemografi lengkap, catatan imunisasi dasar dan data titer antibodi Campak. Pemeriksaan campak dilakukan dengan metode Enzyme-Linked Immunosorbent Assay (ELISA).*

Hasil: *Imunisasi yang tidak lengkap, berjenis kelamin laki-laki, dan kurangnya kebersihan di ruang keluarga berhubungan bermakna dengan rendahnya tingkat antibodi campak pada anak. Setelah masing-masing variabel terkontrol, kelengkapan imunisasi (OR=1,99; p=0,018; 95% CI=1.124-3.544) dan jenis kelamin laki-laki (OR=2.0; p=0.016; 95% CI=1.137-3.515) merupakan variabel yang tetap berhubungan dengan titer antibodi secara signifikan.*

Kesimpulan: *Kelengkapan imunisasi memiliki hubungan yang bermakna terhadap titer antibodi Campak pada anak. Kelengkapan imunisasi merupakan upaya nyata untuk mencapai herd immunity pada anak dan mencegah wabah campak di masyarakat. Promosi kesehatan yang memadai diperlukan untuk mengubah perilaku masyarakat agar percaya akan keamanan dan pentingnya pelaksanaan imunisasi dasar lengkap bagi anak meskipun dalam kondisi pandemi.* ***(Health Science Journal of Indonesia 2021;12(2):97-103)***

Kata kunci: *titer antibodi, imunisasi, anak usia 12-36 bulan, Indonesia, campak*

Immunization intends to provide toddlers' immunity. The immunization policy began in 1956 to eradicate smallpox. It expanded until 1980, including several vaccination types, i.e., BCG, DPT, Polio, and Measles. Hepatitis B immunization had become part of the national program in 1997. Basic Immunization Program in Indonesian toddlers started soon after birth and reached nine months, followed by repeated immunizations at specific periods (Regulation of the Minister of Health No.12 / 2017). The Indonesian Basic Health Research (RISKESDAS) shows no significant change in the prevalence of children receiving complete basic immunization. In 2013, it was reported that only 60% of children aged 12 months had completed the necessary immunizations, while the results of the 2018 survey the prevalence decreased slightly to 57.9%. Incomplete basic immunization coverage experienced a small increase from 32% to 32.9% from 2013 to 2018 and there were still 9.2% of children who did not receive immunizations based on the survey in 2018.[1,2]The global spread of the COVID-19 pandemic has been shown to significantly impact routine immunization services disruption. A rapid study conducted by UNICEF and the Indonesian Ministry of Health in April 2020 found that 84% of all health facilities reported interruption of immunization services. This disruption occurred at various levels of service where there was a decrease in demand due to fear of contact with COVID-19. In addition, there has also been a shift in focus on resources for controlling COVID-19. It was also reported that the limitations of personal protective equipment (PPE) in carrying out safe immunization were one of the problems that disrupted immunization services.[3] This further exacerbates the risk of children getting incomplete immunizations.

Due to the high prevalence of incomplete immunization in children, this has implications for the risk of disease exposure in children under five. In which malnutrition can be one contributor to this condition. Malnourished as a consequence of inadequate intake of food and other multiple predecessor factors in children are at a high risk of child mortality. It is commonly seen in low- and middle-income countries.[4,5] There is a two-way causal relationship between malnutrition and infection. Malnutrition caused by inadequate intake increases susceptibility to infectious diseases, while the condition might worsen infant nutritional status by reducing appetite, repetitive intestinal infection, and nutrient malabsorption. Although it is debatable whether malnutrition increases the incidence of infection or whether it only increases the severity of the disease, studies showed malnourished children are at a higher risk of death after infection.[6,7] Therefore child immunity is very important and can be invested early years of life through the maternal nutritional status.[8]

Nutrition is an essential determinant of the immune response, while malnutrition mostly causes immune deficiency worldwide. Lack of amino acids and carbohydrate intakes are associated with a significant decrease in cellular immunity. Specifically, on the phagocyte function, the complement system, secretory immunoglobulin, antibody concentrations, and cytokine production. Single nutrient deficiency produces an immune response, even when a nutritional deficiency is relatively mild. Micronutrients such as zinc, selenium, iron, copper, vitamins A, C, E, and B-6, and folic acid are essential for immune response. Excessive nutrition and obesity also reduce immunity. Babies with low birth weight have prolonged cellular immunity disruption, which can be partially restored by providing a different diet plus zinc.[9]

Inadequate nutritional intake reduced the body's immunity and body response to form antibodies, especially at newborn and young child of 12–36-month-old. The body's vulnerability at these age groups should be maintained since the fetus. Maternal micronutrient supplementation could prevent the adverse effect of the birth outcome, such as preterm birth and neonatal mortality[10–13] Furthermore, improved breastfeeding practices at postnatal and optimal nutrition intervention would prevent child's immunity and reduce deaths from infection.[14]

We selected children aged 12-36 months to assume that these subjects have completed the necessary immunization and measles booster and the body's immune response against measles formation. Based on the above evidence, to date, there are still limitations to studies using antibody titers in survey data to emphasize the importance of a comprehensive basic immunization program for children in Indonesia. Therefore, this study aims to determine the level of measles immunity in children aged 12-36 months and the factors associated with it.

METHODS

Design and Sample

Riskesdas has been carried out every five years since 2007. In the 2013 survey, data collection was conducted in the period of May-June, in 33 provinces and 497 districts/cities. This survey measures the coverage of health indicators in Indonesia. It measures the content of health indicators—secondary data analysis conducted to produce this article.

Measures

RISKESDAS 2013 blood sampling represented the provincial level. Probability proportional to size with replacement in selecting 177 districts/cities sampling is applied, then census blocks chosen by systematic sampling. The biomedical sample size which includes 1,000 Census Blocks was 49,931 people.[15] Our study consisted of a secondary analysis based on data from 229 children aged 12-36 years. The sample inclusion criteria were children who had complete sociodemographic and basic immunization records, public health and also Measles antibody titer data.

Measles examination was carried out using the Enzyme-Linked Immunosorbent Assay (ELISA) method using a commercial NOVALISA kit, which read at a wavelength of 450/620 nm. Measles IgG antibody titers were divided into two positive categories if the titer is> 220 mIU / ml and negative if it is ≤ 220 mIU / ml. The negative group titers with equivocal values (titers 120 - 220 mIU / ml) have been repeated and included.[16]

The dependent variable is the measles antibody titer (protective/non-protective). In contrast, the independent variables included age, sex, prior immunization status (complete/incomplete), nutritional status (WAZ, HAZ, and WHZ), frequency of illness in the past month (ARI, Diarrhea, and Pneumonia), anemia status (Fe levels in the blood), environmental health status, and settlement status (rural-urban).

Analytic strategy

Data were managed and analyzed using the statistical software SPSS Statistics for Windows, version 21.0 (SPSS Inc., Chicago, Ill., USA). Analysis was performed for univariate, bivariate of Chi-square analysis, and multivariate using stepwise logistic regression. Following are the operational definitions of the variables used in this study.

Operational definition of variables included in this analysis

Terminology	Definition	Category
Batita or children under three years old	Children aged 12-36 months. We adjusted a little bit of this terminology as we included children aged 36 months in the data collected.	1=12-23 months 2=24-36 months
Antibody titer	The level of immunity of Measles at the plasma blood of children	1=protected 2=unprotected
Immunization	The vaccination exemption, namely Measles, DPT, and Hepatitis	1=yes 2=no
Immunization status	Completeness of the primary immunization accepted by the children, taken from child's KIA book record	1= completed 2=uncompleted and unimmunized
Nutritional status	Anthropometric measurement results of weight by age (WAZ or wasting) and height by age (HAZ or stunting) using the cut-off point <-2 SD as malnourished	1=well-nourished 2=malnourished
Disease frequency	Having a history of acute respiratory infection (ARI) or diarrhea or pneumonia at the last month	1= yes 2=no
Anemia status	Level of hemoglobin in the blood using the cut-off point<12 mg/dl	1= anemia 2=not anemia
Environmental health status	The availability of cleaned water and household's clean space in the house	1=yes 2=no
Residential	Urban and rural (based on the CBS criteria)	1=urban 2=rural
Mother's education	Mother's length of education from not schooling up to the highest level of education achieved	1=below high school 2=high school or above

Ethical Clearance

This study is a secondary data analysis from the 2013 RISKESDAS Survey. Ethical approval was granted by the National Ethical Committee (ethic number: 01.1206.207). Informed consent is signed up before the data collection by all study participants. For children younger than 15 years old, parental consent was mandatory.

RESULTS

There were 229 children aged 12-36 months with complete measles antibody titer data analyzed in this study—the frequency distribution for each variable presented in Table 1.

Table 1. The distribution of demographic and child health status

No	Characteristics (N=229)	n	%
1	Titer antibody (protective)	141	61.6
2	Immunization (completed)	147	64.2
3	Not wasted (WAZ)	176	76.9
4	Not stunted (HAZ)	136	59.4
5	No history of ARI	127	55.5
6	No history of Diarrhea	190	83.0
7	No history of Pneumonia	223	97.4
8	Not Anemia	150	65.5
9	Boys	122	53.3
10	Age of 24-36 month	151	65.9
11	Mother's education (high)	70	30.5
12	Urban residence	108	47.2
13	Clean space of the household	172	75.1
14	Clean water available	171	74.4

Of the 229 children, 61.6% had protective measles antibody status and 64.2% had complete immunization status. The proportion of illness history is relatively good, except for ARI experienced by almost half of the total sample (45.5%). Anemia in children under the age of three years reached 34.5%. Maternal education was still relatively low; only about 30% of mothers were high school graduates.

Table 2. Analysis of association between independent variables and measles titer antibody

No	Demography and Health Status	Measles Titer antibody		
		OR	95% CI	P
1	Incomplete immunization	1.91	0.982-3.701	0,05
2	Wasted	0.59	0.220-1.583	0.25
3	Stunted	0.72	0.353-1.469	0.37
4	Ever ARI	0.68	0.450-1.681	0,87
5	Ever Diarrhea	0.85	0.366-2.034	0.72
6	Ever Pneumonia	4.59	0.352-59.885	0.24
7	Anemia	0.86	0.431-1.737	0.68
8	Boys	2.45	1.243-4.843	0.01
9	Age of 12-23 month	1.57	0.807-3.063	0.18
10	Low mother's education	0.68	0.339-1.368	0.28
11	Rural residence	0.99	0.517-1.920	0.99
12	Clean family room	2.21	1.027-4.740	0.04
13	Clean water available	0.59	0.270-1.277	0.18

The bivariate analysis results showed children with incomplete immunization status had two times the risk of lower antibody titers (OR = 1.91; p = 0.05). No association between nutritional status and antibody titer status, nor was illness history. Table 2 shows family room cleanliness is significantly related to Measles antibody titer (OR = 2.21; p = 0.04). Boys have twice antibody titers than girls (OR = 2.45; p = 0.01). The regression analysis runs in the stepwise method, as presented in Table 3.

Fit model shows that having each variable controlled, completeness of immunization influences quality of Measles antibody titer (OR = 1.99; p = 0.01; 95% CI = 1.124-3.544). Boys' measles antibody titer is twice that of girls. No interaction between the completeness of immunization with the sex of the child. Statistically estimated calculation results show that Logit antibody titer = -1,057 +0,691 complete immunization + 0.693 male sex.

The model showed a significant number of Omnibus test p = 0.002, which completeness of immunization and sex could explain 7.6% (based on Nagelkerke R-square) effect on measles antibody variable in children. However, the accuracy of predicting the two variables against the Measles antibody titer was 61.6%.

Table 3. Multivariate regression of risk factors and measles antibody

Factor	Estimated				
	Reg Coeff (β)	Se of β	p-value	Odds Ratio of β	95% CI of β
Constant	-1.057	0.241	0.000	0.347	
Incomplete immunization	0.691	0.293	0.018	1.996	1.124-3.544
Boys	0.693	0.288	0.016	2.000	1.137-3.515

DISCUSSIONS

Completeness of vaccination has a significant effect on a toddler's antibody titer. Results of this study show completeness of immunization are closely related to protective measles antibody titers. There are two aspects in a child's immune system against the Measles vaccine, namely: 1) completeness of immunization shows the discipline of parents to access immunization services so that the child's immunity is protected, and 2) the possibility of antibody titers in Measles vaccine due to booster treatment.

Results of previous studies indicate, in general, mothers knew the benefits of immunization even though they do not fully understand, so mothers try to immunize their toddlers. Yet, those who are socio-economically capable always try to vaccinate their children to the fullest.[17] Besides, higher maternal education leads to better literacy skills and health-seeking behaviors, which increases immunization awareness for their children.[18]

A child's immunization completeness depends on the mother's knowledge and education. Unfortunately, this analysis results do not show any differences in children's antibody titers between mothers with low education and mothers with high education. A relatively small number of samples might cause this. Studies in Indonesia and several countries show maternal education as a determining variable in vaccination and child health. Higher the mother's education leads to higher understanding and awareness about the prevention of infectious diseases by immunization.[19–22]

Primary immunization is a mandatory program globally. The immunization program in Indonesia requires children to complete essential vaccination at the age of 9 months, followed by a measles immunization booster at the age of 18 months.[23] Maternal antibodies are transferred from the mother to protect their child's immune system from the late pregnancy period until the first month after birth or during the child's immune system maturation.[24] Therefore, vaccination is essential to acquire immunity. The health workers implemented immunization to the children through the integrated health post for child health or Posyandu.

A study of multilevel analysis in Indonesia showed the rise of immunization coverage from 47,5% to 61,5% in 2008 and 2013.[19] The 2018 RISKESDAS showed 32.9% of under-fives-year-old children in Indonesia did not get complete immunizations, and 9.2% were not immunized at all.[2] Unfortunately, according to the WHO recommendation (>80%) has not reached the basic immunization completeness coverage. Low immunization coverage has been shown by several studies, among others due to young mother's age, low parental education, limitations on access to health workers and health services, as well as the presence of certain negative beliefs. [19,25] Also, an analysis of data from IDHS 1997 showed that freeing immunization and health services charge did not guarantee mothers would bring their children getting immunized. Mothers' education is a confounder for children immunization.[26]

Vaccine safety is among the main issues for children not being immunized in developed countries such as America.[27] Besides, also the increasing refusal of vaccines based on religious beliefs. Incorrect interpretation of parents or religious leaders leads to clashes between religion and vaccination. Proper communication to illuminate the essence of the theological perspective on vaccination[28] is necessary to solve this issue. Studies on the incompleteness of immunization in Indonesia also underscore the problem of rural-urban disparities, where immunization coverage is lower in rural areas.[25]

Sex difference in measles antibody titers is challenging to explain. A GAVI report shows no difference in immunization coverage between boys and girls, except when gender inequalities existed (e.g., giving priority to boys); on the contrary, gender bias related to immunization inequality is apparent in India. Studies in six regions show that girls and those living in rural areas are less protected by vaccines because they have lower coverage than boys and those living in urban areas.[29]

A previous study from the 2013 RISKESDAS biomedical data analyzed the DPT antibody titer in under-five children in Indonesia found incompleteness on the 3-dosage of DPT's immunization was around 28%, while protective titers for tetanus and diphtheria was 18-30% and for pertussis was only 10%. This study provided a critical recommendation related to the immunization records that should be filled and appropriately stored.[30] The incompleteness of the immunization record caused inaccurate reporting of immunization coverage from surveys conducted in the community.

We used a cross-sectional dataset that cannot answer whether the dependent and independent variables

become our study limitation. Our small sample represented the national biomedical sub-sample of the RISKESDAS 2013. Therefore, future research is needed with a larger sample size to support better generalizability. Nevertheless, this is the only data related to immunization and antibody titer for measles in Indonesia.

In conclusion, immunization completeness and Measles's booster received are significantly protect antibody titer of children. Fully immunized children are more protected and have better Measles antibody titers than those who are incomplete. To avoid Measles and preventable diseases, the completeness of immunization is an important indicator. This study provides recommendations for policymakers in Indonesia to evaluate the ongoing immunization program, maximize health promotion, to educate the public on the importance of necessary immunization completeness. With the condition of the COVID-19 Pandemic which is exacerbating the challenge of providing complete immunizations to children. The reactivation of routine immunization programs must be supported by an effective communication strategy. Adequate health promotion is needed to increase knowledge and change the attitude and behavior of the community to believe in the safety and importance of carrying out complete basic immunization for children even in pandemic conditions.

List of abbreviations

BCG: Bacille Calmette Guerin vaccine; DPT: a class of combination vaccines against three infectious diseases in humans: diphtheria, pertussis (whooping cough), and tetanus; WAZ: Weight for Age Z Score; HAZ: Height for Age Z Score; WHZ: Weight for Age; ARI: Acute Respiratory Infection; IDHS: Indonesia Demographic Health Survey; WHO: World Health Organization; GAVI: The Global Alliance for Vaccines and Immunizations

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Authors contributions

NKA and PPA have contributed the same authorship as the first writer. Conceptualization: VS, NKA. Data curation: NKA, PPA. Formal analysis: NKA, PPA. Funding acquisition: NKA. Methodology: NKA, VS, PPA. Project administration: NKA. Writing - original draft: NKA, PPA. Writing - review & editing: VS, SI, PPA. The Authors declare that there is no conflict of interest.

Conflict of interest

The authors have no conflicts of interest associated with the material presented in this paper.

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