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Cost-effectiveness of rotavirus immunization in Indonesia: Taking breastfeeding patterns into account

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ABSTRACT

Objective: This study aims to assess the cost-effectiveness of rotavirus immunization in Indonesia, taking breastfeeding patterns explicitly into account.
Method: An age-structured cohort model was developed for the 2011 Indonesia birth cohort. Next, we compared two strategies, the current situation without rotavirus immunization versus the alternative of a national immunization program. The model applies a 5 year time horizon, with 1 monthly analytical cycles for children less than 1 year of age and annually thereafter. Three scenarios were compared to the base case reflecting the actual distribution over the different breastfeeding modes as present in Indonesia; i.e., the population under 2 years old with (i) 100% exclusive breastfeeding, (ii) 100% partial breastfeeding and (iii) 100% no breastfeeding. Monte Carlo simulations were used to examine the economic acceptability and affordability of the rotavirus vaccination.
Results: Rotavirus immunization would effectively reduce severe cases of rotavirus during the first 5 years of life of a child. Under the market vaccine price the total yearly vaccine cost would amount to US$ 65 million. The incremental cost per quality-adjusted-life-year (QALY) in the base case was US$ 174 from the societal perspective. Obviously, it was much lower than the 2011 Indonesian Gross Domestic Product (GDP) per capita of US$ 3495. Affordability results showed that at the Global Alliance for Vaccines and Immunization (GAVI)-subsidized vaccine price, rotavirus vaccination could be affordable for the Indonesian health system. Increased uptake of breastfeeding might slightly reduce cost-effectiveness results.
Conclusion: Rotavirus immunization in Indonesia would be a highly cost-effective health intervention even under the market vaccine price. The results illustrate that rotavirus immunization would greatly reduce the burden of disease due to rotavirus infection. Even within increased uptake of breastfeeding, cost-effectiveness remains favorable.

1. Introduction

Despite the growing number of diarrheal disease in Indonesia, the burden of rotavirus diarrhea as the major cause of diarrheal disease is poorly documented [1,2]. Indonesia was one of the countries in Asia, which received support from PATH's Rotavirus Vaccine Program to strengthened the World Health Organization's (WHO)'s expanded immunization recommendations on promoting the global use of rotavirus vaccines [3]. Since 2001, according to the WHO's generic protocol, a longitudinal survey of rotavirus infection through the Indonesian Rotavirus Surveillance Network (IRSN) has been conducted in six hospitals in Indonesia [1]. The prospective surveillance in 2006 showed that rotavirus infections were responsible for the majority of severe diarrhea in children under-5-years occurring throughout the year mainly in children aged between 6 and 24 months old [1].

Breastfeeding is considered to protect against rotavirus infections [4]. The main component of breast milk that is thought to protect against rotavirus infection is lactadherine [4–6]. The WHO estimated that breastfeeding in accordance with the WHO's recommendations would save 1.45 million children's lives each year in developing countries due to averting diarrhea disorders and lower respiratory tract infections [5]. The United Nations Children's Fund (UNICEF) and the WHO issued a recommendation that children should be breastfed for at least six months to reduce the morbidity and mortality rates [7]. In 2003, the Indonesian government

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changed the recommended duration of exclusive breastfeeding from four to six months.

The Indonesian government needs to assess the economic benefits and health outcomes of such a vaccination program before routine rotavirus immunization can be recommended [8]. In terms of economic and financial perspectives, implementation of rotavirus vaccine should ideally be cost-effective. However, still it would be difficult to implement rotavirus immunization in the National Immunization Program (NIP) if the vaccine price is not affordable. Determining the financial resources needed is important to know the entire cost or budget impact of the vaccination program, even at the prevailing market price [9].

Up to now, only one economic evaluation study on rotavirus immunization has been conducted in Indonesia [8], suggesting that implementation of rotavirus immunization in the National Immunization Program (NIP) would be a cost-effective intervention in Indonesia. However, it only evaluated the use of the 2-dose vaccine while the potential impacts of the 3-dose vaccine in the NIP could also be considered. Additionally, the previous study applied the vaccine efficacy without taking breastfeeding patterns explicitly into account. Notably, further increasing breastfeeding would be in line with the WHO's recommendations on that matter. This might impact the economic evaluation results for rotavirus vaccination as maternal protection would be enhanced leaving less room for the preventive effect of the vaccine. Hence, it is important to know whether potential favorable cost-effectiveness remains within the context of the Indonesian policy to enhance the uptake of breastfeeding. The objective of this study is to assess the cost-effectiveness of rotavirus immunization in Indonesia, taking breastfeeding patterns explicitly into account.

2. Methods

2.1. Model

Considering the limitations of previous study and motivated by exploring the impact of breastfeeding in childhood vaccination, we performed a cost-effectiveness analysis on rotavirus immunization focusing on the use of 3-dose Rotateq® as one of the recommended rotavirus vaccines. Differing from previous studies on the same topic and model [8,10–13], we explicitly took breastfeeding patterns into account and compared three scenarios to the base-case reflecting the actual distribution over the different breastfeeding modes as present in Indonesia; i.e., the population under-2-years-old with (i) 100% exclusive breastfeeding (EBF), (ii) 100% partial breastfeeding (PBF) and (iii) 100% no breastfeeding (NBF). The vaccination program was compared to the condition without vaccination in these situations of the actual breastfeeding pattern (base-case) and specific scenarios.

In this study we applied an age-structured cohort model based on a decision tree model, developed by the University of Groningen labeled "Consensus Model on Rotavirus Vaccination" (CoRoVa), that has been used previously for both developing and developed countries [10,11], to assess the cost-effectiveness and affordability of implementing universal rotavirus immunization. We based the analysis on the Global Alliance for Vaccines and Immunization (GAVI)-subsidized vaccine price and market vaccine price in the context of the Indonesian healthcare system (see Fig. 1). We applied this model because of its ability to account for all relevant epidemiological parameters, economic aspects and characteristics of the vaccine, inclusive potential waning immunity [14]. Also, it was readily available to us. In particular, we used the Indonesia 2011 birth cohort of 4,200,000 infants [8] in this age-structured cohort model and applied a 5-year-time horizon with 1 month analytical cycles for children less than 1 year of age and annual cycles beyond 1 year.

2.2. Disease burden estimates

Using the data from the Indonesian Demographic and Health Survey (IDHS) 2007 on age patterns of breastfeeding, we populated the under-5-years-old population based on breastfeeding statuses as the actual distribution over the different breastfeeding modes as present in Indonesia: 3.8% EBF, 59.8% NBF and 36.4% PBF [15]. Health outcomes from this model were classified by the four levels of rotavirus-diarrhea severity that are generally used: mild, moderate, severe and death [2]. We assumed that mild disease requires home treatment, moderate requires general practitioner (GP) treatment and outpatient visits, while severe cases were assumed to require hospitalization [10,11]. This classification is in line with a study which was done previously for global assessments [2]. The model was programmed in Microsoft Excel 2010 and for probabilistic sensitivity analysis, @Risk 4.5.4. was used.

We estimated rotavirus-diarrhea cases from diarrhea cases in Indonesia. Firstly, we classified the Indonesian 2011 population under-5-years-old based on breastfeeding status using data from IDHS 2007 on breastfeeding status by age (0–3 years), extrapolated to the whole under-5-years population. We divided the population into the relevant age groups: 0–6, 6–11, 12–23, 24–35, 36–47 and 48–59 months [15]. In the compared scenarios, we assumed that the proportions of breastfeeding under-2-years-old are 100% EBF, 100% PBF and 100% NBF for scenarios 1, 2 and 3, respectively. We considered 2-year-time-horizon in our breastfeeding scenario as WHO recommended that exclusive breastfeeding for the first six months of life and supplemented breastfeeding continued up to two years or beyond [7]. For 36–47 months, we assumed that the proportions over breastfeeding status are 90% NBF, 10% PBF, 0% EBF, whereas for 48–59 months we assumed 100% NBF. Related to the diarrhea cases in under-5-years-old children, we used 2007 data from a previous study in Indonesia as a base-case [8]. We assumed the same number of diarrhea cases for 2011 as analyzed for 2007. For the scenarios compared, we estimated diarrhea cases explicitly based on breastfeeding distribution. Considering the relative risk of diarrhea from IDHS 2007 and the WHO's algorithm for calculating relative risk of diarrhea morbidity by feeding mode [16], we estimated 2011 diarrhea cases for under-5-years-old depending on breastfeeding status for the base-case and all scenarios. Secondly, we applied the same approach to calculate 2011 rotavirus-diarrhea cases for under-5-years-old in base-case and all scenarios by considering the percentage of patients with rotavirus-diarrhea from the number of patients with diarrhea enrolled in each age group reported in a previous study on the burden of rotavirus-diarrhea in Indonesia [1]. Finally, we classified rotavirus-diarrhea cases into the four levels of severity by applying proportions of 1.1% for death, 22.9% for hospitalization (severe cases) and 76.0% for outpatient visit (moderate and mild cases) on rotavirus-diarrhea cases [8]. Furthermore, we estimated that moderate would make up 38.7% and mild 61.3% from outpatient visit cases, based on a previously published application of CoRoVa to the South East Asia Region (SEAR) [14]. Notably, we obtained the number of rotavirus-diarrhea cases in four levels of severity adjusted by age for the base-case and all scenarios, consistently considering the same age groups in our adjustments (see Fig. 2).

2.3. Vaccine efficacy, waning immunity and between-dose efficacy

Rotavirus vaccine efficacy was estimated to be 84% for the prevention of rotavirus-associated hospitalizations, 70% for the prevention of outpatient visits and 76.5% for prevention of deaths [8]. We assumed these percentages as initial effectiveness of the vaccine for the outcomes: severe, mild/moderate and death, respectively. We applied the vaccine effectiveness from a previous study