Introduction of Rotavirus Vaccine in Indonesia: a New Hope in Reducing Under-Five Mortality

It has been years that diarrhea is one of the major leading causes of mortality among children under-five years old in Indonesia. It is reported that around 15% of mortality among under-five children is caused by diarrhea (United Nations Children’s Fund (UNICEF) 2010). With under-five mortality rate 41/1000 and around 4.2 million annual births, we can extrapolate that among 22 million under-five children, based on Indonesian Statistic Bureau census (Badan Pusat Statistik (BPS) 2010), around 172,000 of them die by any causes, and around 26,000 die due to diarrhea each year.

Personal hygiene and good sanitation condition play important roles in decreasing diarrheal incidence. Meanwhile Indonesia, with its more than 17,000 islands and population around 240 millions, face huge barriers in establishing those living conditions. As a developing country; urban slumps, poverty, and starvation are still around. Access to safe drinking water is still a problem for more than 100 million people and only around 45% could access good sanitation condition (Adisasmito 2007). Thus implementing key interventions to prevent diarrheal disease (e.g. access to safe drinking water, improved sanitation, good personal and food hygiene, and health education about how infections spread) is still far away to reach satisfaction rate (World Health Organization (WHO) n.d).

Moreover Indonesia is also still facing insufficient use of oral rehydration solution (ORS) or salt-sugar solution (SSS) as management of all diarrheal cases including rotavirus infection. In a study in Lombok, Nusa Tenggara Barat Province, it was reported that 56% of mother give ORS as diarrheal treatment and 10% give SSS. Among those mothers who involved in that study, only 37% of them could prepare ORS and 9% could prepare SSS (Widarsa and Muninjaya 1994). Based on National Basic Health Survey 2007, it was reported in a bulletin published by Ministry of Health, that 90% of mothers know about ORS or SSS, but only one out of three children (35%) who had diarrhea was given ORS or SSS (Kementerian Kesehatan Republik Indonesia 2011).

There is also another new hope to prevent diarrheal diseases, especially diarrhea which is caused by rotavirus, through vaccination. As one of disease prevention method, rotavirus vaccination is one of the solutions that we can implement. But it is not that easy to implement such a program, moreover a vaccination program. Since 2000, Indonesia has undergone decentralization including health sector, and it was strengthened by government act number 32/2004 (Pemerintah Republik Indonesia 2004) about districts autonomy. Thus local authorities have more power in regulating health. Vaccination as a vertical program, nowadays is implemented varies among districts based on their priorities, fiscal capacities, geographical barriers and other reasons. There are seven classical obligatory vaccination in Indonesia; BCG, hepatitis B, polio, DTP, and measles, those have been government national programs for years and parents could have their under-five children vaccinated for free in primary health centers. But if we try to add at least one more vaccine that can help to prevent one of the highest burden diseases which contributes to under-five deaths as mentioned above, would it be the government priority? How can we introduce and implement a new vaccination program to prevent diarrhea within decentralization
era? That is the challenge, we have to do more efforts to local authorities and make the program as one of the priorities.

**Burden of rotavirus infection**

Rotavirus infections are reported as the most common causes of diarrheal diseases. At least one episode of rotavirus infection is experienced by all children worldwide, 111 million cases treated at homes, while 25 millions of children have to visit clinics and 2 millions of them have to be hospitalized each year (Rotavirus Vaccine Program (RVP) 2008). Among those numbers, it is estimated that numbers of deaths due to rotavirus infection are 450,000 cases which mostly occurred in developing countries (Parashar et al, 2003).

A systematic review study reported that rotavirus infection contribute to hospitalized diarrheal cases among children around 38% in Asia. The authors also mentioned in their discussion that they found some studies in other regions which stated about rotavirus contribution is around 30% in Latin America, 40% in Europe, and 34-40% in Africa and Middle East (Kawai et al 2012).

Rotavirus infection is also the major cause of diarrheal diseases in Indonesia. It was reported that during period June 1978 – June 1979 in Yogyakarta Municipality, Indonesia, rotavirus infection was responsible 38% of all patients hospitalized with acute gastroenteritis (Soenarto et al 1981). A study held in six participating teaching hospital in six provinces of Indonesia also reported that rotavirus infection was the leading cause of acute diarrhea. It was vary from 39% to 67% depends on the study sites, while from overall 2240 stool samples tested, 60% of them were rotavirus positive. The study also reported that rotavirus is available all year round with peak season during period of June and July which are the highest peak of rainy season (Soenarto et al 2009).

**Development of rotavirus vaccine**

In an editorial (Zaman, 2008), it is mentioned that in 1998, the first licensed rotavirus vaccine was a tetravalent rhesus-human reassortant vaccine, produced by Wyeth Laboratories and licensed in USA under a brand name: RotaShield. It was followed by marketing authorization for Europe in 1999, but no longer after that the vaccine was withdrawn due to associated with increasing risk of intussusceptions (Center for Disease Control (CDC) 1999).

Two new rotavirus vaccines are now available. They are Rotarix, a live attenuated monovalent human rotavirus (HRV) vaccine, by Glaxo-Smith Kline, and RotarIX, a live attenuated pentavalent human-bovine reassortant rotavirus vaccine (WC3), by Merck. Both vaccines perform good efficacy results: HRV vaccine had efficacy of 85% against rotavirus gastroenteritis and rotavirus-associated hospitalization, and up to 100% against more severe rotavirus gastroenteritis, while 42% against hospitalization of diarrhea by any cause (Ruiz-Palacios et al 2006); WC3 vaccine had efficacy of 94.5% against rotavirus gastroenteritis hospitalization, 74.0% against rotavirus gastroenteritis, and 98% for severe rotavirus gastroenteritis (Vesikari et al 2006). In both studies, it was also mentioned of intussusceptions incidents among participants:
for HRV vaccine, 6 recipients among 31,673 infants in vaccine group; while for WC3 vaccine, 12 recipients among 34,035 infants in vaccine group.

In a study held in Mexico, after introduction of monovalent HRV vaccine by December 2007, with an estimated coverage of 74% among children 11 months old or younger. It was reported that diarrhea-related mortality had decreased from annual median of 18.1 to 11.8 deaths per 100,000 among under five children in 2008 (35% reduction), and among 11 months old infants or younger, diarrhea-related mortality had fallen from 61.5 to 36.0 death per 100,000 (41% reduction), while among 12 – 23 months old children, the reduction rate was 29% (Richardson et al 2010).

Another study which is undertaken in rural Matlab, Bangladesh and sub-urban Nha Trang, Vietnam, involved infants aged 4-12 weeks without symptoms of gastrointestinal disorders. The study was double-blind, placebo-controlled trial and participants were randomly assigned to receive three oral doses of pentavalent rotavirus vaccine or placebo. It was reported that the vaccine efficacy was 48.3% against severe rotavirus gastroenteritis during nearly 2 years of follow up, and there was a serious adverse events among 2.5% infants followed in vaccine group, which most frequent one was pneumonia (Zaman et al, 2010).

**Developing countries’ experiences in introducing rotavirus vaccination as a national program**

As recommended by WHO, the two rotavirus vaccine, monovalent HRV and pentavalent WC3, have been adopted in different countries into their routine EPI (expanded program on immunization). Some developing countries also already conducted trials of rotavirus vaccines, included countries where they had poor sanitation and high mortality of diarrheal diseases. In Africa, Rotarix had been evaluated in Malawi and South Africa, while RotaTeq in Ghana, Kenya and Mali; in Asia, Bangladesh and Viet Nam had evaluated RotaTeq (World Health Organization (WHO) 2009).

Latin America and Caribbean (LAC) is running one step further. Many countries within this region had introduced rotavirus vaccine and adopted into their EPI. Brazil, El Salvador, Mexico, Nicaragua, Panama and Venezuela were the first group introduced rotavirus vaccine into their national immunization schedules in 2006. By January 2011, 14 countries in LAC had adopted rotavirus vaccine as a program. It was also reported their coverage of rotavirus vaccine program varied from 49% - 98%, in which Venezuela was the lowest and Nicaragua was the highest. All of those 14 countries in LAC combined the schedule of rotavirus vaccination with DTP3 with coverage range between 78% - 99% (Center for Disease Control (CDC) 2011).

**Has Indonesia adopted rotavirus vaccine into national schedule on immunization?**

So far, Indonesian government keep going with seven classical vaccination programs as mentioned previously. It is already proven that both vaccines which WHO recommended perform good efficacy results. The studies related to rotavirus vaccine might bring new hope to Indonesia in reducing under-five mortality due to diarrhea. It has also been a discussion in
Ministry of Health that there are new rotavirus vaccines available and some studies conducted and still ongoing (Kementerian Kesehatan Republik Indonesia 2011).

There was a study about economic evaluation of rotavirus vaccine if implemented as a routine program. The study calculation was using the model of two doses monovalent HRV rotavirus vaccine due to low participants’ adherence in Indonesia for the third dose of any kind of vaccine. It was reported that the cost of a national rotavirus immunization program would be USD 53.424 million annually, with coverage estimation of 80%, 10% wastage, and 4.2 million annual births. It is such a huge amount of budget that government should provided if Indonesia adopted the program. But then, the study also reported the calculation of total costs that could be saved was USD 15.687 million per year, both medical and non-medical direct costs, if Indonesia adopted rotavirus vaccination as a national program (Wilopo et al 2009)

Discussion

Indonesian government must think very hard if we should implement rotavirus vaccine as a program. It is possible that government get co-payment through GAVI Alliance as we are eligible and already been supported since 2002 for new and underused vaccine support, immunization services support, health system strengthening, injection safety support, and support for civil society organizations (Global Alliance for Vaccine and Immunisation (GAVI) n.d). But rely on GAVI support, the sustainability of the program would be questioned how long that GAVI could support Indonesia and how if someday Indonesia is no longer belong to one of eligible countries to receive GAVI support.

As mentioned before that Indonesia is undergone decentralization, we have some provinces and districts that have high fiscal capacity but also have some provinces and districts that have low fiscal capacity, while if it would be the central government’s burden in covering extra vaccine for 4.2 million annual births among 33 provinces and 483 districts which vary from urban to rural, big islands to small and remote islands, that would be really difficult. Distribution of human resources for health could also be a limitation of this vaccine to be adopted as a program. Most of health workers in Indonesia serve in Java Island, moreover in Jakarta capital city, while the rests mostly serve in other big areas or islands (Heywood & Harahap 2009).

Developing funding mechanism that coordinated by central government might also work. Despite of some limitations issue on the seven previous vaccination programs, nowadays Indonesia has multi-layered social safety nets. It has been initiated since 1999 (after period of financial crisis in South-East Asia), through a program called “Jamkesmas” that now cover around 76.4 million poor people. Also by decentralization, there is such a competition among local authorities in having local safety nets, “Jamkesos” in provincial level and “Jamkesda” in district level (Rokx et al 2010). The idea is to bring health services more affordable to poor people: those who are not covered through Jamkesmas scheme would be covered by Jamkesos then finally by Jamkesda.

So, it might be possible for rotavirus vaccine program get funded through this kind of scheme. The next step is that we need a strong leadership; the central government could initiate
coordinating local governments or by providing new guidelines and regulations. It is absolutely
would be a very long task to do. We need some approaches to legislative and executive members
both local and central. Rotavirus experts also have to do more studies and deeper analysis to get
more evidence in efficacy and safety, cost-effectiveness and feasibility in procuring rotavirus
vaccine.

Some local districts which have high fiscal capacity and small number of population could
initiate adopting rotavirus vaccination as programs and becoming triggers for the others to
implement the same program.

While poor people is covered by social insurance scheme, it might be also a good idea that other
insurance scheme, such as “Askes” (insurance for civil servant) and “Jamsostek” (insurance for
labors and formal workers), could also be encouraged to cover rotavirus vaccination program.

It is also might be a benefit that Indonesian population make colonies in certain areas. Around
58% of Indonesian populations live in Java Island and 21% in Sumatra Island (Badan Pusat
Statistik (BPS) 2010). Government actually could focus on populous areas and pushing the
introduction of rotavirus vaccine as urgent need due to populous areas might have more slumps
area then more potential diarrhea outbreaks happen because of poor living condition, hygiene
and sanitation.

Poor, remote and less populous areas need special effort from government. National Medium-
Term Development Plan 2010 – 2014 stated that government should also consider area
categorizations in order for less developed area could catch up development disparity. It is
divided into seven region of development: Java-Bali, Sumatra, Kalimantan, Sulawesi, Nusa
Tenggara, Maluku, and Papua. Thus in every aspects of development, government could be more
focus in every regions, moreover in remote and neglected areas (Badan Perencanaan
Pembangunan Nasional (Bappenas) 2010). As mandated, if rotavirus vaccination program
implemented nationally, we should also consider those people who are living in remote areas,
and government should also be able to bring the idea of having people living there vaccinated,
might be by providing better infrastructures and distributing human resources equally.

Also there is a new hope that Indonesia can develop its own rotavirus vaccine. In partnership
with Australia (University of Melbourne) and Indonesia (a local pharmaceutical company, Bio
Farma), an alternative innovation of new rotavirus vaccine is under developed. It is a monovalent
rotavirus vaccine (RV3) from neonatal human strain and undergone in phase II clinical trial. The
strain of rotavirus is naturally found in healthy newborns, thus the vaccine might be given to
newborns (Glass 2005). By the end this vaccine is expected to be marketed in lower price in
order to fulfill the needs of Indonesian children in the future, also for other developing countries.

Conclusion

Indonesia is in dire to the need of rotavirus vaccine studies and introduces rotavirus vaccination
as a national program. The burden of diarrhea ranks as one of the major cause of under-five
mortality and the most common agent of diarrhea is rotavirus infection. As recommended by
WHO, Indonesia could implement the new available rotavirus vaccines, either two doses of monovalent HRV rotavirus vaccine or three doses of pentavalent WC3 rotavirus vaccine.

The problem of adopting rotavirus vaccine as a program could be come from funding mechanism due to Indonesia is still a developing country and eligible for co-payment from GAVI alliance. But for sustainability of the program, the government should also think solutions of funding vaccination program without external donors. Decentralization might bring new hope or might be a failure as well. Thus, we need a strong leadership from central government in coordinating local authorities to participate more in funding vaccination program for their own people.

Developing local vaccine as an answer for more affordable and efficacious rotavirus vaccine is urgently needed and now Indonesia, together with Australia is undergone a new rotavirus vaccine development

Millions of children die due to diarrhea, a disease that simply we can manage and prevent. Bring our new hope for brighter future, through rotavirus vaccine.

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