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Conference report

Evidence of reduction of rotavirus diarrheal disease after rotavirus vaccine introduction in national immunization programs in the African countries: Report of the 11th African rotavirus symposium held in Lilongwe, Malawi

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ABSTRACT

The 11th African Rotavirus Symposium was held in Lilongwe, Malawi from May 28th to 30th 2017. Over 270 delegates (73% from Africa) from 40 countries of which 30 (75%) were from African countries attended the symposium. Participants in this symposium included research scientists, clinicians, immunization managers, public health officials, policymakers and vaccine manufacturers. At the time of the symposium, 38 of the 54 (70%) countries in Africa had introduced rotavirus vaccines into their national immunization schedules. Delegates shared progress from rotavirus surveillance and vaccine impact monitoring, demonstrating the impact of the vaccine against rotavirus diarrheal hospitalizations. Data supported the beneficial effect and safety of WHO pre-qualified available vaccines up to 2017 (RotaTeq, Rotarix). This symposium highlighted the dramatic impact of the rotavirus vaccination, called for urgent adoption of these vaccines in remaining countries, particularly those with high disease burden and large birth cohorts (e.g. Nigeria, Democratic Republic of Congo) to attain the full public health benefits of rotavirus vaccination in Africa.

1. Introduction

Since the first introduction of rotavirus vaccine in the Expanded Program of Immunization (EPI) in South Africa in 2009, tremendous progress has been made with regard to the acceleration of rotavirus vaccine introduction in sub-Saharan African countries during the last eight years [1], highlighting the rapid implementation of the vaccine. Rotavirus vaccination has resulted in dramatic reductions in diarrhea hospitalizations and rotavirus-laboratory confirmed diarrhea hospitalizations in Africa, and prevented an estimated 21,000 deaths in 2016 alone [2].

The African Rotavirus Symposia initiated in 1998 has been an effective forum to share research findings, evidence of the high disease burden, lessons learned on the implementation of rotavirus surveillance and vaccine impact dissemination in the African region. The symposium series has been hosted by the African Rotavirus Surveillance Network (AFRSN) - a strong regional network of African institutions and Ministries of Health conducting research/-surveillance on diarrheal diseases in children coordinated mainly by key regional and African institutions and World Health Organization Regional Office for Africa (WHO/AFRO) and key immunization partners. The 11th African Rotavirus Symposium was hosted by the Malawi-Liverpool-Wellcome Trust Clinical Research Programme (MLW), College of Medicine, University of Malawi and the University of Liverpool, Center for Global Vaccine Research, Institute of Infection & Global Health in Lilongwe, Malawi between 28th and 30th May 2017.

At the time of the 11th Rotavirus Symposium, 38 countries in Africa had introduced rotavirus vaccines in their national immunization programs [1] as shown in Fig. 1. This symposium provided opportunities for networking and advocacy to sustain momentum

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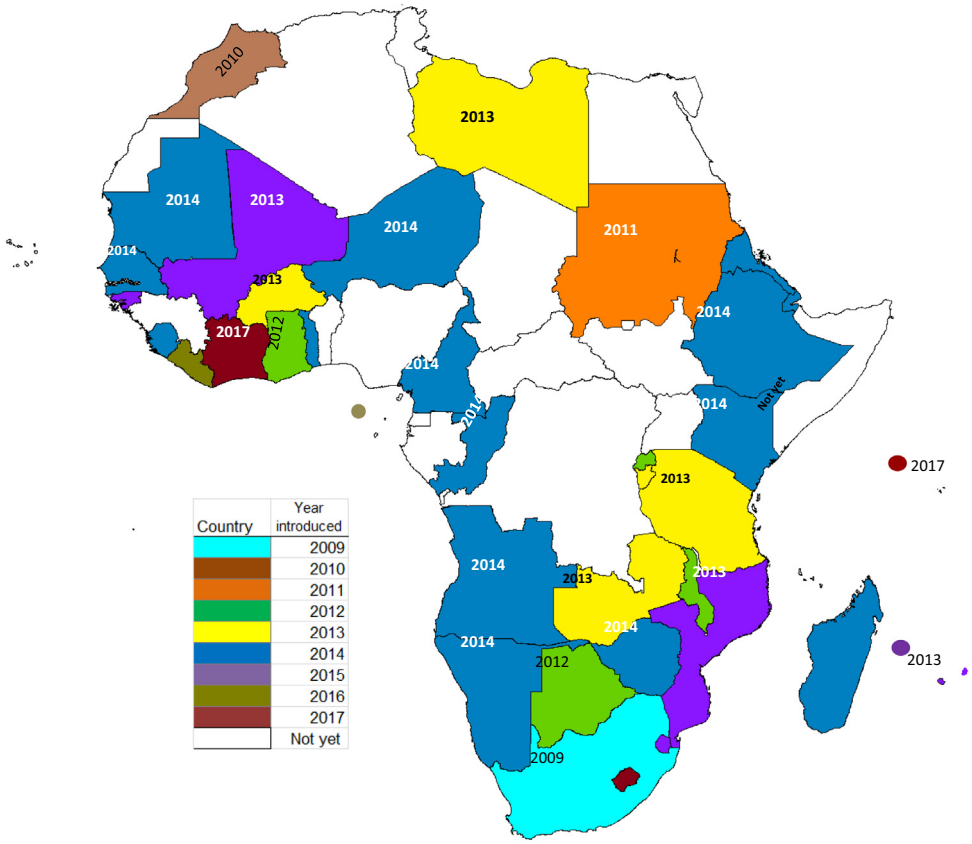

Fig. 1. Status of Rotavirus vaccine introduction in Africa.

to ensure that every child in Africa has the opportunity to be protected from rotavirus diarrhea through timely and full vaccination with rotavirus vaccines. This event also provided a forum to review research and share global epidemiological trends on rotavirus diarrhea; share practical experiences and impact of vaccines on diarrheal disease and safety data on rotavirus vaccines in African countries; and review and shape future agenda for research / surveillance on other diarrhea pathogens in the region [3].

The symposium was officially opened by Dr. Charles Mwansambo, Ministry of Health of Malawi and Dr. Eugene Nyarko, WHO Representative in Malawi. During their opening remarks, they both commended those countries in the WHO African region that had introduced rotavirus vaccine, cited the promising early data on rotavirus vaccine impact/effectiveness from 12 countries, and vaccine safety data from 11 countries monitoring intussusception to fill the existing knowledge gaps. Two hundred seventy-nine participants (73% from Africa, n = 204) from 40 countries (including 30 African countries) who attended this symposium made oral or poster presentations and participated in panel discussions. Key highlights of these presentations and discussions are summarized below. Prof Nigel Cunliffe, University of Liverpool, United Kingdom gave the key note lecture highlighting the tremendous amount of rotavirus-related research conducted in Malawi and the leading role Malawi has played in rotavirus vaccine research in Africa.

2. Regional burden of enteric infections

In this session, regional and global diarrheal disease burden and rotavirus-associated diarrhea was discussed including the importance of long-term and strong disease surveillance for vaccine preventable disease to provide the evidence for policy and decision making.

Dr. Ibrahim Khalil, Institute of Health Metrics and Evaluation (IHME), University of Washington, USA, provided the most recent estimates on the global rotavirus burden, emphasizing the need for continuous refinement of estimates using updated surveillance data provided by wide range of countries in Africa. While diarrhea deaths have continued to decline over the last ten years, diarrhea remains a leading cause of death among children globally [4], and rotavirus is still the leading cause of acute severe gastroenteritis requiring hospitalization. Based on IHME data, globally, in 2015, rotavirus attributable mortality was estimated at 146,480 deaths in Under5 children, a >30% decline from the previous 2013 estimates of 215,000 by the WHO/CDC [5] among children less than 5 years of age. In 2015, the majority of rotavirus-related deaths were recorded for sub-Saharan Africa (74%; 108,600 deaths; 95% CI: 87,400–134,800), where rotavirus caused approximately 112.3 million episodes of diarrhea (95% CI: 85.82–144.9) yearly. Dr. Khalil also discussed the importance of other pathogens contributing to diarrheal disease and deaths in young children globally, including *Cryptosporidium* spp., *Shigella* spp., enterotoxigenic *E. coli* and *Campylobacter* spp.

The contribution of advanced molecular methods such as quantitative PCR (qPCR) and TaqMan Array card (TAC) to identify wide ranging causes of diarrhea in children and to elucidate pathogen-specific etiology more accurately, was discussed by Dr. James Platts-Mills (University of Virginia, Charlottesville, USA) [6]. In addition, he presented data from a more recent study showing a reduction of rotavirus attributable cases from 55% in rotavirus vaccine age-eligible children to approximately 20% after the introduction of rotavirus immunization in the African region [6], suggesting that a proportion of this reduction was attributable to vaccine use. Indeed, rotavirus vaccine implementation accounted for ~45% reduction of all-cause diarrhea admissions in Haydom Hospital,

Tanzania in 2015 [7]. Furthermore, the use of qPCR does improve the detection rates of broader range enteric pathogens compared to ELISA which detects only rotavirus, use of TAC/qPCR may provides better estimates of broad pathogen-specific disease burden. [6]. It is clear that, while rotavirus remains the most significant pathogen associated with acute gastroenteritis (AGE) in young African children, there are several other pathogenic organisms widely circulating in young children in the continent.

Dr. Beckie Tagbo, University of Nigeria Teaching Hospital, Enugu State, Nigeria presented data showing the high rotavirus disease burden in Nigeria where rotavirus accounted for 41% of diarrheal cases detected by ELISA between 2011 and 2015, thus reinforcing the urgent need for Nigeria to consider introducing rotavirus vaccine in their national immunization program. Nigeria has applied for Gavi support and is scheduled for introduction in late 2019.

3. Rotavirus vaccine impact and effectiveness

A major success of the African Rotavirus Surveillance Network (AFRSN) is the utility of this platform for raising awareness and advocacy, and to evaluate rotavirus vaccine impact and effectiveness [8]. During this symposium, representatives of several countries presented data from vaccine impact evaluation and effectiveness analyses. In Burkina Faso, a 44% reduction of rotavirus associated hospitalizations was reported (from 37% in 2014 to 21% in 2016); with estimated vaccine effectiveness of 58% among children aged 6–11 months. Similar remarkable results were observed in Zimbabwe where rotavirus-associated diarrhea hospitalizations dropped from 41% in pre-vaccine period to 20% after vaccine introduction. This observable decline of rotavirus positivity was associated with a shift of rotavirus seasonality from May to September. Preliminary data from the Rotavirus Vaccine Impact in Diarrhea in Africa (VIDA) ongoing in three of the four African GEMS' sites (Mali, Kenya and The Gambia) further highlighted the decline on rotavirus incidence after vaccine introduction

Presentations on the transmission dynamics of rotavirus strains circulating in pre- and post-vaccine introduction in Africa was presented by Dr. Mathew Esona, Centers for Disease Control and Prevention (CDC), Atlanta and Dr. Khuzwayo Jere, University of Malawi. Genome reassortment and antigenic drift mutations were highlighted as the major evolutionary mechanisms driving genetic diversity of G1P [8] strains in Malawi. Atypical DS-1-like G1P [8] strains emerged in 2013 through reassortment between Wa- and DS-1-like human strains that have circulated since the 1990's. These data suggest the need for careful monitoring of circulating strain diversity to continually assess vaccine effectiveness against novel emerging strains in Africa.

4. Monitoring safety of rotavirus vaccines

Monitoring safety of internationally licensed rotavirus vaccines, Rotarix and RotaTeq, has continued in Africa as part of post-marketing surveillance recommended by the WHO. Regional intussusception (IS) surveillance network was established in 2014 and currently 11 countries are monitoring, and reporting IS data to WHO (Fig. 2). Dr. Richard Omore, Kenya Medical Research Institute (KEMRI), Kenya, presented preliminary data from ongoing IS surveillance in Kenya which reviewed retrospective hospital records from 12 referral hospitals and identified 305 cases between January 2002 and October 2014 pre-vaccine, and 248 cases from

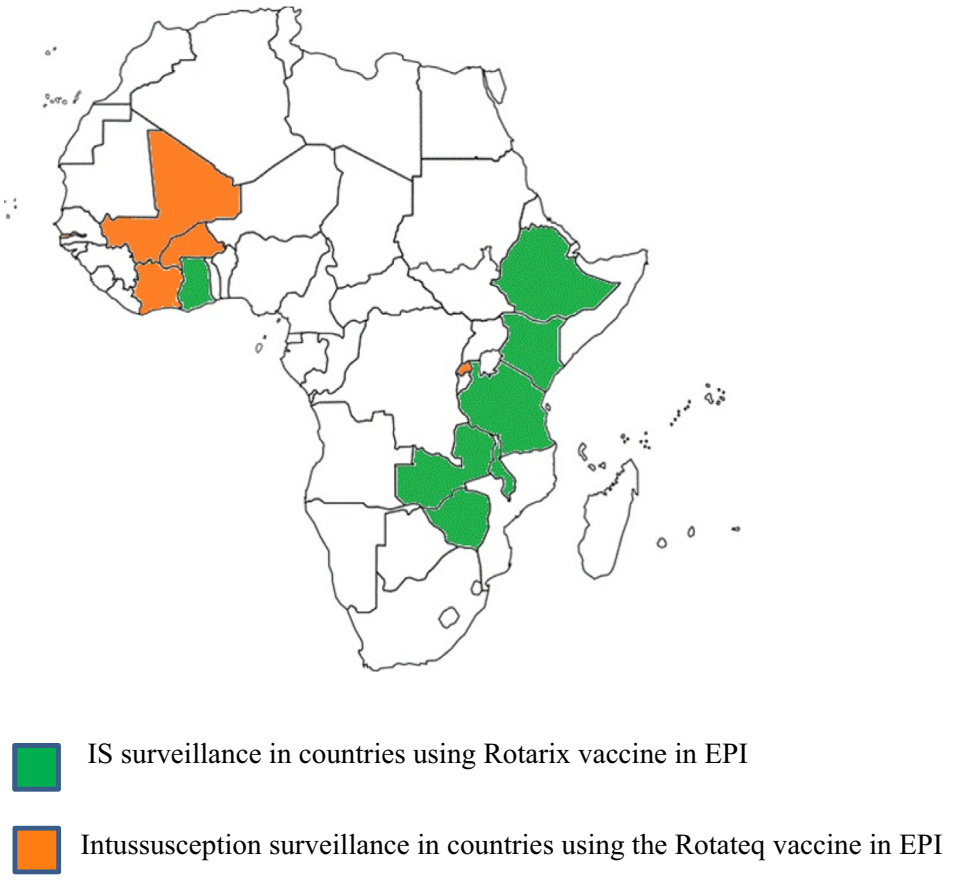

Fig. 2. Countries that are part of the African intussusception (IS) surveillance network.

post-vaccine prospective review of records in 6 referral hospitals between November 2014 and December 2016. IS cases were identified before the use of rotavirus vaccine and there was no increase in IS cases recorded after the vaccine introduction. A multi-country analysis of data from the countries in AFRO IS network utilizing the human monovalent rotavirus vaccine showed no increase of IS risk in pooled data from these 7 countries [9]. This first analysis of pooled data from these 7 countries is very re-assuring and re-affirms the safety of rotavirus vaccines in use in these low resource settings. IS surveillance in countries using the pentavalent bovine-human reassortant vaccine is ongoing through AFRO, with data expected later this year.

5. Rotavirus vaccine cost-effectiveness

Available data from sub-Saharan Africa countries that have introduced the vaccine have demonstrated a decrease in rotavirus-related morbidity and mortality [10] providing further evidence of the benefits of the rotavirus vaccination. Economic models have been used to predict a reduction in economic burden rotavirus-related health costs, this analysis showed vaccine introduction is cost-effective in resource-constrained settings in Africa [11,12].

The speakers from this session showed the importance for economic evaluation of rotavirus vaccine to assess how to achieve the most benefit using limited resources. Dr. Deborah Atherly, PATH, presented cost-effectiveness data and highlighted the importance of measuring and communicating the impact and cost-effectiveness of current and potential rotavirus vaccination, particularly in the upcoming years due to changing health and economic environments in Africa.

Gavi's support is phased out after countries' gross national income per capita surpasses a set threshold (US$1000 per capita), which requires governments to assume responsibility for the continued financing of childhood vaccines [13]. During the period 2016–2020, Gavi's funding will end for 19 countries in Africa that have exceeded the eligibility threshold. Dr. Maite Irurzun-Lopez, (Agence de Médicine Préventive), made a presentation on the cost analysis of surveillance for vaccine preventable diarrheal diseases. Dr. Lopez, highlighted the importance of undertaking specific studies on the costing of disease surveillance systems to guide planning, budgeting and prioritization of allocation of available resources as well to advocate for resource mobilization for vaccine preventable diseases (VPD) surveillance and immunization programs.

Dr. Justice Nonvignon, University of Ghana, Legon, Ghana, presented cost-effectiveness analysis from Ghana which showed rotavirus vaccine will substantially reduce under-five morbidity and mortality. He estimated that the vaccine will avert 2.3 million cases; 11,000 deaths and 369,000 DALYS between 2012 and 2031; estimated $7 – 11 million treatment's saving for the national health system [12]. Dr. Justice suggested that using standard cost-effectiveness thresholds, rotavirus vaccination is an economically viable investment, producing impressive cost-effectiveness estimates over the 20-year period even without any GAVI support. Dr. Justice analysis demonstrated that RV vaccination should remain a priority health investment even after Ghana graduates from GAVI support and indicated that one would expect to see similar findings in other African countries approaching GAVI graduation. Dr. Jangangir Hossain (Medical Research Council, The Gambia), presented the results of the Rotavirus VIDA that showed overall mortality decrease in both moderate-to-severe diarrhea cases and controls, implying an improvement in DALYs in the community overall, despite the increased number of cases that progress to persistent diarrhea in The Gambia.

6. Rotavirus vaccines updates

Dr. Bernd Benninghoff (GSK Biologicals, Rixensart, Belgium) shared the experiences, new data and lessons learned from a decade of vaccinating infants with the monovalent Human Rotavirus vaccine (Rotarix®). Dr. Benninghof summarized the impact of the 2-dose rotavirus vaccine in distinct regional and socio-economic contexts – such as 80% reduction in RV-specific acute gastroenteritis (AGE) admissions in infants <1 year of age and a 63% reduction in RV-specific AGE admissions in children aged 1–4 years in the rotavirus season during 2013/2014 compared with pre-vaccination years in UK [14]. In Latin American countries, where the vaccine has been used longest, it was demonstrated that rotavirus vaccine reduced diarrhea mortality rates in infants aged <5 years [15]. Similarly, substantial reduction in all-cause diarrhea hospitalization rates have been documented in various settings in Africa [7,16], although mortality reduction studies have been limited in scope so far. Dr. Tidiane Nado, Merck Research Co., Pennsylvania, USA also shared experience of the 10 years use of their pentavalent bovine-human reassortant vaccine (RotaTeq) in routine childhood immunization globally.

Since its first approval in 2006, the pentavalent oral, human–bovine reassortant vaccine (RotaTeq, MSD) is licensed in >120 countries and >198 million doses have been distributed worldwide. The effectiveness data are similar to what was observed in clinical trials across different settings. For example, in the US, vaccine impact showed a 94% reduction in rotavirus-related hospitalization (2012). In Nicaragua, 3 dose vaccine effectiveness in those <2 years (2007–8) was 58% against severe rotavirus disease and 77% against very severe rotavirus disease, as well as hospitalizations for diarrhea in <1 year olds decreased by 51% in Rwanda (2014). Diarrhea hospitalizations also declined among older children not vaccinated, suggesting indirect protection. In addition, to evaluating vaccine effectiveness, a randomized, multicenter, double-blind, clinical study in collaboration with IMPAACT (The International Maternal Pediatric Adolescent AIDS Clinical Trials Network) evaluated the safety and immunogenicity of RotaTeq in HIV+ and HIV exposed-uninfected (HEU) infants born to HIV+ mothers in 4 African countries (Botswana, Tanzania, Zambia, Zimbabwe). Immunogenicity was assessed by serum neutralizing antibodies (G1-G4, P1A) and anti-RV IgA. RotaTeq was well tolerated in both HIV+ and HEU infants. Statistically significantly higher immune responses were seen in recipients of RotaTeq compared to placebo recipients in both HIV strata, and post dose 3 antibody levels did not differ by HIV status. Shedding of vaccine virus in stool was similar to that previously reported in uninfected infants and was not prolonged in HIV+ vaccinees.

Other presentations during this session showed the landscape of vaccines under development by various manufacturers, with an emphasis on those that could be utilized in Africa. First, Dr. Sai Prasad, Bharat Biotech Ltd International, Hyderabad, India, described progress of the Indian-licensed ROTAVAC live, orally vaccine. ROTAVAC is a monovalent human Rotavirus vaccine, based on the naturally attenuated neonatal strain, 116E [17]. The vaccine underwent clinical evaluation in India showing clinical efficacy of 56% and 49% in the first year and second year of life respectively [18], was licensed in 2014 and quickly introduced into 4 early adopter states in 2016, through the Universal Immunization Program (UIP)[1]. In 2017, ROTAVAC introduction was expanded into a further 5 States, where >3 million infants have now been immunized. The licensed vaccine was evaluated clinically to assess the need for a gut-acid neutralizing buffer and was shown to generate

[1] ROTAVAC was pre-qualified by WHO in January 2018, after the 11th African Rotavirus Symposium.

comparable immune responses in those infants receiving the vaccine with or without the buffer [19]. The unbuffered product has been approved by the Drugs Controller General of India (DCGI) and is the product currently being utilized in UIP. Currently, post-marketing surveillance for safety with respect to intussusception is ongoing in several districts and states, as requested by the DCGI and WHO. Finally, the rotavirus vaccine product was designed with several similar characteristics to oral poliovirus vaccine (OPV). The vaccine without buffer has the smallest cold chain footprint (~3.2 cm^3/dose), and a delivery profile in 5- and 10-dose vials. ROTAVAC is currently undergoing registration in several countries, including on the continent.

Next, Dr. Sameer Naik, Serum Institute of India, Pune, India described progress with the lyophilized, heat-stable rotavirus vaccine developed by the company. The vaccine is a pentavalent bovine-human reassortant rotavirus vaccine including G1-G4 and G9 strains [20], and also evaluated in clinical studies in India. The vaccine was licensed in India based on a large phase 3 clinical study across different areas of the country which demonstrated 39.5% vaccine efficacy against severe rotavirus gastroenteritis in the per protocol analysis [21]. Additional development in India has demonstrated that the lyophilized vaccine is heat-stable and can be stored at 25 °C for up to 36 months, and that it can withstand extreme temperatures of 37 °C and 40 °C for 18 months [22]. The vaccine is due for introduction in India in 2018[2].

Dr. Celine Langendorf, Medicins sans frontiere (MSF), discussed the results from an efficacy and safety study of this lyophilized and heat-stable stable rotavirus vaccine (RotaSIIL®) in Niger, West Africa. During the conduct of this clinical trial in Niger, the vaccine was stored and transported outside the 2–8 °C cold chain, once it had left the central depot in Niamey. Three doses of this lyophilized rotavirus vaccine or placebo were administered at health centers at 6, 10, and 14 weeks of age with routine EPI vaccinations. Vaccine efficacy against severe gastroenteritis was recorded at 67% in the per protocol analysis and at 69% in the intention to treat analysis [23]. The vaccine is under license application in Niger and other countries.

Finally, Dr. Julie Bines, University of Melbourne, Australia, reported progress of a neonatal vaccine developed in Australia (RV3-BB), utilizing a birth-dose strategy that may offer novel opportunities to overcome challenges faced with the oral rotavirus vaccines. A birth dose of a rotavirus vaccine may offer safety advantages as intussusception is rare in the first weeks of life, may overcome or avoid interference from maternal antibody, may avoid potential interference from other gut pathogens, etc. RV3-BB vaccine was developed from a human neonatal rotavirus strain, RV3 (G3P[6]), identified in the stool of asymptomatic infants in Melbourne and provided protection from severe rotavirus gastroenteritis during the first 3 years of life, with strong heterotypic serological responses to community strains. Clinical trials conducted in New Zealand and Indonesia provide evidence that RV3-BB vaccine is well tolerated and immunogenic in either a neonatal vaccine schedule (doses at 0–5 days, 6–8 weeks and 12 weeks) or infant vaccine schedule (6–8 weeks, 12 weeks and 16 weeks). Furthermore, RV3-BB vaccine showed robust efficacy in a small study conducted in Indonesia in both the traditional infant schedule and in a neonatal schedule [24].

Dr. Duncan Steele (Bill & Melinda Gates Foundation), drawing together these various presentations, provided a pragmatic view of the current situation for rotavirus vaccines in Africa, and a strategic vision of what we can expect in the next 5-year horizon. Pragmatically, rotavirus vaccines are being widely implemented across the continent and demonstrating clear impact on rotavirus-associated hospitalizations, overall diarrheal hospitalizations and deaths [2]. However, the full impact of rotavirus immunization on diarrheal mortality has not yet been reached due to (i) the lack of implementation in the largest African countries with highest rotavirus-associated mortality, or (ii) lack of full access to all children in hard-to-reach areas in some countries using the vaccines. Secondly, the vaccines have clearly been documented to be cost-effectiveness in all settings in Africa and will continue to be [11,12]. However, 19 countries in the continent will 'transition' from Gavi vaccine subsidy support in the next 5-years and will likely pay increased costs for rotavirus vaccines, and have to prioritize as they cover all the routine vaccine costs for the EPI.

With the recent 2018 WHO pre-qualification of both India vaccines (ROTAVAC, Bharat Biotech and RotaSIIL, Serum Institute), new opportunities present themselves for the continent. First, countries already approved for Gavi-vaccine subsidy, such as DRC, Nigeria Benin, now have 4 rotavirus vaccine products to choose from and should not have to delay national introduction due to perceived supply constraints. Furthermore, these new entrants developed in partnership with the global public health community, are available at lower pricing per course than the current vaccines and may provide long-term pricing sustainability for countries. Despite this scenario, much remains to be done including better access and outreach to the most vulnerable infant populations with these life-saving vaccines. Equitable coverage in many countries of the region remains an elusive but worthwhile goal for all childhood vaccines.

7. Immunological responses to enteric vaccines

It is well recognized that live, attenuated oral rotavirus vaccines operate sub-optimally in infants in developing countries and several factors, whether host-specific or vaccine-specific, have been identified as contributors to that. Several presentations covering the latest development is this field were presented. Dr Nick Grassly, Imperial College of London described studies conducted with oral poliovirus vaccine that might offer insights into the immune responsiveness to rotavirus vaccines. Interestingly, enteric virus-associated inflammation (but not bacteria related), at the time of immunization could accurately predict OPV responsiveness. This might be an important angle to pursue given the high proportion of AGE in young children that was attributable to enteric viruses in previous studies [6,7].

Further studies reported that histo-blood group antigens (HBGAs) and the Lewis and secretor antigens are associated with susceptibility to rotavirus infection in a genotype-dependent manner and may have a role to play. Studies conducted in Burkina Faso and Nicaragua highlighted that the VP8* domain of genotype P[4] and P[8] rotavirus strains show strong binding to the Lewis B and H-type 1 glycans, while the P[6] genotype binds to the H type 1 glycan. Preliminary data from Nicaragua showed that no infants with the Lewis A phenotype sero-converted to immunization with either Rotarix or RotaTeq after the first dose [25]. Dr. Svensson concluded that differences in the HBGA expression appear to be a contributing factor to vaccine take and possibly vaccine efficacy in different ethnic populations. Interestingly, none of the three new rotavirus vaccine candidates (ROTAVAC, RotaSIIL and RV3-BB) which all have different VP4 proteins unrelated to the P[8]1A, have been studied yet, and is a line of investigation that is required. Dr. Laban, Center for Infectious Disease Research in Zambia (CIDRZ) reported data from Zambia supporting the conclusion that HBGAs have a differential immune responsiveness to rotavirus vaccine where AB subjects sero-converted best.

Dr. Roma Chilengi, CIDRZ described the role of an innate antiviral glycoprotein in breast milk that was associated with blunting of

[2] RotaSIIL was prequalified by WHO in September 2018 and introduced into the UIP of Jharkhand State in April 2018.

the vaccine-take and immune response in Zambian infants. Higher concentrations of lactadherin in the breast milk were negatively correlated with the sero-conversion rates in infants [26]. Finally, also from CIDRZ, Dr. I Mwape, described an analysis of rotavirus vaccine take in children and its potential relationship to environmental enteric dysfunction (EED). A range of biochemical markers for EED were assessed in children, including soluble CD14, endotoxin core IgG antibodies, intestinal fatty acid binding protein and Zonulin, and correlated to sero-conversion to Rotarix. Interestingly, Zonulin and intestinal fatty acid binding protein were positively associated with vaccine sero-conversion [27].

7.1. Challenges related to the use of rotavirus vaccines in Africa

The final session focused on the challenges to rotavirus vaccine introduction in Africa. Dr. Mwenda, AFRO, highlighted some of the issues that may hinder progress of rotavirus vaccine roll-out in Africa and that are likely to impact the sustainability of rotavirus vaccine implementation in Africa. The pending global rotavirus vaccine supply shortage and the transition of some countries from Gavi-eligibility, constitute enormous challenges to enhancing the potential full impact of rotavirus vaccine in Africa. Dr. Mwenda noted that 19 African countries, including those with large birth cohorts of Nigeria and DRC, are yet to introduce rotavirus vaccines into their EPI. Planned introductions have been impacted by the global vaccine supply resulting in delays in introductions or a shift in priorities. Furthermore, as some countries transition from Gavi support and have to consider to fully cover the costs for all their vaccines, cost and cost-effectiveness become key issues for consideration. This session also summarized some of the major challenges for rotavirus vaccines, including cold chain storage, modest efficacy in low-income settings, and questions around optimizing the dose and schedule [3].

Ms. Zoey Diaz, Vaccine Delivery at the Bill & Melinda Gates Foundation discussed the challenges and opportunities to rotavirus vaccine introduction, sustainability and continental scale-up. Using the UNICEF Healthy Market Framework, Ms. Diaz explored how ensuring vaccine demand at the country level contributes to a healthy and cost-effective global supply. New entrants into this field will ultimately support this framework.

Dr. Dawda Sowe, EPI Manager, The Gambia presented the serious issues related to limited capacity for vaccine storage at all levels from the central- to the health-facility level. The lack of cold room capacity at the central level resulted in cancelation of shipments and the increased frequency of distribution to the regional level depots. At the health facility level, the major challenge was related to vaccine stock-outs, which were due to local cold chain storage limitations, thus impacting the vaccine coverage and the effectiveness of the vaccine. These challenges ultimately increased the cost of the vaccine delivery across all levels. Dr. Sowe concluded that despite these challenges RotaTeq® has contributed greatly in reducing diarrhea diseases associated with rotavirus. However, these challenges have been mentioned as a major reason for both The Gambia and Rwanda to switch from RotaTeq® to Rotarix® vaccine during 2017.

A final presentation from Dr. Carl Kirkwood, Bill & Melinda Gates Foundation, provided an update to the African surveillance network of the WHO Polio endgame and how this would impact laboratories with archival or prospectively collected diarrheal stool samples.

8. Conclusions

Presentations from this symposium highlighted the impact of rotavirus vaccines in reducing diarrheal morbidity and mortality in many countries although rotavirus remains the leading pathogen associated with severe dehydrating diarrhea among young children in Africa. Rotavirus vaccine was shown to be very cost-effective resulting in an estimated $7–11 million treatment's saving for the health system in Ghana, a Gavi-transitioning country. In addition, intussusception surveillance in the WHO African region has provided additional data confirming the safety of the currently available vaccines. Together, the evidence presented, reinforces the urgency to accelerate the introduction of rotavirus vaccine into the remaining 19 WHO African Region countries, and particularly large countries with high disease burden (e.g. Nigeria and DRC). Recent analyses highlighted what the full potential of rotavirus immunization in sub-Saharan Africa could be with full implementation [2,28]. Implementation of rotavirus vaccines has substantially decreased hospitalizations from rotavirus and all-cause AGE. Hospitalizations and emergency department visits due to rotavirus AGE were reduced by a median of 67% overall and 71%, 59%, and 60% in countries with low, medium, and high child mortality, respectively [28]. On the other hand, if all African countries had introduced rotavirus vaccine, over 270,000 hospitalizations and almost 50,000 deaths could have been prevented in 2016 (2 years after introduction) [2]. This needs to be our focus in the years ahead.

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Conflict of interest statement

The authors have declared no conflict of interest.

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