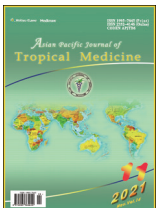

Review Article

Asian Pacific Journal of Tropical Medicine

apjtm.org

doi: 10.4103/1995-7645.331255

5-Year Impact Factor: 2.285

Recent emergence and outbreak of rotavirus gastroenteritis in Samoa: A scoping review of risk factors, containment measures and public health preparedness

Lawal Olatunde Olayemi✉, Vicky Yemoh, Alec Ekeroma

School of Medicine, Faculty of Health Sciences, National University of Samoa, Samoa

ABSTRACT

Diarrheal diseases have been known to cause death in many children below the age of five years, and rotavirus infection represents a major health problem in the world today, particularly in developing countries. The recent outbreak of rotavirus gastroenteritis in Samoa led to the introduction of her debut national immunization program on rotavirus vaccination for infants. Despite the introduction of anti-viral and anti-emetic drugs as of the containment approaches towards the virus, risk factors, preventive measures and public health preparedness against rotavirus infection are poorly understood in Samoa. This review aims to use available evidence on rotavirus literature to elucidate and map preventive strategies for the recently emerged rotavirus infections in Samoa. We conducted a search strategy using online medical literature databases and retrieval systems. A designated set of keywords such as rotavirus, gastroenteritis, outbreak, risk factors, containment measures, vaccination and Samoa were inserted in electronic databases to retrieve articles. The databases included PubMed, Google Scholar, MEDLINE, Scinapse, and EBSCO host. Findings from this review addressed the impact of rotavirus infection, associated threats and other preventive measures. Introducing useful health frameworks in pursuing possible methods such as improved water quality, exclusive breast feeding, improved laboratory diagnostics and outbreak surveillance, may be essential in addressing alternate approaches towards containment of the disease in Samoa and other Pacific Island Countries and Territories.

KEYWORDS: Rotavirus; Gastroenteritis; Outbreak; Risk factors; Containment measures; Vaccination; Pacific Island Countries and Territories; Samoa

1. Introduction

Acute gastroenteritis is a common infectious disease confronting people of all ages globally, especially the pediatric population[1]. It represents a significant public health threat, particularly in developing countries. Enteric microbial pathogens, viruses, parasites, or bacteria remain the most frequent causative agents of acute gastroenteritis among children under the age of five[2]. Acute gastroenteritis is commonly acquired through the fecal-oral route, contaminated surfaces and from unhygienic water sources[3,4]. Rotavirus gastroenteritis can be recurrently acquired in persons during childbirth and until old age, although infants in their early years are mostly affected[5]. The virus is extremely communicable and this can be assumed that after one year of age, about two-thirds of children would have experienced at least one rotavirus infection and one-third a second rotavirus infection[6]. Most infections could present as either asymptomatic or episodes of mild enteric symptoms, which may not be noticed in infected persons. Despite this, a large number of infections lead to severe disease sequelae with diarrhoea, need for hospitalization, and in rare cases death[7]. There are also considerable disparities in the severity of disease amongst primary and successive infections[6]. Among the classical symptoms of rotavirus infections, the most alarming and critical include high fever, vomiting, diarrhoea and marked dehydration According to the Ministry of Health in Samoa, as of the 22nd of July 2021, rotavirus outbreak among children had resulted in over 31 rotavirus cases, which were confirmed by laboratory testing[8]. Further investigations and contact tracing were still ongoing to ascertain the source of transmission of the virus in affected persons. Except for Fiji and the Philippines, the burden of rotavirus in the Asia-Pacific region is largely unknown[9,10]. With the growing and continuous drive towards vaccine-preventable disease and in achieving the World Health Organization (WHO) goal of global eradication of childhood infectious disease mortality, Pacific Island Countries and Territories (PICTs) may be the principal beneficiaries

✉To whom correspondence may be addressed. E-mail: Olayemis2002@yahoo.com

How to cite this article: Olayemi LO, Yemoh V, Ekeroma A. Recent emergence and outbreak of rotavirus gastroenteritis in Samoa: A scoping review of risk factors, containment measures and public health preparedness. Asian Pac J Trop Med 2021; 14(11): 479-485.

Article history: Received 9 September 2021 Revision 22 November 2021
Accepted 23 November 2021 Available online 30 November 2021

of rotavirus vaccination due to risks of severe disease outbreaks[11]. In achieving such stride, urgent public health strategies and plans must be continuously introduced in mitigating the dangers associated with the spread of rotavirus infections in reducing the burden of the disease. Strengthening infectious disease diagnostics, introducing and consolidating emergency prevention and containment programs as well as socio-cultural networks in the PICTs may help in achieving this.

This paper briefly elucidates the current emergence of rotavirus infections in Samoa, including associated risk factors, improved containment measures and public health interventions. It further addresses the significance of rotavirus vaccination in Samoa and also the need for further research to identify post-vaccination effectiveness, acceptance rate measures and psychosocial levels amongst affected individuals.

2. Search strategy, study selection and eligibility

A search strategy was performed using online medical literature databases and retrieval systems. Databases included PubMed, Google Scholar, MEDLINE, Scinapse, and EBSCO host. A designated set of keywords from Medical Subject Heading (MESH) such as "Rotavirus", "Gastroenteritis", "Outbreak", "Risk-factors", "Containment measures", "Vaccination" and "Samoa" were inserted in electronic databases to retrieve articles published between 1996 and 2021. Only articles in English were included in this review. Though no original research had been carried out on rotavirus in Samoa, studies that closely addressed the key entities, risk factors, containment measures and public health emergency preparedness towards rotavirus were included in this article to elucidate and map a conceptual public health framework for the prevention of rotavirus in Samoa.

3. Results

Findings from this review revealed various entities, which addressed the knowns and unknowns that characterized the outbreak of rotavirus gastroenteritis in Samoa. These ranged from risk factors of the rotavirus disease, importance of containment methods and diagnostics to the impact of rotavirus vaccination, public health emergency response and preparedness.

3.1. Associated risk factors for rotavirus infection

Significant risk factors attributed to rotavirus disease may predict the progression of rotavirus infection to severe illnesses, including hospitalization and death, due to debilitating the clinical effects of rotavirus in susceptible people. These could also contribute to the development of intussusception, autoimmunity, gastrointestinal disease, and immune deficiency[12]. There could be an upsurge in the severity of biological and social risk factors among affected populations, who are mostly young children, unimmunized teenagers and adults. These risk factors may range from nutritional status, malignancy, cardiac disease, and gastroparesis to breastfeeding, socio-economic levels, low gestational age and central nervous system complications. Previously available evidence indicated that the rate of hospitalizations due to childhood diarrhoea in Samoa decreased from 68% in 2009 to 62% in 2014[13] and 57.4% in 2019[14]. The reduction rate was largely attributed to the use of oral rehydration therapy (ORT) in syndromic case management of children who presented to a health facility[13]. However, in the recent rotavirus outbreak, children below the age of five years were the most affected with typical clinical manifestations as observed by attending clinicians at the emergency wards of the government hospital and following laboratory confirmations[8]. Moreover, studies have shown the highest burden of rotavirus infection amongst paediatric populations below the age of two years, where children below the age of six months experienced lower rates of infection and a decrease in the rate of infection was observed amid children above two years of age[15]. The disparity in the rates of rotavirus infection between the age groups may be explicated by the protective effect of maternal antibodies in newborns less than 6 months old, and the development of innate immunity after recurrent infections in children above two years of age[16]. These could largely be due to the peculiarity of individual risk factors for rotavirus gastroenteritis in at-risk age groups or populations in Samoa. Likewise, being malnourished, underweight, history of low-birth weight, drinking untreated water, and being born to an uneducated mother have also been shown to be identified as independent risk factors of rotavirus infection[15]. Infant feeding practices of using unboiled tap water to prepare formula milk also increases the risk of developing rotavirus infection[17]. These further explain the possibilities of the rotavirus outbreak and the spread of the infection in Samoa, where there may be lack of quality drinking water and poor hygiene practices, especially in rural and suburban areas. Despite the likelihood of government efforts in bridging the education gap and improving socio-economic living standards, there may still be challenges of poor health literacy and access to proper health education.

3.2. Role of containment measures

3.2.1. Rotavirus biology and genotype distribution

As an RNA virus, rotavirus belongs to the family Reoviridae. It is non-enveloped, measures 60-80 nm in diameter, and its genome length is approximately 18.5 kb. Its genome is made up of 11 segments of double-stranded RNA and encodes six structural proteins (VP1-7) and six nonstructural proteins (NSP1-6)[18,19]. Rotavirus A is one of the main causative agents of diarrhea in young humans and animals[18,20]. It is ubiquitous in the environment and relatively resistant to disinfectants. Rotavirus exists in different genotypes and serotypes, and throughout the world, studies have identified common co-circulating rotavirus types, and G2P[21], G1P, G3P, and G4P are the predominant strains[22]. However, due to antigenic drift and variations in viral ecology, other less common genotypes, such as G9P, G5P[22] and G8P[23], are predominant in many countries. Molecular characterization of rotavirus genotypes could help underpin efficient global surveillance of rotavirus infections. There is a tremendous diversity amongst the human

and animal strains of rotavirus, especially the human pathogenic rotavirus type A. The presence of such diversity among rotavirus isolates offers insight into the evolution of these strains which can occur based on point mutations, inherited reorganization and re-assortment, and interspecies spread[24–26]. Despite the advent of rotavirus vaccination in most countries globally, circulating rotavirus strains tend to be more diverse, thereby enhancing the prevalence of non-vaccine strains. This eventually impairs vaccine effectiveness towards circulating strains, with much lower vaccine efficacy[27]. Using the surveillance and distribution of predominant rotavirus genotypes in some Asia-Pacific countries (Table 1) may assist in understanding the pattern of spread and concentration of pathogenic rotavirus genotypes currently circulating in Samoa and other PICTs. This could further help explicate the efficacy and effectiveness of rotavirus vaccines during the pre- and post-vaccination periods.

3.2.2. Significance of improved rapid diagnostic testing and surveillance networks against rotavirus infections

Laboratory diagnosis of rotavirus infection is achieved using various conventional and molecular techniques. Enzyme immunoassays (EIAs) are used as the standard diagnostic test for rotavirus infection in many parts of the world[55]. Numerous polymerase chain reaction (PCR)-based protocols for the uncovering of human enteric viruses with higher sensitivities have been published, but only a few allow simultaneous detection of most enteric viruses in one assay, especially during viral outbreak screening and surveillance activities[56,57]. This is essentially vital to understand the disease burden associated with viral gastroenteritis caused by rotavirus and other enteric viruses, which may be unknown and currently circulating in Samoa.

Furthermore, studies to solve hypotheses on diagnostic interventions and concerns surrounding their effectiveness in providing reliable and accurate data should be pursued. The potential benefits would help avail the challenges of misdiagnoses and under-diagnoses of diarrheagenic rotavirus infections in situations of outbreak cum community transmission. Clinical diagnoses and testing for rotavirus in Samoa are carried out at the major tertiary health centre-Tupua Tamasese Maeole Hospital (TTM Hospital), which is located in the center of the Capital City. Testing or baseline assessment for rotavirus infection is rarely done in remote regions, where laboratories have insufficient resources and limited human and medical capacities. In developing countries like Samoa, rapid serological EIAs may be the only available laboratory choice of investigation. Though reliable, this may not provide complete information on viral load, and will have low sensitivity and specificity, unlike molecular methods for rotavirus detection[58,59]. Molecular assays like rapid multiplex PCR, quantitative RT-PCR and RT-PCR platforms have been documented to have better performance than EIAs and conventional PCR, due to better detection of PCR products and reduced ambiguity in negative and positive samples[58,59]. Improved molecular and diagnostic techniques for virus' genomic characterization and personal training are much needed in containment measures for the rotavirus epidemic in Samoa. Despite immunization against the rotavirus, future investigations into circulating rotavirus genotypes in Samoa is pertinent and will assist in evaluating post-vaccination outcomes and measuring vaccine effects. Provision of prompt diagnostic services is imperative in curbing the spread of the virus through laboratory surveillance, pathogen identification and confirmation. Hence, concerted efforts are required by all health stakeholders involved in public health prevention of enteric diarrheagenic diseases and rotavirus infections, to create functional systems and networks for syndromic and laboratory surveillance in specific locations in rural and suburban communities in Samoa, where there is little or non-existing accessible screening facilities.

3.2.3. Upscaling and preventive role of rotavirus vaccination

Interventions with proven ability can only be effective when necessity warrants their accessibility. To maintain practical sustainability, aggregated efforts toward investment and ongoing acceptance of vaccination should be channelled to timely delivery of vaccination materials. Undoubtedly, the effectiveness of rotavirus vaccines has offered huge benefits in pediatric and adult populations susceptible to diarrheagenic rotavirus disease. In geographically isolated communities which are culturally diverse and sensitive such as Samoa, huge challenges face the surveillance, effectiveness and safety assessment of vaccine-preventable disease[60]. Sensitization on rotavirus vaccination for both adults and children could assist in preventing early infection transmission, early death, drastically reduce rotavirus morbidity and confer herd immunity within the communities. Certain studies had revealed that children who did not receive a second dose of the rotavirus vaccine suffered 3.96 times more from diarrheal morbidity compared to those in receipt of the

Table 1. Distribution of predominant human rotavirus genotypes in some Asia-Pacific countries at pre- and post-vaccination era.

Countries	Predominant rotavirus genotypes	Year(s) of surveillance	References
Fiji	G2P(8), G3P(8), G8P(8), G12P(4) G1P(8), G2P(4), G3P(8), G12P(8)	2005-2018	[28]
Philippines	G1P(4), G2P(8), G9P(8), G8P(6)	2012-2014	[29]
Indonesia	G1P(8), G3P(8)	2009-2018	[30–35]
Singapore	G1P(8), G9P(8)	2015	[36,37]
Lao DPR	G1P(8), G2P(4), G3P(8), G9P(8)	2009-2015	[38,39]
Malaysia	G1P(8), G2P(4), G9P(8)	2008-2010	[39,40]
Cambodia	G1P(8), G2P(4), G8P(8), G9P(8), G3P(8)	2010-2016	[41]
Vietnam	G1P(8), G2P(8), G8P(8)	2012-2015	[42]
Myanmar	G1P(8), G12P(4), G2P(4), G3P(8), G9P(8)	2009-2015	[43,44]
Thailand	G2P(4), G1P(8), G3P(8)	2008-2018	[45–53]
Turkey	G1P(8), G2P(8), G3P(8), G9P(8)	2012-2014	[54]

second dose of the rotavirus vaccine[56]. Health regulations on child vaccination should be firm on compliance to avoid unwarranted complications from diarrhea morbidities. Thus, two-dose rotavirus vaccines (doses 1 and 2) should be given to children as part of a comprehensive approach to control diarrhea[61]. Studies on the safety and efficacy of rota-vaccines administered in Africa and Asia revealed the vaccines dramatically reduced severe diseases among infants in developing countries, where a majority of rotavirus-related deaths occurred[62,63], thereby overrating the effectiveness of RV1, RV5 and Rotavac vaccines to be safe at preventing diarrhea[64]. In Fiji, the introduction of rotavirus vaccines helped reduce confirmed gastroenteritis admissions at the main referral hospital by 87% amongst young infants[60]. There was an 81% reduction in case fatality from cause associated diarrheagenic patients and a decline of 89% of the outpatient burden of rotavirus gastroenteritis[60]. Another study by Jenney *et al*. reported huge reductions in rotavirus confirmed diarrhoea in both hospital inpatients and outpatients in children below age of five years following the introduction of the rotavirus vaccine on a national scale. Likewise, there were demonstrable reductions in severity (81% fall in mortality), the total burden of rotavirus (above 80% decline) and all-cause diarrhoea (36% decline) amongst children. The mortality rate was further decreased from all cause-specific diarrhea admissions in those age groups, who were not eligible for vaccination[65]. This could be as a result of high, full-dose vaccine coverage and lower rates of malnutrition and gut enteropathy[57]. Replicating similar preventive interventional models in Samoa could help to halt the surge of a rotavirus outbreak and its absolute eradication. It may also rapidly reduce the incidence of community transmission and potential spread of the virus across borders of Samoa and neighbouring countries, as seen in other developed and developing regions of the world, with positive outcomes following the recommendation to introduce the rotavirus vaccines[66]. Although rotavirus-associated diarrhoea could be prevented with rotavirus vaccine or treated with low-osmolarity oral rehydration salt (ORS) and zinc, a lack of awareness of effective preparedness strategies towards diarrhoea prevention and management could lead to late presentation of ill children to the clinic and poor adherence to prescribed interventions[67]. Additionally, low supply of rotavirus vaccines, under vaccination and challenges associated with lack of transparent government policies amongst others may come to bear in mitigating containment measures, awareness and upscaling vaccination towards the rotavirus disease in Samoa.

3.3. Public health preparedness: Public awareness and health education for communities

In Samoa, the rotavirus vaccination (Rotarix) for children is provided by the Ministry of Health at no cost, and the schedule includes two doses administered at 6 weeks and 10 weeks along with Penta 1, PCV1, PCV 2 and Penta 3. However, despite the vaccination implementation, there is a great need for public awareness *via* billboards, social media (TV, radio, Facebook, Instagram, *etc*.), community campaigns and education on the effects of the virus on infants and children. Low coverage rates are currently a public health challenge in Samoa, since vaccination was offered to children under five and half months, and parents had little information about the virus, thereby, resulting in vaccination hesitancy amongst parents.

A study on the knowledge of rotavirus conducted in Italy discovered that, though the majority of participants (89%) had agreed with the statement that the rota-vaccine was not harmful, among those who did not immunize their children, a large proportion reported they were not willing to obtain vaccination mainly due to lack of knowledge on the disease and concerns of side effects[68]. This emphasizes the importance of public health awareness and education towards at-risk populations, especially those with misconceptions regarding vaccinations, to eradicate their uncertainties about safety. Similarly, a mother's lack of education may increase the risk for the development of diarrhea in her children, thus an educated mother is more likely to be empowered to take care of her offspring[69]. Previous studies had also shown children of highly educated mothers were at low risk of cause-specific morbidity and mortality due to diarrhea because they had the necessary knowledge and observed good hygiene and sanitation practices[64,66,70]. This further explains the importance of health education in creating public awareness regarding disease prevention at both household and community levels. Moreover, improving sanitation and water quality provided a beneficial advantage for reducing diarrheal disease in low-income countries[67]. Different systematic analytic studies on the prevention of diarrheagenic rotavirus disease have shown campaigns on hand-washing reduced the incidence of gastrointestinal infections by 30% (95% *CI* 19%-43%)[68].

Furthermore, studies had revealed positive associations between breast milk and the prevention of rotavirus disease. Breast milk contains special nutritious and bioactive compounds, which are known to boost immunity in infants. Exclusive breastfeeding for four months and partial breastfeeding thereafter are linked with lower rates of acute gastroenteritis in the first year of life[69] and decreased rates of hospitalization from the diarrheal disease[67]. A study by Shumetie *et al.* also depicted the odds of diarrheal morbidity were 2.69 times higher among under-five children who were not exclusively breastfed for six months[33]. Essentially, introducing health policies to tactically address vaccination challenges are germane in disease prevention and surveillance. A systematic and adoptable contextual framework could drastically help in reducing rotavirus epidemics in unvaccinated populations (Figure 1). This should be modeled to suit the population's health literacy, communal way of living and socio-behavioural standards. Huge expectations bequeath on policymakers, including non-governmental and community-based organizations in creating support and efficient health systems to ensure enforcement, accountability and sustainability of preventive programs for collective health benefits. Implementation of strategies on rotavirus vaccination as discussed and previously studied may be pertinent in bridging the lapses, hitherto disease spread, case detection and management as well as surveillance of rotavirus in Samoa.

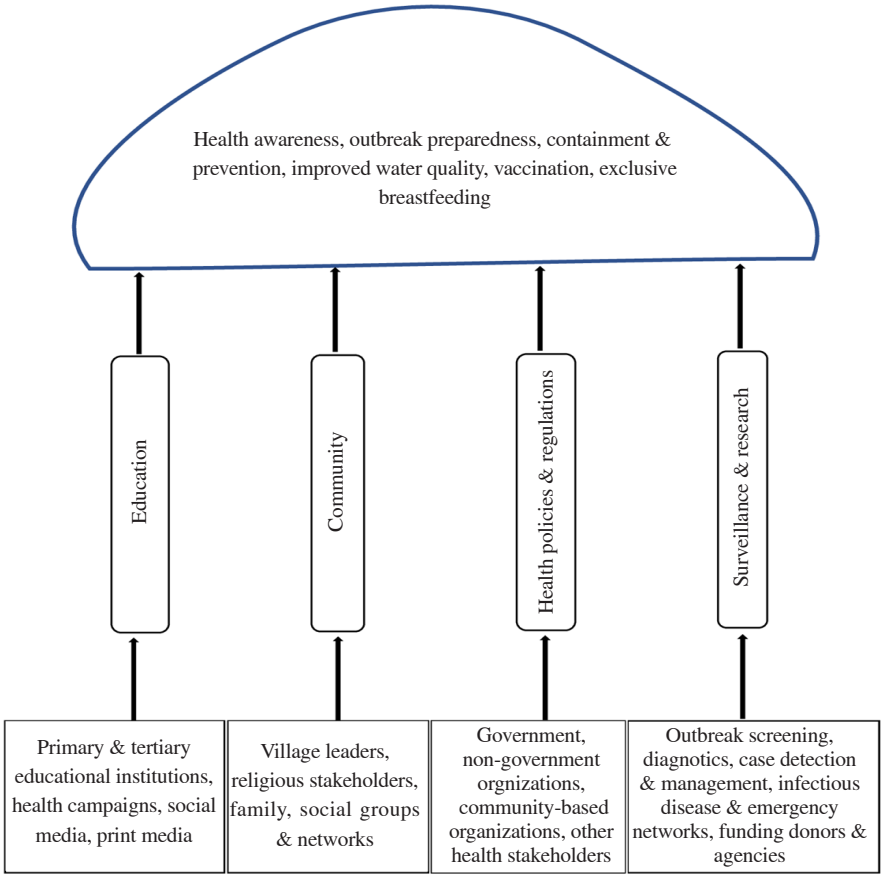

Figure 1. An adoptable conceptual framework for public health community and socio-preventive mechanism against the spread of rotavirus infection in a developing society.

4. Conclusions

The introduction of rotavirus vaccination in Samoa is a good achievement and has provided an opportunity for the government, community-based organizations and other stakeholders to re-evaluate and address gaps in the health system. Implementing effective rotavirus vaccination programs, encouraging good sanitation and hygiene, hand-wash practice, exclusive breastfeeding and improving the quality of water would help to reduce childhood diarrheal morbidity in the country. However, due to the impact of environmental dynamics on virus antigenic variations or mutations and the resultant effects on the effectiveness of rotavirus vaccines, continuous monitoring of rotavirus disease burden and strain distribution in Samoa must be prioritized. Further scientific-based evidence should be carried out on the effectiveness of public health education and awareness of associated risk factors, safety and program preparedness on rotavirus infection in Samoa and other PICTs.

Conflict of interest statement

All authors have no conflict of interest to declare.

Authors' contributions

L.O.O and V.Y conceptualized and wrote the initial version of the study. L.O.O, V.Y and A.E designed and coordinated the study. L.O.O, V.Y and A.E searched and designed the images. L.O.O, V.Y and A.E performed literature search, wrote the article and contributed to the final version of the manuscript.

References

[1] Salami A, Fakih H, Chakkour M, Salloum L, Bahmad HF, Ghssein G. Prevalence, risk factors and seasonal variations of different Enteropathogens in Lebanese hospitalized children with acute gastroenteritis. *BMC Pediatr* 2019; **19**(1): 137.

[2] Chhabra P, Payne DC, Szilagyi PG, Edwards KM, Staat MA, Shirley SH, et al. Etiology of viral gastroenteritis in children <5 years of age in the United States, 2008-2009. *J Infect Dis* 2013; **208**(5): 790-800.

[3] Cheng W, Jin Y, Duan Z, Xu Z, Qi H, Zhang Q, et al. Human bocavirus in children hospitalized for acute gastroenteritis: A case-control study. *Clin Infect Dis* 2008; **47**(2): 161-167.

[4] Dennehy PH. Infectious gastroenteritis. In: Domachowske J (ed). *Introduction to clinical infectious diseases: A problem–based approach*. Sham: Springer International Publishing; 2019, p. 157-168.

[5] Bishop RF. Natural history of human rotavirus infection. *Arch Virol Supp* 1996; **12**: 119.

[6] Velázquez FR, Matson DO, Calva JJ, Guerrero ML, Morrow AL, Carter CS, et al. Rotavirus infection in infants as protection against subsequent infections. *N Engl J Med* 1996; **335**: 1022-1028.

[7] Parashar UD, Gibson CJ, Bresse JS, Glass RI. Rotavirus and severe childhood diarrhea. *Emerg Infect Dis* 2006; **12**: 304-306.

[8] Samoa observer. *No plans to shut schools over rotavirus*. 2021. [Online]. Available from: https://www.samoaobserver.ws/category/samoa/88062. [Accessed on 28 August 2021].

[9] Jenney A, Tikoduadua L, Buadromo E, Barnes G, Kirkwood CD, Boniface K, et al. The burden of hospitalized rotavirus infections in Fiji. *Vaccine* 2009; **27**: F108-F111.

[10]Lopez AL, Raguindin PF, Esparagoza J, Fox K, Batmunkh N, Bonifacio J, et al. Impact of rotavirus vaccine on diarrheal hospitalization and outpatient consultations in the Philippines: First evidence from a middle-income Asian country. *Vaccine* **2018**; 36: 3308-3314.

[11]Jones FK, Ko AI, Becha C, Joshua C, Musto J, Thomas S, et al. Increased rotavirus prevalence in diarrheal outbreak precipitated by localized flooding, Solomon Islands, 2014. *Emerg Infect Dis* 2016; **22**(5): 875-879.

[12]Huppertz HI, Salman N, Giaquinto C. Risk factors for severe rotavirus gastroenteritis. *Pediatr Infect Dis J* 2008; **27**(1): 11-19.

[13]Samoa Bureau of Statistics, Government of Samoa, Census-Surveys and Demography Division, Apia, Samoa. *Samoa demographic and health survey, 2014*. [Online]. Available from: https://pacificdata.org/data/dataset/oai-www-spc-int-2dbf934c-46d1-49c4-bdf9-cebb1485eebb. [Accessed on 8 October 2021].

[14]Samoa Bureau of Statistics, Government of Samoa, Census-Surveys and Demography Division, Apia, Samoa. *Samoa DHS–MICS 2019–20 preliminary results–July 2020 Samoa demographic and health survey–Multiple indicator cluster survey (DHS–MICS) 2019–20*. [Online]. Available from: https://pacific.unfpa.org/en/publications/fact-sheet-samoa-dhs-mics-2019-20. [Accessed on 8 October 2021].

[15]Fidhow AM, Samwel A, Ng'ang'a Z, Oundo J, Nyangao J, Wences A. Molecular epidemiology and associated risk factors of rotavirus infection among children < 5 yrs hospitalized for acute gastroenteritis in North Eastern, Kenya, 2012. *Pan Afr Med J* 2017; **28**(1): 3.

[16]Kargar M, Zare M, Najafi A. Molecular epidemiology of rotavirus strains circulating among children with gastroenteritis in Iran. *Iran J Pediatr* 2012; **22**(1): 63-69.

[17]Nimri LF, Hijazi S. Rotavirus-associated diarrhoea in children in a refugee camp in Jordan. *J Diarrhoeal Dis Res* 1996; **14**(1): 1-4.

[18]Zhou X, Wang YH, Ghosh S, Tang WF, Pang BB, Liu MQ, et al. Genomic characterization of G3P (6), G4P (6) and G4P (8) human rotaviruses from Wuhan, China: Evidence for interspecies transmission and reassortment events. *Infect Genet Evol* 2015; **33**: 55-71.

[19]Desselberger U. Rotaviruses. *Virus Res* 2014; **190**: 75-96.

[20]Cho YI, Han JI, Wang C, Cooper V, Schwartz K, Engelken T, et al. Case-control study of microbiological etiology associated with calf diarrhea. *Vet Microbiol* 2013; **166**(3-4): 375-385.

[21]Enweronu-Laryea CC, Sagoe KWC, Glover-Addy H, Asmah RH, Mingle JA, Armah GE. Prevalence of severe acute rotavirus gastroenteritis and intussusceptions in Ghanaian children under 5 years of age. *J Infect Dev Ctries* 2011; **6**(2): 148-155.

[22]Mészner Z, Balogh Á, Bányai K, Kovács J, Pazdiora P, Mrukowicz J, et al. The clinical burden of rotavirus disease. *Pediatr Infect Dis J* 2008; **27**(1): 33-41.

[23]Salinas B, González G, González R, Escalona M, Materán M, Schael IP. Epidemiologic and clinical characteristics of rotavirus disease during five years of surveillance in Venezuela. *Pediatr Infect Dis J* 2004; **23**(10): 161-167.

[24]Kirkwood CD. Genetic and antigenic diversity of human rotaviruses: Potential impact on vaccination programs. *J Infect Dis* 2010; **202**: S43-S48.

[25]Jain S, Vashistt J, Changotra H. Rotaviruses: Is their surveillance needed? *Vaccine* 2014; **32**(27): 3367-3378.

[26]Gentsch JR, Laird AR, Bielfelt B, Griffin DD, Banyai K, Ramachandran M, et al. Serotype diversity and reassortment between human and animal rotavirus strains: Implications for rotavirus vaccine programs. *J Infect Dis* 2005; **192**: 146-149.

[27]Leshem E, Lopman B, Glass R, Gentsch J, Bányai K, Parashar U, et al. Distribution of rotavirus strains and strain-specific effectiveness of the rotavirus vaccine after its introduction: A systematic review and meta-analysis. *Lancet Infect Dis* 2014; **14**(9): 847-856.

[28]Thomas S, Donato CM, Covea S, Ratu FT, Jenney AWJ, Reyburn R, et al. Genotype diversity before and after the introduction of a rotavirus vaccine into the national immunisation program in Fiji. *Pathogens* 2021; **10**: 358.

[29]Bonifacio J, Igoy MA, Tandoc A. Reassortment of human rotavirus gene segments into G9P (8) rotavirus strain over a four-year period: 2013-2016. *Int J Infect Dis* 2018; **73**: 195.

[30]Nirwati H, Hakim MS, Aminah S, Dwija IBNP, Pan Q, Aman AT. Identification of rotavirus strains causing diarrhoea in children under five years of age in Yogyakarta, Indonesia. *Malays J Med Sci* 2017; **24**(2): 68-77.

[31]Sudarmo SM, Shigemura K, Athiyyah AF, Osawa K, Wardana OP, Darma A, et al. Genotyping and clinical factors in pediatric diarrhea caused by rotaviruses: One-year surveillance in Surabaya, Indonesia. *Gut Pathog* 2015; **7**: 3.

[32]Mulyani NS, Prasetyo D, Karyana IPG, Sukardi W, Damayanti W, Anggraini D, et al. Diarrhea among hospitalized children under five: A call for inclusion of rotavirus vaccine to the national immunization program in Indonesia. *Vaccine* 2018; **36**(51): 7826-7831.

[33]Utsumi T, Wahyuni RM, Doan YH, Dinana Z, Soegijanto S, Fujii Y, et al. Equine-like G3 rotavirus strains as predominant strains among children in Indonesia in 2015-2016. *Infect Genet Evol* 2018; **61**: 224-228.

[34]Cowley D, Nirwati H, Donato CM, Bogdanovic-Sakran N, Boniface K, Kirkwood CD, et al. Molecular characterisation of rotavirus strains detected during a clinical trial of the human neonatal rotavirus vaccine (RV3-BB) in Indonesia. *Vaccine* 2018; **36**(39): 5872-5878.

[35]Athiyyah AF, Utsumi T, Wahyuni RM, Dinana Z, Yamani LN, Soetjipto, et al. Molecular epidemiology and clinical features of rotavirus infection among pediatric patients in East Java, Indonesia during 2015-2018: Dynamic changes in rotavirus genotypes from equine-like G3 to typical human G1/G3. *Front Microbiol* 2019; **10**: 940.

[36]Phua KB, Tee N, Tan N, Ramakrishnan G, Teoh YL, Bock H, et al. A hospital-based surveillance of rotavirus gastroenteritis in children < 5 years of age in Singapore. *Pediatr Infect Dis J* 2013; **32**(12): e426-e431.

[37]Phua KB, Lim FS, Lau YL, Nelson EAS, Huang LM, Quak SH, et al. Rotavirus vaccine RIX4414 efficacy sustained during the third year of life: A randomized clinical trial in an Asian population. *Vaccine* 2012; **30**(30): 4552-4557.

[38]SoukAloun D, Douangbouphaa V, Phetsouvanh R, Sibounheuang B, Vongsouvat M, Chanmala K, et al. Rotavirus diarrhea in hospitalized

children under 5 years of age in Vientiane, Lao PDR 2009-2015. *Vaccine* 2018; **36**(51): 7878-7882.

[39]Bonifacio J, Igoy MA, Tandoc A. Reassortment of human rotavirus gene segments into G9P (8) rotavirus strain over a four-year period: 2013-2016. *Int J Infect Dis* 2018; **73**: 195.

[40]Lee WS, Lim BT, Chai PF, Kirkwood CD, Lee JK. Rotavirus genotypes in Malaysia and universal rotavirus vaccination. *Hum Vaccin Immunother* 2012; **8**(10): 1401-1406.

[41]Angkeabos N, Rin E, Vichit O, Chea C, Tech N, Payne DC, et al. Pediatric hospitalizations attributable to rotavirus gastroenteritis among Cambodian children: Seven years of active surveillance, 2010-2016. *Vaccine* 2018; **36**(51): 7856-7861.

[42]Huyen DTT, Hong DT, Trung NT, Hoa TTN, Oanh NK, Thang HV, et al. Epidemiology of acute diarrhea caused by rotavirus in sentinel surveillance sites of Vietnam, 2012-2015. *Vaccine* 2018; **36**(51): 7894-7900.

[43]Theingi WM, Hlaing MT, Ye MK, Khin MA, Mo MW, Htin L, et al. Sentinel surveillance for rotavirus in children < 5 years of age admitted for diarrhoael illness in Yagon Children's Hospital, Myanmar, 2009-2014. *Vaccine* 2018; **36**(51): 7832-7835.

[44]Giri S, Priya HR, Arumugam R, Sherchand JB, Thu HM, Galagoda G, et al. Molecular epidemiology of rotaviruses in the south-east Asian region from 2009 to 2015. *Vaccine* 2018; **36**(51): 7851-7855.

[45]Khananurak K, Vutithanachot V, Simakachorn N, Theamboonlers A, Chongsrisawat V, Poovorawan Y. Prevalence and phylogenetic analysis of rotavirus genotypes in Thailand between 2007 and 2009. *Infect Genet Evol* 2010; **10**(4): 537-545.

[46]Sakpaisal P, Silapong S, Yowang A, Boonyasakyothin G, Yuttayong B, Suksawad U, et al. Prevalence and genotypic distribution of rotavirus in Thailand: A multicenter study. *Am J Trop Med Hyg* 2019; **100**(5): 1258-1265.

[47]Maiklang O, Vutithanachot V, Vutithanachot C, Hacharoen P, Chieochansin T, Poovorawan Y. Prevalence of group a genotype human rotavirus among children with dirarrhea in Thailand, 2009-2011. *Southeast Asian J Trop Med Public Health* 2012; **43**(4): 904-916.

[48]Yodmeeklin A, Khamrin P, Kumthip K, Malasao R, Ukarapol N, Ushijima H, et al. Increasing predominance of G8P (8) species rotaviruses in children admitted to hospital with acute gastroenteritis in Thailand, 2010-2013. *Arch Virol* 2018; **163**(8): 2165-2178.

[49]Chieochansin T, Vutithanachot V, Phumpholsup T, Posuwan N, Theamboonlers A, Poovorawan Y. The prevalence and genotype diversity of human rotavirus a circulating in Thailand, 2011-2014. *Infect Genet Evol* 2016; **37**: 129-136.

[50]Intamaso U, Poomipak W, Chutoam P, Chotchuang P, Sunkkham W, Srisopha S, et al. Genotype distribution and phylogenetic analysis of rotaviruses in Thailand and emergence of uncommon genotypes. *Arch Clin Microbiol* 2017; **8**(4): 60

[51]Guntapong R, Tacharoenmuang R, Singchai P, Upachai S, Sutthiwarakom K, Komoto S, et al. Predominant prevalence of human rotaviruses with the G1P (8) and G8P (8) genotypes with a short RNA profile in 2013 and 2014 in Sukhothai and Phetchaboon provinces, Thailand. *J Med Virol* 2017; **89**(4): 615-620.

[52]Tacharoenmuang R, Komoto S, Guntapong R, Upachai S, Singchai P, Ide T, et al. High prevalence of equine-like G3P (8) rotavirus in children and adults with acute gastroenteritis in Thailand. *J Med Virol* 2020; **92**(2): 174-186.

[53]Chan-It W, Chanta C. Emergence of G9P (8) rotaviruses in children with acute gastroenteritis in Thailand, 2015-2016. *J Med Virol* 2018; **90**(3): 477-484.

[54]Durmaz R, Kalaycioglu AT, Acar S, Bakkaloglu Z, Karagoz A, Korukluoglu G, et al. Prevalence of rotavirus genotypes in children younger than 5 years of age before the introduction of a universal rotavirus vaccination program: Report of rotavirus surveillance in Turkey. *PLoS One* 2014; **9**(12): e113674.

[55]Saketa, ST, Merilles OE, Bar-Zeev N. Welcome evidence of vaccine impact in the Pacific. *Lancet Reg Health West Pac* 2020; **6**: 100068.

[56]Shumetie G, Gedefaw M, Kebede A, Derso T. Exclusive breastfeeding and rotavirus vaccination are associated with decreased diarrheal morbidity among under-five children in Bahir Dar, northwest Ethiopia. *Public Health Rev* 2018; **39**: 28.

[57]World Health Organization. Rotavirus vaccines: An update. *Wkly Epidemiol Rec* 2009; **84**(50): 533-540.

[58]Parashar UD, Johnson H, Steele AD, Tate JE. Health benefits of rotavirus vaccination in developing countries. *Clin Infect Dis* 2016; **62**: S91-95.

[59]Soares-Weiser K, Maclehose H, Bergman H, Ben-Aharon I, Nagpal S, Goldberg E, et al. Vaccines for preventing rotavirus diarrhoea: Vaccines in use. *Cochrane Database Syst Rev* 2012; **15**(2): CD008521.

[60]Giaquinto C, Dominiak-Felden G, Van Damme P, Myint TT, Maldonado YA, Spoulou V, et al. Summary of effectiveness and impact of rotavirus vaccination with the oral pentavalent rotavirus vaccine: A systematic review of the experience in industrialized countries. *Hum Vaccin* 2011; **7**(7): 734-748.

[61]Bosomprah, S, Beach LB, Beres LK, Newman J, Kapasa K, Rudd C, et al. Findings from a comprehensive diarrhoea prevention and treatment programme in Lusaka, Zambia. *BMC Public Health* 2016; **16**: 475.

[62]Napolitano F, Ali Adou A, Vastola A, Angelillo IF. Rotavirus infection and vaccination: Knowledge, beliefs, and behaviors among parents in Italy. *Int J Environ Res Public Health* 2019; **16**(10): 1807.

[63]Claudine U, Kim JY, Kim EM, Yong TS. Association between sociodemographic factors and diarrhea in children under 5 years in Rwanda. *Korean J Parasitol* 2021; **59**(1): 61-65.

[64]Irfan M, Zaidi SMH, Waseem HF. Association of socio-demographic factors with diarrhea in children less than five years: A secondary analysis of multiple indicator cluster survey SINDH 2014. *Pakistan J Public Heal* 2017; **7**: 85-89.

[65]Jenney AWR, Reyburn R, Ratu FT, Tuivaga E, Nguyen C, Covea S, et al. The impact of the rotavirus vaccine on diarrhoea, five years following national introduction in Fiji. *Lancet Reg Health West Pac* 2020; **6**: 100053.

[66]Bado AR, Susuman AS, Nebie EI. Trends and risk factors for childhood diarrhea in sub-Saharan countries (1990-2013): Assessing the neighborhood inequalities. *Glob Health Action* 2016; **9**(1): 30166.

[67]Clasen TF, Alexander KT, Sinclair D, Boisson S, Peletz R, Chang HH, et al. Interventions to improve water quality for preventing diarrhoea. *Cochrane Database Syst Rev* 2015; **2015**(10): CD004794.

[68]Aiello AE, Coulborn RM, Perez V, Larson EL. Effect of hand hygiene on infectious disease risk in the community setting: A meta-analysis. *Am J Public Health* 2008; **98**(8): 1372-1381.

[69]Duijts L, Jaddoe VW, Hofman A, Moll HA. Prolonged and exclusive breastfeeding reduces the risk of infectious diseases in infancy. *Pediatrics* 2010; **126**(1): 18-25.

[70]Quigley MA, Kelly YJ, Sacker A. Breastfeeding and hospitalization for diarrheal and respiratory infection in the United Kingdom Millennium Cohort Study. *Pediatrics* 2007; **119**(4): e837-e842.