ORIGINAL ARTICLE

INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACEUTICAL SCIENCES

Published by Pharmascope Publications Journal Home Page: www.pharmascope.org/ijrps

The effectiveness of rotavirus vaccine and its impact on demographic characteristics for children in Babylon city, Iraq

Laith M Abbas Al-Huseini*[1], Manal Khalid Abdulridha[2], Qassim Mahdi Mutlak[3]

[1]Department of Pharmacology and Therapeutics, College of Medicine, University of Al-Qadisiyah, Iraq
[2]Department of Clinical Pharmacy, College of Pharmacy, Al-Mustansiriyah University, Iraq
[3]Babylon Health district, Ministry of Health, Iraq

Article History:

Received on: 14.03.2018
Revised on: 17.05.2018
Accepted on: 21.05.2018

Keywords:

Rotavirus,
Diarrhea,
Vaccine,
Effectiveness,
Demographic

ABSTRACT

Gastroenteritis caused by rotavirus infection is one of the major healthcare problem affecting millions of children all over the world. WHO has recommended vaccine against rotavirus to be involved in the national immunisation programmes. In Iraq, rotavirus vaccine has been started since 2012 and in the current study, we aimed to estimate the effectiveness of rotavirus vaccine in Babylon city, Iraq. Faecal samples were obtained from children presented with diarrhoea during the period beginning in October 2016 until August 2017. The age range was 6-60 months and history of rotavirus vaccine was checked. Latex test for detection of Rotavirus analysed specimens. We examined 349 children with diarrhoea; the rotavirus antigen was detected in 169 faecal specimens from children with diarrhoea (48%). For those who are infected with rotavirus antigen, 44 (26%) were previously vaccinated against rotavirus and 125 (74%) were not. These results indicated that children who did not receive rotavirus vaccination have 4.679 folds increased the risk of having positive rotavirus antigen infected diarrhoea. Furthermore, low percentages of vaccinated children with positive rotavirus antigens detected in their stool were seen in most age groups except for those between 25–36 months with no gender differences. Additionally, more percentages were in the urban area and artificial feedings. The effectiveness of rotavirus vaccine, in the present study, has been confirmed in reducing the burden of rotavirus gastroenteritis in young children in Babylon city, Iraq. However, huge effort needs to be done in order to have more children received rotavirus vaccine.

* Corresponding Author

Name: Laith M Abbas Al-Huseini
Email: laith.abbas@qu.edu.iq

ISSN: 0975-7538

DOI: https://doi.org/10.26452/ijrps.v9i3.1560

Production and Hosted by

Pharmascope.org

INTRODUCTION

In developing countries, diarrheal illnesses in the first five years of life are responsible for mortality of 4.9 per 1,000 children per year (Kosek, Bern *et al.,* 2003). Rotavirus infection is the most prevalent pathogen accountable for acute gastroenteritis in children worldwide (Parashar, Gibson *et al.,* 2006). Every year, rotavirus causes more than 150 million episodes of diarrhoea that require medical care and more than 500,000 deaths in children younger than five years (Grimwood and Lambert 2009). In Iraq, rotavirus infection was confirmed in (24-37%) of children with acute gastroenteritis (Ahmed, Coulter *et al.,* 2006, Alrifai, Alsaadi *et al.,* 2009).

Rotaviruses are highly contagious with the faecal-oral route is the predominant transmission method (Dennehy 2000), and the disease usually presented clinically in the infected children with a variety of symptoms from transient mild diarrhoea to severe episodes of acute fever, vomiting, and

watery diarrhoea. The significant sequelae of rotavirus infection are dehydration and electrolyte disturbances which commonly occur in the youngest children (Desselberger 2014).

Improving personal hygiene and living standards have been found inadequate to decrease the risk of developing diarrhoea in children especially in developing countries. Therefore, development of effective and safe vaccine became a priority in order to significantly reduce this disease outcome in the form of health-care attendance, hospitalisation or even death.

In published data, available licensed rotavirus vaccines appear to be safe and well-tolerated (Wang, Chen *et al.,* 2015, Velazquez, Linhares *et al.,* 2017). They provide 80-100% protection against rotavirus infection in Europe, Japan and USA (Dennehy, Brady *et al.,* 2005, Vesikari, Karvonen *et al.,* 2007, Dennehy 2008). Whereas in developing countries, the effectiveness of rotavirus vaccines showed a huge heterogeneity in the results (20-60%) which is in general much less than in developed countries (Gruber, Hille *et al.,* 2017).

Analyzing the effect of vaccination in early adopter countries is a great challenge for policymakers worldwide and it is rather essential to assess if the benefits compensate the costs and support wider propagation of these vaccines. In developing countries, rotavirus vaccines remain to be thoroughly evaluated due to reduced difficulties in reaching target populations, greater strain diversity and immunogenicity of oral vaccines which might decrease immunisation program performance. In Iraq, rotavirus vaccine (Rotarix®) has been introduced into the national immunisation programme since 2012 and subsequently, no survey has been done to evaluate its effectiveness. The Iraqi ministry of health calls for studies to be taken in order to estimate the effectiveness of the vaccine and this is the aim of our current research.

Patients and Methods

Patients: A cross-sectional study was conducted at Babylon teaching Hospital for maternity and children in addition to three major primary health centres in Babylon city. A total of 450 children presented acute diarrhoea have been collected at the time of study application during the period from the 1st of October 2016 to the 1st of August 2017. However, data were only could be obtained from (349) children. The other 101 children we could not have access to their vaccination history. Information including age, gender, residence, type of feeding, place of sample collection and duration of diarrhoea were taken according to the WHO criteria. The objectives and methodology of this study were explained to all parents or guardians of the patients in the study to gain their verbal consent.

Stool Collection: At least 4–8mg of stool was directly collected and stored in a sterile plastic container. Samples were kept at 2–8°C, for a maximum of 8 days, until they were transported to the laboratory where they were stored at −20°C before analysis.

Latex test for human Rotavirus Antigen: LA was performed by using the commercial latex agglutination kit (Blasmatec, Germany). The test was considered positive for rotavirus if distinct agglutination was observed with test latex but not with control latex and indeterminate if agglutination was observed in test and control latex, this test was performed according to the manufacturer's specifications.

Data Collection

A. Inclusion Criteria: All vaccinated children presented with acute diarrhoea from the age of 6 months to the age of 60 months.

B. Exclusion Criteria

(1) Infant younger than 6 months.

(2) Children older than 5 years.

(3) Hypersensitivity to a vaccine.

(4) Gastrointestinal Tract Congenital Malformation.

(5) History of Intussusception.

(6) Severe Combined Immunodeficiency Disease.

Data Analysis: Statistical analysis was carried out using SPSS version 17. Categorical variables were presented as frequencies and percentages. Pearson's chi-square (X2) and Fisher-exact test were used to find the association between categorical variables. A p-value of ≤ 0.05 was considered significant.

RESULTS

The effectiveness of rotavirus vaccine among children in Babylon city: For those 349 children who have diarrhoea, we found 169 patients had positive stool samples for rotavirus. Retrospective analysis revealed that 44 patients of them (28.2%) were fully vaccinated for rotavirus infection while 125 patients (71.8%) were not vaccinated as shown in Table 1 and Figure 1.

The percentage of children with negative rotavirus stool test was significantly higher in vaccinated patients compared to not vaccinated 71.8% vs 35.2%

Table 1: Effectiveness of Rotavirus Vaccine according to positive rotavirus test

Variables	Not vaccinated	Vaccinated	p-value
Number	193	156	-
Rota test			<0.001
Negative	68 (35.2%)	112 (71.8%)	
Positive	125 (64.8 %)	44 (28.2%)	
Chi-square test			

as illustrated in Table 1. Children that did not receive rotavirus vaccination had 4.679 folds increased the risk of having positive rotavirus infection as illustrated in Table 2. To estimate the benefit of vaccination to reduce the risk of positive rotavirus infection we found the odds ratio = 0.213, after conversion to ARR (i.e., by subtracting it from 1.0) resulted in 79%, which mean that vaccination predicts 79% lower risk of having positive rotavirus infection.

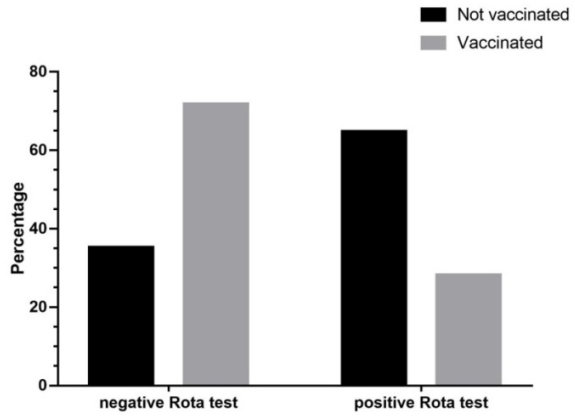

Figure 1: Rotavirus vaccine reduced the number of patients with a positive stool for rotavirus

Table 2: correlation between vaccination status and rotavirus test outcome

Risk factor	OR	95% CI of OR	P value
Not vaccination	4.679	2.963 – 7.390	<0.001
Binary logistic regression			

Demographic characteristics in vaccinated vs not vaccinated children who have diarrhoea with a positive stool for rotavirus: We compared the demographic characteristics of children who have positive rotavirus gastroenteritis taking into consideration if they are rotavirus vaccinated or not vaccinated.

Age: Rotavirus vaccinated children showed a significant reduction in rotavirus infection in all age groups except for 25-36 months compared to unvaccinated children as shown in Table 3, Figure 2 and 3. The lowest percentage of positive rotavirus infection in vaccinated children was observed in the age group of 6-12 months.

Gender: There was no significant difference (P> 0.05) in the gender between vaccinated and not vaccinated children with positive rotavirus test as illustrated in Table 4 and Figure 4.

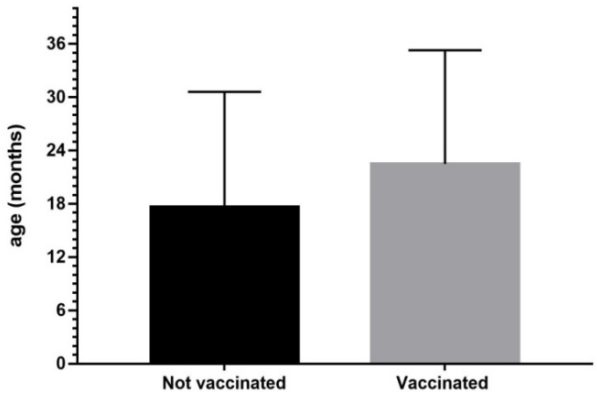

Figure 2: Vaccination status according to age for children with positive rotavirus infection

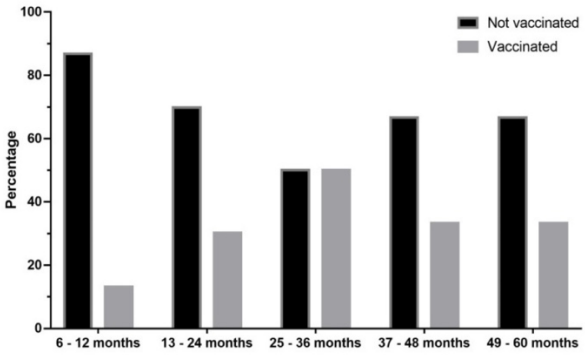

Figure 3: Comparison of different age groups according to vaccination status for children with positive rotavirus infection

Residence: The Higher percentage of vaccinated children with positive rotavirus infection was found in the urban area (29.1%) comparing to a rural area (21.2%). Inversely, the higher percentage of non-vaccinated children with positive rotavirus infection was among the rural area (78.8%) more than urban (70.9%). However, the difference was not as significant as illustrated in Table 5 and Figure 5.

Place of sample collection: The severity rotavirus infection can be estimated from place for sample collection where the highest percentage of vaccinated children with positive rotavirus infection was observed in cases collected from hospital

(30.5%) followed by primary care centre (18.8%) and the lowest percentage was seen in cases collected in private clinics (8.0%), meanwhile, in non vaccinated children private clinics reflects the majority of cases (92.0%), though statistically near to significance between groups (P> 0.05). As shown in Figure 6 and Table 6.

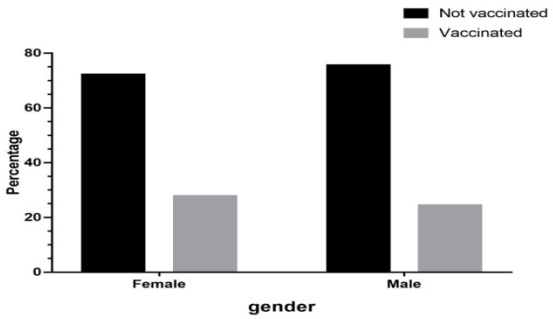

Figure 4: Gender distribution according to vaccination status for children with positive rotavirus infection

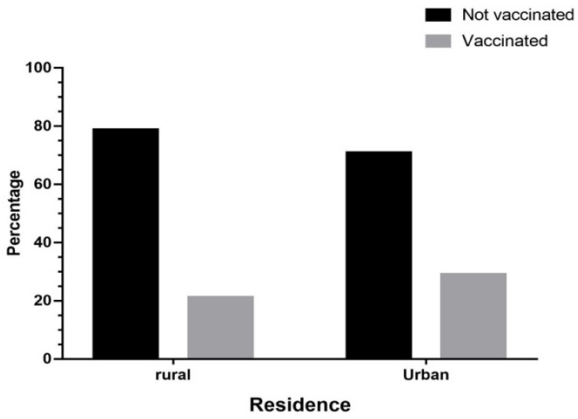

Figure 5: Residence distribution according to vaccination status for children with positive rotavirus infection

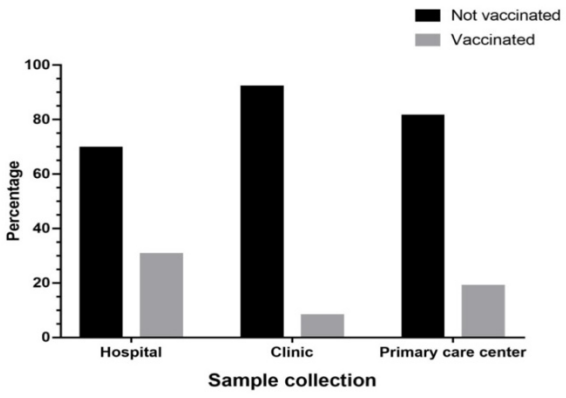

Figure 6: Sample collection distribution according to vaccination status for children with positive rotavirus infection

Type of feeding: As illustrated in Table 7 and Figure 7, the vaccinated children with rotavirus infection was seen in higher percentage with those on breastfeeding (37.0%), followed by artificial feeding (24.6%), food (20.0%), then mixed feeding (18.4%) respectively. On the contrary, in not vaccinated children those on breastfeeding presented with the least percentage of rotavirus infection (63.0%). However, the difference was not significant (P> 0.05) between both groups.

Duration of diarrhoea according to vaccination status: Vaccinated children with positive rotavirus infection were associated with longer duration of diarrhoea compared to non-vaccinated children as shown in Table 8 and Figure 8.

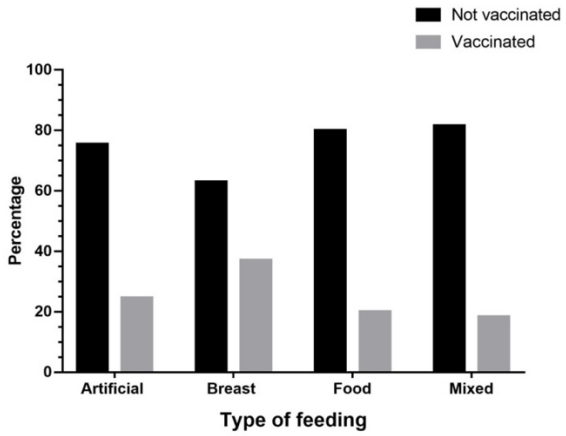

Figure 7: Feeding distribution according to vaccination status for children with positive rotavirus infection

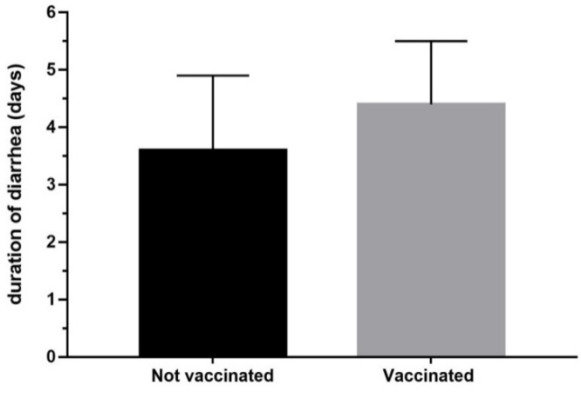

Figure 8: Duration of diarrhea according to vaccination status

DISCUSSION

Childhood diarrhoea is a main community health concern in developing countries, including Iraq (AL-Khafaji and H.J. 2013). Viruses cause about 70% of episodes of acute infectious diarrhoea in the pediatric age group (Imade and Eghafona 2015). Rotavirus infection is endemic worldwide especially in the first few years of life; and usually correlated with high rates of morbidity and mortality in developing countries due to poor nutrition and health care (Junaid, Umeh *et al.,* 2011).

Table 3: Comparison of age according to vaccination status for children with positive rotavirus infection

Variables	Not vaccinated	Vaccinated	p-value
Number	125	44	-
Age (months), mean ± SD	17.6 ± 13.0	22.5 ± 12.8	0.034
Age groups			
6 – 12 months	59 (86.8%)	9 (13.2%)	0.012
13 – 24 months	37 (69.8%)	16 (30.2%)	
25 – 36 months	9 (50.0%)	9 (50.0%)	
37 – 48 months	12 (66.7%)	6 (33.3%)	
49 – 60 months	8 (66.7%)	4 (33.3%)	
Independent t-test; Chi-square test (using linear by linear association) after correction using Monte Carlo methods of asymmetrical p-value			

Table 4: Comparison of gender according to vaccination status for children with positive rotavirus infection

Variables	Not vaccinated	Vaccinated	p-value
Number	125	44	-
Gender, no. (%)			0.615
Female	57 (72.2%)	22 (27.8%)	
Male	68 (75.6%)	22 (24.4%)	
Chi-square test			

Table 5: Comparison of residence according to vaccination status for children with positive rotavirus infection

Variables	Not vaccinated	Vaccinated	p-value
Number	125	44	-
Residence			0.253
Rural	52 (78.8%)	14 (21.2%)	
Urban	73 (70.9%)	30 (29.1%)	
Chi-square test			

Table 6: Comparison of place for sample collection according to vaccination status for children with positive rotavirus infection

Variables	Not vaccinated	Vaccinated	P value
Number	125	44	-
Sample collection			0.051
Hospital	89 (69.5%)	39 (30.5%)	
Clinic	23 (92.0%)	2 (8.0%)	
Primary care center	13 (81.3%)	3 (18.8%)	
Chi-square test			

Table 7: Comparison of feeding according to vaccination status for children with positive rotavirus infection

Variables	Not vaccinated	Vaccinated	P value
Number	125	44	-
Type of feeding			0.218
Artificial	49 (75.4%)	16 (24.6%)	
Breast	29 (63.0%)	17 (37.0%)	
Food	16 (80.0%)	4 (20.0%)	
Mixed	31 (81.6%)	7 (18.4%)	
Chi-square test			

Table 8: Correlation between length of diarrhoea and vaccination status

Not vaccinated	Vaccinated	OR	95% CI of OR	P value
3.6 ± 1.3	4.4 ± 1.1	1.561	1.181 – 2.065	0.002
Binary logistic regression				

Studies focus on vaccine effectiveness will provide the health administered comities with the required data on outcomes and safety and significant long-term public health statistics. Such information will be useful in guiding decision-maker personnel with respect to the maintenance, modification and extension of rotavirus vaccine programs in developing countries.

Phase III clinical trials of rotavirus efficacy have involved more than 70,000 infants 6 through 12 months of age in 11 countries against rotavirus gastroenteritis of any severity was 74%, and against severe rotavirus gastroenteritis (defined by severity of fever, vomiting, diarrhea and changes in behavior) was 98% (Correia, Patel *et al.,* 2010, de Palma, Cruz *et al.,* 2010, Velazquez, Linhares *et al.,* 2017).

The present study demonstrated that non vaccinated children presented with higher percentages of positive rotavirus infection (64.8%), and those children had (4.679) folds increased risk of having positive rotavirus gastroenteritis in comparison to vaccinated children which represented the effectiveness of (79%). Within Europe, US and Latin America vaccine effectiveness against rotavirus-induced gastroenteritis are ranged from (68% to 98%), based on data from clinical trials (Karafillakis, Hassounah *et al.,* 2015, Paternina-Caicedo, Parashar *et al.,* 2015, Kirkwood, Ma *et al.,* 2017). However, many publications have been implicated lower efficacy (34%-74%) of rotavirus vaccine in developing countries include African and Asian countries (Zaman, Dang *et al.,* 2010, Gruber, Gruber *et al.,* 2017).

The safety and effectiveness of rotavirus vaccines in the developing world are not well documented because the burden of rotavirus is greatest and the disease has more common fatal outcomes (Masters 2007). The efficacy of live oral vaccines is remaining a challenging issue with lower results in low-income than in the middle- and upper-income countries. Numerous hypotheses have been suggested to explain these differences that could provide clues to develop the ultimate achievement of these novel vaccines (Zeller, Heylen *et al.,* 2017). Even though introduction at present of constant fairly effective vaccines will reduce the morbidity and mortality associated with rotavirus in low-income settings, the investigation is urgently needed to understand why these differences in efficacy happen and what could be done to improve vaccine outcome to enhance the life-saving profits of vaccination. Many factors influence the immune response to live oral vaccines, including the concentration of acquired maternal antibody transmitted transplacental, breast milk immune and non-immune components, micronutrient malnutrition, the gastric acid amount in the digestive tract, interfering with gut flora, and diarrheal and general immune system diseases (Patel and Parashar 2009).

In conclusion, the results highlight the real picture of the effectiveness of rotavirus vaccine after the introduction of it is by Iraqi national immunisation programme in 2012 in Babylon city and the importance of certain demographic characteristics like age, residence, place for sample collection and duration of diarrhoea in the course of rotavirus infection.

Acknowledgements

Authors wish to thank Al-Mustansiriyah University for approving the study plan. This work was done according to the list of annual research plan of the Iraqi ministry of health in 2016. The authors have no conflict of interest.

REFERENCES

Ahmed, H. M., J. B. Coulter, O. Nakagomi, C. A. Hart, J. M. Zaki, A. A. Al-Rabaty, W. Dove and N. A. Cunliffe (2006). "Molecular characterisation of rotavirus gastroenteritis strains, Iraqi Kurdistan." Emerg Infect Dis. 12(5): 824-826.

AL-Khafaji, Y. A. R. and A.-J. H.J. (2013). "Detection of Rotavirus in diarrhoea stool samples of children with acute gastroenteritis in Babylon governorate, Iraq." International Research Journal of Microbiology 4(3): 4.

Alrifai, S. B., A. Alsaadi, Y. A. Mahmood, A. A. Ali and L. A. Al-Kaisi (2009). "Prevalence and aetiology of nosocomial diarrhoea in children < 5 years in Tikrit teaching hospital." East Mediterr Health J. 15(5): 1111-1118.

Correia, J. B., M. M. Patel, O. Nakagomi, F. M. Montenegro, E. M. Germano, N. B. Correia, L. E. Cuevas, U. D. Parashar, N. A. Cunliffe and T. Nakagomi (2010). "Effectiveness of monovalent rotavirus vaccine (Rotarix) against severe diarrhoea caused by serotypically unrelated G2P[4] strains in Brazil." J Infect Dis. 201(3): 363-369. doi: 310.1086/649843.

De Palma, O., L. Cruz, H. Ramos, A. de Baires, N. Villatoro, D. Pastor, L. H. de Oliveira, T. Kerin, M. Bowen, J. Gentsch, D. H. Esposito, U. Parashar, J. Tate and M. Patel (2010). "Effectiveness of rotavirus vaccination against childhood diarrhoea in El Salvador: the case-control study." BMJ 340: c2825.

Dennehy, P. H. (2000). "Transmission of rotavirus and other enteric pathogens in the home." Pediatr Infect Dis J. 19(10 Suppl): S103-105.

Dennehy, P. H. (2008). "Rotavirus vaccines: an overview." Clin Microbiol Rev. 21(1): 198-208. doi: 110.1128/CMR.00029-00007.

Dennehy, P. H., R. C. Brady, S. A. Halperin, R. L. Ward, J. C. Alvey, F. H. Fischer, Jr., B. L. Innis, H. Rathfon, A. Schuind and B. De Vos (2005). "Comparative evaluation of safety and immunogenicity of two dosages of an oral live attenuated human rotavirus vaccine." Pediatr Infect Dis J. 24(6): 481-488.

Desselberger, U. (2014). "Rotaviruses." Virus Res 190: 75-96.

Grimwood, K. and S. B. Lambert (2009). "Rotavirus vaccines: opportunities and challenges." Hum Vaccin. 5(2): 57-69. Epub 2009 Feb 2008.

Gruber, J. F., L. M. Gruber, R. P. Weber, S. Becker-Dreps and M. Jonsson Funk (2017). "Rotavirus Vaccine Schedules and Vaccine Response Among Infants in Low- and Middle-Income Countries: A Systematic Review." Open Forum Infect Dis. 4(2): ofx066. doi: 010.1093/ofid/ofx1066. eCollection 2017 Spring.

Gruber, J. F., D. A. Hille, G. F. Liu, S. S. Kaplan, M. Nelson, M. G. Goveia and T. C. Mast (2017). "Heterogeneity of Rotavirus Vaccine Efficacy Among Infants in Developing Countries." Pediatr Infect Dis J. 36(1): 72-78.

Imade, P. and N. Eghafona (2015). "Viral Agents of Diarrhea in Young Children in Two Primary Health Centers in Edo State, Nigeria." International Journal of Microbiology 2015(Article ID 685821): 5 pages.

Junaid, S. A., C. Umeh, A. O. Olabode and J. M. Banda (2011). "Incidence of rotavirus infection in children with gastroenteritis attending Jos university teaching hospital, Nigeria." Virol J. 8:233.(doi): 10.1186/1743-1422X-1188-1233.

Karafillakis, E., S. Hassounah and C. Atchison (2015). "Effectiveness and impact of rotavirus vaccines in Europe, 2006-2014." Vaccine 33(18): 2097-2107.

Kirkwood, C. D., L. F. Ma, M. E. Carey and A. D. Steele (2017). "The rotavirus vaccine development pipeline." Vaccine 7(17): 30410-30413.

Kosek, M., C. Bern and R. L. Guerrant (2003). "The global burden of diarrhoeal disease, as estimated from studies published between 1992 and 2000." Bull World Health Organ 81(3): 197-204.

Masters, J. D. (2007). "Gastroenteritis and the rotavirus vaccine." infant 3(6): 224-227.

Parashar, U. D., C. J. Gibson, J. S. Bresee and R. I. Glass (2006). "Rotavirus and severe childhood diarrhoea." Emerg Infect Dis. 12(2): 304-306.

Patel, M. M. and U. D. Parashar (2009). "Assessing the effectiveness and public health impact of rotavirus vaccines after introduction in immunisation programs." J Infect Dis. 200(Suppl 1): S291-299. doi: 210.1086/605059.

Paternina-Caicedo, A., U. D. Parashar, N. Alvis-Guzman, L. H. De Oliveira, A. Castano-Zuluaga, K. Cotes-Cantillo, O. Gamboa-Garay, W. Cornell-Rodriguez and F. De la Hoz-Restrepo (2015). "Effect of rotavirus vaccine on childhood diarrhea mortality in five Latin American countries." Vaccine 33(32): 3923-3928.

Velazquez, R. F., A. C. Linhares, S. Munoz, P. Seron, P. Lorca, R. DeAntonio and E. Ortega-Barria (2017). "Efficacy, safety and effectiveness of licensed rotavirus vaccines: a systematic review and meta-analysis for Latin America and the Caribbean." BMC Pediatr. 17(1): 14. doi: 10.1186/s12887-12016-10771-y.

Vesikari, T., A. Karvonen, R. Prymula, V. Schuster, J. C. Tejedor, R. Cohen, F. Meurice, H. H. Han, S. Damaso and A. Bouckenooghe (2007). "Efficacy of human rotavirus vaccine against rotavirus gastroenteritis during the first 2 years of life in European infants: randomised, double-blind controlled study." Lancet. 370(9601): 1757-1763.

Wang, C. M., S. C. Chen and K. T. Chen (2015). "Current status of rotavirus vaccines." World J Pediatr. 11(4): 300-308. doi: 310.1007/s12519-12015-10038-y. Epub 12015 Oct 12511.

Zaman, K., D. A. Dang, J. C. Victor, S. Shin, M. Yunus, M. J. Dallas, G. Podder, D. T. Vu, T. P. Le, S. P. Luby, H. T. Le, M. L. Coia, K. Lewis, S. B. Rivers, D. A. Sack, F. Schodel, A. D. Steele, K. M. Neuzil and M. Ciarlet (2010). "Efficacy of pentavalent rotavirus vaccine against severe rotavirus gastroenteritis in infants in developing countries in Asia: a randomised, double-blind, placebo-controlled trial." Lancet 376(9741): 615-623.

Zeller, M., E. Heylen, S. Tamim, J. K. McAllen, E. F. Kirkness, A. Akopov, S. De Coster, M. Van Ranst and J. Matthijnssens (2017). "Comparative analysis of the Rotarix vaccine strain and G1P[8] rotaviruses detected before and after vaccine introduction in Belgium." PeerJ. 5:e2733.(doi): 10.7717/peerj.2733. eCollection 2017.