



Original Research Article

**EPIDEMIOLOGY AND PHARMACOTHERAPY OF ROTAVIRUS AND
IMPACT OF VACCINATION TO PREVENTION ITS MORTALITY**

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ABSTRACT

Rotavirus is a type of virus that primarily affects infants and young children, causing gastroenteritis, which is inflammation of the stomach and intestines. It is one of the leading reasons for severe diarrhea worldwide, especially in developing lands. The virus is highly contagious and can spread through the fecal-oral route, primarily through contaminated food, water, and surfaces. The introduction of the rotavirus vaccines has had a significant impact on reducing the burden of rotavirus-related illnesses. Many countries have incorporated rotavirus vaccination into their national immunization programs. The vaccines have significantly reduced rotavirus-related hospitalizations, deaths, and overall disease burden in countries where vaccination coverage is high. Here, we will discuss the recent developments in epidemiology, diagnosis, and treatments of rotavirus-induced gastroenteritis. Moreover, suggestions to prevent incidences of infection have been elegantly discussed.

Keywords: rotavirus, vaccines, diarrhea, challenges, immunization programs, diagnosis

Introduction:

Acute infant diarrheal disease is majorly caused by rotavirus (RV) which persuades high morbidity and mortality in children under the age of five. Data show that nearly one-half of the rotavirus-related mortalities are observed in countries including the Democratic Republic of Congo, India, Nigeria, and, Pakistan (1). RV was termed as it resembles a wheel shape under an electron microscope. Many species of birds and young animals are principally susceptible to RV where it induces diarrhea. These viruses are members of the reovirus family and make up their genus inside the larger family of viruses known as Reoviridae (derived from respiratory enteric orphan virus) (2). Entirely, they have 11 fragments of double-stranded ribonucleic acid (dsRNA) that are encased in three layers of protein, thus making up their genome (Figure 1).

Each segment of the RV genome is responsible for the production of a specific viral protein (VP) synthesis however, except segment number 11, which is responsible for two proteins in certain species. Collectively, RV consists of twelve proteins: VP1-VP4, VP6, and one accessory VP7 (six structural proteins) and NSP1-NSP6 (six nonstructural proteins) (Figure 1). The VP7 and VP4 proteins (that define G and P genotypes) on the outer capsid of RVs, offer the basis for the binomial categorization of these viruses (3). The external region of the RV protein coat is composed of VP4 and VP7 and the mesial region is composed of VP6 protein. Based on particular antigens present on the VP6 protein layer, RVs are classified into 8 groups (groups A to H). Group A, B, C, and H are responsible for the disease in humans where Group A accounts for ninety percent of all reported cases (4). RV majorly infects enterocytes (the mature cells of the epithelium of the small intestine) and subsequently, it causes diarrhea and death of enterocytes. The processes involve stimulation of the enteric nervous system because of its disruption and interruption of blood flow (5). Clinical presentations comprise multiple episodes of watery diarrhea, fever, vomiting, feebleness, excessive vomiting, and loose stools instigating water and salt loss in the body. If untreated, this may lead to life-threatening conditions (6). Gastrointestinal infections bring osmotic and secretory diarrhea, the former stimulates the intrinsic nervous system and the latter occurs due to malabsorption. Emesis, cholelithiasis, acid regurgitation, abdominal distention, and indigestion are major gastrointestinal infection symptoms (7). Laboratory methods and techniques for example, reverse transcription polymerase chain reaction (RT-PCR), antigen detection assay, virus extraction, latex agglutination and polyacrylamide gel electrophoresis (PAGE) are routinely applied for diagnosis of the virus. Treatment and management of the disease aim to alleviate the severity of infection. Oral rehydration solutions (ORS) are used as a first-line agent in the management of dehydration. As well, probiotics, anti-secretory, and antiviral drugs are used in the treatment. Anti-emetics (ondansetron) and antibody preparations are usually applied as an adjunct in therapy, particularly to hospitalized and immunosuppressed patients (8). The immune system is prominently affected by malnutrition in children and they are prone to other diseases as well (9). Nevertheless, avoiding the risk of RV infection in children is challenging as it implicates strict hygienic measures (10). The incidence of RV-induced diarrhea can be alleviated by the administration of vaccines as it had played a pro-vital role in downscaling of disease load globally (11). In infants, breastfeeding and maternal antibodies offer immunity against RV infection (12). Further surveys have supported the positive impact of vaccination as RV group A caused 40.3% of diarrheal diseases worldwide, but only a 12.2% fraction in countries where universal immunization was made compulsory (13). In 2009, WHO approved two oral vaccines named RotaTeq (Merck and Co, Kenilworth, NJ) and Rotarix (RV1) (GlaxoSmithKline, Brentford, United Kingdom) respectively. Two more live, oral RV vaccines, Rotasil, and Rotavac were prequalified in 2017 by WHO (14).

By January 2022, more than 100 countries have included the RV vaccine as part of their national

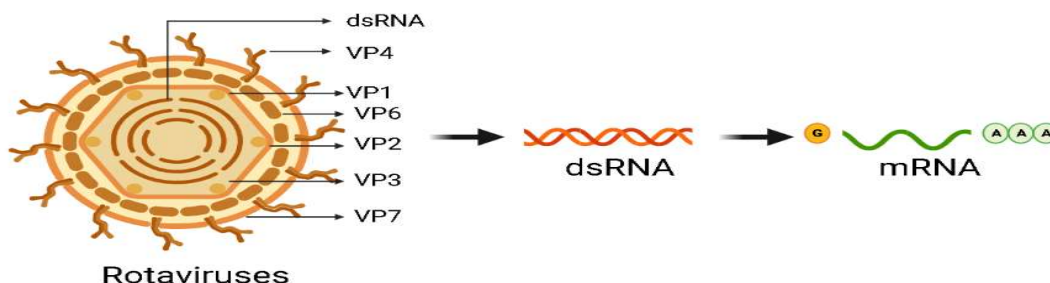


Fig1. Cross-sectional schematic of the rotavirus triple layer particle. It consists of spike proteins (VP4), the outer capsid layer (VP7), the middle capsid layer (VP6), and the inner capsid core (VP2). After its proteolytic cleavage, VP4 turned into VP5 and VP8. VP1 (the enzymatic protein), VP2 (the structural protein), and the viral genome (dsRNA) constitute the virion core. The genetic material processing of the

virus occurs by the direct formation of messenger RNA from a double-stranded RNA genome. The Figure was adopted from (22).

Epidemiology

Unhygienic surroundings, high population burden, and shortage of public cleanliness offer viruses a place of convergence and the untroubled spread of disease (23). Unhygienic surroundings as well as the use of contaminated water for domestic purposes give rise to a high prevalence of diarrheal disease. United Nations International Children's Emergency Fund (UNICEF) claimed that only 29% and 52% of people had approached sufficient cleanliness services and quality water sources (Figure 2). All these conditions ensure viruses have basic reproducing ground and transmission (24). The yearly worldwide prevalence rate of diarrhea is around 1.7 billion cases (25). WHO claims that 1,600,000 people die annually due to digestive system upset and is listed as the 9th major cause of fatality in children with age less than 5 years. Until now, diarrhea is a considerable disease in underdeveloped countries because of poor medical care approaches and contaminated habitats (26). In this regard, RV infection is responsible for more than 50% of diarrheal prevalence. Globally, 1.14 billion RV diarrheal cases are reported annually (27). RV causes between 352,000 and 592,000 mortality, with another 111 million cases of gastroenteritis in young children needing just at-home care, twenty-five million cases requiring urgent care centers, and 2 million hospitalized cases in younger under five years of age (28)(29). Globally, estimated 440,000 deaths occur due to RV (30).

In Europe, 30% of people are prone to diarrhea and 320,000 (20%) die annually (31). Children living in Asia, Africa, and poor countries (32) are more susceptible to RV diarrheal disease and have high mortality rates due to overpopulation, inadequate sanitation, poor living standards lack of cleanliness, and contaminated water (33). More than half of the fatality stress is due to RV diarrheal cases reported in volunteers from 6 states including Indians, Nigerians, the Congos, Ethiopians, Chinese, and Pakistanis (34). The data show that the incidence of illness due to RV is significant without immunization nevertheless, the mortality rate is lesser in Europe and America where vaccine is a must for long (35). 11% Prevalence rate and 26,400 deaths due to RV recorded in Europe each year (36). While in Asia 45% diarrheal prevalence rate is recorded and 560,000 deaths occur each year (37, 38). RV accounts for a 30 % prevalence rate and a 101,200 per year mortality rate (39).

In Pakistan overpopulation and ecological circumstances contribute considerably to uncontrolled virus sprouting. Due to frequent diarrheal events, an 11% prevalence rate and 150,000 deaths per year are observed which is the main cause of undernourishment and stagnant growth in children under the age of five (40). The prevalence rate of the virus is almost 7%. G1p, G2p, and G9p are the most prevalent genotypes in this country according to microscopic epidemiological studies (12). In Punjab, 3.5% diarrheal frequency with a mortality rate of 30,000 annually has been recorded (41). Low-income countries tolerate more than half of the mortality load caused by diarrhea (42). Out of 194 observed countries, Pakistan is enumerated among 23 in the catalog due to diarrhea-associated deaths as reported by WHO (43). The prevalence of RV is particularly high in Punjab 2% and the mortality rate is 1.1% (estimated 5078 deaths) (44). Across the world, both in progressed and emergent countries, RVs are now believed to be the primary cause of 40-50% of diarrhea in youngsters under 5 (45). Global Monitoring Network and reported data from hospitals claimed that the frequency of RV-associated diarrhea among younger under five lies in the range of 6% to 56% (46).

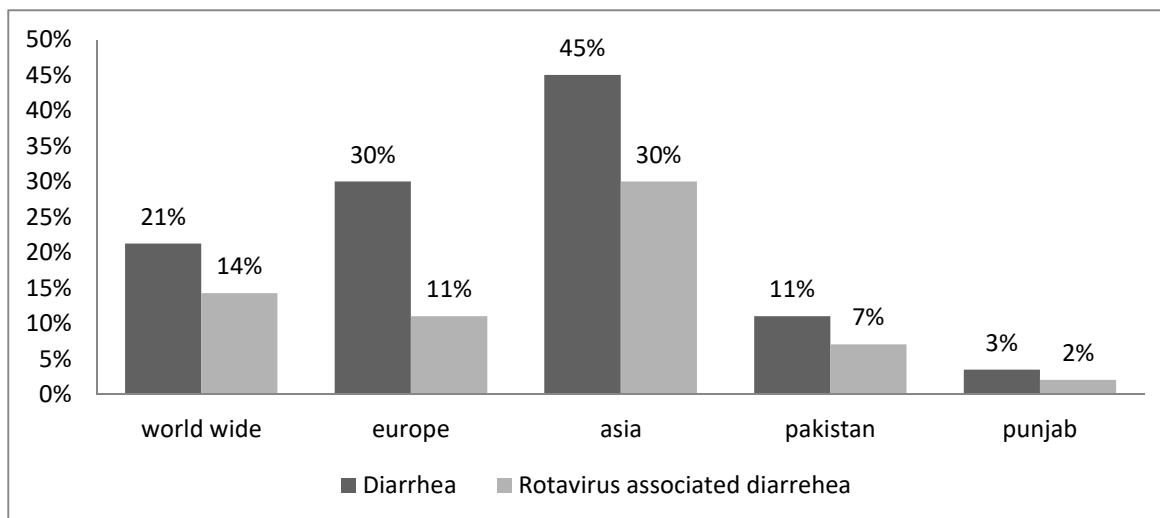


Figure 2. Epidemiological data shows the prevalence of diarrhea and rotavirus-associated diarrhea in different regions of the world including Pakistan.

Mode of transmission of Rotavirus

The virus is majorly spread in the population via the faecal-oral route. It may also transfer through feces-pollutant water in impoverished nations. RV may also be transmitted from one younger to another younger through the unclean caretakers' hands by contaminated objects. The passage of small particle aerosol into the lungs has also been suspected, but not proven in humans (47). The period required for the appearance of first symptoms is 1 to 3 days and the number of persons with that virus frequently arise in outbursts is among the circumstantial evidence for RV gastroenteritis spreading through the air. In some individuals, RV was observed in bronchial discharge. Moreover, up to 50% of patients with RV develop bronchial upset and otitis media (48). In kids' day-care centers, as well as family day-care homes, RV transmission is facilitated by recurrent and constant confront among susceptible hosts, with nappy changing being more likely for alike transference. The virus was found in diaper wastage bins, playing tools, faucets, nappy change areas, hand washing regions, and even kitchens. This observation acclaims that RV can affect all over in homes or baby care centers, not j only in the regions directly polluted by faeces(49).

Replication cycle

RV multiplies into the cell cytoplasm of the suspect person. Viruses enter the host cell via endocytosis, and viral mRNA is transcribed into structural protein units of the capsid utilizing the viral RNA polymerase that is already present in the virion. The mRNA segments are associated with the immature capsid, which is subsequently replicated to create the double-stranded RNA genome (50). The RV replication cycle comprises the following steps including fitment, conciliated by VP4 and VP7, perforate and uncoating, strand ssRNA production mediated by VP1, VP2, and VP3, viroplasm production, facilitating RNA packing, minus strand, RNA synthesis and double layer particle (DLP) formation (51). A detailed elaboration of the mechanism is elegantly presented in Figure 3. Clathrin-induced endocytosis of the virus into the host cell is mediated by the attachment of the viral VP4 protein to host receptors. Particles are partially uncoated in endolysosomes (loss of the VP4-VP7 outermost layer) and penetrate the cytoplasm via permeabilization of the host endosomal membrane. Inside these newly formed DLPs, viral polymerase performs early transcription of the dsRNA genome, preventing dsRNA from ever being exposed to the cytoplasm. The nascent (+) RNAs are extruded into the cytoplasm and serve as a template for viral protein synthesis (52). Cytoplasmic virus factories create progeny cores with replicative activity (also called viroplasm). This implies the synthesis of complementary (-) RNA and initiates steps of viral morphogenesis. These

components are covered with VP6 at the edges of virus factories, developing into immature DLPs that bud across the endoplasmic reticulum membrane and acquire a temporary lipid membrane that is modified with the ER-resident viral glycoproteins NSP4 and VP7. These temporary membranes are removed when the particle enters the ER cisternae, and the viral surface proteins VP4 and VP7 rearrange to form the outermost virus protein layer, resulting in mature infectious triple-layered particles. Mature virions are likely released after host plasma membrane breakage brought on by cell death (53).

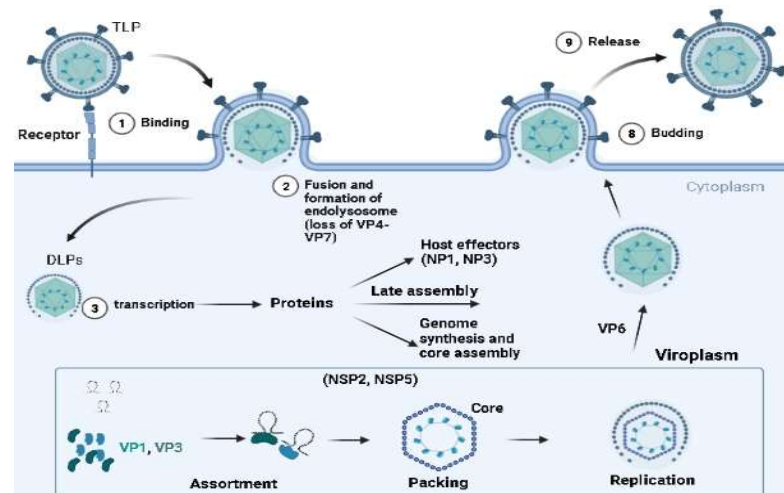


Figure 3. Steps of the replication cycle of rotavirus inside the host cell are presented. Knowing the mechanism is imperative to devise strategies against virus replication and disease management. Here, TLP denotes triple-layer particles, and DLP denotes double-layer particles.

Clinical presentation

Studies have established that fever, vomiting, and diarrhea are the most prevalent clinical symptoms. Among the clinical symptoms reported by sick children, vomiting is more common among those who test positive for RV than among those who test negative. Fever was also a common clinical manifestation (54). Blood in the stool and mucous stool were less common clinical signs of RV infections. Diarrhea caused by the virus can induce mild to severe dehydration. Acute dehydration affected 60%-100% of hospitalized patients (55). RV gastroenteritis patients typically have more severe symptoms and so are more likely to need hospitalization than patients with other types of acute gastroenteritis (vomiting, diarrhea, dehydration, etc.). These patients may experience electrolyte imbalances and severe dehydration. Abdominal pain and watery diarrhea that lasts for three to eight days are likewise common symptoms. The infected children may experience coughing and a runny nose as well. Severe dehydration reveals itself through fatigue, loss of consciousness, an inability to drink enough, puffy eyes, and a very lengthy recovery period (> 2 seconds) when the skin is pinched. Mild dehydration was characterized by agitation, irritation, sunken eyes, excessive drinking, thirst, and a delay in the restitution of pinched skin (56). Neurological symptoms, including afebrile or febrile convulsions, meningo-encephallitis, encephalopathy, and cerebellitis, appear to be the most common extra-intestinal effects (57). The effects of RV infection on the brain can range from a moderate form of encephalitis with a reversible specific lesion to a severe form of acute encephalitis with biphasic convulsions and late reduced diffusion, and even acute necrotizing encephalopathy (58). Most infants with RV infection would not show any symptoms at all, but if left untreated, they could develop

necrotizing colitis, a potentially fatal form of diarrhea. Accompanying symptoms include high body temperature, blood in the stool, abdominal pain, and distention (59). Vaccinated children have experienced fewer severe cases, less dehydration, and less vomiting than unvaccinated children (60).

Diagnosis

A stool sample analysis may be performed alongside symptoms and a physical examination to confirm a diagnosis. There are several methods for detecting RV in stool samples. Electron beam microscopy, reverse transcription polymerase chain reaction (RT-PCR), antigen detection test, polyacrylamide gel electrophoresis, latex-agglutination, immune-chromatography testing, and extraction of the virus are among them. RT-PCR further comprises real-time RT-PCR (RT-rPCR), multiplex real-time RT-PCR (RT-mPCR), and quantitative RT-PCR (RT-qPCR). Weighing test results according to their sensitivity, specificity, and predictive values may help enhance diagnostic accuracy. Faulty diagnostic tests that fail to effectively detect the full extent of the disease could increase the mortality toll in a community because they delay and cloud the therapeutic response (61). The details of the individual diagnostic test have been described here.

Electron microscopy

The first case of equine RV was discovered in 1975 in the United Kingdom in a diarrheic sample from a foal (62). An Electron microscope (EM) illustrates the structural, and functional aspects, a broad spectrum of interactivity, resistance, and mechanisms of viral particles or viruses, it also offers a significant illustration of virion due to its extreme resolving power which permits the nanoscale study of viruses, diagnosis, and research (63). Despite electron microscopy's high level of specificity, however, the procedure is labor-intensive, expensive, and takes a lot of time as it requires the assistance of trained professionals (5).

Reverse transcription polymerase chain reaction

It can be used to find the DNA of a targeted organism, such as a virus. Every laboratory uses PCR to assess the prevalence of virus strains. When working with unanticipated viral species or variations in closely related virus genomes, primer selection has more importance (64). By use of primers, nucleic acid is detected by the RT-PCR technique at the molecular level (65).

Real-time RT-PCR

Due to its superior sensitivity, specificity, and ease of data interpretation, real-time RT-PCR assays may replace traditional RT-PCR testing for detecting group A viruses. In the early trials using real-time RT-PCR, SYBR Green was employed to amplify the VP6 gene (66). Due to their superior sensitivity and specificity, real-time PCR assays have supplanted culture-based methods for detecting GI pathogens in stool samples (67).

Multiplex real-time RT-PCR

Greater efficiency in high-throughput genotype characterization of RV using multiplex real-time RT-PCR allows for the detection of new strains of circulating wild-type RV (68). To detect and identify a wide variety of GI pathologies, real-time multiplex PCR diagnostics such as those provided by BioMerieux's Bio Fire® Film Array® Gastrointestinal Panel, Luminex Corporation's xTAG® Gastrointestinal Pathogen Panel, and Abbott's Allplex™ Gastrointestinal Panel Assays may be used (Seegene). These platforms provide challenges for laboratories seeking to maximize efficiency and productivity due to their poor throughput or lack of automation (67). PCR-based multiple diagnosis temperature analysis has been used for high specificity and short duration of the method.

Quantitative RT-PCR

Although RT-qPCR is known as the gold standard for RV identification in clinical practice, the high cost of this technique makes it impractical for early diagnosis. Therefore, the current investigation assessed the performance of a commercial LAT technique for fast diagnosis of RV in pediatric outpatients, with RT-qPCR serving as the gold standard (69). Quantitative RT-PCR identifies the viruses at the growing stage rather

than the plateau phase which prevents a host from severe illness due to early diagnosis. It eliminates the uncertainty in positive or negative analysis and is used as a reference for its high performance (70).

Antigen detection assay

Enzyme-linked immunosorbent assays (ELISA) can also be used to identify RV antigens. RV Antigen ELISA Kit by EDI (California-based), Prospect Viral Microplate Assay by Oxoid (United Kingdom-based), Rota Antigen Test Device by Cambridge, and Premier Rota clone by Meridian Bioscience, Inc. (United States-based) are all in use. ELISA is a specialized method for identifying the virus because of its high sensitivity and the fact that it can detect RV-specific IgM (68). Although electron microscopy and enzyme-linked immunosorbent assay (ELISA) both detect RV antigens, ELISA seems to be more effective and accurate (5).

Polyacrylamide gel electrophoresis

Different RV strains were analyzed for their phenotypes using SDS-polyacrylamide gel (PAGE). Western blots are a method for isolating denatured proteins by molecule sieving out across pores of poly(n PA) gel in the addition of ionic surfactants (i.e., sizing). For on-membrane immunoglobins, the sizing of protein bands enables exact calculations of hundreds to millions of combined cells. Time and effort are required for the lengthy procedures (68). The polyacrylamide gel electrophoresis approach is fast, straightforward, and reproducible when it helps prepare RNA from RV for gel electrophoresis analysis in affinity chromatography (71).

Latex agglutination

The latex agglutination slide test is a rapid diagnostic procedure in which antigens from fecal supernatant are coated onto latex particles. A human observer can read the results of this test in under a minute (72). Drugs, viruses, proteins, bacteria, and Hormones can be identified through this technique. Interference and non-specific interactions can result in false positive and negative results (73).

Immunochromatography test

The immunochromatography strip test is a fast and accurate field method for analyzing feces samples taken from the calf's side for pathogens. Dipsticks are kept in the solution with homogenized feces, the result is positive if both the control and indicator lines turn red otherwise regarded as null (61). Compared to alternative processes, clinical veterinarians and researchers may prefer using immunochromatographic rapid test kits since they can be used in any laboratory office setting, including those found in private clinics or even the field (74).

Virus extraction

The practice of isolating viruses is utilized in a limited capacity (5). Extraction of viruses from the culture or sample gives terminal evidence of virus connection with illness but it is a more effortful and less precise technique as compared to others (73). Since it is compatible with a wide variety of viral genomes and architectures, this method of nucleic acid extraction has the potential to boost viral recovery. There are many different nucleic acid extraction kits available, and they have all been proven to successfully recover viral and bacterial nucleic acids in lab tests. It was concerning to learn that contaminants in certain extraction kits routinely created false-positive results (75).

Management of rotavirus

The management of RV includes primary management and secondary management. Primary management further covers preventive measures and secondary management includes pharmacological and non-pharmacological treatment.

Preventive measures

Avoiding contact with infectious children

The best strategy to lower the chance of developing the infection is to stay away from affected people (76). Given the prevalence of RV infection, the fact that some people infected with RV are asymptomatic but are even contagious and the disease is often shed in the feces for longer periods after the infection, and the

possibility that children are probable to get sick of the virus in daycare health institutions, this strategy has constrained useful value (77). Thus, RV can be prevented by decreasing the total numeral of kids admitted to the hospital and acute RV occurrence can be avoided (78).

Improved sanitation and hand hygiene

Improving cleaning and hand hygiene can help to reduce the strain. To inhibit the spread of disease, disinfectants are used to raise awareness about the significance of proper hand washing. To stop the spread of RV, apply a disinfectant such as a hypochlorite or sodium dichlorocyanurate. The virus is likewise rendered inactive by a 70% ethanol solution (79). RV is removed from the skin by alcohol-based hand hygiene products; medicated or non-medicated soap is less successful at lowering RV titers on fingertips than 70% isopropanol and 70% ethanol (80). Since polluted eating things or direct person-to-person contact are the main ways that the agents of acute gastroenteritis spread, sanitation, proper hand washing, and sanitary practices can stop the spread.

Use of probiotics

Probiotics can improve the health of the host when given in sufficient doses. Research has shown that the use of probiotic bacteria may mitigate the effects of acute RVGE and stop its spread in hospitals and other healthcare facilities and the general public (81). Infants who used *Lactobacillus* as a preventative medicine had a considerably lower chance of developing nosocomial diarrhea, particularly RV-induced gastroenteritis. As it reduces the time the virus is shed in faeces and the duration of the symptomatic period, LGG is more efficacious in the treatment of RV infection (82). Two randomized, controlled clinical trials compared *Streptococcus thermophilus* and *Bifidobacterium bifidum* against *Lactobacillus GG* for their ability in preventing diarrhoea. It was revealed that lactic acid-producing organisms like *Streptococcus thermophilus* and *bifidobacteria*, which make up the majority of an infant's gut flora when nursed, can prevent severe diarrhea (83).

Breastfeeding

There are conflicting findings on breastfeeding's ability to effectively protect against RV infection. Initially, it was thought that a significant factor reducing the efficacy of the RV vaccine was the oral transmission of breast milk components in children at the time of inoculation (84). Withholding nursing at the time of the RV vaccine had no effect, according to studies on children in South Africa and India. Breastfeeding offers some RV protection, according to different studies. Lactadherin, a protein found in breast milk that inhibits the RV enzyme, is what gives breastfeeding its anti-RV effects (85).

Vaccination

After proving its effectiveness against the widespread RV gastroenteritis, a rhesus human reassortant RV vaccine was granted US licensure in 1998. Two live RV vaccines were created: the monovalent human vaccine Rotarix from GSK Biologicals and the pentavalent bovine human reassortant vaccine RotaTeq from Merck. In the United States, the Advisory Committee on Immunization Practices (ACIP) recommends vaccinating infants against RV at 2, 4, and 6 months of age. The optimal age for the first dose is between 6 and 12 weeks old child (86). Five bovine-human reassortantRVes that express either human VP4 or VP7 from RV strains G1, G2, G3, G4, and P1A make up the live attenuated, pentavalent RV5 vaccine. The WHO has currently pre-qualified four oral vaccines (ORVs) for widespread use: RotaTeq, Rotarix, Rotavac, and Rotasiil. Each vaccine is an oral, live-attenuated shot. In clinical trials carried out in higher-income areas, RotaTeq and Rotarix both showed outstanding vaccine effectiveness (87).

In the EU, infants aged 6-32 weeks are recommended to receive the three-dosed pentavalent vaccine (RotaTeq) to prevent RV gastroenteritis (RVGE) (88). The vaccine is delivered orally and can be combined with other popular pediatric vaccinations. It has been demonstrated that Rotasiil, a lyophilized, heat-stable ORV, is stable when stored for up to 18 months at 37°C–40°C. At six and ten weeks (Rotarix) or (6, 10, and 14 weeks) RotaTeq, Rotavac, or Rotasiil is advised (89). Delayed administration is recommended as it may lessen the inhibitory effects of maternal antibodies (90). However, less is known about how breast milk

affects ORV responsiveness. In vitro, both antibodies found in breast milk and non-antibody components like lactoferrin and human milk oligosaccharides make RV less infectious, even in vaccine strains (91).

Table 1. Chronological history of the approved vaccines, their manufacturers, schedule, and approved dose.

Vaccine	Manufacturer	Dosage	EPI Schedule	WHO pre-qualification time
RotaTeq	Merck & Co., Inc	2-2.8 × 10 ⁶	6, 10, 14 weeks	Oct 2008
Rotarix	Glaxo Smith Kline Biologicals	>10 ⁶ CCID ₅₀	6, 10 weeks	March 2009
Rotavac	Bharat Biotech International Ltd.	>10 ⁵ FFU	6, 10, 14 weeks	Jan 2018
Rotasill	Serum Institute of India Pvt, Ltd.	>10 ^{5.6} FFU/serotype	6, 10, 14 weeks	Sep 2018
RotasilThermo	Serum Institute of India Pvt, Ltd.	>10 ^{5.6} FFU/serotype	6, 10, 14 weeks	Jan CC2020

CCID₅₀ denotes median cell culture infectious dose, FFU denotes focus-forming units

Secondary management

The management of RV includes the following treatments.

Non-pharmacological management

Oral rehydration

A replacement of fluid and electrolyte loss is the main focus of the treatment of RV infections. There are a variety of options for rehydration, including the WHO's recommended method and commercial products (92). Children who are mild to moderately dehydrated can be helped by these formulas. If the child cannot swallow or will not drink, intravenous fluids should be used. Homemade solutions include water, sugar, and salt which are used if ORS isn't available (93).

Dietary management

Severely dehydrated patients should fast for four to six hours after beginning rehydration therapy (94). Some research suggests that lactose-free formulas can aid some children, especially those who need to be hospitalized (95). Breastfeeding should be motivated and never prohibited. Immunoglobulins and other vital elements found in breast milk support an infant's growth and survival. Lactadherin, a protein found in breast milk, is thought to be responsible for inactivating the virus that causes diarrhea and anti-RV property of breast milk is due to this protein (96). The WHO recommends daily zinc supplements for infants and children in low-income regions if they have a diarrhea episode. The latest advice for avoiding diarrheal dehydration fatality is oral rehydration therapy with zinc supplements (97). One of the most popular traditional therapies is mashed bananas, utilized by parents when their children have diarrhea. It expedites healing and promotes nutrient absorption and mucosal damage (98). Due to its high starch content which is resistant to amylase and produces short-chain fatty acids, which improve salt and water absorption from the colon, bananas have anti-diarrheal properties (99).

Adjunctive therapy

Other probiotics may be more effective than a placebo in treating RV-induced diarrhea when used as an adjunctive therapy. Supplementation with bifidobacteriumlactis enhanced the effectiveness of treatment for RV gastroenteritis. Probiotics can decrease the total numerals of days you have to deal with diarrhea from several days down to just a couple (100). A daily dose of 10 billion colony-forming units of the Lactobacillus

rhamnosus GG is efficacious in decreasing the extent of diarrhea and the risk of long-term hospitalization (101).

Pharmacological treatment

When treating children with acute RV gastroenteritis, anti-emetics like ondansetron are usually used as adjunctive (102). The best outcome might get when ondansetron is used early in the management of children with RV infection (103).

In another study, nitazoxanide, a broad-spectrum antiviral, has been shown to have a cytoprotective impact against RV and shorten the duration of diarrhea as compared to placebo control. Also, Nitazoxanide interferes with viral morphogenesis to prevent RV replication (104). Other products that have been investigated for the treatment of acute diarrhea and RV gastroenteritis include zinc, vitamin A, probiotics, and immunoglobulins (105). Racecadotril and smectite are two more possible treatments for gastroenteritis brought on by the virus. Racecadotril, an intestinal enkephalinase inhibitor that lowers the gut's production of water and electrolytes, has been demonstrated to dramatically reduce diarrhea output 48 hours after treatment without increasing the frequency of adverse effects according to a meta-analysis of seven randomized trials. Racecadotril therapy is superior to a placebo or no intervention in reducing the length of illness and stool production in children with acute diarrhea (106). In a meta-analysis of largely open-label trials in children with acute diarrhoea, smectite (a natural adsorbent) that binds to endotoxins, exotoxins, bacteria, and viral particles, has been shown to shorten the duration of acute diarrhea by 18–29%. Smectite has also been demonstrated to boost the cure rate at day 5 without increasing the risk of adverse effects, suggesting that it may be helpful for some people with RV sickness (107).

Herbal medicine has also shown its potential against the virus so far. In this regard, GegenQinlian decoction is considered an excellent remedy for RV enteritis (RVE) (108). It is made up of four herbal medicines, Pueraria lobate, Scutellariabaicalensis, Coptischinensis, and Glycyrrhizauralensis which correspond to the four roles of "monarch, minister, assistant, and guide," according to the fundamental rule of prescription composition in traditional Chinese medicine. It has a curative impact on RVE, which is marked by a reduction in fever, vomiting, and diarrhea. A study showed that the modulation of calcium ions, serotonin, and gastrointestinal hormone ions, which may all have an impact on the intestinal nervous system, has effectively alleviated the symptoms of RVE (109). Also, Puerarialobata's root (Wild) Ohwi is an edible and medicinal Chinese herb used to treat diarrhea and increase the Yang Qi (energy) of the spleen and stomach. RV gastroenteritis is frequently treated clinically with Puerarialobata root extract. The Puerarialobata's primary constituent is the isoflavone compound puerarin. The influenza virus, the RV, and epidemic diarrhea viruses are all susceptible to puerarin's antiviral properties (110).

CONCLUSIONS:

Rotavirus is the leading cause of severe diarrhea in children worldwide. It is appraised that rotavirus causes approximately 37% of death due to diarrhea in children under the age of 5. It is most prevalent in low-income countries and regions with poor sanitation and inadequate access to health care, where a majority of deaths ensue. Testing can identify the presence of the rotavirus antigen or genetic material. Physical examination and medical history can also help to confirm a diagnosis. Treatment typically involves managing symptoms with rest, fluid, and anti-diarrheal medications. However, with the widespread use of rotavirus vaccines, the prevalence of the virus has declined significantly in many countries. Despite this, rotavirus remains a major global issue, especially in areas with limited access to vaccination. Diagnosis is typically made through laboratory testing of stool samples. Governments must include the vaccine in their national immunization programs, and put into practice novel policies that can help tackle this lethal virus.

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