REVIEW ARTICLE

MORBIDITY AND MORTALITIES BY ROTAVIRUS: REVIEW FOR STRATEGIC MEASURES

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ABSTRACT

Despite, the improved healthcare system, diarrhea is considered as leading cause of child morbidity and mortality. Young children under age of 5 years have more propensity to be affected by water-borne infections particularly diarrhea, according to an estimation over 200,000 mortality of children occur annually by preventable diseases due to poor hygienic conditions, lack of sanitary facilities and contaminated water. Rotavirus is the main causative agent for inducing diarrheal hospitalization. Since 2006, vaccines for rotavirus has introduced by WHO and recommended for countries to make the part of their national immunization program. Generally, 2 licensed vaccines are used internationally and these have high effectiveness. Many other vaccines are still in developing phase. Though, some others pre-qualified vaccines are used in developing countries. Yet, coverage for rotavirus vaccination is not reached to satisfactory level. Except the efforts, certain barriers exist for vaccination including high cost of vaccine, limited perception and knowledge of families and health priorities. To overcome these barriers, there is need of distinguished role of community health workers and pharmacists.

Keywords: Barriers, Coverage, Diarrhea, Morbidity, Mortality, Rotavirus infection, Vaccination.

INTRODUCTION

Primarily rotavirus infects young children and account for approximately 40% hospitalization due to diarrhea and 200,000 mortalities globally with the huge number of deaths occurring in developing countries[1]. Rotavirus induced annual morbidity rate ranges from 0 to 112/100,000 and mortality rate with an average of 39/10,000 in under five year children[2]. Currently the best estimation approach indicates that every child under 5 years of age will be infected by rotavirus, one in five of them will require hospital visit, one in sixty five will be hospitalized and one in two ninety-three will have fatal consequences[3].

In 2006 two vaccines against rotavirus were licensed and have been included in immunization programs in 95 countries by April 2018[1]. Rotavirus vaccination (RVV) significantly decrease the diarrheal hospitalization by rotavirus among various settings but coverage for RVV lagged in Asia[4].

Rotavirus was first discovered in 1973 by Ruth Bishop and his colleagues, he isolated it from duodenal mucosa of children[5]. Rotavirus being a member of Reoviridae family, consists of eleven double stranded RNA segments protected by 3 layers of protein[6]. RNA of rotavirus is encoded with six structural and six non-structural proteins represented as (VP, VP2, VP3, VP4, VP6, VP7) and (NSP1, NSP2, NSP3, NSP4, NSP5, NSP6)[7]. According to the genetic characterization of rotavirus, seven groups has been classified from A to G, out of them A, B and C affect human mostly[8]. In developed countries group A rotavirus is the leading cause of deaths among children. On the basis of VP6 capsid gene rotavirus ID further classified into different genotypes. G1P, G2P4, G3P8, G4P8, G9P8 and G12P8 are the main six genotypes combinations, that are associated in rotavirus induced gastroenteritis in humans[9].

Schematic view of rotavirus replication is shown in (fig-1) that shows that rotavirus triple layer particle (TLP) after entering into cytoplasm of infected cell becomes double layered particle

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(DLP) which leads to transcription and translation processes. After this formation of viroplams (an important viral structure) takes place which upon maturation leads to TLP rotavirus[10]. Pathophysiology of rotavirus infection involves the formation of mature enterocytes after replication near the tip of villi, which leads to alteration of epithelium function of small intestine that causes diarrhea[11]. It is further ascribed as excessive loss of fluid due to various mechanisms including exudation, osmosis and abnormal intestinal motility[12]. The major symptoms of rotavirus infections arewatery diarrhea, fever, and vomiting, and dehydration are the common symptoms of rotavirus gastroenteritis[13].

Rotavirus can be directly diagnosed from faecal specimen containing viral load of 1×101 per gram of stool. In public health and clinical laboratories most frequently used test, for the detection of virus, is enzyme immunoassay. This test shows the greater than 90% specificity and sensitivity of Rota virus. Other diagnostic procedures like latex agglutination and lateral flow immune assay are also available to facilitate patients at point of care. Instead the presence of viral nucleic acid, the illness and clinical symptoms correlate more effectively with the presence of the rotavirus antigen. Because with laboratory diagnosis different mild infections are also identified. Several latest and expensive molecular detection test that target different pathogens associated with gastroenteritis also show high sensitivity (>90%) towards rotavirus[14,15].

Burden of Rotavirus Disease

Rotavirus gastroenteritis, mainly affects children below 5 years of age, this leads toward high rate of mortality and morbidity. Approximately, 2 and 2.15 million annual hospitalization and deaths were reported respectively[16]. Studies estimated that highest number of deaths occurs in Asia and Africa. Annual number of deaths are high in India (146,000). Whereas, in other countries like Nigeria, China, Pakistan, Congo and Ethiopia, the number of deaths are mentioned respectively (47,500), (41,000), (36,500), (29,000), (29,000)[17]. There is no seasonal disease observed in topical countries in contrast to temperate environment countries where diarrheal epidemic spread usually in winters[18]. Almost 90% of deaths by rotavirus occur in African and Asian region[19]. (fig-II) representing the mortality globally among

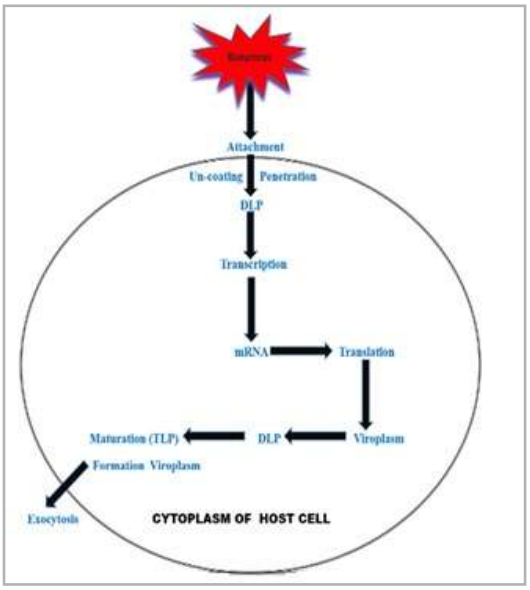

Figure-1: Replication Cycle of Rotavirus.

regions defined by (WHO). African region was observed to be the highest burdened region with total deaths of 510,046 while european region was

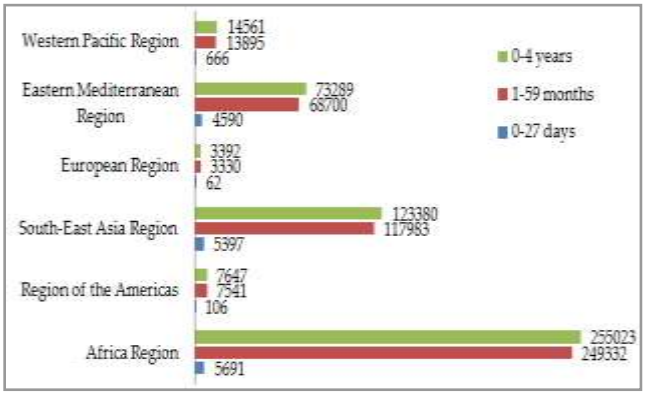

Figure-2: The number of deathsin different age groups by diarrhoeal diseases estimated by WHO region in 2016[16].

observed the lowest burdened region with total deaths of 6784.

Prevention Strategies against Rotavirus Infection

There are two basic ways through which enteric infections can be prevented by vaccination and by improving Hygienic conditions including water and sanitation[21]. Results of study revealed that handwashing and interventions in quality of water results in reduction in diarrhea by 40% and 27%[22]. A decrease in mortality and morbidity, and hospitalization were observed in children who received rotavirus vaccination[23]. Many of the countries use 1 of the 2 vaccines available globally, Rotarix (RV1) monovalent or RotaTeq (RV5) pentavalent[24]. Vaccination schedule for monovalent (RV1) vaccine is 2 doses given at two and four months of age whereas, for Pentavalent (RV5) dosing schedule is 3 doses given at two, four and six months of age[25]. Rotateq covers G1, G2, G3, G4 and P8 genotypes, while Rotarix includes onlythe G1P[8] strain[26]. National immunization programs started by low middle income countries use Rotarix (monovalent) in greater extent rather than rotateq (pentavalent) because of less number of doses[23]. Whereas, effectiveness and efficacy vary in countries, lowest (46%-59%) in under developed or developing countries and highest (91%) in developed countries[27] (table). elaborating the available brands of licensed and in developing phase vaccines globally.

Table: List of licensed vaccines and vaccine candidates in clinical trial phases of development[25].

Vaccine	Status	Comments
LLR®	License is restricted	Employed in China
Rotavin-M1®	License is restricted	Employed in Vietnam
Rotavac®	License is restricted	Employed in India
UK reassortant (Rotasiil®)	License is restricted	Phase 3 study
RV3BB	Recent development in clinical era	Early phase two studies
Tetanus toxoid P2 protein and a Truncated VP8 subunit	Recent development in clinical era	Phase one/two study
Rotashield®	First time it was licensed in USA in 1998, But withdrawn,	It has undergone the clinical trial with 2 dose regimen starting with the first thirty days of life exhibiting effectiveness of 63% for the twelve months of life
RotaTeq®/Rotarix®	globally license	twelve years, globally distributed and highly effective

Barriers against Rotavirus Vaccination

Vaccines of rotavirus are generally prescribed by private doctors. Hence its high cost is the most important element to the access of vaccine. Other factors like limited perception and knowledge of families, health priorities, access to public health authorities and doctors and safety and quality of vaccines are other important barriers[28]. Pakistan is one of the largest birth region in all over the world, there are 5 million children born every year. In Pakistan, the child mortality and morbidity is associated with improper intake of vaccination. The data showed 78 or 89 deaths out of 1000 births of >5 year children take place annually due to communicable diseases. The major barriers associated with non-compliance of vaccination are poor knowledge regarding the importance of vaccination program, no guidelines about follow-up doses, shortage of health care provider or vaccine, the over burden of house chore on mother and deferral till the next time[29].

Role of Community Health Workers In Vaccination

Health care system involves community health workers to serve the humanity and improved the health outcomes in individuals. With the efforts of community health workers, better health conditions have been observed in various countries. Community health workers consider it a crucial part of their job to provide social support. The most cited reason by health workers to vaccinate themselves is to protect their near ones (patient and non-patient). A positive doctor and patient relationship is required for promotion of

vaccination. American Pharmaceutical Association (APhA) defines three major roles of pharmacist in immunization coverage which includes, work as immunizer, facilitate other health workers and promote vaccination by motivating other people. Whereas, pharmacies are considered as preferred site for vaccination.

Treatment of Rotavirus Infection

Oral rehydration is the immediate attempt for the management of diarrhea. Nitazoxanide effectively decrease the time period of rotavirus caused diarrhea, buthas no effect on the proportion of children requiring parenteral rehydration. Probiotics can also be use as alternative or supportive therapy in rotavirus infection. They reduce the time duration of diarrhea hence reducing fluid loss and nutrition through it. Probiotics also found to be effective in reducing the time of vomiting and fever.

CONCLUSION

From the previous years, rotavirus vaccination coverage has been increased to some extent, through which death rate of children has been decreased. But in developing countries especially in Pakistan where the knowledge regarding the rotavirus disease is not sufficient and lack of basic health care facilities also play exaggerating role in worsening the conditions. Hence, some special guidelines are needed to be introduced to enhance the coverage of rotavirus vaccination, including addition of rotavirus into the national program of immunization, provision of basic information to public through media for awareness of this harmful disease, there must be the initiation of special training sessions for health workers regarding to rotavirus infection, its vaccination, and prevention strategies.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by author.

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