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FOODBORNE VIRUSES PAPER II – ROTAVIRUS

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ABSTRACT Rotavirus diarrhea causes considerable morbidity and mortality in young children all over the world including India with the highest burden among children less than 2 years of age. It is a highly contagious infection and spreads very fast within families, institutions, child care settings and hospitals. High shedding titer and fecal-oral and person-to-person transmission makes it extremely infectious. Vaccination is the only effective way to prevent rotavirus infection. Currently, two rotavirus vaccines are available in the global market. Moreover, one candidate vaccine is under development by Indian manufacturers and may be licensed in near future.

KEYWORDS :

1. Foodborne Viruses Paper II – Rotavirus

1. Introduction

In spite of child mortality and morbidity resulting from rotaviral gastroenteritis is declining, rotavirus infection continues to be the most common cause of hospitalization and mortality in children owing to the severe diarrhea and dehydration that result from infection (Lin *et al*, 2014). Rotaviruses were discovered in animals in the 1960s and then were subsequently identified in humans via electron microscopic examination of the duodenums of children who were suffering from severe diarrhea (Bishop, 1973)

Rotavirus belongs to genus *Rotavirus* and family *Reoviridae*. Under electron microscopy, the virus structure is observed to have a 70 nm, non-enveloped, icosahedral symmetry that surrounds a double-stranded RNA genome. The genomic RNA of rotavirus is surrounded by a triple-layered capsid (Estes *et al.*, 2007). The rotavirus genome consists of 11 RNA segments which encode for the VP1-VP4, VP6 and VP7 structural and NSP1-NSP6 nonstructural viral proteins. The middle capsid layer is formed by VP6 protein and it is responsible for the group-specific antigenic determinants. The VP7 and VP4 are the major outer capsid surface proteins and act as independent neutralizing agents. Therefore, serotypes of rotavirus are determined by VP7 and VP4 proteins. NSP4 is also antigenic and acts as an enterotoxin that is capable of producing diarrhea. Rotaviruses are characterized into different genotypes according to the particular NSP4 proteins expressed (Estes *et al.*, 2007)

Human rotaviruses are remarkably diverse in nature. Thus by far, at least 42 different P-G serotype combinations have been recognized due to independent variety and segregation of the G and P proteins, resulting in the production of different strains. Fortunately, only few of the different rotavirus strains circulating globally are capable of causing illness to humans (Lin *et al*, 2014).

2. Global burden of disease

Rotavirus infection results in severe gastroenteritis in newborns and young children all over the world. Worldwide, at least 525000 children under 5 years of age die from diarrhea with severe dehydration and electrolyte and acid-base imbalance each year (WHO, 2016). The World Health Organization estimated that globally 215 000 (197 000 - 233 000) child deaths occurred during 2013.

Nationwide estimations of rotavirus attributable deaths in children under five years of age stretched from 47 100 (India) to less than 5 deaths (79 countries). Twenty-two percent of all deaths from rotavirus under five years of age occurred in India. Four countries namely - India, Nigeria, Pakistan and the Democratic Republic of the Congo accounted about half (49%) of all rotaviral deaths under age five in 2013.

3. Epidemiology

a. Occurrence

Rotavirus infection occurs all over the world. The incidence of rotavirus is comparatively more in developing parts of the world such as south-east Asia than in the developed countries

b. Reservoir

The gastrointestinal tract and stool of infected humans are the reservoirs of rotavirus. Though, rotavirus infection is observed in many mammals, transmission to humans of animal rotaviruses is said to be infrequent and probably does not cause clinical illness

c. Transmission

Rotaviruses are shed in the environment in high concentration in the feces of infected humans. Transmission of disease occurs by feco-oral route through close person-to-person contact and by fomites such as toys and other environmental surfaces contaminated by feces. Contaminated water or food appears to be unusual routes of rotavirus transmission (CDC, 2018).

d. Temporal pattern

Globally, seasonality of rotavirus infection has been observed to vary greatly. Various past studies have been performed to enhance understanding of factors supporting the disparity in occurrence of rotavirus infection by season and locality. In a review of 34 studies carried out before 1990, Cook et al. observed that rotavirus infection characteristically occurred during the winter months of the year in temperate regions, while year-round patterns were often seen in the warmer tropical regions (Cook *et al*., 1990). Efforts to find a connection between seasonal incidence of rotavirus disease and many factors of climate, such as temperature, relative humidity, rainfall and barometric pressure have produced contradictory findings (Purohit *et al*., 1998; Levy *et al*., 2009; Hashizume *et al*., 2007; D'Souza *et al*., 2008).

e. Communicability

Rotavirus infection is highly transmissible, as demonstrated by the nearly worldwide infection of children by age of 5 years in the prevaccine era. A huge quantity of virus is shed in the stools beginning 2 days prior the onset of diarrhea and for up to 10 days after onset of symptoms by the infected person. In immunodeficient persons, rotavirus can be detected in the stools for more than 30 days after infection.

4. Clinical Features

Rotavirus diarrhea has short incubation period, usually less than 48 hours. According to the type of infection such as first infection or reinfection, the clinical manifestations of the infection differ. The first infection which occurs after 3 months of age is usually more severe. Infection may be asymptomatic, may result in self-limiting watery diarrhea, or may lead to severe dehydrating diarrhea with vomiting and fever.

The clinical signs and characteristics of stool of rotaviral diarrhea are nonspecific and similar clinical feature can be developed by other pathogens. Therefore, laboratory testing is required to confirm diarrheal illness.

5. Rotavirus in India

Previously, several studies across India were carried out by investigators on the cause of diarrheal diseases, especially owing to rotavirus, in children under 5 years. Several factors such as variation in study populations, study design, recruitment strategies and the tests employed resulted in fragmented information. The outcome of these studies was not similar. 20% of total diarrheal deaths that occur worldwide because of rotaviral diarrhea are estimated to occur in India alone. Recent estimates have shown that about 872,000 hospitalizations and 78,500 deaths occur due to rotavirus infections annually in India (John *et al*., 1990).Thus, with the goal of systematic data collection and need of sustainable surveillance programme, in 2005, Indian Council of Medical Research (ICMR) in association with Centers for Disease Control and Prevention (CDC), Atlanta, USA, has founded a network for hospital-based surveillance of rotavirus in different parts of the country. The National Rotavirus Surveillance Network (NRSN) comprises one coordinating center at National Institute of Epidemiology, Chennai and one coordinating laboratory at CMC, Vellore. It also includes four referral centers, seven regional centers and around 30 peripheral centers scattered all over India.

Mehendele *et al*. (2016) conducted a surveillance study all over India between 2012 and 2014 in 3 phases. The study shown that out of 10207 diarrheal cases in children under 5 years of age, 39.6% were caused by rotavirus. The study also revealed that rotavirus infections were observed more frequently during the winter months (September – February). The highest prevalence was seen for the period of December – February and lowest during June – August. Genotype investigation of rotavirus positive samples indicated that G1 P [8] was the predominant strain.

6. Prevention and Control

There is no specific treatment exists for rotavirus gastroenteritis and reinfection is common in children (Gladstone *et al*., 2011). Though hygiene and sanitation improvements have had a great impact on diarrheal diseases caused by bacteria and parasites, it has had less effect on disease caused by rotavirus. This is revealed by the constant presence of rotavirus in high income settings (Chandran *et al*., 2010). So far, the only specific prevention strategy for rotavirus infection is immunization with rotavirus vaccines.

Presently, two rotavirus vaccines are available in the international market. Rotarix (GlaxoSmithKline, Rixensart, Belgium) is a monovalent vaccine (RV1) which is produced by attenuating a highly antigenic strain of human G1P[8] rotavirus (Ruiz-Palacios et al). Another vaccine available in the market is RotaTeq (Merck and Co., Whitehouse station, USA) is a pentavalent (RV5) created by reassorting G and P antigens from human rotavirus G1, G2, G3, G4 and P[1] with a bovine rotavirus strain (Vesikari *et al*., 2006).

Additionally, third vaccine Rotavac manufactured by Indian manufacturer is under trial. It is in the pre-vaccine stage and will be available in the market in the span of 1 to 2 years. This vaccine will be useful in reducing rotavirus incidence rate in low and middle income countries.

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