Commentary

**Rapid diagnosis of rotavirus infection: key to prevent unnecessary use of antibiotics for treatment of childhood diarrhoea**

Rotavirus is an important aetiological agent of acute diarrhoea below 4 years of age. It has been estimated that each year rotavirus infection is responsible for an estimated 111 million episodes of diarrhoea requiring only home care, 25 million clinic visits, 2 million hospitalizations, approximately 4,40,000 deaths in children < 5 years of age and most of it occurs in developing countries (1). An estimated 1,205 children die from rotavirus diseases each day and 82% of this death occurs in children in poorer countries of the world. A recent review of 27 prospective studies from 20 countries estimated the incidence of diarrhoea as 3.8 episodes per child per year for children < 11 months of age and 2.1 episodes per child per year for children 1-4 years of age (1).

Since every child will be infected at least once in first five years of life and 82% of total death toll occurs in developing countries, control of rotaviral diarrhoea is an important proposition from public health point of view. The need to develop a safe and efficacious rotavirus vaccine to reduce disease burden and prevent deaths remains a very high priority for control of diarrhoeal diseases. Vaccine for control of rotavirus diarrhoea developed are either against a single serotype of animal or human origin or a quadrivalent vaccine comprising of 4 important serotypes (Serotypes 1-4) to reduce severity of diseases. The vaccines conferred protection to children in countries of their origin but failed during field trial in some developing countries. On the other hand, a vaccine with very high efficacy is yet to be developed. As an Indian initiative, two rotavirus vaccines were developed by using a nursery strain, 116E (2) and by using an asymptomatic naturally occurring human - bovine reassortant strain, I321 (3) that are currently under phase I trial.

Though the ability of natural rotavirus infection and rotavirus vaccine to reduce the severity of rotavirus gastroenteritis has been proved, the lack of reliable laboratory marker that can predict immunity has hampered due to a clear understanding of the mechanism of protective immunity against rotavirus (4,5). It is likely that mucosal immunity in small intestine is critical in the defense against rotavirus infection (6,7).

The segmented nature of rotavirus genome provides a unique mechanism for the generation of genetic diversity by the process of genetic reassortment that occurs during mixed infections *in vivo* as well as *in vitro* (8). When this occurs between bovine and human strains, the progeny becomes asymptomatic (9). On the other hand, one such reassortant strain between human and porcine has been implicated for its association with an outbreak of infantile diarrhoea (10,11). Development of an efficacious vaccine to control rotavirus diarrhoea is not forthcoming and naturally occurring reassortment involving VP6 and NSP4 of porcine origin, two crucial proteins thought to be responsible for host range restriction and pathogenicity has been implicated in an epidemic of acute infantile gastroenteritis (11), therefore, the only option left is rehydration of the infants with ORS / or IV fluid therapy.
In developing countries, the treatment of diarrhoea cases starts with feeding ORS solution / IV fluid therapy followed by treatment with antibiotics. It is well known that administration of antibiotics will not be of any help in case of rotavirus diarrhoea or any other viral diarrhoea. Therefore, rapid diagnosis of rotavirus infection is the need of the day.

A number of diagnostic assays have been developed to detect the virus and / or to demonstrate the serological response induced by the viruses in the host. A number of diagnostic tests have been developed for detection of rotaviruses, however they are not routinely used due to low sensitivity and or specificity. On the other hand, detection of rotaviruses by reverse transcriptase polymerase chain reaction (RT-PCR) method for detection of rotaviruses is highly sensitive, however the system needs costly equipments, reagents and trained manpower and cannot be performed as a routine laboratory diagnostic test for detection of rotaviruses in developing countries. The only diagnostic test, the enzyme linked immunosorbent assay (ELISA) is considered to be highly sensitive tool for screening of rotaviruses from hospital or field samples, because of its ability to detect positive isolates even at low concentrations. The pitfalls of ELISA test include failure to detect viral antigen in stool samples containing a high titer of the corresponding antibody and false positive results. However, regardless of its limitations, ELISA is still the method of choice in almost all laboratories for the identification of rotaviruses.

The article by SD Kelkar and colleagues in this issue of the Journal (12) addresses the need of a rapid diagnosis of rotaviruses by ELISA test. The investigators have developed an ELISA kit by using cell culture adapted semi purified simian rotavirus strain SA11 as antigen and compared the same with the ELISA kit (NIV-ELISA) developed by them previously. The sensitivity and the specificity of the short duration (< 4 hours) ELISA were as good as when compared with NIV-ELISA. On the other hand, the optical density values of positive samples were higher than NIV-ELISA. In addition, the plates pre-coated with antigen that are stable for over two weeks in a refrigerator, thereby substantially reducing the incubation period during the test. During development and evaluation of the ELISA kit, they have used only 155 stool samples, which are very small in number, and the kit needs to be tested in different laboratories to substantiate their claim. On the contrary, the new ELISA kit with short duration of incubation developed by NIV investigators seems to be very useful in providing diagnosis of rotaviruses in a short duration thereby helping the clinicians and saving unnecessary use of antibiotics and expense for treatment of diarrhoeal diseases.

Multi-drug antibiotic resistance was reported during an epidemic of Shigellosis in eastern India in the year 1984 due to indiscriminate use of antibiotics for treatment of Shigellosis. Therefore rapid diagnosis of rotavirus infection in children will reduce the unnecessary use of antibiotics and chances of development of antibiotic resistant strains.

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References


