Incidence of rotaviral diarrhea and its clinical profile comparison in under 5 children

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Abstract
Introduction: Rotavirus causes 40% of all hospital admissions due to diarrhea in under 5 children worldwide.
Objectives: To study the incidence and clinical profile of rotaviral diarrhea and comparison of clinical, lab and demographic parameters with non rotaviral causes.
Materials and Methods: Children presenting with acute diarrhea, defined as passage of 3 or more loose watery stools in under 5 years were examined for rotavirus using latex agglutination test. The incidence was calculated and the statistical difference in various clinical parameters plotted using chi square technique.
Results: A total of 188 cases were enrolled for the study. 40 cases were tested positive accounting for 21%. Peak age group was 7 months to 2 years. Socioeconomically lower and middle groups, severe dehydration and hospital stay more than 4 days were more closely associated with rotaviral diarrhea.
Conclusion: The incidence of rotaviral diarrhea was 21% in our study among 188 enrolled cases of acute diarrhea. Age group, severe dehydration, socioeconomic group and duration of hospital stay were significantly different in rotaviral diarrhea children.

Keywords: Rotaviral diarrhea, Non-rotaviral diarrhea, Hospital stay, Dehydration.

Introduction
Diarrhea is the second most common cause of death worldwide in under five children. Diarrhea is defined as the passage of three or more liquid or watery stools per day or more frequently than normal for an individual. Most episodes are mild but acute cases can lead to significant loss of fluid and dehydration which may cause death or other severe consequences.

One out of five child deaths is due to diarrhea1. Together, pneumonia and diarrhea are responsible for an estimated 40% of all deaths around the world each year. Rotavirus causes approximately 111 million cases of diarrhea per year in under five children globally. Of these 111 million cases, 18 million cases are considered moderately severe. It accounts for at least 5 lakhs to 6 lakh deaths in under five children per year.2 17% of world’s rotaviral deaths occur in India3. The disease burden calculated in India showed 5 lakhs diarrhea associated deaths in under five children every year out of which 95000 to 1.2 lakh deaths have been attributed to rota virus alone.

Repeated attacks of diarrhea also aggravate the compromised nutritional status of under privileged children with a consequent heightened susceptibility to infections. Hence diarrhea is an important contributory factor for malnutrition, which in turn predisposes the child to further diarrhea, initiating a vicious cycle.

Rotavirus comes from the family reo viridae which consists of four genera – ortho virus, colti virus, orbi virus, rota virus. All of them have double stranded RNA genome by which they differ from other arbo viruses. Rota viruses are double walled viruses presenting a characteristic appearance under electron microscope, resembling little wheels with short spokes radiating from a wide hub to a clearly defined outer rim. The name is derived from rota in latin meaning wheel. Both complete and incomplete particles are seen. Rotaviruses have been classified into five species A to E, plus two tentative species F and G, based on antigenic epitopes on the internal structural protein vp6. Group A rotaviruses are the most frequent human pathogens. Outer capsid proteins VP4 and VP7 glycoproteins carry epitopes important in neutralizing activity with VP7 being the predominant antigen.

Molecular epidemiological studies have analyzed isolates based on differences in the migration of the 11 genome segments following electrophoresis of the RNA in polyacrylamide gels. These differences in electrophoretic types can be used to differentiate group A viruses from other groups, but they cannot be used to predict serotypes.4 Sub Classification of Rotaviruses: The classification system is based on the antigenic specificity of vp6 capsid proteins and the pattern of electrophoretic mobility of RNA segments of viral genome. Further typing schemes are based on the proteins of outer capsid vp7 and vp4. Variability in the genes encoding two outer capsid proteins vp7 and vp4 decides the sub classification of group A rotavirus into G and P genotypes respectively. G serotypes correspond with genotypes but more P genotypes than serotypes are identified5.7 Rotavirus strain is now identified by a G genotype, indicated by a number, followed by its P type.

Group A includes the common human pathogens as well as animal viruses. Group B has been reported in China and Bangladesh.8,9 G1 and G2 are the most commonly identified strains in India followed by G4.

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G3 is comparatively rare. They are found in many studies throughout the country. Recently G6 G8 G10 G12 are added to the list. The P type found commonly was P8 followed by P6 and P4. The common strains worldwide are G1P(8), G2P(4), G3P(8), G4P(8).

Rotaviruses infect cells in the villi of the small intestine. It does not infect gastric mucosa and colonic mucosa. They multiply in the cytoplasm of enterocytes and damage their transport mechanisms. One of the rotavirus encoded proteins, NSP4 is a viral enterotoxin and induces secretion by triggering a signal transduction pathway. Damaged cells may slough into the lumen of the intestine and release large quantities of the virus, which appear in the stools (up to $10^{10}$ particles per gram of faeces). The excretion of virus in stools usually lasts 2 to 12 days in healthy patients whereas it is prolonged in malnutrition. Rotaviral diarrhea is due to impaired sodium and glucose absorption as damaged cells on villi are replaced by non absorbing immature crypt cells. It may take 3 to 8 weeks for normal function to be restored. Rotavirus survives for up to 4 hours in human hands. It survives in water for days to weeks.

**Laboratory Diagnosis of Rotaviral Infection:** Direct electron microscopy of stools for rotavirus has a sensitivity of 80% but it requires expensive equipment and trained personnel. Recent diagnostic tests include latex agglutination test, reverse passive hemagglutination assay, solid phase agglutination of coated erythrocytes, enzyme immune assay, polyacramide gel electrophoresis. The most widely used ones are latex agglutination test, ELISA, PAGE. ELISA uses polyclonal sera and requires confirmatory or blocking ELISA for validation. PAGE though a highly specific test lacks sensitivity. RT-PCR is found to be a highly sensitive and specific method for diagnosis of rotavirus in stool samples from patients with acute diarrhea.

WHO sets out a 7 point plan that includes a treatment package to reduce childhood diarrhea deaths and a prevention package to make a lasting impact on the disease burden in the medium and long term. The prevention package includes rotavirus vaccination. The world wide improvement in sanitation and hygiene has reduced the number of diarrheal episodes across the world. The proportion of hospitalizations of children with diarrhea have come down over the past 20 years. There seems to be a disproportionate non reduction in the rate of rotaviral diarrheal hospitalizations compared to non rotaviral diarrheal hospitalizations. The hospitalizations for diarrhea due to rotavirus has not decreased over the years compared to non rotaviral diarrhea. The role of breast feeding in the prevention or amelioration of rotaviral infection is small according to various studies. Vaccines offer the best hope for the control of these infections. The first vaccine was a trivalent one introduced in USA during 1998. It was linked to a high risk of intussusception. It was withdrawn subsequently in 1999.

**Aim of the Study**
To study the incidence and clinical profile of rotaviral diarrhea and to compare all data with non rotaviral diarrhea in children under 5 years attending tertiary set up.

**Objectives**

To study the incidence of rotaviral diarrhea in under five children.

To study the clinical profile of rotaviral diarrhea and to compare the demographic, clinical features and laboratory parameters of rotaviral diarrhea with non rotaviral diarrhea.

**Materials and Methods**

It is a descriptive study done at government raja mirasad hospital thanjavur. The period of study was 6 months from May 2012 to October 2012 and the study population was all children admitted in paediatric ward under 5 years with acute diarrhea. Exclusion criteria included parents not consenting for the study and children with dysentery and those with chronic illness.

**Manoeuvre:** All cases were subjected to latex agglutination for rotavirus other investigations like stool leukocyte count, complete blood count, e reactive protein were done and reports entered in data collection form.

**Rotavirus Latex Agglutination Test:** The samples should be tested immediately. If the fecal samples cannot be tested immediately, they should be stored at 20 degrees Celsius. The fecal sample should be added to 1 ml extraction buffer in an airtight vial. The sample should be 10% prepared by adding 0.1 g of feces to 1 ml of buffer solution. After complete mixing, it should be allowed to stand for 2 minutes. After preparation of fecal specimen, the specimen should be mixed well with vortex mixer. It should be left to stand for 10 minutes. The sample should be centrifuged for ten minutes. One drop of supernatant fluid should be placed on the test slide and another drop placed over the control slide. One drop of test latex reagent is added to both circles. A positive result is indicated by agglutination of test latex circle. The sensitivity of the test is 97.2 % and the specificity is 97.1%.

**Results**

The incidence of rotavirus positive cases was 21% among 188 cases tested. 40 out of 188 cases tested positive. Among positive cases, 65% were male and 35% female.
Incidence of rotaviral diarrhea and its clinical profile.  

Age distribution of rotavirus diarrhea: Out of the 40 rotavirus cases, 33% occurred in 0 to 6 months children. 63% occurred in 7 months to 2 years children and 4% occurred in 2 to 5 years children.

Dehydration status in rotaviral diarrhea:
55% children suffered from some dehydration while 36% had severe dehydration and only 9% had no dehydration.

### Table 1: Clinical features in rotaviral diarrhea

| Clinical parameters | Number | Percentage |
|---------------------|--------|------------|
| Fever               | 9      | 22         |
| Vomiting           | 7      | 18         |
| Abdominal pain       | 9      | 23         |
| Number of episodes <6 | 16     | 41         |
| Number of episodes >6 | 24     | 59         |
| Duration of hospital stay >4 days | 26 | 65 |
| Duration of hospital stay <4 days | 14 | 35 |

| Lab parameters            | Number | Percentage |
|---------------------------|--------|------------|
| Stool neutrophil >5       | 3      | 8          |
| Stool neutrophil <5       | 37     | 92         |
| Total count 5000 to 15000 | 37     | 93         |
| Total count <5000/15000   | 3      | 7          |
| CRP positive              | 2      | 4          |
| CRP negative              | 38     | 96         |

### Table 2: Comparison of clinical features of rotaviral and non-rotaviral diarrhea

| Clinical parameters | Rotaviral n % | Non-rotaviral n % | P value |
|---------------------|---------------|------------------|---------|
| Fever               | 9(22%)        | 56(38%)          | 0.07    |
| Vomiting            | 7(18%)        | 26(18%)          | 0.992   |
| Abdominal pain       | 9(23%)        | 40(37%)          | 0.563   |
| Number of episodes >6| 24(59%) | 71(46%)        | 0.177   |
| Duration of hospital stay >4 d | 14(35%) | 87(59%) | 0.007 |
| Severe dehydration   | 14(35%)       | 12(26%)          | 0.001   |

### Discussion

The incidence of rotaviral diarrhea in the study sample is 21%. 40 out of 188 subjects tested positive for rotavirus.

### Table 3: Incidence studies from various authors

| Authors            | Incidence          |
|--------------------|--------------------|
| Agarwal et al      | 7% and 21%         |
| Chakravarti et al  | 15% and 18%        |
| Bhan et al         | 24% and 31%        |
| Patwari et al      | 6%                 |
| Hussain et al      | 14%                |
| Malik et al        | 19%                |
| Broor et al        | 18%                |
| Singh et al        | 16%                |
| Huilan et al       | 18%                |
| Aijaz et al        | 22%                |
| Ballal et al       | 15%                |
| Kelkar et al       | 26%                |
| Present study      | 21%                |

Incidence studies done abroad at south west Ethiopia showed 26.6% while at Thailand showed 43.6%. In India, northern states incidence hovers around 6 to 45%. In western India, around 28 to 30% positive rate was reported from Pune. In Kolkata
incidence was 5 to 22%. In south India, 16 to 22% was reported from Chennai, vellore and Bangalore. Few data are available about the G type and P type distribution in India. G1 and G2 were the most prevalent. G1 24.7% G2 23.4%. The P type distribution was p(8) 27%, P(6) 21%, P(4) 20%.

Comparison studies of rotaviral and non rotaviral diarrheas was done by an ethiopian study which showed statistical significance in severe dehydration, vomiting and duration of hospital stay.

Conclusion

The incidence of rotaviral diarrhea in the study sample spanning 6 months was 21%. 5 variables showed significance in comparison between rotaviral and non rotaviral diarrheas. They were:

- Age less than 2 years
- Low socio economic status
- Duration of hospital stay more than 4 days
- Severe dehydration
- C Reactive protein negativity

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