

In this issue, Juneja, *et al.* [10] have evaluated a Hindi translation of the Ages and Stages Questionnaire on Indian infants. They confirmed their results by assessing the same children by the Development Assessment Scales for Indian Infants (DASII), which is considered the gold standard. They found a fairly high sensitivity (83.3%) and good specificity (75.4%) at 18-24 months of age. This test can be translated in other Indian languages and more studies can be done to validate it even further. It can help in identifying developmental delays in both the high risk and low risk children, who can then be referred for more definitive diagnosis.

Considering the prevalence of developmental delays, the primary care provider must be vigilant in identifying those children who require further evaluation and referral. Early identification leads to early treatment and ultimately improved long-term outcomes.

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Prevention of Rotavirus Diarrhea in India: Is Vaccination the Only Strategy?

RAKESH LODHA AND DHEERAJ SHAH*

*Department of Pediatrics, All India Institute of Medical Sciences and *Department of Pediatrics,
University College of Medical Sciences and GTB Hospital, New Delhi, India. rakesh_lodha@hotmail.com*

Diarrheal diseases continue to be an important cause of morbidity and mortality in under-fives in India despite various preventive and standardized case management strategies [1]. It was estimated that in 2005, 302000 children age 1- 59 months died due to diarrheal diseases giving a mortality rate of 11.1 per 1000 live births [1]. The WHO and UNICEF have proposed a 7-point action plan to reduce the childhood diarrheal morbidity and mortality [2]. The treatment package of this plan includes: (i) fluid replacement to prevent dehydration and (ii) zinc treatment, while the prevention package includes (iii) rotavirus and measles vaccinations, (iv) promotion of

early and exclusive breastfeeding and vitamin A supplementation, (v) promotion of hand washing with soap, (vi) improved water supply quantity and quality, including treatment and safe storage of household water, and (vii) community-wide sanitation promotion.

The etiology of childhood diarrhea has been determined in a few studies in India, most of which have been hospital based. In this issue of the journal, Kahn, *et al.* review the epidemiology and prevention of rotavirus gastroenteritis in India, with main focus on the issue of introduction of a vaccine to help control rotavirus disease [3]. This review adds to the previous publications of the

group on the subject. A few issues need discussion to view the results of the review in proper perspective and in an unbiased manner.

Based on the etiology studies conducted in the country, it is estimated that approximately 40% of cases of diarrhea among hospitalized children are due to rotavirus. Most of these studies included in this review aimed to identify rotavirus infection only and not all etiologic agents of childhood diarrhea [3]. The case fatality rates in the rotavirus and non-rotavirus diarrheas in these studies have not been reported. So, the authors of the current review [3] have extrapolated the proportion of hospitalized childhood diarrhea cases where rotavirus infection was demonstrated to estimate the numbers of deaths caused by rotavirus diarrhea. A recent study from Kolkata reported that of the 493 cases positive for rotavirus, 285 (57.8%) were co-infected with other pathogens; children had a higher co-infection rate than adults [4]. In such a scenario, attributing all deaths to rotavirus where rotavirus infection was reported would be inappropriate and would lead to an overestimation of the numbers of deaths attributable to rotavirus diarrhea. Available data suggests that only 12% of all deaths attributed to diarrheal diseases took place in health facility [1]. Are the causes of death in children with diarrhea who die at home same as those in hospitalized children? Evidence suggests that malnutrition and systemic infection are major associates of fatal diarrhea in hospitalized children rather than dehydration [5].

Arguing that rotavirus infections continue to persist in high income settings and the proportion of diarrhea caused by rotavirus does not vary widely between developed and developing countries, the authors conclude that sanitation and hygiene have less of an impact on rotavirus disease and emphasize that immunization with rotavirus vaccines is the only specific prevention strategy [3]. Does a child in the developed world have the same number of episodes of diarrhea as one does in the developing world? It is essential to know the incidence rates of diarrhea in the developed countries, which unfortunately the authors of the current review have chosen to ignore; this is important for understanding the differences in the epidemiology of childhood diarrhea in the developed and developing countries. Available data from the WHO shows that the burden of childhood diarrheal illness (DALY 2004) per capita was, as compared to that in high income countries (0.0012), 11 times higher in middle income countries (0.0134) and 51 times higher in low income countries (0.0611) [6]. Part of the difference is due to the high death rate in low and middle income countries, but the difference in the per capita burden persists even after removing the

contribution of deaths. This indirectly provides evidence of the impact of economic development, better sanitation, safe water supply and better health systems on the diarrheal disease burden in children, including that due to rotavirus.

Substantial gains in the control of diarrheal diseases in the industrialized countries were made before introduction of rotavirus vaccines. Even in India there are significant differences in the mortality rates due to diarrhea in children 1- 59 months age among various states: these vary from 0.3 (95 % CI: 0.0- 1.6) in Kerala to 17.8 (95 % CI 15.9-19.8) per 1000 live births in Bihar [1]. The rates are 2.5 times higher in the lower-income Indian states compared with higher-income states (14.8 vs 5.8). This suggests that reduction in the mortality rates due to diarrheal illnesses can be achieved even in the absence of rotavirus vaccines; most of this may be due to better sanitation, water supply and better health systems.

There are systematic reviews supporting the important role of good sanitation, hand washing and safe water supply in reducing the morbidity due to diarrheal diseases [7]. In such a scenario, excessively greater weightage assigned to the use of rotavirus vaccine for prevention of rotavirus diarrhea by the authors of the review appears unjustified. The authors have inappropriately dismissed the importance of other strategies for prevention of rotavirus diarrhea without providing strong scientific evidence. Improving sanitation, ensuring supply of safe drinking water, promoting good hygiene and hand washing are likely to have substantial gains not just for childhood diarrheal diseases but also for reducing the burden of enteric diseases in all age groups; the disease burden in older children and adults in India is also substantial. Fischer Walker *et al.* have provided evidence for the impact of a multi-pronged strategy including the WASH (water, sanitation and hygiene) interventions for diarrhea prevention using the Lives Saved Tool analysis [8].

The rotavirus serotypes prevalent in the country appear to be different from that in the west. In a multi-center study enrolling 4243 children with diarrhea (39% tested positive for rotavirus), the most common types of strains were G2P(4) (25.7% of strains), G1P(8) (22.1%), and G9P(8) (8.5%) [9]. The authors of the study observed that 22.1% of the strains identified in this study would be covered by Rotarix (GSK Biologicals) and 47.9% by RotaTeq (Merck) [9]. While there is some evidence to suggest that there may be cross-protection, the same has not been shown in India.

There have been no trials in Indian children evaluating efficacy of the two available vaccines against

rotavirus diarrhea; the efficacy data from other countries may not be applicable to the country. One study evaluated the immunogenicity of Rotarix vaccine [10]. In this study, it was observed that 27% of the 8-week old infants were initially seropositive; the seroconversion rate observed one month post-dose 2 in the Rotarix group was 58.3% (95% CI: 48.7; 67.4) [10]. In another study evaluating the immunogenicity of Rotateq vaccine it was observed that 20% of 6- 12 week old infants had serum anti rotavirus IgA ≥ 20 IU/mL at baseline [11]. 83% infants demonstrated seroconversion (increase in the anti rotavirus IgA titers by a factor of 3 or more from baseline to approximately 6 months) in the per protocol analysis [11]. The percentage of patients who demonstrated 3 fold increase in G1 neutralizing antibody titre was 38.2%, for G2, G3, G4 and P1 were 14.7%, 30.4%, 37.2% and 30.4% respectively. The low rate of seroconversion against G2 may be of concern as this is an important serotype in Indian scenario. It is surprising that these two vaccines have been approved for marketing in India by the regulators despite insufficient immunogenicity and absent efficacy data in Indian children. In such a scenario, there is need for efficacy data for the existing and newer rotavirus vaccines in Indian children; this is particularly important to address the issue of adding the vaccine to the UIP.

While all Indian children should benefit from the available, safe and efficacious vaccines, the decisions to incorporate new vaccines in national schedule will need discussions with policy makers where various issues other than the safety and efficacy will also be important. The current estimate of disease burden itself shows major gaps. Cost of the vaccine is important; however, with various options available, the same can be worked around. One also has to assess the capacity of the health systems to determine if the intervention will be delivered effectively. The overall immunization rates are still inadequate. Particularly important for rotavirus vaccination is the time of administration of the doses; for Rotateq vaccine, immunization should not be initiated beyond 12 weeks of age. In such a scenario, will the health care system be able to deliver the rotavirus vaccine to children efficiently, particularly to those who need it the most? The prevention of rotavirus diarrhea in children can be best achieved with a multi-pronged strategy; introduction of the rotavirus vaccine at some stage may be

one of them, provided there is sufficient and reliable efficacy and effectiveness data from the country.

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