Chapter 3
Exposition of the study
Group A rotaviruses, members of the family *Reoviridae* are the major etiologic agents of severe acute gastroenteritis in infants and young children, worldwide. A total of 114 million cases, 24 million out-patient visits and 2.4 million hospitalizations have been attributed to rotavirus diarrhea in children <5 years of age (Glass et al., 2006). Annually, global mortality from rotavirus gastroenteritis has been estimated to be about 527,000 with majority of the deaths occurring in the low-income countries. India alone accounts for approximately 1,22,000 - 1,53,000 infant deaths per annum due to rotavirus disease (Parashar et al., 2009; Tate et al., 2009).

Naturally occurring point mutations, reassortment, genome rearrangement and interspecies transmissions steadily generate diversity in rotaviruses at genetic and antigenic levels resulting in reinfections and escape from host immunity and thus pose a challenge in planning vaccine strategies. Hence, monitoring the diversity of rotavirus strains in a single community over time is essential for better understanding of commonly circulating and emerging rotavirus strains that can influence rotavirus vaccine efficacy.

A binary system has been followed to classify group A rotaviruses into G and P genotypes based on the specificities of the VP7(G) and VP4(P) encoding genes respectively (Estes and Kapikian, 2007). To date, 27G and 35P genotypes have been identified (Matthijnessens et al., 2011). More than 60 different G-P combinations have been found in humans infected with rotaviruses (Patel et al., 2011). Several studies have shown that approx 90% of these rotavirus infections constitute G1P[8], G2P[4], G3P[8], G4P[8] and G9P[8] specificities (Santos and Hoshino, 2005). However, only the five most common types (G1–G4, P[8]) have been targeted in rotavirus vaccines. Countries considering use of these vaccines conduct surveillance to identify the most common strains in circulation so that subsequent impact of vaccines on circulating strains can be assessed. Majority of such studies have been carried out in infants and children. Group A rotaviruses are also known to cause gastroenteritis among adults in a variety of settings including epidemic outbreaks, travel-related gastroenteritis, infections transmitted from children to adults and endemic disease (Hrdy, 1987). Adults infected with group A
rotavirus could act as a source of infection to susceptible individuals and affect the epidemiology of rotavirus disease in infants and young children (Hrdy, 1987; Nakajima et al., 2001; Barnes et al., 2003; Anderson and Weber, 2004). Adolescents and adults also encounter sporadic infections and outbreaks of group B rotavirus more frequently than infants and children. Characterization of rotaviruses circulating in different age groups is expected to provide a key for understanding the spread of rotavirus in the community.

Prior to the initiation of present study, the data available on the rotavirus infections in adolescents and adults from India, was limited to serological and molecular identification of group A and group B rotaviruses (Kelkar et al., 1996; Krishnan et al., 1999; Ray and Kelkar, 2004a; 2004b; Kelkar and Zade, 2004; Awachat et al., 2006; Kelkar et al., 2007; Ray et al., 2007). In order to have better understanding of epidemiological and molecular features of rotavirus infections occurring in adolescents and adults over the time, an extensive study entitled “Characterization of rotaviruses recovered from adolescent and adult cases of acute gastroenteritis” covering two time points, 1993-1996 and 2004-2007 was undertaken with the following objectives:

➢ To know the contribution of group A rotaviruses in causing acute gastroenteritis in adolescents and adults from Pune, western India
➢ To examine the seasonal variations in group A rotavirus associated gastroenteritis in adolescents and adults
➢ To detect and characterize the rotaviruses in ELISA negative specimens
➢ To understand the inter and intra genotypic diversity in the VP7 and VP4 encoding gene sequences of group A rotavirus strains
➢ To characterize the NSP4 and VP6 encoding genes of group A rotavirus strains and study their linkage
➢ To comprehend the linkage between VP4, VP6, VP7 and NSP4 encoding genes of genotyped group A rotavirus strains

To achieve the above mentioned objectives, the study was divided into six parts. Part I detects and characterizes group A rotavirus infections in adolescents and adults from Pune, western India: 1993-1996 and 2004-2007;
Part II deals with detection and characterization of rotaviruses in ELISA negative specimens, Part III and Part IV analyze respectively sequences of VP7 and VP4 genes of group A rotavirus strains; Part V characterizes the VP6 and NSP4 genes of group A rotavirus strains and analyzes their linkage while Part VI analyzes linkage between all four genes encoding VP7, VP4, VP6 and NSP4 proteins of group A rotaviruses. These parts (I-VI) have been detailed in Chapters 4-9 respectively.