Chapter 3

Purpose of the study
For several years, routine diagnosis for non-bacterial AGE was restricted to only rota and enteric adenoviruses [Ramirez et al., 2006:1656-1662]. With the introduction of molecular techniques in diagnostics, the etiology of other enteric viruses in AGE has emerged. As a consequence, NoVs are recognized as the most common cause of outbreaks of AGE, accounting for ~50% of all-cause outbreaks worldwide [Patel et al., 2009:1-8]. These viruses also play an important role in causing sporadic infections of AGE. The variable rates (5.5-44%) of NoV infections have been reported in AGE cases from different parts of the world [O’Ryan et al., 2000:1519–1522; Parashar et al., 2004:1088–1092; Kirkwood et al., 2005:96-101; Lindell et al., 2005:1086-1092; Nguyen et al., 2007:582-590].

NoV infections are reported in all age groups. However, these infections are often high in children ≤ 5 years and in elderly [Green et al., 2002:133-146; Fankhauser et al., 2002:1-7; Kirkwood et al., 2005: 96–101; Medici et al., 2006:1486-1492]. NoV infections are usually associated with winter month seasonality [Xi et al., 1990:1580-1583; Mounts et al., 2000:S284-287; Inouye et al., 2000:S270-274; Liu et al., 2006:69-72]. However, many recent reports associate them with spring or summer months [Böga et al., 2004:2668-2674; Marshall et al., 2005:321-331; Eric et al., 2007:2205-2211]. Although, NoV infections have been noted to be higher in relatively low humidity or dry weather conditions, there are reports on increase in NoV activity in rainy season also [Dey et al., 2007:218-223; Nguyen et al., 2008:102-113; Lopman et al., 2009:e6671].

With the advancement of molecular cloning technology, the complete genomes of NV and related viruses were successfully cloned in 1990s [Jiang et al., 1990:1580–1583]. Complete genome studies played an important role in establishing phylogenetic and evolutionary relationship of NoVs with other members of the genogroup/ genotype circulating worldwide. Full-length human NoV genome sequencing has been done for over 100 strains from around the world [Thackray et al 2007:10460-10473].

Molecular epidemiology data has revealed that the variants of genogroup II genotype 4 (GII.4) causes majority of outbreaks and sporadic infections worldwide [Noel et al., 1999:1334-1378; Castilho et al., 2006:3947-3953]. However, recombinant NoV GII.b/GII.3 has emerged recently as the main causative agent for many outbreaks across Europe, Australia and Asia [Ambert-Balay et al., 2005:5179-
At the time of initiation of this study, knowledge about NoV infections in India was limited to only two studies— one from Vellore, South India that reported NoV prevalence rate of 8% with predominance of genotype GII.4 (Grimsby-like strains) in sporadic cases of AGE and other from New Delhi, North India documenting involvement of genotype GII.3 in a food-borne outbreak occurred in a nurses' hostel of a civil hospital located in West Delhi [Kang et al. 2000:1-3; Girish et al. 2002:603-607]. However, this data was inadequate for epidemiological and molecular information on NoV infections in a country like India with vast population and geographic diversities. Other aspects such as the relationship between age and NoV susceptibility, the seasonal variations of NoV infections and complete genome analysis of circulating strains in Indian population were also not studied in any of the earlier studies from India. In view of this, the present study was initiated on 'Identification and molecular characterization of NoV strains in patients with AGE from western India' with the following objectives:

1. To determine the contribution of NoVs in causing AGE in western India during 2005-07.
2. To establish the relationship between age and NoV susceptibility.
3. To find out the seasonal variations in NoV infections.
4. To genotype the NoV strains circulating in the region.
5. To characterize recombinant or other unusual strains identified.
6. To characterize full-length genomes of selected NoV strains from western India.

To achieve the above-mentioned objectives, the study was divided into three parts. Part I deals with epidemiological, clinical and molecular features of NoV infections in western India. In Part II, recombinant NoV strains identified in the molecular epidemiology study were characterized while in Part III, complete genomes of commonly circulating NoV strains were characterized.