Chapter 7: Conclusive summary

The present study, for the first time, determines the prevalence of SaV, HBoV and salivirus in sporadic cases and outbreaks of acute gastroenteritis from western India. It highlights the genetic diversity among the virus strains detected in the study region and describes the epidemiological features of SaV, HBoV and salivirus infections. The study elucidates the clinical manifestations and severity of acute gastroenteritis associated with emerging HBoV and salivirus. In summary, this study has helped in understanding the contribution of these three viruses in sporadic cases of acute gastroenteritis from Pune, western India and emphasizes on their routine surveillance for better diagnosis and effective management of the disease in the Indian context.

Prevalence of SaV, HBoV and salivirus in acute gastroenteritis cases
- SaV, HBoV and salivirus were detected at following frequencies in sporadic cases of acute gastroenteritis: 2.7% (21/778), 6% (46/778) and 2.6% (20/778), respectively.
- While SaV and salivirus were not detected in any of the outbreak cases, HBoV was detected in the 2011 outbreak at a frequency of 4.3% (2/47).

Closing the diagnostic gap
- Before the present study was undertaken, 54% (418/778) of the sporadic cases of acute gastroenteritis remained undiagnosed for a causative agent.
- Detection of SaV, HBoV and salivirus has significantly decreased the diagnostic gap for such cases. A total of 15% (63/418) cases of unknown aetiology were attributed to SaV (3.6%, 15/418), HBoV (9%, 38/418) and salivirus (2.4%, 10/418).

Epidemiological features of viral infections
- Highest incidences of viral infection occurred in children up to 2 years of age, suggesting their strong correlation with age.
- Seasonality with respect to viral acute gastroenteritis cases was found to vary. While SaV infections predominantly occurred in summer months, HBoV and salivirus infections peaked during monsoon months.
Severity and disease association

- Results from the case control study for HBoV and salivirus revealed that while HBoV was significantly associated with gastroenteritis (6% vs 0%. p=0.00), such evidence could not be established for salivirus (2.6% vs 1.93%, p=0.57)
- Salivirus mono-infections did not exacerbate severity of acute gastroenteritis while SaV and HBoV infections resulted in severe disease.
- Enteric HBoV genotypes (HBoV2-4) showed a strong clinical and statistical association with gastroenteritis then HBoV1.

Genetic diversity in SaV, HBoV and salivirus study strains

- Four new genotypes (GI.3, GI.5, GI.V.1 and GV.1) of SaV, which have not been reported previously from India, were identified. Two of the study strains also showed evidence of intragenotypic recombination between genotypes GII.2 and GII.4.
- Similarly, all four HBoV genotypes (HBoV1-4) associated with acute gastroenteritis were identified in the study region. HBoV1 strains were observed to be homogenous (>99% nucleotide identity) while HBoV2-4 showed more variation (92-96%).
- The salivirus study strains reveal the presence of a novel cluster (Salivirus A1 Cluster2) which has not been reported so far. This cluster could represent a variant lineage.

The aetiology of viral gastroenteritis is well established with respect to important enteric viruses such as RV, NoV, AdV and HAstV, which have been detected at high frequencies in acute gastroenteritis cases globally. The widespread introduction of RV vaccine in immunization programs in various countries has led to a decreased burden of RV gastroenteritis worldwide (Benett et al., 2016). Since 2006, two RV vaccines have been licensed in over 100 countries and as of 2015, they have been implemented in national immunization programs of 36 low income group countries (Parashar et al., 2016). Following this, the incidence of RV hospitalizations was observed to
reduce significantly. Interestingly, as the incidence of RV gastroenteritis reduced, caliciviruses were predominantly detected in Nicaragua (Bucardo et al., 2014; Becker-Dreps et al., 2014). In recent times, several enteric viruses have been associated with acute gastroenteritis but, their aetiological role has not been studied in detail. With the introduction and implementation of RV vaccine, these newer emerging viruses could have an important role to play in the development of acute gastroenteritis. Identification of such viruses will help in better diagnosis and effective management of this disease which remains to be a leading public health problem worldwide.