Chapter 3
Exposition of the study
A striking rise in the polio-free AFP cases has been reported over the last decade during AFP surveillance carried out in India and worldwide for eradication of polio (www.who.int, Vashisht and Puliyel, 2012). Isolation of NPEVs is documented frequently from such cases as a part of the requirement of PSPs (www.npsspindia.org, Heim, 2005). However, they have no programmatic significance and are not studied further. In India, genotypic characterization of NPEVs isolated from AFP cases has been reported occasionally (Kapoor et al., 2001, Dhole et al., 2009, Rao et al., 2012), although occurrence of such viruses has often been recorded (www.npsspindia.org). There is limited understanding of the attributes of NPEV infections in the backdrop of different geographical/meteorological zones. Hence, in the post-polio eradication era, it is vital to carry out the studies on the epidemiological and virological characteristics of NPEV infections associated with AFP cases in varied climatic zones.

The most intriguing feature of the NPEVs is their ability to be involved in a wide range of infections from asymptomatic to fatal. Severity of the pathological conditions associated with NPEV infections has been described in part due to genetics/immune status of the host or the initial viral load during infection or the viral genetics or quasispecies diversity in the viral population. However, among these, analysis of the viral genome has been considered important to understand the issue of disease causation (Tracy et al., 2006). The genotyping approaches that are based on sequencing of the variable genomic region are unable to differentiate NPEV strains of the same genotype responsible for different clinical manifestations (Nasri et al., 2007). This issue has been further complicated by frequently described phenomenon of recombination in NPEVs, which allows independent evolution of the viral genome fragments even at a micro-evolutionary scale (Lukashev, 2005, Bessaud et al., 2011, Kyriakopoulou et al., 2015). The diversity in disease manifestations associated with some of the strains of the same NPEV type has been proposed to be attributable to profound biological
effects of some mutations that do not affect the phylogenetic positions of the virus strains (Tracy et al., 2006). However, the genetics of NPEV strains of high and low virulent phenotypes is yet to be understood. Hence, it is imperative to analyze the strains of same NPEV genotype, responsible for variable spectrum of infections/diseases, at the complete genomic level for fine scale mapping of genetic determinants that could be associated with neurological manifestations.

With this background, the present study was designed with the following objectives:

- To examine different features associated with NPEV infections among AFP cases from different geographical/meteorological zones.
- To carry out genotypic characterization of the NPEV strains associated with AFP.
- To determine and analyze the full-length genomes of selected NPEV strains, of the same genotype recovered from AFP patients and their asymptomatic contacts from the same region, during the same period.

In order to achieve the above mentioned objectives the study was performed in the following three parts as mentioned below and is presented in the upcoming chapters of this thesis.

- Characterization of the non-polio enterovirus infections associated with acute flaccid paralysis in south-western India
- Genomic characterization of Coxsackievirus type A24 strains associated with acute flaccid paralysis
- Genomic characterization of Coxsackievirus type B3 strains associated with acute flaccid paralysis in south-western India