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Commentary

The genetics of post-polio syndrome - much to be unravelled!

Post-polio syndrome (PPS) affects 20-40 per cent of polio survivors and manifests as neuromuscular complications. The incidence, symptoms and severity of PPS vary and some patients are known to develop weakness, atrophy, fatigue, muscle and joint pain and other complications; however, the absence of its incidence or severity has also been reported in some polio survivors¹. There have been reports that even non-paralytic polio patients succumb to PPS².

The exact cause for PPS and reasons for the differences in its span are still unclear. The treatment generally focuses on reducing the symptoms and improving the quality of life³. An early diagnosis of PPS would be helpful in reducing the severity of PPS. There are no diagnostic tests for PPS available. It is difficult to identify who is more susceptible and or at a higher risk.

There has been an interest in analysing the genetic basis of infectious diseases recently^{4,5}. Poliovirus has a common receptor known as poliovirus receptor (PVR) that belongs to immunoglobulin superfamily CD155, a poliovirus cell surface receptor which is located on chromosome 19q13.2^{6,7}. *PVR* gene polymorphism in patients with progressive muscular atrophy was reported by Saunderson *et al* in 2004⁸. Later, Ala67Thr polymorphism in the *PVR* gene was reported to be a possible risk factor for the aetiology of poliomyelitis⁹. The heterozygous single nucleotide polymorphism (SNP) (Ala67Thr) in *CD155* gene has been reported in healthy population (6.8 to 8.5%) and the incidence has been shown to be significantly higher in polio paresis (13.3%) and progressive muscular atrophy (20%) patients^{8,9}. Nandi and colleagues¹⁰ in this issues have reported development of an SNP assay to detect the single nucleotide substitution (GCGaACG) in *CD155/PVR* gene. The assay seems to be suitable for large scale screening of PPS samples for identification of

heterozygous SNP in the *CD155/PVR* gene¹⁰. However, the screening for *PVR* gene polymorphism (Ala67Thr) should be further confirmed on a large sample of PPS patients in different population groups in India. SNPs used are the most powerful tools for human genetic studies¹¹. SNPs as genetic markers can be used to identify the inheritance patterns of chromosomal regions from generation to generation in human genetic diseases¹².

It has been reported¹³ that a number of viruses produce chromosomal abnormalities in circulating lymphocytes during infections in humans (such as, measles virus, chicken pox and mumps viruses and hepatitis virus) with the first report being the chromosome breakage due to herpes simplex virus in culture¹⁴. However, these chromosomal abnormalities due to direct or indirect effects, as well as the immediate or delayed effects of viruses have not been completely understood. Bhattacharya *et al*¹⁵ reported a significant increase in chromosome aberrations in PPS patients than in controls showing a delayed effect of the poliovirus in humans. However, many questions still remain unanswered.

Centers for Disease Control and Prevention¹⁶ reported a drop in the incidence of polio myelitis worldwide from an estimated 350,000 in 1988 to 407 in 2013, that is, more than 99 per cent decline in the reported cases. According to the global polio surveillance data (March 9, 2016)¹⁷, five wild poliovirus cases from Pakistan and one from Afghanistan were reported.

Although India has efficiently eradicated polio and 80 per cent of the world's people now live in polio-free areas, the increase in the prevalence of a polio-like condition known as acute flaccid paralysis (AFP) has

been recorded¹⁸. Many cases of non-polio enteroviruses have also become common in infants and children¹⁹. It has been reported that Enterovirus 71 (EV 71) causes AFP and is linked to meningitis, encephalitis, hand, foot and mouth diseases¹⁹. Hence, the research needs to address whether the single nucleotide polymorphism (Ala67Thr) in *CD155/PVR* gene known to be utilized for screening PPS will also pick up AFP individuals or any motor neuron diseases or will it be specific for PPS alone? Further research analysis will provide characterization of human diversity at the nucleotide level and demonstrate the feasibility of large-scale screening of human SNPs.

Though the cytogenetic studies have shown a significant increase in the frequency of various chromosomal anomalies, the specific chromosome regions where rearrangements occurred have to be analysed in depth. This chromosome specific rearrangement could result in disease specific marker/probe for screening PPS. Ala67Thr polymorphism in *PVR* gene is known to occur in many motor neurons related diseases⁸. Therefore, a well designed study with a large sample size in other population groups is recommended using this SNP assay and the DNA sequencing method for validation. Further, a study related to the pattern of inheritance of the Ala67Thr polymorphism in the PPS families and a correlation between genotype-phenotype could be addressed at the cytogenetic and molecular levels.

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