Molecular characterization of severe combined immunodeficiency in North India

INTRODUCTION- Severe combined Immunodeficiency (SCID) is one of the most severe forms of primary immunodeficiency and a medical emergency. It manifests clinically in the form of severe, life-threatening infections during early infancy. Mutations in more than 30 different genes have been detected in different forms of SCID. The clinical and immunological phenotypes are quite variable and dependent on the underlying genetic defect. However, environmental factors and gene modifiers have also been implicated because different clinical and immunological phenotypes have been observed in siblings with the same genetic defect. The genetic basis of severe combined immunodeficiency also depends on the geographical location largely due to the affects of consanguinity and endogamy. Data on SCID from India is limited to case reports only. We have diagnosed 52 cases of SCID over the last 2 decades. Molecular defects were characterized in 22/52 cases.

MATERIALS AND METHODS- Mutation analysis was performed at the Department of Pediatrics and Adolescent Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong, Kazusa DNA Research Institute, Kisarazu, Chiba, Japan, National Defense Medical College, Saitama Japan and Duke University Medical Center, Durham, North Carolina, USA.

RESULTs- Mutations in the RAG1 and RAG2 genes were the commonest and detected in 4 patients each. One patient had a mutation in RAG1 gene on one allele and mutation on the RAG2 gene on the other allele. IL2RG mutations were detected in 6 patients. Mutations in IL7RA and ADA gene were detected in 2 patients each. Mutations were also detected in PNP, DCLRE1C and NHEJ1 genes in one patient each.

CONCLUSION: This series of 22 SCID patients with a well characterized underlying genetic defect is the largest from India. Mutations in the recombinase activating genes 1 and 2 were commonest being detected in 9 patients followed by mutation in the IL2RG gene in 6 patients. Two patients from unrelated families had similar mutation in the IL2RG gene indicating a possible founder effect.