Abstract

Inherited arthropathies are monogenic conditions caused by alterations of genes encoding proteins that play an important role in osteochondrogenesis. Detailed clinical and molecular evaluation of 146 Indian patients (121 families) with common inherited arthropathies was carried out in this study by Sanger sequencing. Our cohort primarily comprised patients with progressive pseudorheumatoid dysplasia (PPD, 98 families) and multicentric osteolysis nodulosis and arthropathy (MONA, 15 families). The molecular analysis revealed twenty-six pathogenic variants (5 reported and 21 novel) in WISP3 and 10 pathogenic variants (4 reported and 6 novel) in MMP2. For the novel missense mutations, \textit{in silico} structural analyses of the proteins were performed to predict the pathogenicity. No specific genotype phenotype correlation was established in our study. Our study is the largest reported cohort of patients with PPD and MONA. The results of the study helped in defining the genotype and phenotype of PPD and MONA. We also identified \textit{EXOC6B} and \textit{ARSK} as the likely cause of two uncharacterized arthropathies.