Chapter 7

Summary and conclusions
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We evaluated clinical and molecular aspects of 121 Indian families with various inherited arthropathies. We studied the largest reported series of patients with PPD (98 families; 118 patients). We found slipped capital femoral epiphysis, corner fractures and rhizomelia as additional clinical features in a few patients. The Sanger sequencing of the \textit{WISP3} gene revealed 26 pathogenic variants (five reported and 21 novel). p.(Cys78Tyr) and p.(Cys337Tyr) were the most common and population specific mutations with a frequency of 23.3% and 28.8%, respectively. No specific genotype phenotype correlation was observed in this cohort.

We analysed 18 patients with multicentric osteolysis nodulosis and arthropathy (15 families). This is the largest series of patients with MONA in literature till date. The clinical and radiological evaluation characterized the natural history of this condition. Sanger sequencing identified ten pathogenic variants (4 reported and 6 novel) in \textit{MMP2} gene. The mutation, p.(Asn430Thrfs*68) was the most common variant (27.8%) noted in our study cohort. Establishing genotype-phenotype correlation was challenging due to the small sample size.

In addition to these, we studied four patients with hyaline fibromatosis syndrome. The molecular evaluation revealed four mutations (3 novel and 1 reported) in \textit{ANTXR2}. Two families with hyperphosphatemic familial tumoral calcinosis were evaluated. We identified biallelic mutations in \textit{GALNT3} and \textit{FGF23} in these families. Exome sequencing in two families with uncharacterized arthropathies revealed mutations in \textit{EXOC6B} and \textit{ARSK} as the molecular basis of their condition.