

Muscle Diseases in India

A wide spectrum of myopathies is routinely encountered in India. The clinical load of these patients is shared to a large extent by paediatricians and physicians and a proportion of these patients are then referred to the neurologists for further evaluation. This is not surprising as the number of neurologists servicing the large population of India is only just over a thousand.¹ Lack of availability of large scale laboratory facilities, especially in the fields of immunocytochemistry and genetic testing limits the molecular analysis of those myopathies seen in India and hence the available data may not be representative of the true situation. Also most of the prevalence data are based on hospital series and are not population based.

Muscular dystrophies

The most common muscular dystrophies are Duchenne muscular dystrophy (DMD) and limb girdle muscular dystrophy (LGMD). Of the 1950 patients studied by Das,² 27.4% were muscular dystrophies with 30% having DMD and 29.2% LGMD subtypes. In a tertiary neuromuscular center in Mumbai, DMD formed the main myopathy of childhood while limb girdle dystrophy was the most common diagnosis of adolescent and adulthood myopathies.

Duchenne Muscular Dystrophy: This is by far the most common muscular dystrophy. Though no ethnic variations have been observed, one hospital based study suggested a higher prevalence among certain Hindu communities.³ The phenotype of DMD has been studied in detail by a number of investigators. The differential muscle wasting and hypertrophy giving the 'Valley sign' as described by Pradhan⁴ can aid the diagnosis of DMD/BMD patients in cases without calf hypertrophy or late presentation. Due to the prevalent religious concepts and illiteracy, more than one case of dystrophinopathy in a family is not too uncommon in India. In general, familial cases with DMD seem to follow similar clinical courses but on occasions, striking intra-familial phenotypic variability has been seen (Figure 1). For example, one family has been described in which three brothers were suffering from a dystrophinopathy; one with a DMD phenotype, the second with a BMD phenotype and the third cousin had only cramp-myalgia syndrome.⁵



Figure 1: Index case with DMD and maternal uncle with BMD phenotype: Both had the same in frame mutation in exon 45-48.

Gene studies In dystrophinopathy: Multiplex PCR has been used to study the dystrophin gene in many centres in India and information is available from large centres in the north, west and south of the country. The deletion rates have been consistently around 70%⁵⁻⁸, with the dele-

tions being seen in the central and proximal hot spots of the dystrophin gene. In one study, the proximal deletions were essentially seen in the familial cases and sporadic patients tended to have deletions in the central hot spot.⁵ An interesting phenomenon of double deletions has also been noted. These patients have two non-contiguous hot spot deletions in the dystrophin gene. The significance is not clear as there are only few reports in the world literature.⁵ Becker muscular dystrophy has been genetically analysed and the frame shift hypothesis seems to hold true in the majority of patients.

Rehabilitation: Due to a lack of awareness of muscle diseases, parents of affected children often do not know where to seek help. Illiteracy is also an issue which makes counselling difficult. The social structure in India is also not kind to the physically challenged with no availability of ramps for public modes of transport. Home rehabilitation programs,⁹ designed for those patients who cannot come for regular visits, has proved to be more successful than clinic based programs, in Mumbai and other centers.

DMD-look-a-likes (Phenocopies): Information on the myopathies presenting in early life with a DMD phenotype is scarce. Case reports of a severe childhood autosomal recessive muscular dystrophy [SCARMMD] phenotype with immunohistochemical characterisation are available.¹⁰ A series of adhalinopathy children has also been reported from the south of India. An unusual family with severe autosomal recessive muscular dystrophy with mental retardation and chorea has been documented as well.¹⁰

Limb Girdle Muscular Dystrophy: LGMD is the most common muscle disease seen in the adult population. Sarcoglycanopathies and dysferlinopathies have been characterised.

Sarcoglycanopathies: The age at onset and tempo of the disease show a lot of variation. Proximal pelvic girdle involvement with later involvement of the shoulder girdle appears to be the most common phenotype. Due to severe involvement of the hip adductors and relative sparing of the hip abductors, the hip abduction sign has been observed.¹¹ Three series have been reported on this condition, with multiple sarcoglycan deficiencies most often being seen on the immunocytochemical studies.^{11,12,13} In northern India, gamma sarcoglycan deficiency has been found to be more common.

Genetics of sarcoglycanopathies: There is as yet very little information available on the genetic aspects of sarcoglycanopathies. In a study from Mumbai, 16 patients were found to have abnormalities in the sarcoglycan genes. In this small study, the most common abnormalities were encountered in the gamma sarcoglycan gene, followed by alpha, delta and a single instance of a beta sarcoglycan gene defect. A noteworthy point was the prevalence of the 525delT deletion mutation amongst those with the gamma SGP abnormality. This mutation is seen in select Mediterranean populations and its appearance in Western India is curious. It may relate to the pattern of human migration or may simply reflect a hot spot region in the gene.

Dysferlinopathy: Data on dysferlinopathy is lacking with only one series of 14 patients having been reported.¹⁴ Nine patients had a distal presentation with calf atrophy. 'Calf head on a trophy', an appearance resulting from focal



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The wide spectrum of myopathies seen in India is expected to be genetically characterised further in the coming years. Efforts need to be intensified for better rehabilitation of these chronic myopathies

muscle wasting¹⁵ and the diamond sign¹⁶ were described in those with dysferlinopathies by Pradhan, emphasising the focal and patchy wasting of various muscles. Large scale genetic data is not available and case reports have shown a variety of genetic abnormalities within the dysferlin gene.

Other muscular dystrophies: Facioscapulohumeral dystrophy (FSHD) is not uncommon but published data is scarce. In a series of 211 cases of muscular dystrophy, Srinivas¹⁷ saw only five (2.3%) patients with FSHD and Das² in only 8 (1.3%). The differential wasting in certain muscles with relatively preserved bulk or mild hypertrophy of the muscles around the shoulder girdle describes the 'poly hill sign' of Pradhan.¹⁸ Myotonic dystrophy is less common in India. Gourie Devi¹⁹ found myotonic dystrophies to form only 8% of all muscular dystrophies. Basu et al has studied the CTG repeats in these patients with myotonic dystrophy and found similarity in the molecular anatomy of 90% of the Indian patients with Caucasians. In the remaining 10%, the expansion of the CTG repeat was of a new haplotype suggesting a unique founder effect probably indigenous to the Indian population.²⁰

Congenital myopathies: In a study from Bangalore, 100 cases of congenital myopathies (CM) were diagnosed over a period of 20 years and the spectrum of CM consisted of centronuclear myopathy (39), congenital fiber type disproportion (35), central core disease (9), multicore disease (7), myotubular myopathy (5), nemaline myopathy (4) and one case of congenital myopathy with tubular aggregates. In a north Indian study, 4 nemaline myopathy cases out of 15 were identified.²¹

Mitochondrial myopathy: Case series of mitochondrial myopathies have been published. In a large study from Hyderabad,²² the most common clinical syndrome associated with ragged red fibres (RRFs) on muscle biopsy was progressive external ophthalmoplegia with or without other signs. Kearns-Sayre syndrome and myoclonic epilepsy with RRFs was seen less often.

Osteomalacic myopathy: Though it is less common at present in India, Irani²³ reported 15 female patients of whom eight had constantly worn the burkha when outdoors. Notably these patients were multiparous with prolonged periods of lactation. The striking features were bone pains and pelvic limb girdle weakness.

Inflammatory myopathies: All types of inflammatory myopathies are encountered,^{24,25,26} although of interest is that inclusion body myositis is rare. Gayathri²⁷ reported five patients (four sporadic and one hereditary), and all had progressive muscle weakness with spared cranial nerve innervated muscles.

Conclusion

Thus a wide variety of myopathies are encountered in India and as the diagnostic facilities become more easily available, further useful information will come to light.

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With this paper, the series 'Neurology In India' comes to an end. In this six part series, we have dealt with major areas of neurological interest, which constitute the mainstay of work for the practicing Indian Neurologists. As can be appreciated from the papers, at one end, sub specialty work is catching on. Increasing numbers of neurologists are willing to spend time in their areas of interest. This trend has as yet not percolated to the research laboratories and clinical observations need support

from collaborative work; often outside the country. On the other hand, the number of clinical neurologists in India is clearly inadequate to service the large population and hence only a small proportion of neurology patients reach the neurologists. In the next few years, we hope for and expect a significant rise in the neurology work force to study and service patients with neurological disorders encountered in this vast country.

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