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# Clinical, electrophysiological and pathological evaluation of limb girdle weakness

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## ABSTRACT

**Introduction**: Limb girdle weakness is one of the frequent clinical diagnoses in neurological clinics. Their etiology, treatment and prognosis are varied in different geographical regions of the world. **Materials and methods**: Patient cohort of 68 patients with limb girdle weakness from a tertiary hospital in South India were studied. **Results**: Most of the patients were found to have muscular dystrophies with LGMD variety being the highest reported. Out of 48 cases of muscle disorders LGMD [17/48] and DMD [14/48] formed the majority. Very few of them had a family history and they had little evidence of cardiac involvement. Males were more affected in DMD and BMD. LGMD males outnumbered female patients in this study. **Conclusion**: Our study reports that muscular dystrophies claim a major share of limb girdle weakness. It is very important to understand the precise etiology and to identify patients prone to life threatening cardiac, pharyngeal or respiratory muscle involvement.

**Keywords:** Limb girdle syndrome; muscular dystrophies; limb girdle dystrophy; myopathies; muscular disease.

## Introduction

The term "limb girdle weakness" refers to a clinically heterogeneous group of disorders mainly characterized by proximal muscle weakness of the shoulder girdle and pelvic girdle. Typically patients with hip girdle weakness manifest with difficulty in getting up from floor or a toilet without hand rails. People with quadriceps weakness find great difficulty in descending stairs and those with hip extensor weakness while climbing up the steps. Weakness of hip abductors, results in Trendlenburg gait. In patients with shoulder girdle weakness, a feeling of tiredness often is the first expression as the weight of arm is sufficient to cause fatigue. Patients experience fatigue on performing sustained tasks with hands held up, especially over the head. The problematic activities include painting the ceiling, shampooing, shaving or trying to lift an object off a high shelf [1].

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As these are the symptoms with which patients present to the clinics, the distribution of various etiologies causing these symptoms is useful for diagnosis. Regional information regarding the relative frequencies and morbidities associated with these diseases can help to understand the priorities for public health planning and research. The etiological and clinical profile is also different in different countries. We present our profile of patients presenting with Limb Girdle Muscle Weakness to a tertiary neurocare centre in a developing country.

## Materials and methods

This is an observational study of patients admitted in the Neurology Department, Osmania Medical College and Hospital and in Niloufer Paediatric Hospital, Hyderabad, India with features suggestive of limb girdle weakness. Sixty eight patients were evaluated in the Department of Neurology, Osmania General Hospital, Hyderabad between October 2008 and January 2011.Cases were chosen based on the diagnosis by Clinical examination in all affected patients and family members, the family members were considered to be symptomatic if they had hypertrophy of any muscles with or without weakness. The cranial nerve involvement (especially facial, ocular and bulbar) pattern of wasting, atrophy and hypertrophy

(symmetrical or asymmetrical) of muscles were noted. For all the patients, muscle biopsy, immunohistochemistry, CPK [creatinine phosphokinase] levels in the blood and other routine blood investigations were carried out.

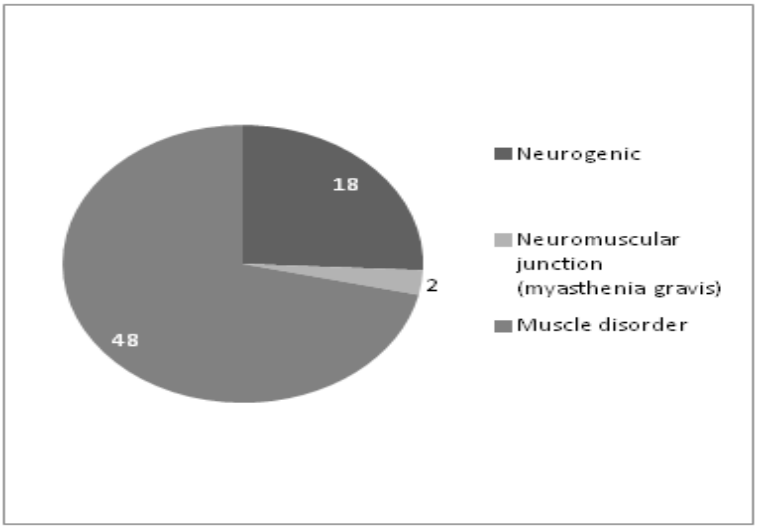
Patients with predominant distal muscle weakness, combined LMN [lower motor neuron] and UMN [upper motor neuron] weakness , generalized weakness and Onset of the disease at birth were excluded from study.

The study was approved by the Institutional Ethical Committee and informed consent was obtained from patients.

**Results**

During the study period a total of 68 patients with limb girdle weakness were examined.

**Figure 1: Distribution of limb girdle weakness**




Muscle disorders constituted the majority [48/68] of cases . Forty two of these were muscular dystrophies. Neurogenic causes formed a significant number, among which most of the patients [15/18] were diagnosed with CIDP [chronic inflammatory demyelinating neuropathy]

**Table 1: Muscle disorders**

| Diseases | No of patients | Percentage |
|---|---|---|
| **Muscular dystrophies** | 42 | 87.5 |
| **Metabolic myopathy** | 5 | 10.4 |
| **Polymyositis** | 1 | 1.1 |

42 cases of muscle disorders were muscular dystrophies of all the cases.

**Table 2: Family History and Limb girdle weakness**

| Disease | No of patients with +ve family history | Inheritance |
|---|---|---|
| **Duchenne Muscular Dystrophy** | 2 | X-linked |
| **Becker Muscular Dystrophy** | - | - |
| **Limb Girdle Muscular Dystrophy** | 2 | AR |
| **Myotonic dystrophy** | - | - |
| **Fascioscapulohumeral Muscular Dystrophy** | 1 | AD |

Inheritance is associated with muscle weakness.

**Table 3: Cardiac involvement in Limbgirdle weakness**

| Disease | Abnomal ECG | Echocardiography |
|---|---|---|
| **Duchenne Muscular Dystrophy** | 4 | Normal |
| **Becker Muscular Dystrophy** | 1 | Normal |
| **Limb Girdle Muscular Dystrophy** | 6 | Cardiomyopathy |
| **Myotonic dystrophy** | - | - |
| **Fascioscapulohumeral Muscular Dystrophy** | - | - |

Limb Girdle Muscular Dystrophy has highest cardiac involvement with Cardiomyopathy.

**Table 4: Comparison between different subtypes of muscular dystrophies**

| | Duchenne Muscular Dystrophy (n=14) | Becker Muscular Dystrophy (n=4) | Limb Girdle Muscular Dystrophy (n=17) | Fascioscapulohumeral Muscular Dystrophy (n=4) |
|---|---|---|---|---|
| **M:F** | 13:1 | 4:0 | 11:6 | 3:1 |
| **Mean age of presentation** | 7yrs | 19yrs | 20yrs | 25yrs |
| **Mean age of onset** | 4yrs | 5yrs | 3yrs | 19 yrs |
| **Mean disease duration** | 2yrs | 4yrs | 2yrs | 4yrs |
| **Inheritance** | x-linked (2) | - | AR (2) | AD (1) |
| **Calf hypertrophy** | 10 | 4 | 6 | - |
| **EDB hypertrophy** | 10 | 3 | 5 | - |
| **Valley sign(2)** | 6 | 1 | 6 | - |
| **Scapular winging** | 6 | - | 8 | 5 |
| **Hip abductor sign(3)** | - | - | 10 | - |
| **Mean CPK (ng/mL)** | 2687 | 2603 | 2881 | 1163 |
| **Muscle biopsy** | Dystrophic (70%) myopathy (30%) | Dystrophic (60%) Myopathy (40%) | Dystrophic (80%) Myopathy (20%) | Dystrophic (75%) Myopathy (25%) |

**Table 5: Muscle Biopsy Findings**

| | Duchenne Muscular Dystrophy (14) | Becker Muscular Dystrophy (4) | Limb Girdle Muscular Dystrophy (17) | Fascioscapulohumeral Muscular Dystrophy (4) | Myotonic dystrophy (3) |
|---|---|---|---|---|---|
| **Fiber size variation** | 14 | 4 | 17 | 3 | 1 |
| **Central nuclei** | 4 | 1 | 10 | 1 | - |
| **Round fibers** | 5 | 3 | 6 | 3 | - |
| **Necrosis** | - | - | 1 | - | - |
| **Split fibers** | 5 | 3 | 10 | - | 1 |
| **Increased connective tissue** | 6 | - | 3 | 2 | 2 |
| **Atrophic fibers** | 4 | - | 5 | - | - |
| **Hypertrophi c fibers** | 6 | 4 | 15 | 4 | 2 |
| **Angulated** | - | - | - | - | - |
| **Lymphocytic infiltration** | 3 | - | - | 2 | - |

*DMD:; BMD: Becker Muscular Dystrophy; LGMD: Limb Girdle Muscular Dystrophy; FSHD: Fascioscapulohumeral Muscular Dystrophy;*

There were two cases of Myasthenia gravis. In all of the patients, the weakness started in the pelvic girdle

muscles followed by shoulder girdle weakness except in FSHD, in which hip girdle muscles were involved early. 15/68 of patients had only pelvic girdle muscle weakness at presentation.

In two DMD cases deletion of dystrophin gene was identified. We could get positive family history in 5 of the cases of dystrophies. One case of FSHD had total asymmetry.

Out of the five cases of metabolic myopathy, one female patient was on eptoin since the last nine years for generalized seizure disorder, one patient presented with vitamin D resistant rickets, there was one case of steroid induced myopathy [the patient was admitted for acute exacerbation of chronic bronchitis, was treated in ICU with ventilatory support, and developed proximal muscle weakness after recovery from illness], one female patient with polymyositis and in two other patients the cause for osteomalacia was not known.

**Discussion**

In our series, the maximum number of the cases with limb girdle weakness were due to muscle disorders [48/68] followed by neurogenic causes [18/68].

Out of 48 cases of muscle disorders LGMD [17/48] and DMD [14/48] formed the majority. The incidence and distribution of dystrophies correlated with previous Indian studies [Table 6].

Males were more affected in DMD and BMD. LGMD males outnumbered female patients in this study.

**Table 6: Comparison of muscular dystrophies in various other Indian studies**

| | Present study | Das(4) et al | Srinivas(5) |
|---|---|---|---|
| **Limb Girdle Muscular Dystrophy** | 40.5% | 29.2% | 30% |
| **Duchenne Muscular Dystrophy** | 33.3% | 30% | 60% |
| **Becker Muscular Dystrophy** | 9.5% | 6% | - |
| **Fascioscapulohumeral Muscular Dystrophy** | 9.5% | 0.1% | 2.5% |

Metabolic myopathies especially osteomalacia in females contributed to quite a good number of proximal muscle weakness cases. This type of osteomalacia is more common in asian peoples. The dysregulation of calcium metabolism in osteomalacia can manifest as muscle weakness[1]. Most cases of CIDP presented with predominant proximal muscle weakness. ECG changes were common, but echocardiography didn't reveal any abnormality which is typical of Indian patients(6). Symptomatic cardiac involvement was seen only in one case. The low familial tendency [5 cases] noted in our study may be explained by the lack of ancestral information as in other studies[6].Since decades, across neuromuscular centers in India, dystrophies have been documented which were clearly distinct from the then well-described dystrophinopathies, myotonic disorders, fascio-scapulo humeral dystrophies and the likes. Initial observations on LGMD in India were made in 1975, when Srinivas, in a survey of 211 patients of myopathies seen over 25 years, diagnosed almost half the patients to have muscular dystrophy. Amongst them, 82 were Duchenne Muscular Dystrophy (DMD), 35 LGMD, five fascio-scapulo humeral dystrophies and 14 ocular-oculopharyngeal myopathies. [5] In a hospital-based study of 126 cases of muscular dystrophy by Mondkar and Bhabha, [7] 12 were designated as "girdle dystrophy" (three females) as they did not fit in Duchene or Becker muscular dystrophies. Four cases (three males) with affected sisters were labeled "Autosomal recessive dystrophy of childhood". Das published a large series of 1950 biopsy-proven myopathies, of which 535 were dystrophies. Among them, 29.2% were labeled as LGMDs, 5.6% severe dystrophies were seen in young girls, resembling DMD and 2.2% had autosomal recessive dystrophies in young boys. [4] In the more recent times, immunocytochemical stains have been used to study Indian patients with LGMDs and information based on immunostaining has emerged. Initial case reports of "Adhalinopathy" (alpha-sarcoglycanopathy) appeared in 2001. [8,9,10] This was followed up by case reports of beta and gamma-sarcoglycanoathy from pediatric centers in New Delhi. [11,12] In 2002, the first series analyzing 25 cases of sarcoglycanopathy came from a neuromuscular center in Mumbai, where phenotypic features were studied in detail and some unique features were pointed out. [6] Soon, as more and more centers across the country got involved with immunostaining of myopathies, further reports, one from New Delhi in 2004, a study of 13 pediatric cases [13] and the other from Hyderabad in 2007, detailing 26 adult cases of sarcoglycanopathies became

available.[14] Indeed, sarcoglycanopathy is the best characterized LGMD in India. The second type of LGMD to be immunocharacterized in India is dysferlinopathy. The initial series of 14 Indian patients with dysferlinopathy from Mumbai was published in 2004.[15] The second study comprising nine cases was recently reported from northern India by Pradhan in 2008.[16] A third series comprising 28 patients from south India has been made available in 2008.[17]

## Conclusion

Our study reports that muscular dystrophies claim a major share of limb girdle weakness. However, as a hospital based study, our work only gives a glimpse of the true epidemiology of the diseases. It shows that several conditions mimic myopathies, and hence it is very important to understand the precise etiology and to identify patients prone to life threatening cardiac, pharyngeal or respiratory muscle involvement.

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