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Original Research Article

# A Study of Clinical Profile of Muscle Dystrophies in Rural Western India

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**Abstract:** The muscular dystrophies are progressive, hereditary, degenerative, diseases of skeletal muscle. One of the problems in the diagnosis of the muscular dystrophies and in understanding their nature is the close resemblance between those and the spinal muscular atrophies. This study was conducted to study the inheritance patterns and clinical presentation of muscular dystrophies in western rural India. Forty patients with a diagnosis of Muscular Dystrophy were selected for the study. The types of Muscular Dystrophies studied were Duchenne Muscular Dystrophy (DMD), Becker's Muscular Dystrophy (BMD), Limb Girdle Muscular Dystrophy (LGMD), Facio-Scapulo-Humeral Dystrophy (FSH) and Myotonic Dystrophy (MD).A careful history of muscle disease in a vertical transmission up to 2 to 3 generations and disease in other male siblings of the patient were carefully elicited. The subjects were examined thoroughly and investigated in detail including Manual muscle testing, serum muscle enzymes, electromyography and 2D-Echocardiography and muscle biopsy. The study revealed the Muscle dystrophy patients in India seem to present much earlier with deformities and fixed contractures and are incapacitated much earlier in the disease process with a mean age of inability to walk at seven years of illness. The sample population is small when divided into its different subgroups. A longer study is necessary to further evaluate this observation for the significance. CPK levels cannot be used as an index of the severity of the disease since they remain elevated till very late in the disease.
**Keywords:** Muscle Dystrophy, Inheritance, Clinical Profile, Muscle Enzymes

## INTRODUCTION

The muscular dystrophies are progressive, hereditary, degenerative, diseases of skeletal muscle[1]. The innervation of the affected muscles, in contrast to that of the neuropathic and spinal atrophies, is normal. Indeed, the final proof, that the origin of these disorders is in the muscle itself comes from the demonstration of intact spinal motor neurons, muscular nerves, and nerve endings in the presence of muscular weakness and atrophy, intact sensibility and preservation of reflexes.

The study of the progressive degenerative disorders of muscle began in the mid-19th century especially in France and Germany[2]. Aran (1850) and Wachasmuth (1855) reviewed the subject but did not try to classify them. Meryon (1952) was the first one to give a clear account of progressive muscular paralysis in young boys and demonstrated 'granular degeneration' of the muscles with no changes in the anterior horn cells. Later, Duchenne (1868) gave a vivid description of this disorder, now given his name.

Duchenne and Gowers, in 1879, emphasized the 'pseudohyertrophic' enlargement of certain muscles. Leyden (1976) and Mobius (1879) described a familiar form of degeneration affecting the muscles of the pelvic girdle. In 1884 Erb described a juvenile or scapula-humeral form of the disorder. The classical description of the FSH form was published by Landouzy and Dejerine (1884).

One of the strange and difficult problems in the diagnosis of the muscular dystrophies and in understanding their nature is the close resemblance between them and the spinal muscular atrophies (SMA). Fortunately the commonest muscular dystrophy (Duchenne) have no neurogenic phenocopies. Clinically, evidence of marked asymmetry of muscle involvement, areflexia in mildly affected muscles and a very profound contrast in power between weak and strong adjacent muscles are all points in favour of SMA[3]. Above all, SMA should be suspected when the distribution of muscle weakness, although approximately that of one of the muscular dystrophies

does not conform to it precisely. In these cases, diagnosis is confirmed on EMG and Muscle Biopsy.

## AIMS AND OBJECTIVES

To study the inheritance patterns and clinical presentation of muscular dystrophies in Indian population.

## MATERIALS AND METHODS

Forty patients with a diagnosis of Muscular Dystrophy were selected for the study. The types of Muscular Dystrophies studied were Duchenne Muscular Dystrophy (DMD), Becker's Muscular Dystrophy (BMD), Limb Girdle Muscular Dystrophy (LGMD), Facio-Scapulo-Humeral Dystrophy (FSH) and Myotonic Dystrophy (MD).

The subjects were either hospitalised or followed up on an outpatient basis. The subtypes in the group studied consisted of 13 with DMD variety, 7 with BMD, 5 with LGMD, 12 with FSH and 3 with MD. A careful history of muscle disease in a vertical transmission up to 2 to 3 generations and disease in other male siblings of the patient were carefully elicited. The subjects were examined thoroughly, a detailed neurological, cardiovascular and general examination were done. After a clinical diagnosis of the type of muscular dystrophy was made, the patients were investigated. Manual muscle testing, along with electrocardiogram, Chest X-ray, Serum Muscle Enzymes, Electromyography and 2D-Echocardiography were done.

Twelve controls ware carefully chosen from the Neurology and Medicine Departments. The controls were matched with age, sex and body surface area[4]. A detailed history was taken and a family history of muscle disease in the siblings and in the family unto 2 generations was carefully asked for. None of those chosen as controls have a family history. They were examined and muscle function testing, EGG and ECHO were done. The controls were not subjected to invasive tests like EMG and Muscle Biopsy.

### Physical Examinatnion

In order to quantify the degree of musculoskeletal involvement, Manual Muscle Testing(MMT) was performed on each patient and the result expressed as the percent of normal muscle function remaining. Each muscle group was assigned a numerical value as follows:

1. No motions but visible or palpable contraction.
2. Full range of motion, with gravity eliminated
3. Full range of motion against gravity with no other resistance.
4 Full range of motion against gravity with moderate resistance.
5. Full range of motion against gravity with strong resistance.

The MMT score obtained by summing the weighted results of all muscle groups was divided by the total points obtainable for normal function and expressed as a percentage of normal. A score of 100 percent represented normal function while a score under 40 percent represented severe musculoskeletal dysfunction. The patients with muscular dystrophy were examined and on the degree of muscle involvement were divided into two groups early and late. Early was greater than 50% and late less than 50% score. A system of grading was also used to classify these patients into groups based on skeletal muscle functional capacity with a rating of 1 to 9 used in the Muscle Clinic of University Hospitals, Cleveland, Ohio for many years and found to be reliable and reproducible. Group I included patients in classes I to 5 and group II included patients in classes 6 to 9. Both methods of assessment were then correlated with each other and the degree of muscle involvement compared.

CLASS FUNCTIONAL CAPACITY

1. Walks and climbs stairs without assistance
2. Walks and climbs stairs with aid of railing
3. Walks and climbs stairs with aid of railing (for 8 standard steps).
4 Walks unassisted and rises from chair but cannot climb stairs
5. Walks unassisted but cannot rise from chair or climb stairs.
6. Climbs only with assistance
7. Walks but requires assistance for balance.
   Stands but unable to walk even with assistance.
8 Stands but unable to walk even with assistance
9. Wheelchair or bed bound; can only perform limited activities involving lower arm and hand muscles.

### Muscle Biopsy

All patients had a muscle biopsy done. The quadriceps, the gastrocnemius, the biceps, and the deltoid muscles were the usual sites chosen for the biopsy.

### Statistical Analysis

The data obtained was analysed using the student 't' test for significance and correlation coefficient. Linear regression was used to show the correlation[5].

## RESULTS

The results of physical examination, muscle biopsy, serum creatinine phospho- kinase are presented.

### Physical Examination:

Forty patients were examined. The subjects ranged from 3 years to 40 years. There were 33 males and 7 females. The types and sex distribution of muscular dystrophy patients studied are given in Table 1 and Table 2.

**Muscle Assessment:**

The patients tested with MMT grading based on functional capacity were found to correlate well with each other and with the degree of muscle involvement. There were ambulatory patients with mild to moderate skeletal muscle impairment (classes 1 to 5) with greater than 50% residual muscle function and patients with more severe impairment (classes 6 to 9) with less than 50% of normal residual muscle function. Five patients were bed bound or had to be carried by relatives.

In the patients studied, a family history of a similar illness in other family members was obtained in only 17 of 40 patients (42.5%). 23 patients (57.5%) gave no family history A diagnosis of sporadic involvement was carefully looked into by examining the other siblings in the absence of disease in the family up to 2 generations. Patients who had no male or other siblings, with no family history were included in the sporadic group. In the DMD group 11 out of 13 patients (84.6) were sporadic in onset (Table 4). There is a high incidence of consanguinity present in the study group. 18 patients (45%) have a history of consanguinity (Table 5).

**Serum CPK Enzymes**

Serum Creatinine Phosphokinase (CPK) Levels were elevated in all the 13 patients with DMD,11 out of the 12 patients with FSH, 4 out of 5 with Limb girdle and variably in the BMD and not at all in the MD.CPK levels after exercise checked in parents and siblings of the patients with Muscular Dystrophy were not elevated (Table 6). Thirty-four out of 40 had elevated CPK levels. DMD cases had very high CPK levels. FSH, LGMD and BMD had moderately elevated levels. MD cases typically showed no rise in enzymes. This was consistent with the western literature.

No correlation was noticed between the staging of muscle involvement and the CPK levels (Table 7).

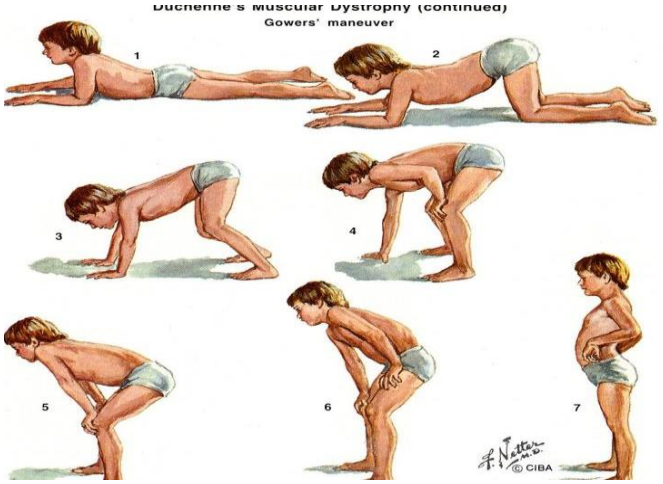



**PLATE I- Gower's Manoeuvre in DMD**

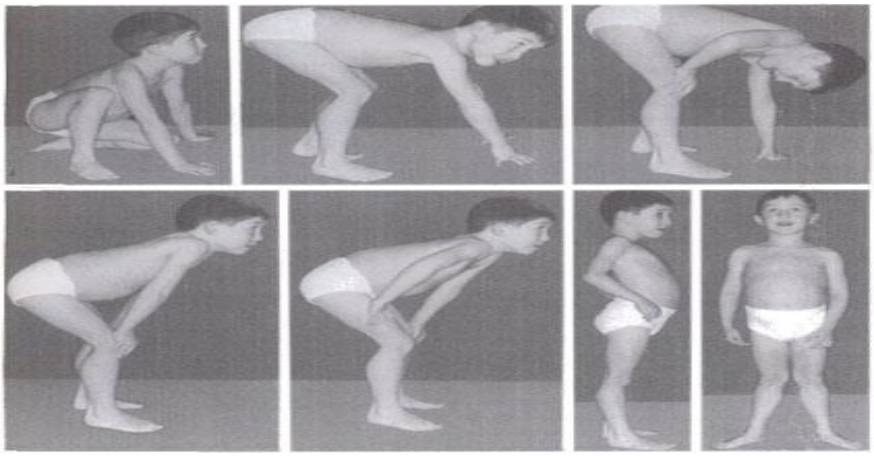


**PLATE II- Muscular Atrophy due to FSH**

**TABLE I: TYPES OF MUSCULAR DYSTROPHIES**

| SEX | DMD | BMD | LGMD | FSH | MD | TOTAL |
|---|---|---|---|---|---|---|
| **MALE** | **13** | **4** | **3** | **10** | **3** | **33** |
| **FEMALE** | **-** | **3** | **2** | **2** | **-** | **7** |

**TABLE- II: AGE AND SEX DISTRIBUTION**

| AGE (years) | 0-5 | 6-10 | 11-15 | 16-20 | 21-25 | 26-30 | 21-35 | 36-40 | > 40 |
|---|---|---|---|---|---|---|---|---|---|
| **MALE** | 1 | 11 | 4 | 5 | 3 | 3 | 5 | - | 1 |
| **FEMALE** | 1 | 1 | 2 | 1 | - | 1 | - | 1 | - |

**TABLE- III: MANUAL, MUSCLE TESTING AND PHYSICAL ABILITY**

| STAGE | DMD | BMD | LGMD | FSH | MD | TOTAL |
|---|---|---|---|---|---|---|
| **EARLY (50% MMT CLASS 1-5** | 8 | 6 | 5 | 12 | 3 | 34 |
| **LATE (50% MMT CLASS 6-9** | 5 | 1 | 0 | -- | -- | 6 |

**TABLE IV: GENETIC PATTERN OF INHERITANCE**

| TYPE | SPORADIC | | FAMILY HISTORY | | TOTAL |
|---|---|---|---|---|---|
| | NUMBER | PERCENTAGE | NUMBER | PERCENTAGE | |
| **DMD** | 11 | 84.6 | 2 | 15.4 | 13 |
| **BMD** | 1 | 12.5 | 6 | 87.5 | 7 |
| **LGMD** | 2 | 40.0 | 3 | 60.0 | 5 |
| **FSH** | 8 | 66.67 | 4 | 33.33 | 12 |
| **MD** | 1 | 33.33 | 2 | 66.67 | 3 |

**TABLE V: CONSANGUINOUS/ NON CONSANGUINOUS**

| TYPE | CONSANGUINEOUS | | NON-CONSANGUINEOUS | | TOTAL |
|---|---|---|---|---|---|
| | NUMBER | PERCENTAGE | NUMBER | PERCENTAGE | |
| **DMD** | 6 | 46.2 | 7 | 53.8 | 13 |
| **BMD** | 5 | 71.4 | 2 | 28.6 | 7 |
| **LGMD** | 3 | 25.0 | 9 | 75.0 | 12 |
| **FSH** | 2 | 40.0 | 3 | 60.0 | 5 |
| **MD** | 2 | 66.7 | 1 | 33.3 | 3 |

**TABLE VI: CPK LEVELS**

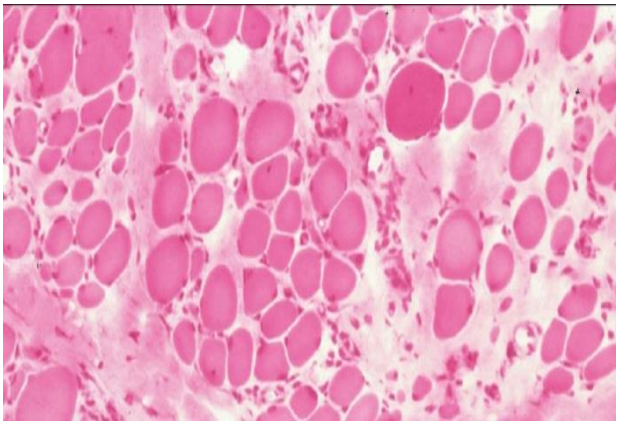
| CPKLEVEL (U/L) | DMD | BMD | FSH | LGMD | MD | TOTAL |
|---|---|---|---|---|---|---|
| 10-100 | -- | 2 | 1 | -- | 3 | 6 |
| 100-1000 | 1 | 3 | 6 | 3 | -- | 13 |
| 1000-10000 | 12 | 1 | 5 | - | - | 18 |
| 100000- 1000,000 | - | 1 | -- | 2 | - | 3 |
| TOTAL | 13 | 7 | 12 | 5 | 3 | 40 |

**TABLE VII: CPK LEVEL (U/L)**

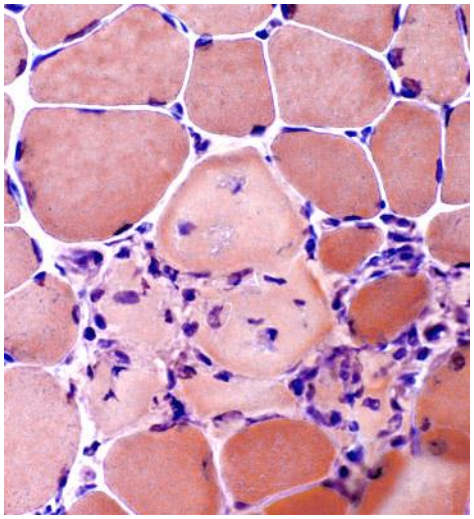
| MMT SCALE | CPK LEVEL (U/L) | | | | |
|---|---|---|---|---|---|
| | 10-1000 | 100-1000 | 1000- 10,000 | 10,000- 100,000 | TOTAL |
| **100-80%** | 3 | 2 | 2 | 1 | 8 |
| **80-60%** | 1 | 7 | 7 | 2 | 17 |
| **60-40%** | 2 | 4 | 9 | -- | 15 |
| **40-20%** | - | - | - | - | - |
| **20-0%** | - | - | - | - | - |
| **TOTAL** | 6 | 13 | 18 | 3 | 40 |

**Muscle Biopsy:**

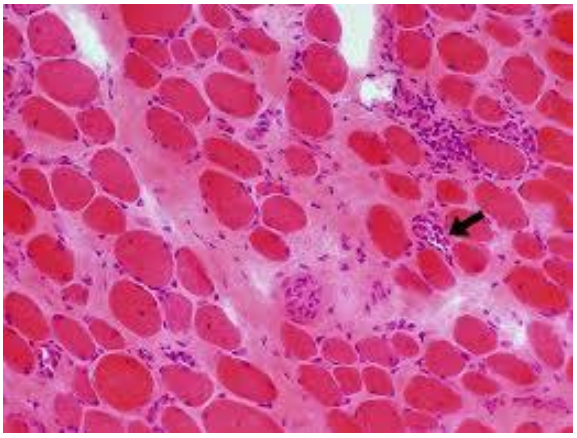
On gross examination of the muscle it was found to float in the formalin instead of sinking. The muscle was yellowish and showed evidence of fat infiltration. It was pale and more fibrous and did not bleed easily. The slides were studied under light microscopy using low power (x 160), and high power magnification. The histopathologic findings of muscle biopsy are given in Slides 1, 2 and 3. These changes were typical of muscular dystrophies described in literature[6].



**SLIDE 1: Shows marked muscle fiber size variation. Some bundles appear very large and some normal sized or smaller. Internalization of nuclei were seen quite clearly with slight thickening of endomysium.**



**SLIDE 2: Shows muscle splitting which is very characteristic of muscular dystrophies and can be clearly differentiated from artifact which occurs on processing.**



**SLIDE 3: shows phagocytosis of entire. muscle fibre bundles with presence of segmental areas of necrosis within muscle fibres.**

**Electromyography**

In the group with Muscular Dystrophy the configuration of the Motor Unit action potential was polyphasic (greater than four phases) because of patchy loss of muscle fibers. Spontaneous fibrillation was occasionally recorded.

## DISCUSSION

**Clinical Presentation Of Muscular Dystrophy In An Indian Population:**

In the study group DMD patients were noticed to have an earlier onset of contractures and deformities. In two patients a Tendo-Achilles contracture was the presenting complaint and it was only later that the muscle disease was diagnosed. The patients had a far more rapid course than their western counterparts being almost completely disabled by three years from the detected onset of the disease with a mean age of inability to walk at 7 years. Usually, in DMD the mean age at inability to walk is about 9.5 years, but varies from about 7 to 14 years. Contractures may develop from about 8 years of age and seem to result from the posture which the boys adapt[7]. In the BMD type, the mean age at the onset was 11 years. This was similar to Skinner and Emery's study (1976). Since the subtypes studied are small it may be difficult to explain why the differences occur.

The following are the probable reasons for this occurrence.

1. There is very poor awareness about the disease entity of Muscular Dystrophy in India.
2. Furthermore, these patients, because they are clumsy due to muscle weakness are not encouraged to walk, but are carried by mothers and relatives. Contractures and deformities as a result seem to appear much earlier in them[8,9].
3. Minor infections and fever cause them to be confined to bed. Physiotherapy is not instituted early and the functional severity appears earlier in the course of the diseases. This is probably because of ignorance about the disease, poverty leading to delay in approaching the physician, poor supportive care and paucity of physiotherapy facilities.

**Inheritance Patterns**

One interesting feature noticed among the study group was the genetic patterns of inheritance. It was found that 11 out of 13 cases (84,6%) with DMD were sporadic and only 2 out of 13 (15.4%) gave a family history of similarly afflicted siblings. A study by Roses et al showed approximately only 40% of patients have a negative family history and are said to represent mutations[9,10]. In our study group, sporadic cases were noted in 66.7% and 40% of cases of F.S.H and LGMD respectively. The relation of consanguinity to sporadic onset is noted, but has not been studied. Roses et al found a careful examination of mothers of patients with DMD had shown slight involvement in as many as half of mutant cases but in this study this was not observed.

**Serum Creatinine Phosphokinase Enymes (CPK)**

CPK levels were elevated in all patients with DMD from the range of 1000 to 10,000. Mothers and immediate siblings of the patients also had CPK values done after exercise which were not elevated. In the BMD group, two brothers with a strong family history of horizontal transmission had very high CPK levels in the range of 10,000 to 15,000 u/l. All the others had moderately elevated levels. The FSH group also had elevated CPK levels ranging from 1000 -10,000 u/l. The serum CPK activity is often normal and rarely exceeds 5 times normal as documented in western literature. The MD group showed normal CPK levels and the LGMD group showed moderate elevation.

An interesting feature noticed in the majority of the patients was that the serum CPK levels remained high throughout the illness and did not decline when the disease became severe. This could be explained by the fact that since contractures and incapacitation occurs earlier in the disease, functional impairment occurs early. Muscle damage is still at its height, amount of muscle tissue is not drastically reduced and fatty change has not set in. This gives a clinical picture of severe disease with high serum CPK levels. There was therefore no correlation noticed between degree of muscle involvement and serum CPK level ($r = 0.062$) unlike in western literature where it has been reported that the level of CPK in DMD patients appears to reach its peak in one to two years, then it may be more than 200 times normal (normal ranges from 6 to 200 depending upon the method)[11]. It then declines gradually and is at or near normal levels in the advanced stages of the disease.

## CONCLUSION

1. Indian patients seem to present much earlier with deformities and fixed contractures and are incapacitated much earlier in the disease process with a mean age of inability to walk at seven years of illness.
2. There is a higher percentage of sporadic onset of Muscular Dystrophy in our group of patients. The role of consanguinity in the inheritance pattern is an observation which, has to be studied further. The sample population is small when divided into its different subgroups.
3. CPK levels cannot be used as an index of the severity of the disease since they remain elevated till very late in the disease.

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