



Myotonic dystrophy in Otago, New Zealand

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Abstract

Aims To determine the prevalence of myotonic dystrophy (DM) in Otago, the ethnic distribution of the disease, any founder effect, the complications and adequacy of health care, and the quality of life of sufferers in this region.

Methods DM patients were identified through hospital records and assessed using a structured questionnaire, neurological examination, and review of hospital records. Quality of life was evaluated using the SF-36 Health Survey, and compared to patients with other neuromuscular conditions and New Zealand norms.

Results 21 patients were identified, giving a prevalence of 11.6 per 100,000. All were of European descent. There was no evidence of a common ancestor. Not all patients had had essential investigations such as electrocardiogram and many had not been seen by the genetic service. DM patients had higher scores on the bodily pain subscale of the SF-36 Health Survey, compared to neuromuscular controls and the general population. Subjects differed significantly from New Zealand norms on four of the eight subscales.

Conclusions DM is relatively common in Europeans in Otago, but we found no cases in other ethnic groups. The disease affects aspects of quality of life, and management could be improved by use of a clinical care pathway.

Myotonic dystrophy (DM) is a dominantly inherited, multisystem disorder, with at least two genetic variants—type 1, due to a trinucleotide (CTG) repeat expansion on chromosome 19; and the rare type 2, due to an expanded CCTG repeat on chromosome 3q.¹ The clinical features include weakness, myotonia, cataracts, cardiomyopathy, and gonadal atrophy.

DM is the most common form of adult muscular dystrophy, and the prevalence in the Western World has been reported to range from 2.2–5.5/100,000.² Studies of DM in South Africa^{3,4} and Canada⁵ have shown evidence for a founder effect—where most individuals are descendants of a common ancestor. The prevalence in New Zealand is not known, and there has been no report of a founder effect.

There are also striking ethnic differences, DM being less prevalent in South-East Asians and extremely rare in central and southern Africans.⁶ There have been no reports of the prevalence in different ethnic groups in New Zealand, but anecdotally, DM seems to be rare in Polynesians.

Because DM is a multisystem disorder, patients require management by multiple specialties, and it is important to ensure well-planned and consistent care.⁷ It is also likely to impact on quality of life, but there has been no study of quality of life issues in a pure population of DM sufferers.

The aims of this study were therefore multiple. To determine:

- The prevalence of the condition in Otago;
- The ethnic distribution;
- Whether there is a founder effect in Otago;
- Whether patients receive adequate medical care and whether their quality of life is affected.

Methods

Patients with a clinical diagnosis of DM and resident in Otago were identified through a search of computerised medical records in the Neurology Department at Dunedin Hospital, and through a database of members of the Muscular Dystrophy Association of New Zealand. Other involved family members were identified through the index cases. Subjects were recruited via a letter inviting them to take part in the study.

Patients were assessed at the hospital or in their home. They were given a structured interview, a full neurologic examination, and they also completed the SF-36 Health Survey.⁸ The investigators were not blinded to the diagnosis, as the typical facial appearance usually made this impossible.

For the quality of life survey, age and sex matched control subjects with other neuromuscular diseases were identified from Neurology Department records and recruited by letter. Results were also compared with New Zealand norms.⁹

Student's t-test was used to evaluate the results of the SF-36 Health Survey, using the SPSS-PC software package (SPSS Inc, Chicago, Illinois, USA).

The study was approved by the Otago Ethics Committee and informed written consent was obtained from all participants.

Results

Prevalence and demographics of myotonic dystrophy in Otago—Twenty-one patients with a diagnosis of DM were identified, of whom 18 agreed to participate. With a population base of approximately 181,539 (New Zealand 2001 Census¹⁰) this represents a prevalence of 11.6 per 100,000. Ten patients had DNA confirmation of the diagnosis, including two that did not participate. For those patients without DNA testing, diagnosis was based on clinical findings and electromyography. No cases of type 2 DM were identified, either clinically or with molecular genetics. The mean age of our patients was 45 years with a range of 16 to 74 years (Table 1); 61% were male and all were of European descent but born in New Zealand, with no knowledge of Māori ancestry.

Table 1. Demographic characteristics of myotonic dystrophy (DM) patients and controls

Variable	Age (years), SD	Range (years)	Sex (n (%))	
			Male	Female
DM Patients	45.0±13.9	16–74	11 (61)	7 (39)
Controls	47.8±15.0	15–75	11 (61)	7 (39)

Genetic aspects—There were 12 families: 4 parent-child pairs, 2 sibling pairs, and 6 patients with no other family members in Otago with DM. When the pedigrees of the 12 families were investigated, one previously unknown link was found between two

of the families. In most families it was possible to trace back the lineage only by two generations. But it was nevertheless clear that the families were otherwise unrelated.

Clinical features—Fourteen patients were mildly affected by the disease. Their most prominent symptom was muscle stiffness (myotonia), with mild weakness and minimal impact on gait and walking. Three were moderately affected—patients found it difficult to walk large distances, and had some dysphagia. One was severely affected, with difficulties with walking and swallowing. All subjects were ambulant.

The most common initial symptom was myotonia, noted in 7 (38%). Fatigue was the most debilitating symptom according to 8 (44%) patients; 17 of the 18 patients reported significant myotonia, and 4 reported significant muscle pain.

All had weakness of typical distribution and myotonia, either clinically or electrophysiologically, leaving little doubt about the diagnosis.

Several complications of the disease were present in the patients, as shown in Table 2.

Table 2. Complications of myotonic dystrophy

Complications	n (%)
Respiratory	
Sleep apnoea	2 (11)
Type II respiratory failure	1 (6)
REM-related hypoventilation	1 (6)
Cardiovascular	
1 st -degree AV block	3 (17)
Ventricular tachycardia and pacemaker	2 (11)
Swallowing	
Minor swallowing difficulty	13 (72)
PEG tube	1 (6)
Ophthalmologic	
Cataract operation	9 (50)
Minor visual problem	1 (6)
Endocrine	
Diabetes mellitus	2 (11)
Libido/impotence problems (in men, n=11)	5 (45)

AV=atrioventricular; PEG=percutaneous endoscopic gastrostomy.

Management and access to specialist services—Five patients lived in rural settings (more than 1 hour from a major hospital), and 13 lived close to (or in) an urban centre (less than 1 hour from a major hospital).

Six patients had been referred to a respiratory specialist for sleep problems (4 from urban communities, and 2 from rural locations); 15 patients had seen a cardiologist (11 from urban communities, and 4 from rural locations); 16 had had an ECG on record and 11 had had an echocardiogram; 5 patients had been referred to a speech language therapist (all from urban communities); and 9 patients had been referred to an ophthalmologist (5 from urban communities, and 4 from rural locations). Only four patients recalled having been seen by genetic services. Seven were members of the [Muscular Dystrophy Association of New Zealand](#).

Quality of life—18 out of 22 invited control subjects with neuromuscular disorders agreed to participate. Their diagnoses were polymyositis (3 patients), dermatomyositis (1), myasthenia gravis (4), Charcot-Marie-Tooth disease (5), Becker muscular dystrophy (1), facioscapulohumeral muscular dystrophy (2), myotonia congenita (1), and limb girdle muscular dystrophy (1). They were not significantly different from the DM patients in age and sex ratio, and like the DM patients they were all of European descent (Table 1).

There was no significant difference between the DM patients and their matched controls in overall scores as measured by the SF-36 Health Survey. However, the DM patients had significantly higher scores on the bodily pain subscale than their paired controls (mean difference=20.22, $t=2.692$, $p=0.015$), and the New Zealand norms (Table 3). Both the DM patients and the controls differed significantly from the New Zealand norms on the subscales for physical functioning, role physical, general health and vitality, but not for social functioning, role emotional, and mental health (Table 3).

Table 3. Myotonic dystrophy (DM) patients and controls compared to New Zealand (NZ) norms⁹.

Variable		SF-36 mean	NZ Mean ⁹	T statistic	P
Physical functioning	DM	65.00±26.07	86.00	-3.42	0.0033
	Controls	50.83±29.42		-5.08	0.0001
Role physical	DM	52.78±37.27	80.70	-3.18	0.0055
	Controls	48.61±38.80		-3.51	0.0027
Bodily pain	DM	88.11±17.20	77.90	2.52	0.0220
	Controls	67.89		-1.49	0.1547
General health	DM	45.78±28.16	73.80	-4.23	0.0006
	Controls	53.11±26.69		-3.29	0.0043
Vitality	DM	39.44±19.55	65.60	-5.69	0.00003
	Controls	42.22±23.34		-4.25	0.0005
Social functioning	DM	86.81±17.92	86.60	0.05	0.9609
	Controls	73.61±26.39		-2.09	0.0521
Role emotional	DM	81.48±32.78	85.00	-0.46	0.6546
	Controls	81.48±32.78		-0.46	0.6546
Mental health	DM	79.78±12.76	78.00	0.59	0.5621
	Controls	74.44±17.74		-0.85	0.4062

Discussion

This study shows that the Otago region has a prevalence of DM that is more than double that reported in Western Europe.¹ The population base was derived from the 2001 census¹⁰, and the Otago population may have increased slightly, but this is unlikely to affect the result by more than 2%, which was the growth of the Otago population between 1996 and 2001. The reason for the high prevalence is unclear, and it may just be chance that produced this result, as the population studied was quite small.

As the neurology service for the region is concentrated in our hospital, with limited private practice, case ascertainment may have been better than previous studies. Our department's subspecialty interest in neuromuscular diseases was not a factor, because we excluded patients not domiciled in Otago. There was no evidence for a founder effect. As we may have missed patients who had not been diagnosed or had not been referred and were not members of the Muscular Dystrophy Association of New Zealand, the true prevalence of DM may be even higher.

All patients indicated that they were of purely European descent and none were Māori. This may reflect the high proportion of Europeans (93.7%) and low proportion of Māori (6%) in the Otago population,¹⁰ or indicate that Māori are less likely to seek medical care. However, an informal (unpublished) survey of all neurologists in New Zealand found no DM patients of Māori or Pacific Island ancestry.

DM is rare in sub-Saharan Africans, and this is reflected in a lower frequency of large-sized normal alleles (CTG repeats) in this part of Africa.^{6,11} Outside of Africa, the frequencies of large-sized normal alleles and the prevalence of DM are highest in West Europeans and Japanese and lowest in South-East Asians⁶. As larger alleles are more unstable, it is postulated that people with large-sized normal alleles provide a pool of individuals, who may have descendants with DM.

The original expansion of CTG repeats into the large-sized normal range may have occurred in a north-eastern African population prior to the migration of the ancestors of the European and Asian population out of Africa, and most cases of DM may be descendants of these individuals.⁶

The prevalence of DM in Polynesian populations is unknown, but our inability to identify any cases in the Māori or Pacific Islander populations suggests that it is low. If so, the prediction would be that Polynesians have a low frequency of large-sized triplet repeats, perhaps reflecting their origins in South-East Asia. However, the frequency of large sized alleles is high in Micronesian and Australo-Melanesian populations (also thought to originate from South-East Asia), while the prevalence of DM is unknown.⁶ In Polynesians, neither the prevalence of DM or the frequency of large alleles is known, and more research is clearly needed.

We attempted to assess the standard of care of patients with DM. As this is a multisystem disorder, management can be complex and requires input from several specialties. It is not clear from our data whether patients received adequate input from other specialties. However, it is concerning that not all patients had a recent electrocardiogram, and there was one patient with visual symptoms who had not yet been referred for ophthalmological evaluation.

The low rate of referral to genetic services probably reflects the lack of a genetic service in this region at one time, but does suggest a degree of inertia in referring patients already known to our service. Review of the notes suggested that care was haphazard and non-systematic. It has been recognised that clinical guidelines and integrated clinical care pathways are important in the management of complex genetic disorders.⁷ Our findings emphasise the need to make use of such protocols in myotonic dystrophy, and we plan to introduce a clinical care pathway into our clinical practice.

Although overall quality of life, as measured by the SF-36, was no different to patients with other neuromuscular conditions, DM patients had significantly higher scores on the bodily pain subscale than paired controls and New Zealand norms. Surprisingly, only four DM patients reported significant muscle pain during the interview, so it was not clear why they scored so high on this subscale. Muscle pain has been commonly reported in other studies however.¹

Both the DM patients and the controls had worse scores for physical functioning, role physical, general health, and vitality, when compared with New Zealand norms. DM patients and neuromuscular controls were not significantly different to the general population for social functioning, role emotional, and mental health, which is surprising for a disabling group of diseases.

No previous studies of muscular dystrophy have utilised the SF 36 Health Survey. However, several Swedish studies have examined quality of life in muscular dystrophies, including myotonic dystrophy, using the Sickness Impact Profile and the Kaasa test.¹²⁻¹⁵ In these studies, no significant differences were found between types of muscular dystrophy, and increasing disability over 5 years was correlated with decreased coping and quality of life. Quality of life was significantly related to forced vital capacity and fatigue, but less so to other respiratory and cardiac parameters and performance of activities of daily living.

Myotonic dystrophy is an important neuromuscular disease in Otago, affecting quality of life and requiring significant health resources. Management of these patients could be improved with the use of an appropriate clinical care pathway.

The apparent low prevalence of myotonic dystrophy in Māori and other Polynesians is intriguing and, if confirmed, may help inform theories of the genetic origins of these populations.

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