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Prevalence of myotonic dystrophy type 1 in adults in western Sweden

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Abstract

Myotonic dystrophy type 1 (DM1) is the most common inherited muscle disorder in adults. The prevalence differs widely between countries, but a figure of 13/100.000 is most frequently cited. It is a multi-organ disorder classified into four categories: congenital, childhood, adult/classical and late-onset/mild. The purpose of this study was to estimate the total and age adjusted prevalence of DM1 in adults in western Sweden (the Västra Götaland Region, VGR) as well as in the city of Gothenburg and also in the VGR except Gothenburg.

Patients with the diagnosis of DM1 in the VGR were traced by outpatient registers at the Neuromuscular Center, contacted by regular mail and thereafter telephone interviewed about organ manifestations in order to ascertain the age at onset and thus the disease category. Medical records were examined to obtain detail accuracy. We detected 230 adult DM1 patients in the VGR which gives a prevalence of 17.8/100.000. The prevalence of DM1 in Gothenburg was 14.1/100.000, which was significantly lower than in the remaining region which was 19.7/100.000. There was no gender difference. The age adjusted prevalence rates showed that DM1 is most prevalent in the age group 35–44 years (23.9/100.000) and 45–54 years (25.8/100.000). DM1 prevalence in the western Sweden thus seems to be somewhat higher than elsewhere in Europe, and is especially high in the less densely populated areas of the region. The disease burden in the community is larger than what was known previously.

Keywords: Myotonic dystrophy type 1; Prevalence; Age adjusted; Sweden

1. Introduction

Myotonic dystrophy type 1 (DM1) is the most common muscular dystrophy in adults. The repeat expansion $(CTG)_n$ in the *DMPK* gene [1] results in accumulation of $(CUG)_n$ RNA repeats in the cell nuclei as *foci*. This leads to the deregulation of RNA-binding proteins and abnormal splicing of several proteins, which is hypothesised to explain the multisystem nature of the disease [2,3].

The manifestations include symptoms from muscle (including respiratory impairment), brain, gastro-intestinal tract, eyes, the endocrine system, and the heart. DM1 symptoms typically begin with muscle wasting and weakness localised to the head/face and distal parts of both lower and upper extremities [4] but the first symptom may be from any of the organs.

DM1 can be grouped into four forms depending on onset of symptoms: congenital, childhood, adult/classical and late-onset/mild [4]. The congenital form, which gives obvious symptoms either at birth or during the first year of life, typically shows a more or less severe generalised muscle weakness and various degrees of mental retardation and frequently also autism spectrum disorders [5]. The childhood form defined as having first symptoms between the age of 1 and 10 is less severe than the congenital form [5]. The adult/classical form has onset between 10 and up to approximately 40 years with progressive muscle weakness, myotonia and cognitive impairment and fatigue [4]. The late-onset/mild form of DM1 has a symptom onset occasionally from age 20 but usually after 40–50 years of age, with relatively minor symptoms from muscles or cataract [4,6,7].

Correct diagnose is a prerequisite for medical follow-up, genetic counselling, detection of treatable complications such as respiratory and cardiac conduction failures and also for the patient and families to seek further information regarding their disease. Knowledge of the prevalence of DM1 in a particular geographic area such as VGR is important to identify the scope of burden on society and thereby may be used in order to plan healthcare resources. This is since there are several areas of need for DM1 patients – the lifelong disabilities of a patient with congenital DM1 as well as with age, the increasing need of medical follow up (mainly respiratory and cardiac) and need of care by others in the childhood and adult/classical forms.

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The prevalence of DM1 in Sweden or worldwide is not known in detail. The epidemiology of DM1 was described in two recent reviews [8,9]. The lowest prevalence is found in Asia [10], while in New Zealand [11] and in Europe a prevalence of 10–12/100.000 is found [3,12–15]. A higher prevalence (18/100.000) was found in Croatia [16]. In Finland the DM1 gene frequency in blood donors was reported to be 2 in 4520 (44.2/100.000) [17], and is even higher in a province in Quebec, Canada [18]. The only previous Swedish study is from Örebro County, published in 1993, which reported a prevalence of DM1 of 18/100.000 inhabitants [19].

The primary aim of the research was to estimate the total and age adjusted prevalence of DM1 in adults in western Sweden (the Västra Götaland Region, VGR) with a total population of 1.6 million inhabitants. Our clinical impression about differences in where patients with DM1 live leads us to investigate if there is a difference in prevalence between the larger city Gothenburg and the VGR except Gothenburg.

2. Methods

The Neuromuscular Center (NMC) at the Department of Neurology, Sahlgrenska University Hospital in Gothenburg has, for more than 15 years, been a reference centre for adult patients with neuromuscular disorders in the VGR. All DM1 patients have been offered yearly follow-up.

Diagnosed patients with DM1 in the VGR were traced by outpatient registers at the NMC. These patients were contacted by regular mail, and thereafter telephone interviewed regarding their onset symptoms of the DM1 diagnosis. We further traced patients by checking patients who were positive for the genetic test for DM1, but these patients were not contacted, and thus we have no clinical data regarding age of onset.

The different DM1 subgroups were defined by age at first occurrence of any of symptoms that could be associated with DM1 and not obviously were caused by another disorder: Congenital 0 to <1 year, Childhood 1 to <10 years, Adult/Classical 10 to <40, and Mild/Late onset as symptoms presenting at age 40 or later. Patients asymptomatic at the time of investigation were not included in the calculations of prevalence of the different subgroups or prevalence in the different age groups, but included in the total prevalence figure.

The DM1 diagnosis was verified by DNA test, except in a few cases. All of these non-DNA verified patients were seen by us in the Neuromuscular Center and had typical symptoms and at least one relative with DM1 who was DNA verified. There are four other neurology services in the VGR, and they were asked to report any adult DM1 patients who were not also seen by our centre. Patients under the age of 18 were not included in the study. The prevalence date was set to 1 July 2014. The adult population in VGR was 1.290.100 and the adult population of the city of Gothenburg was 432.207 persons.

2.1. Ethics

Approval had been obtained from the ethics committee of Gothenburg University. Patients gave written informed consent in order to take part in the study.

2.2. Statistical methods

Prevalence of adults with DM1 in western Sweden was assessed per 1 July 2014. Further, 95% confidence intervals were calculated and given for the age adjusted prevalence. Difference in prevalence was assessed using Fisher's exact test by use of IBM SPSS software package. The population statistics was obtained from the website of Statistics Sweden (SCB/www.scb.se). The age adjusted prevalence was calculated by dividing the number of DM1 patients in each age group with the number of inhabitants (in 100.000).

3. Results

We identified in all 230 DM1 cases in the VGR (113 males/117 females) which gives a prevalence of DM1 in adults of 17.8/100.000. In addition, 5 patients were identified by tracing genetic tests, but they were not contacted and thus not part of the study. Six of the 230 included patients were pre-symptomatic. In Gothenburg city we found 61 cases (29 males/32 females) while we found 169 cases in the remaining VGR (84 males/85 females). The prevalence of DM1 in Gothenburg city was 14.1/100.000 which was significantly lower than in the remaining region which was 19.7/100.000 ($p = 0.027$). There was a tendency for lower prevalence in the city of Gothenburg in all four subgroups of DM1, although none of the differences reached statistical significance. There was no gender difference in prevalence.

The age adjusted prevalence within each of the four disease categories is shown in Table 1. Total DM1 prevalence reached a maximum in the age groups 35–44 years (23.9/100.000, 95% CI 20.5–27.3) and 45–54 years (25.8/100.000, 95% CI 22.4–29.2). There are very few adults with congenital DM1. The age adjusted prevalence of the congenital and childhood forms is very low in the age groups 45 years and older. Since six patients were presymptomatic, the number of reviewed symptomatic DM1 patients was 224 (Table 1). By reviewing results of DM1 DNA tests, we found five additional patients, who were not contacted and thus not included in our calculations.

4. Discussion

The observed prevalence of DM1 in adults in the VGR, approximately 17.8/100.000, seems to be somewhat higher than estimated elsewhere in Europe which in studies may refer to a prevalence of about 13.5/100.000 [3]. In fact, the prevalence of DM1 outside Gothenburg (19.7/100.000) is, as far as we are aware, the highest prevalence of DNA verified cases in Europe. To our knowledge this is the first report on age adjusted prevalence rates, and our data show that DM1 is most prevalent in the age groups 35–44 and 45–55 years where approximately 25/100.000 has DM1. We found few adults with the congenital and childhood onset forms. In the study of Darin et al. [20] the prevalence of congenital and childhood DM1 in children (up to 18 years of age) was 5/100.000; this is compatible with what we found of congenital and childhood DM1 in the age groups 18–24 and 25–34 years. Thereafter congenital and childhood DM1 is less prevalent probably due to a significant mortality of these DM1 groups.