Myasthenia Gravis in South Trinidad

J Maharaj[1], S Bahadursingh[2], K Ramcharan[2]

ABSTRACT

Objective: *There is no previous research on Myasthenia Gravis (MG) in Trinidad and Tobago. This study sought to determine the prevalence and to characterize MG in South Trinidad.*
Methods: *A cross-sectional study was performed over 30 months in South Trinidad to identify, interview and statistically analyse data on MG cases.*
Results: *Among 36 prevalent patients, female:male ratio was 1.6:1. Estimated MG point prevalence in South Trinidad on March 31, 2010 was 78 per million. Mean age of prevalent patients was 50.5 years. Mean age of onset was 35 years. A higher prevalence was detected in Africans than East Indians (178 vs 68 per million;* p = *0.003). Ocular and extremity muscle weakness were the most common initial symptoms. Autoimmune conditions (mainly thyroid disease) co-existed in 25.7%. Treatment involved pyridostigmine and/or immunosuppressants for all except two that went into remission with just steroids. Generalized MG occurred in 60%; 42.9% expressed social and/or professional handicap. One case with suggestive clinical features tested positive for muscle specific tyrosine kinase antibody.*
Conclusions: *While many features of MG in South Trinidad were similar to international data, the unique, statistically significant higher prevalence in Africans than East Indians warrants further research, given the paucity of reports from Africa and India. Patients with MG suffered a diminished quality of life, necessitating improved health planning.*

Keywords: Myasthenia gravis, prevalence, Trinidad

Miastenia Gravis en el Sur de Trinidad

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RESUMEN

Objetivo: *No existen investigaciones previas sobre la miastenia gravis (MG) en Trinidad y Tobago. Este estudio tuvo por objeto determinar la prevalencia y caracterización de la MG en el sur de Trinidad.*
Métodos: *Se realizó un estudio transversal por espacio de más de 30 meses en el sur de Trinidad, con el fin de identificar, entrevistar, y analizar estadísticamente los datos sobre los casos de MG.*
Resultados: *Entre los 36 pacientes prevalentes, la proporción hembra:varón fue 1.6:1. La prevalencia puntual estimada MG en el sur de Trinidad el 31 de marzo de 2010, fue 78 por millón. La edad promedio de los pacientes prevalentes fue 50,5 años. La edad promedio al inicio de la enfermedad fue de 35 años. Se detectó una mayor prevalencia en los africanos que en los indios orientales (178 vs 68 por millón;* p = *0. 003). La debilidad del músculo ocular y las extremidades fueron los síntomas iniciales más comunes. Las condiciones autoinmunes (principalmente la enfermedad de tiroides) coexistían en 25,7%. El tratamiento implicó la administración de piridostigmina y/o inmunosupresores para todos, excepto dos que entraron en remisión con esteroides solamente. La MG generalizada se produjo en un 60%; el 42,9% expresaron sus handicaps sociales y profesionales. Un caso con características clínicas sugestivas resultó positivo en la prueba de anticuerpos de tirosina quinasa específica del músculo.*
Conclusiones: *Si bien muchas características de la MG en el sur de Trinidad fueron similares a las que aparecen en los datos internacionales, la prevalencia única, y según las estadísticas significativamente mayor en los africanos que en los indios orientales, indica la necesidad de que se realicen investigaciones ulteriores, dada la escasez de informes procedentes de África y la India. Los*

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pacientes con MG sufrieron una disminución en la calidad de vida, lo cual requiere una planificación para mejorar la salud.

Palabras claves: Prevalencia, miastenia gravis, Trinidad

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INTRODUCTION

Myasthenia gravis (MG) is an autoimmune disorder of skeletal muscles, with decreased acetylcholine receptor (AChR) availability (1). Symptoms vary from purely ocular to generalized, severely debilitating disease. Myasthenia gravis may begin at any age. However, paediatric MG is very rare (2). Point prevalence of MG varies from 3.05 to 200 per million (2, 3). Epidemiological studies are vital for health service planning for this frequently overlooked group. Despite research in Jamaica (4, 5), Cuba (6) and the Dutch Antilles (7), there remains a paucity of information on MG in the West Indies. There are no previous studies on MG in Trinidad and Tobago (T&T). Prevalence reports on MG in India and Africa are also limited (8, 9). South Trinidad contains 39.2% of T&T's population in the regional communities of San Fernando, Point Fortin, Penal/Debe, Princes Town, Couva/Tabaquite/Talparo and Siparia. The ethnic distribution of South Trinidad includes 59.0% East Indians, 26.3% Africans, 13.7% Mixed, 0.2% Chinese, 0.2% White and 0.6% Other. The ethnic distribution of North Trinidad, comprising the communities of Port-of-Spain, Diego Martin, Arima, Tunapuna/Piarco and San Juan/Laventille, includes 46.7% Africans, 30.6% Mixed, 19.0% East Indians, 0.7% Chinese, 0.2% Syrian/Lebanese, 1.4% Whites and 0.3% Other, per Central Statistical Office (CSO) data in 2000. This study aimed to report statistical and clinical data on MG in adults in South Trinidad with a predominantly East Indian/African population and to produce an estimated prevalence of MG.

SUBJECTS AND METHOD

A cross-sectional study was conducted from October 1, 2007 to March 31, 2010. Ethical approval was obtained from the regional health authority ethics committee. Patients were recruited from the San Fernando General Hospital (SFGH) Medicine Department (where all inpatients above age 11 years with presumed MG are referred), SFGH outpatient neurology clinic and the only private neurology practice in South Trinidad. San Fernando General Hospital is the largest healthcare institution and has the only public neurology service in South Trinidad.

San Fernando General Hospital is the only one of three university teaching hospitals in Trinidad located in South Trinidad. The current healthcare system in Trinidad operates on a geographical basis. Patients from South Trinidad are first referred to public or private neurology services in South Trinidad. Similarly, patients located in North Trinidad needing neurology services are referred to either one of the two public university teaching hospitals or one of the three private neurologists in North Trinidad. A few patients from North Trinidad may occasionally self-refer to a private neurologist in South Trinidad for a second opinion and *vice versa*. While no statistics were available on the number of patients who self-referred, which remained a limitation, the healthcare system in Trinidad is designed to serve patients only within specific geographic areas and this made it unlikely that most patients would regularly be followed up in a region remote from their home location.

Patients meeting the inclusion criteria of a diagnosis of MG constituted the study population. The diagnosis of MG was based clinically (history and examination findings of fluctuating and fatigable muscle weakness that improved with rest), and supported by a positive Tensilon test and/or serological demonstration of AchR or muscle specific tyrosine kinase (MuSK) antibodies. All patients were screened for thymic abnormalities with chest-computed tomography. Most were tested for other autoimmune diseases. Electrophysiological studies were done in 60% (most with generalized MG). Patients who died during the study period and those without a conclusive diagnosis were excluded.

The inpatient register was screened weekly over the study period to identify all inpatient MG cases (new or chronic). Outpatient cases were identified through SFGH neurology clinic (all cases above age 11 years in the public health sector are referred and regularly followed here) and the only private neurology practice in South Trinidad.

Following informed consent, all patients were interviewed *via* a standard questionnaire including demographical details (name, age, gender, age at initial presentation, ethnicity), disease duration, type of doctor first seen, time period to diagnosis, clinical course (initial symptoms, hospitalizations, thymectomy), clinical test results, family history of MG, other medical history (including autoimmune diseases), pharmacotherapy and MG's effects on social/professional life. Data were kept strictly confidential. Patients were classified according to the Osserman criteria (10).

Statistical analysis was done using SPSS Student version 16.0. All patients alive on March 31, 2010, were included in the prevalence estimate. Point prevalence was calculated as the total number of living cases detected, divided by the total population of South Trinidad. Population values were taken from the latest (2000) CSO data. Chi-squared test was used to calculate the significance of association between MG and each of gender and ethnicity; *p*-values less than 0.05 were considered significant.

RESULTS

Thirty-six patients from South Trinidad were found with MG on March 31, 2010. Point prevalence for South Trinidad's population of 412 810 was 78 per million. Two new cases occurred during the study period.

There were 61.1% females and 38.9% males. Prevalence of MG was higher among females (119 per million females) than males (74 per million males), but statistically unrelated to gender (p = 0.22). Regarding ethnicity, 19 patients were African, 15 East Indian and two White, yielding a prevalence of 193 per million Africans and 68 per million East Indians. This higher prevalence among Africans than East Indians was statistically significant (p = 0.003).

Figure 1 shows age and gender distribution. Mean age of prevalent patients was 50.5 (males 49.5, females 51.2, standard deviation 12.3, range 20–71) years. Figure 2 depicts age of onset – the overall mean was 35.0: males 35.8, females 34.4 years (standard deviation 15.0; range 2–68) years. Median duration of MG was 14.0 years (interquartile range 17.0, range < 1– 48).

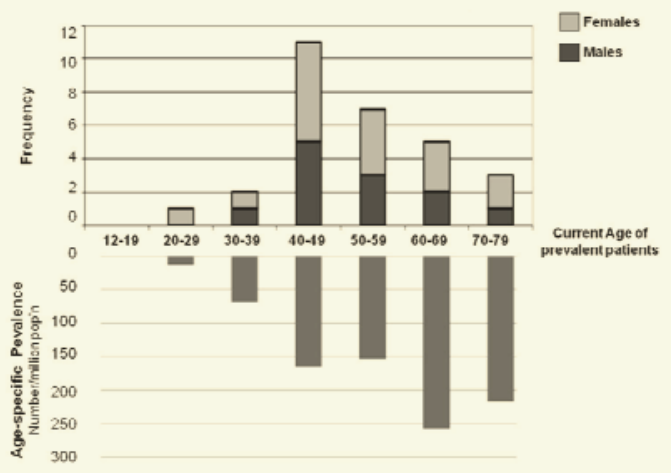

Fig. 1: Frequency of myasthenia gravis according to age and gender.

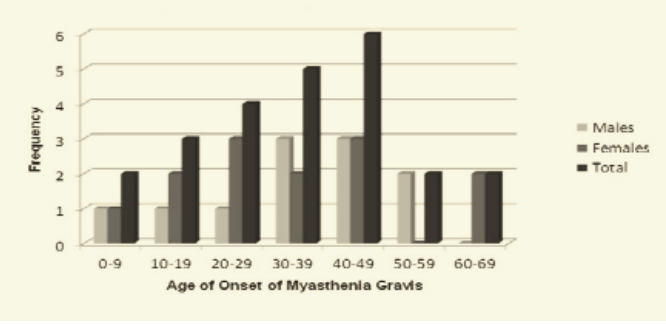

Fig. 2: Age of onset of myasthenia gravis in males, females and overall.

Initial presenting complaints were ocular muscle weakness (94.3%), girdle/extremity muscle weakness (77.1%), bulbar muscle weakness (48.6%), generalized weakness (34.3%) and difficulty breathing (22.9%). All five complaints were present in 11.4%; 17.1% – four, 31.4% – three, 17.1% – two and 22.9% – one complaint. Familial MG was found in 11.4% (two pairs of siblings). The ages of onset of the cases with familial MG were 18 and 38, and 33 and 60 years, making congenital or juvenile MG unlikely; 25.7% of patients had co-existing autoimmune conditions (seven cases with thyroid disease, one systemic lupus erythematosus and one rheumatoid arthritis). Diabetes mellitus Type 2 co-existed in 17.1%.

Initial medical contacts were general practitioners (34.3%), ophthalmologists (22.9%), emergency medicine physicians (20.0%), internists (11.4%), neurologists (5.7%), ear/nose/throat specialists (2.9%) and general surgeons (2.9%). Median time to medical contact after symptom onset was 14 days (interquartile range: 105 days, range: immediately to 10 years). Following medical contact, median time to diagnosis was 28 days (interquartile range: 105 days, range: immediately to 25 years). Five patients had delayed diagnoses beyond one year. Reasons were unclear in four; the fifth was initially misdiagnosed with rheumatoid arthritis. Eighty per cent had Tensilon testing which was positive. Ten patients had AchR antibody testing: 57% tested positive. There was one case, with positive Anti-MuSK antibodies, which was previously published (11).

Pharmacotherapy involved acetylcholinesterase inhibitors (pyridostigmine) for all except two cases in remission: one with poor drug response and the Anti-MuSK positive patient treated with steroids and azathioprine. Eighty-seven per cent reported difficulty in obtaining pyridostigmine; 51.4% used steroids (oral prednisolone – average maintenance dose of 5 mg daily) and 14.3% azathioprine (average dose of 100 mg daily). Anticholinesterase side effects (gastrointestinal upset, increased salivation and lacrimation) were experienced by 35.5% on pyridostigmine. Amongst steroids users, 50.0% reported weight gain, 11.1% had osteoporosis and 11.1% recurrent infections. Imaging revealed thymic enlargement in four patients. Thymectomy was done in six patients: two had thymomas, two had thymic hyperplasia and two had normal thymus glands. Thereafter, three (of which two had thymoma and one a normal thymus gland) noted no improvement and three reported initial symptomatic improvement but were still unable to achieve remission.

Most patients met Osserman's class IIa (Fig. 3); 28.6% required hospital admission for MG management. Six patients required Intensive Care Unit (ICU) admission at some point; five of these six were intubated and required mechanical ventilation for an average of 10.5 days. With the exception of one patient with Osserman's class IIa disease, all patients requiring ICU care had class IIb, III or IV disease. Three patients required plasmapheresis – all had good short-term responses with two having no relapses and one having recurrent subsequent relapses. One patient received human immune globulin. Of the patients without initial generalized MG, 42.9% developed generalized MG; 11.4% gained

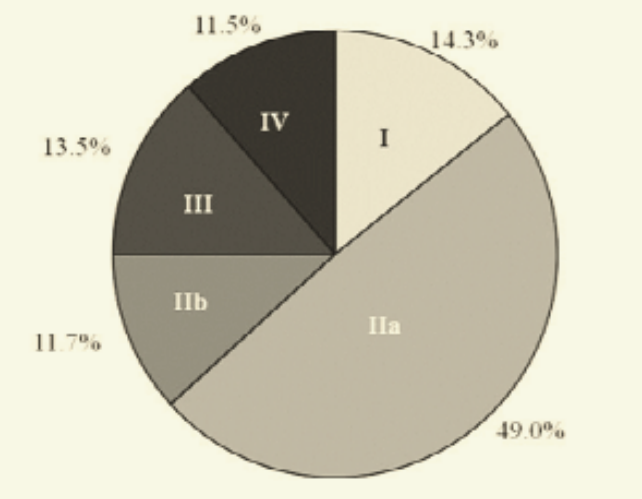

Fig. 3: Percentage of patients falling into each of Osserman's categories I to IV.

remission. Sixty per cent maintained that MG handicapped their social and/or professional life. One patient reported co-treatment for depression.

DISCUSSION

In this first study on MG in Trinidad and Tobago, estimated point prevalence was 78 per million in South Trinidad. International prevalence data range from 5.6 to 200 per million (3, 4, 6, 12–17). The actual prevalence (determined in a total population study) in South Trinidad may be higher:

* There may have been a few 'symptom-free' patients in remission who did not seek medical attention during the study period.
* There may be a few cases age 11 years and under, not covered by our sample population. There is no public or private paediatric neurology-specific clinic in South Trinidad, making accountability in this age bracket difficult. As paediatric MG is very rare it is assumed that the estimate from our sample popula-tion is close to the real value.
* There may be a few undiagnosed patients with a mild pure ocular disorder.

The higher female:male prevalence ratio of 1.6:1, with a higher female proportion below age 40 years and above 70 years is consistent with most previous published reports (3, 7, 18–22). The latter might be explained by a slightly higher life span of women with MG compared to men (18). The reported earlier onset for females and later onset for males were also observed (18).

One unique finding of this study is the statistically significantly higher prevalence in Africans compared to East Indians in the sample population. Association of HLA B8, DR3 and D4 in Caucasian and African American populations, respectively with MG has been documented (22). Our present finding supports the need for further genotypic/phenotypic analyses to investigate allelic combinations in establishing a precise immunogenetic basis for MG.

Ocular muscle weakness as the most common clinical presentation was comparable to conventional data (9, 19–21). However, familial MG occurrence was higher than other reports (12, 18). The frequency of co-existing autoimmune conditions, especially thyroid disease highlighted the importance of screening for such conditions in MG patients. The common co-existence of diabetes mellitus was noteworthy, as steroids are often used in management.

Hospitalizations for myasthenic crises required ICU care for 17%, demanding substantial healthcare resources. Plasmapheresis (for acute fulminant cases) was not available locally, but two patients received this in Caracas, Venezuela. Sixty per cent indicated social and/or professional handicap. The huge fraction initially presenting to general practitioners emphasizes the need for heightened awareness of MG among local health professionals. This might decrease the time to diagnosis (up to 25 years in one case). Eighty-seven per cent reported difficulty in obtaining pyridostigmine. Variable supply and high cost of pyridostigmine are thus critical issues for future health service planning.

In conclusion, the prevalence of MG in South Trinidad was at least 78/1 000 000, with a higher prevalence in Africans. A study in North Trinidad with a higher African population and a much lower Indian population, and further publications from Africa and India may aid in elucidating the novel findings in our multi-ethnic population. The outstanding clinical and socio-economic impacts of MG highlight the need to improve management strategies for MG patients.

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