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Epidemiology and 10-year clinical care of juvenile myasthenia gravis in England: a retrospective cohort study

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ABSTRACT

Background Published evidence is limited on the clinical burden of juvenile myasthenia gravis (JMG). We aimed to assess epidemiology and the clinical characteristics of JMG in England.

Methods We performed a retrospective analysis of patients with newly diagnosed JMG identified in England via primary care and hospital data between 2010 and 2019.

Results 32 children (aged 2–17 years) with newly diagnosed JMG were included. Prevalence of JMG ranged from 2.2 (95% CI 1.5 to 3.1) in 2012 to 2.5 (95% CI 1.8 to 3.4) per 100 000 in 2018. The annual incidence ranged from 0.8 (95% CI 0.1 to 5.7) in 2015 to 3.8 (95% CI 1.6 to 9.0) per million per year in 2017. Incidence fluctuated in females from 1.6 (95% CI 0.2 to 11.3) in 2016 to 6 (95% CI 2.3 to 16.1) per million per year in 2018. Overall, 20 patients received first acetylcholinesterase inhibitors or corticosteroids with no prior therapy during the study period. During the follow-up period (median, 3.3 years), 17 patients (53.1%) with JMG experienced a hospitalisation. No deaths were observed.

Conclusions This study confirms the rarity of JMG in England, with steady incidence and prevalence rates over a decade. Further research is required to assess unmet needs in JMG therapy and the importance of effective treatments for this condition.

INTRODUCTION

Juvenile myasthenia gravis (JMG) is a rare, autoimmune disorder affecting neuromuscular junction transmission in children and young people. Both adult MG and JMG are characterised by fatigable muscle weakness.[1] Prevalence estimates of MG have been increasing in adult populations, with an average incidence of 1 (range 0.3–2.8) per 100 000 over recent decades.[2 3] Limited studies from single centres or registries have established the epidemiology of JMG, reporting incidence rates of 0.3–8.9 per million.[4–6] According to the international consensus guidance for MG management, acetylcholinesterase inhibitors (AChEIs), with or without corticosteroids, are considered as first-line therapy for adult MG and JMG.[1 7 8] There is a lack of real-world data describing the clinical burden of JMG and treatment practice for the condition. The aim of this study is to estimate the prevalence and incidence of JMG and to describe clinical characteristics using a longitudinal cohort of patients with JMG from primary care and hospitals in England.

METHODS

We retrospectively identified and analysed all patients with a reported diagnosis of JMG between 1 January 2010 and 31 December 2019 in England, using the Clinical Practice Research Datalink (CPRD) Aurum database (from primary care), Hospital Episode Statistics (HES) data and the Office for National Statistics in England (online supplemental materials). Cases were classified as new-onset JMG if they had at least one code (first MG diagnosis from 2 to <18 years of age) recorded from January 2010 with 12 months data available prior to the index date (first MG diagnosis) (online supplemental figure 1). Patients with any congenital myasthenia syndrome codes were not included in this study. In addition, we searched databases for information about MG treatments, hospitalisations, procedures (such as thymectomy) and intensive care unit (ICU) admissions (online supplemental tables 1 and 2). MG hospitalisation was defined as a hospitalisation with either MG diagnosis as the primary reason or MG diagnosis during the first episode of that hospitalisation. Myasthenic crisis was defined as an ICU admission for respiratory failure or ICU admission requiring ventilatory support. We estimated annual prevalence (per 100 000 persons) and incidence (per million per year) through 2012–2019 using SAS statistical software

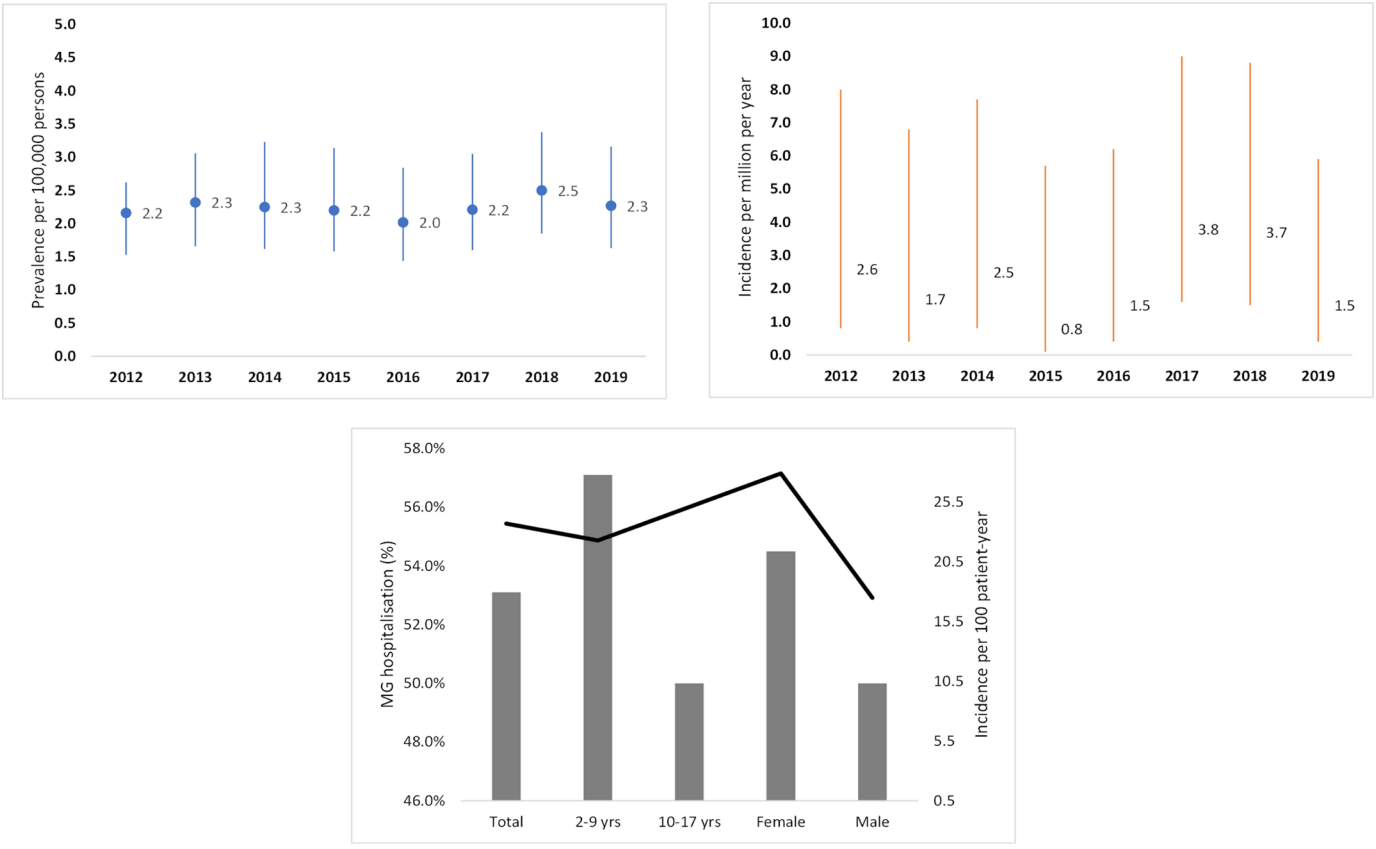

Figure 1 Prevalence (A), incidence (B) of juvenile myasthenia gravis (JMG) and (C) incidence of myasthenic hospitalisation in the newly diagnosed cohort in England in years 2010–2019. (A) Prevalence for each year was calculated as point prevalence on 31 December of the year of interest, dividing the number of patients with a diagnosis of MG at any time in their CPRD Aurum/HES by the population (ie, those that are up-to-standard) with data linked to HES on 31 December of that year. (B) To calculate the incidence of JMG, the number of patients with incident diagnosis of JMG (ie, number of patients with a first-ever MG diagnosis between the start and end of that year) was divided by the number of patients at risk (ie, the population registered at all the eligible CPRD Aurum practices, for at least 1 year prior to MG diagnosis, with data linked to HES without JMG diagnosis at the start of that year, excluding prevalent patients. (C) Myasthenic hospitalisation was defined as hospitalisation with MG (excluding hospitalisation for thymectomy) or treatment with IVIg/PLEX. The bars (y-axis on the left) depict the percentage of events, in total and by subgroups, and the line (y-axis on the right) corresponds to the incident rate of event per 100 patient-year. CPRD, Clinical Practice Research Datalink; HES, Hospital Episode Statistics; IVIg, intravenous immunoglobulin; PLEX, plasma exchange.

V.9.4 (SAS Institute) (see more details in online supplemental materials).

RESULTS

Out of 13 799 patients with a diagnosis of MG between 2010 and 2019 in either the CPRD Aurum or HES data, a total of 32 incident JMG cases (68.7% female) were included (online supplemental tables 3 and 4). The mean age at index date of JMG was 10.2 (minimum and maximum, 2 and 17) years; 18 patients had symptom onset before the age of 12 years.

In total, there were 47 prevalent cases of JMG between 2010 and 2019. During the study period, the prevalence of JMG remained stable in the overall population, ranging from 2.2 (95% CI 1.5 to 3.1) per 100 000 in 2012 to 2.5 (95% CI 1.8 to 3.4) per 100 000 in 2018 (figure 1, online supplemental table 5). For children aged 12 years and above at the index date, prevalence ranged from 3.7 (95% CI 2.1 to 6.3) per 100 000 in 2012 to 4.6 (95% CI 2.9 to 7.1) per 100 000 in 2018. The annual incidence of JMG ranged from 0.8 (95% CI 0.1 to 5.7) per million per year in 2015 to 3.8 (95% CI 1.6 to 9) per million per year in 2017 in the overall paediatric population and slightly increased from 1.6 (95% CI 0.2 to 11.3) per million per year in 2016 to 6 (95% CI 2.3 to 16.1) per million per year in 2018 for females (figure 1, online supplemental table 6).

We observed that 16 out of 32 newly diagnosed (incident) cases with JMG had records of AChEIs use as first-line therapy, mainly in the first (46.9%), second (32.1%) and third (34.8%) year after diagnosis. Corticosteroid (mean dosage, 20 mg/day, anytime during the study) was used in 10 patients (31.3%). A total of 20 patients received AChEIs or corticosteroids with no prior treatments at any time during the study period. The use of immunosuppressive therapies like

azathioprine or mycophenolate mofetil was identified in fewer than five patients. The use of intravenous Ig infusions or plasma exchangewas also identified in fewer than five patients during the first 3 years. Thymectomy was reported in fewer than five patients with JMG in the first 3 years after the index date. The median (first, third quartiles) duration of follow-up for JMG patients was 3.3 (1.6, 6.7) years. During the follow-up period, 17 patients (53.1%) experienced a hospitalisation, with an incidence of 23.7 (95% CI, 15.6 to 35.9) per 100 patient-years (figure 1, online supplemental table 7); fewer than five patients experienced a myasthenic crisis. No deaths were observed during the entire study period.

DISCUSSION

This longitudinal cohort study based on national health data demonstrates that the prevalence and incidence of JMG remained steady in England during the 10-year study period. In females, the incidence of JMG appears to have fluctuated from 1.6 to 6 per million per year over the period 2016–2018. Our results are consistent with previous studies from European populations like Nordic countries, which have reported incidence rates ranging from 1.6 to 2.2 per million per year.[4 5]

Real-world evidence generated from analysing routine practice data outside of traditional cohorts and clinical trial settings is very limited in the healthcare landscape of JMG. Yet such evidence plays an important role in informing clinical trials and clinical decision making.[9] Here, we provide observational evidence that over 50% of children with newly diagnosed JMG had hospital admissions in England between 2010 and 2019. Patients were mainly treated with AChEIs and corticosteroids during the study period. Furthermore, these results increase awareness of the clinical burden of JMG and highlight the need for JMG-specific international clinical guidelines that include treatment strategies with increased efficacy and fewer side effects (such as novel immunotherapies) than traditional treatments for MG.[7]

While this is one of the largest JMG cohorts in England, this study has several limitations. First, due to the rarity and clinical heterogeneity of JMG, the generalisability of our findings to other settings remains unknown. Second, the data linkage between primary care and HES does not provide detailed information on diagnosis and treatments. Third, potential misclassification of JMG is plausible because case definition relies on standard medical codes rather than unstructured data from neurologists' notes, and MG symptoms can mimic other neurological disorders.[10] Furthermore, the new treatment options which have been approved since 2020 were not available in our study. Fourth, given the nature of electronic medical records in clinical practice, information about treatment discussions, treatment side effects and adherence to treatments may not be available.[10] This could contribute to potential under-reporting of treatment data in the databases as we noted that only 20 out of 32 patients were taking AChEIs or corticosteroids. We would have expected more of the study population to be taking these first-line therapies, given that all included children with JMG were aged 2 years or above and had a medical diagnosis for MG, including JMG, generalised MG or not otherwise specified MG. However, the databases did not capture anti-AChR antibody status or allow us to differentiate between generalised and ocular forms of JMG. While routine primary care data are updated monthly, medications prescribed in specialty care may not be captured as frequently.[11] The low use of first-line treatments and thymectomy observed in our study might also reflect delays in updating medical records and receiving feedback from specialists' referral, or delaying (underutilising) the surgical procedure. Also, the initial diagnosis of MG could have been potentially revised to an alternative diagnosis. Fifth, the incidence of myasthenia hospitalisation could have been artificially overestimated because the main cause for hospital admissions and procedures cannot be determined from the databases.[12] Finally, it is also possible that some patients with JMG have received treatments in other specialised centres outside of England. Further research is warranted to leverage more comprehensive information that involves combining specialised datasets such as patient registries, outpatient specialty clinics or rare disease services.

CONCLUSIONS

This observational study that analysed data from primary care and the HES database corroborates the rarity of JMG in England. Over the study period 2010–2019, incidence and prevalence rates were steady, with the incidence slightly increasing in females. Although JMG patients in this cohort had a high number of hospitalisations, further research is needed to assess the generalisability of our findings and to identify potential unmet needs for the management of children with this chronic condition.

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Competing interests KB, AS, FT and SN are employees of UCB and/or hold the UCB stock shares. SJ has served as an international advisory board member for Alexion, Alnylam, argenx, Immunovant, Regeneron, and UCB; is currently an expert panel member of the Myasthenia Gravis consortium for argenx and has received speaker fees from Terumo BCT and Eisai Pharmaceuticals. SR has

served on advisory board for Novartis, Sarepta, Argenx and Roche, has been investigator in clinical trials for Sarepta, Roche, Wave, Genetx, Argenx, Inois and Santhera, and received Speaker fees for educational meetings from Novartis and Roche. AA and PZ report that contract work with UCB, and have no competing interest.

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REFERENCES

1 Punga AR, Maddison P, Heckmann JM, *et al*. Epidemiology, diagnostics, and biomarkers of autoimmune neuromuscular junction disorders. *Lancet Neurol* 2022;21:176–88.
2 Vissing J, Atula S, Savolainen M, *et al*. Epidemiology of myasthenia gravis in Denmark, Finland and Sweden: a population-based observational study. *J Neurol Neurosurg Psychiatry* 2024;95:919–26.
3 Deenen JCW, Horlings CGC, Verschuuren JJGM, *et al*. The Epidemiology of Neuromuscular Disorders: A Comprehensive Overview of the Literature. *J Neuromuscul Dis* 2015;2:73–85.
4 Popperud TH, Boldingh MI, Brunborg C, *et al*. Juvenile myasthenia gravis in Norway: A nationwide epidemiological study. *Eur J Paediatr Neurol* 2017;21:312–7.
5 Parr JR, Andrew MJ, Finnis M, *et al*. How common is childhood myasthenia? The UK incidence and prevalence of autoimmune and congenital myasthenia. *Arch Dis Child* 2014;99:539–42.
6 Lai CH, Tseng HF. Nationwide Population-Based Epidemiological Study of Myasthenia Gravis in Taiwan. *Neuroepidemiology* 2010;35:66–71.
7 Munot P, Robb SA, Niks EH, *et al*. 242nd ENMC International Workshop: Diagnosis and management of juvenile myasthenia gravis Hoofddorp, the Netherlands, 1–3 March 2019. *Neuromuscul Disord* 2020;30:254–64.
8 Sanders DB, Wolfe GI, Benatar M, *et al*. International consensus guidance for management of myasthenia gravis: Executive summary. *Neurology (ECronicon)* 2016;87:419–25.
9 Blonde L, Khunti K, Harris SB, *et al*. Interpretation and Impact of Real-World Clinical Data for the Practicing Clinician. *Adv Ther* 2018;35:1763–74.
10 Mahic M, Bozorg A, Rudnik J, *et al*. Treatment patterns in myasthenia gravis: A United States health claims analysis. *Muscle and Nerve* 2023;67:297–305.
11 Herrett E, Gallagher AM, Bhaskaran K, *et al*. Data Resource Profile: Clinical Practice Research Datalink (CPRD). *Int J Epidemiol* 2015;44:827–36.
12 Harris L, Graham S, MacLachlan S, *et al*. A retrospective longitudinal cohort study of the clinical burden in myasthenia gravis. *BMC Neurol* 2022;22:172.