**Ethnic differences in dystonia prevalence and phenotype**

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**Introduction**

Ethnic differences, both in dystonia prevalence (e.g. higher DYT-*TOR1A* prevalencein Ashkenazi Jewish populations) and phenotype are well recognised, but have not been systematically characterised in large multi-ethnic cohorts1. In order to further define such differences, we examined dystonia frequency and phenotypes across ethnic groups in 4 tertiary movement disorder centres in the UK.

**Methods**

Demographic (age, sex, ethnicity) and clinical (dystonia phenotype, age of onset) data from all patients with dystonia attending our adult tertiary movement disorder clinics at the National Hospital for Neurology and Neurosurgery, St George’s University Hospital, University Hospital Birmingham and Liverpool University Hospital as of June 2020 were retrospectively reviewed. Ethnicity was defined according to the Racial and Ethnic Categories and Definitions for NIH Diversity Programs and for Other Reporting Purposes.

A representative control population was defined using publically available data from the UK office for national statistics (calculated based on the ethnic makeup of each hospital’s catchment population and weighted according to their relative contributions to the study).

The Kruskal-Wallis test with post-hoc Bonferroni-corrected Dunn’s test was used to examine age of onset differences between groups. A chi-square test of independence was used to assess difference in frequency of isolated and combined dystonia, and of focal, segmental and generalized dystonia amongst ethnic groups. In a post-hoc analysis with Bonferroni-correction, we compared each ethnic group to Whites.

**Results**

Data from 1215 people with dystonia was reviewed (table 1). Dystonia was more common in Whites compared to those of Black, Asian or mixed ethnicity. The most common dystonia phenotype in Whites was cervical dystonia, either focal or segmental with additional upper limb or facial involvement. Dystonia involving the face was highly prevalent in Blacks. Age at dystonia onset was significantly earlier in Asian and mixed populations compared to Whites, likely because of the observed differences in dystonia phenotypes. Age at onset was not statistically different between Whites and Blacks, but small numbers in the latter group may have influenced our ability to detect such differences. Frequency of isolated Vs combined dystonia differed between ethnicities (χ2 =44.9; p<0.00001), as did dystonia phenotypes. In post hoc analysis, only Asians and mixed ethnicities differed significantly to Whites.

**Discussion**

This study identified significant inter-ethnic differences both in frequency and phenotypes of dystonia. The over-representation of white ethnicities was striking. While one might argue that this could represent ascertainment bias (healthcare utilization being lower among immigrants compared with their non-immigrant counterparts)2, our data aligns with previous studies which found a lower prevalence of dystonia in Black, Asian and Hispanic individuals compared to Whites, both in their native lands and in emigrant populations 1, 3-7.

 Phenotypes also varied considerably. For instance, the dictum that cervical dystonia is the most common late-onset focal dystonia only held true in Whites8. Limb, facial and oromandibular dystonia were particularly prevalent in Blacks. Asians and Blacks also had higher rates of generalized and combined dystonia, perhaps due to higher prevalence of consanguineous marriage9. Such phenotypic differences have previously been touted. Studies from Japan and Tunisia suggested blepharospasm as a common phenotype 9, 10, while focal hand dystonia was prevalent in Africa and India3, 11, 12 . In a Kenyan study, ‘oropharyngeal’ dystonia had equal prevalence to cervical dystonia (both 25% of all focal dystonia cases)3, and in a study of Black emigrants with dystonia, over 30% had craniofacial onset and >25% had laryngeal onset1.

These differences merit probing for numerous reasons. First, classic descriptions of dystonia may need to be re-worked in a way that more accurately reflects inter-ethnic differences. In increasingly multi-ethnic societies, this becomes important not only for medical education, but also for healthcare planning and resource allocation e.g. training in oromandibular botulinum toxin injections in hospitals serving predominantly Black populations. Second, dissecting the relative contributions of genetic, epigenetic and environmental factors to these differences may further our understanding of dystonia pathophysiology and its determinants. Further, controlling for these differences is important in clinical trial settings to avoid introducing bias13. Finally, it is important to ensure that structural and other factors(e.g. cultural healthcare beliefs, social stigma), which may affect the likelihood of seeking medical attention, are addressed if present.

By virtue of its retrospective nature, our study has inherent limitations. Clinical data was not available for all patients. Ethnicity was self-reported and may therefore have been affected by under- or mis-reporting. The small number of patients in the Black and Mixed groups will have limited the validity of some statistical testing. This was also a select population referred to tertiary centres (many with a high proportion of non-White ethnicities in their catchement populations) and thus may not be representative of the dystonia community at large. Further studies are therefore needed to confirm and further explore these findings.

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**Author roles**

1. Research project: A. Conception, B. Organization, C. Execution

2. Statistical Analysis: A. Design, B. Execution, C. Review and Critique

3. Manuscript Preparation: A. Writing of the first draft, B. Review and Critique

EM 1A, 1B, 1C, 2A, 2B, 3A

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GDL 1A, 1B, 1C, 2C, 3B

SB 1B, 1C, 2C, 3B

JD 1B, 1C, 2C, 3B

SH 1B, 1C, 2C, 3B

NM 1B, 1C, 2C, 3B

AB 1B, 1C, 2C, 3B

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**Ethical Compliance Statement**

This study was approved by the relevant audit and service evaluation committees at each institution. Informed consent was obtained. We confirm that we have read the Journal’s position on issues involved in ethical publication and affirm that this work is consistent with those guidelines

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Table 1: Demographic and clinical characteristics of people with dystonia across various ethnicities

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|   | **White** | **Asian** | **Black** | **Mixed + Other** |
| Demographics |   |   |   |   |
| Total patient no | 1098 | 78 | 25 | 14 |
| % of dystonia population | 90.5 | 6.5 | 2 | 1 |
| % of control population | 68 | 18 | 7 | 7 |
| F:M ratio | 1.9 : 1 | 1.1 : 1 | 2.6 : 1 | 1.8 : 1 |
| Mean age at onset (+/-SD) | 49+/-16 | 44+/- 17 | 40+/-23 | 34+/-20 |
| % isolated | 96 | 85 | 80 | 69 |
| % combined | 4 | 15 | 20 | 31 |
| **χ2**  |   | 20.8 | 15.0 | 20.2 |
| **Bonferroni-corrected p-value** |   | <0.0001 | <0.001 | <0.0001 |
| **Multifocal dystonia** | 1(<1%) | 0 | 0 | 0 |
| **Hemidystonia** | 2(<1%) | 1(1%) | 0 | 0 |
| **Focal Dystonia** |   |   |   |   |
| Isolated cervical | 707 (64%) | 39(50%) | 5(20%) | 8 (57%) |
| Focal limb/task specific dystonia | 75(7%) | 6 (8%) | 2(8%) | 0 |
| Blepharospasm | 27(2%) | 2(3%) | 2(8%) | 0 |
| Oromandibular dystonia | 3 (<1%) | 0 | 2 (8%) | 0 |
| Other focal dystonia | 24(2%) | 0 | 3(12%) | 2(14%) |
| **Segmental Dystonia** |   |   |   |   |
| Involving cervical region (cervical+orofacial OR cervical +upper limb) | 121(11%) | 7(9%) | 4(16%) | 0 |
| Isolated Bi-brachial | 91(8%) | 10(13%) | 2(8%) | 0 |
| Isolated Meige | 4 (<1%) | 2(3%) | 2(8%) | 1(7%) |
| Other | 4(<1%) | 1(1%) | 0 | 0 |
| **Generalised Dystonia** | 39(4%) | 10(13%) | 3(12%) | 3(21%) |
| **χ2**  |   | 18.7 | 7.7 | 12.9 |
| **Bonferroni-corrected p-value** |   | <0.0001 | 0.06 | <0.005 |