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Headaches in multiple sclerosis: Cross-sectional study of a multiethnic population

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ABSTRACT

Objectives: Headaches in MS are common, but there is little data on the influence of race, comorbidities, MS disability and socioeconomic issues on headaches, especially migraine. We aimed at looking at prevalence and type of headache across a multiethnic MS population, and relationship between MS related clinical factors and migraine.

Patients and methods: This is a cross-sectional study of 233 MS patients at two clinical sites, one at a county hospital, and the other a private academic center clinic. We collected demographic data, MS characteristics, and headache histories using validated survey instruments including Headache Impact Test (HIT-6) and Patient Health Questionnaire-9 (PHQ-9). The relationship between MS and migraine was examined using logistic regression.

Results: Majority of our patients were female ($N = 156$, 67%), average age 44 years, with relapsing remitting MS ($N = 214$, 92%). Our cohort was multi-ethnic predominantly Whites ($N = 106$, 46%) and Hispanics ($N = 87$, 37%). Public sector patients were significantly disadvantaged in socioeconomic measures ($p < 0.0001$) and younger (40 vs 47 yrs, $p < 0.0001$), compared to the private sector patients who had a higher MS burden. Headaches were common, regardless of sector ($N = 115$, 49.4%), the most common type being migraine ($N = 83$, 36%). Chronic migraine was more common among Hispanics (82%) than Whites (18.2%) ($p = 0.012$). Headache impact on daily life, measured by HIT-6 score ($p = 0.006$) and PHQ-9 score ($p = 0.004$) were significantly higher in the public sector. After controlling for income and education, female gender (OR 2.59, 95% CIs 1.312–5.127) and ambulatory disability were found to be more likely to suffer from migraines.

Conclusion: Headache, especially migraine is common among MS patients regardless of socio-economic status and treatment setting. Female MS patients with walking disability and longer disease duration tend to get migraines. Hispanic MS patients have a higher likelihood of suffering from chronic migraines. Thorough headache evaluation and headache treatment are essential to comprehensive MS care.

1. Introduction

Headaches are a common symptom in multiple sclerosis (MS) [1,2]. Lifetime prevalence of headaches in MS patients can range between 4–58%, with migraine without aura and tension-type headache being the most frequently reported [3,4]. A higher incidence of migraine in relapsing remitting MS (RRMS) has been reported [2,5]. Less is known about how MS disability impacts migraine [1,5]. Recent observational studies suggest that headaches are more often reported among younger and less disabled individuals suffering from MS while others suggest it to be a common pain syndrome [1–3].

Population-based studies in the U.S. have observed an inverse relation between migraine prevalence and household income [6–8]. The current reports have been limited to mainly white cohorts with similar socioeconomic backgrounds [9]. Similarly, socioeconomic and cultural background has been related to quality of care of MS patients [9]. However, this is not clear if migraine in MS varies by race and ethnicity. Because socioeconomic factors are known to influence headache in general, understanding headache prevalence and managements in different race and ethnic backgrounds affected by MS is important. The purpose of this study was to examine the prevalence and type of headache among a

Abbreviations: MS, multiple sclerosis; HIT-6, Headache Impact Test; PHQ-9, Patient Health Questionnaire-9; RRMS, relapsing remitting MS; EDSS, Expanded Disability Status Scale; MIDAS, Migraine Disability Assessment MIDAS; OR, Odds Ratio OR; CIs-95%, Confidence Intervals.

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multiethnic population with MS and investigate its relationship with socioeconomic factors, MS- related disability and depressive symptoms. Even though, the Hispanic population is the fastest growing immigrant population in the US, there is limited data related to the prevalence of headaches among Hispanics [10] and our study aims to highlight important issues related to pain and comorbidities in this population.

2. Patients and methods

2.1. Sample population

Between March 2010–June 2011, we interviewed 233 consecutive patients with multiple sclerosis seen at two specialty clinics affiliated with the University of Southern California (USC): the MS Comprehensive Care Center which serves English speaking patients with private health insurance, and the MS clinic at the County with uninsured, immigrant, non-English speaking, underserved population. Patients in both clinic settings are seen by the same neurologists. Less than 5% MS patients approached for interview, declined to participate mostly due to time constraints. Exclusion criteria included: secondary headaches including headache related to MS disease modifying treatment, age less than 18, prisoners, pregnant women and employees.

Using a structured, in-person questionnaire, demographic data such as gender, ethnic background, birthplace, annual household income, education and medical history were obtained by one of the co-authors, a medical student who is fluent in Spanish and English (SLW). MS characteristics that were collected included age of onset of MS-related symptoms, and ambulatory index as measured by the Expanded Disability Status Scale (EDSS) which was performed by a neurologist (LA). EDSS is an ordinal scale ranging from 0 to 10, 0 is normal neurological examination, and 10 = death. An EDSS of 6 is equivalent to ambulatory impairment that requires assistive device and is used to mark severe disability in MS [11]. Patients were also interviewed to obtain information related to headache history, types of headaches and associated symptoms. Type of headache was diagnosed using the International Classification of Headache Disorders-2 (ICHD-2) Criteria [12]. The headache specialist making the headache diagnosis was blinded to MS-related clinical data (SS). Primary headaches included Migraine (with and without aura), Tension-type Headaches, Trigeminal Neuralgia, Occipital neuralgia and other headaches, whereas chronic headache was defined as 15 or more headache days in a month per ICHD-2 Criteria. Temporomandibular Joint (TMJ) pain was diagnosed based on the headache neurologist's examination. The Institutional Review Board at USC approved this study and all patients gave informed consent prior to participation.

2.2. Survey instruments

Survey instruments included International Headache Society Criteria to diagnose migraine and other headache types, a validated Migraine Disability Assessment (MIDAS) tool to assess the migraine severity and the Headache Impact Test (HIT-6) total score were used to measure the level of migraine disability [13]. Score range is 36–78. Score of 49 or less: no Headache impact, 50–55: some impact, 56–59: substantial impact, 60 or more: severe impact: To assess the potential co-existence of depressive symptoms and its impact on headache, the well-validated Patient Health Questionnaire-9 (PHQ-9) was added [14,15]. PHQ-9 scoring system for depression severity is as follows: 0–4: none, 5–9: mild depression, 10–14: moderate depression, 15–19: moderately severe depression, 20–27: severe depression. Validated Spanish versions of all survey instruments were used for Spanish speaking patients [15–17].

2.3. Statistical analysis

All analyses were conducted on individuals affected with MS as defined by the revised McDonald Criteria [18]. Baseline sample descriptive statistics by location were performed and reported with mean and standard deviation values. We stratified the sample population by location where they received care, either private or public clinic. For hypothesis testing, two-tailed sample *t*-tests were used to test for statistically significant differences in the means of continuous variables (i.e., age, age of disease onset, disease duration) between the two locations. Unlike age, disease duration was not normally distributed and therefore treated under Wilcoxon's nonparametric analysis. Binary or categorical variables were analyzed using chi-square and Fisher's exact tests, respective to the sample size included in the analysis. Logistic regression was used to calculate the Odds Ratio (OR) and 95% Confidence Intervals (CIs) associated with migraine type, adjusting for age, gender and disease duration. Although factor analysis was not conducted for the selection of variables used under analysis, previous reports have suggested that the variables (age, gender, and disease duration) are commonly correlated with MS and headache. Logistic models were thus built using age, gender, disease duration and ambulatory status as independent variables and presence of migraine was the outcome variable. Supplemental aggregate models were also used to include education level, annual income, and PHQ-9. The PHQ-9 was scored and the proportion on individuals in each category was recorded. Individuals that had a score of >5 were determined to have some degree of depression and a categorical variable was created which was then used in the logistical model. All statistical analyses were performed on SAS 9.2 and set at a priori α-level of 0.05 to declare statistical significance.

3. Results

3.1. Clinical characteristics

The clinical and demographic characteristics of study participants are presented in Table 1. Participants were predominantly women (67%; with a ratio of 2:1), had relapsing remitting MS (92%) and of non-Hispanic white background (~46% followed by Hispanic (37%) with an average age of 44 years). In contrast to the private clinic, the public clinic saw a significantly younger population (40 ± 12.6 vs 47 ± 11.6; $p < 0.0001$) and more diverse racial/ethnic population (Hispanic: ~57%, African–American: ~23, Asian: 5%; $p < 0.0001$). Comparably, a larger sample size of whites comprised the private clinic (65%). Details of MS characteristics are described in Table 2. There were no differences in age of first symptoms or age of diagnosis by clinic location. However, the average disease duration was significantly longer in the private clinic compared to the public clinic (Mean 13.5 ± 11 vs 9.4 ± 8.2 $p = 0.0023$), respectively. Relapsing remitting MS was the most common type of MS reported, and the majority of patients were ambulatory (EDSS < 6). MS Treatment did not differ by clinic setting, and included Glatiramer Acetate 77(33%), Interferon 69(30%), No therapy 44(19%), Natalizumab 32(14%), Fingolimod 3 (1%), and others (Azathioprine, Alentuzumab, Rituximab) 8(3%).

3.2. Socioeconomic characteristics

Annual income and educational history were used as predictive social economic determinants. As expected, significant differences were found between the private and public clinics in annual income ($p < 0.0001$) and educational level ($p < 0.0001$). Participants in the