Urban/Rural Differences in Hospital Admissions with Multiple Sclerosis in Selected Counties in Ohio 1999-2004

Sadik A. Khuder[*,1], Melissa Foos[1], Nabeel A. Herial[1,§], Anand B. Mutgi[1,§], Basil S. Khuder[1,§] and Rose Jung[2,§]

[1]*College of Medicine, University of Toledo, Toledo, Ohio, USA*

[2]*College of Pharmacy, University of Toledo, Toledo, Ohio, USA*

Abstract: *Context*: Regional differences in the prevalence of Multiple Sclerosis (MS) have been reported with higher rates in rural areas.

Purpose: Using hospital admission data from eight counties in Ohio (1999 to 2004), we described the pattern of admissions for MS patients and examined the rural/urban differences.

Methods: Adjusted admission rate ratios (ARR) for rural regions were calculated using Poisson regression models.

Findings: The estimated admission rate was 70 per 100,000 in 1999 and increased to 90 per 100,000 in 2004 ($p<0.0001$). A significant association between degree of urbanization and MS admission rates was found with higher rate in rural area (ARR=1.23, 95% CI 1.17-1.35) and in female (ARR=2.45, 95% CI 2.37-2.54).

Conclusions: Admission rate for MS is increasing and rural residence is associated with higher hospitalization rate.

Keywords: Multiple Sclerosis, hospital admission, urban, rural.

INTRODUCTION

Multiple sclerosis (MS) is a neurodegenerative disease characterized by inflammation of the central nervous system due to the action of the immune system [1]. It mostly affects young adults aged 20 to 40 years, and in developed countries, MS is a major non-traumatic cause of neurological disability for this age group [2].

The exact number of people with MS in the United States is not known. Published estimates range between 250,000 and 350,000 patients with MS diagnosed by a physician [3]. Data from the National Health Interview Survey provided a prevalence estimate of 85 per 100,000 for the period 1989 to 1996. A 50% increase was observed in the number of women reporting MS for 1991 through 1994 compared to an earlier estimate for 1982 through 1986 [4]. Recent review indicates that almost one in 1,000 people in the United States have MS [5].

Little is known about the aetiology of MS. Epidemiological studies suggest that increased risk may be related to an interaction between genetic predisposition and several environmental factors. Among these are infectious agents, radiation, occupational exposures, nutritional factors, smoking, and exposure to organic solvents [6-10].

*Address correspondence to this author at the College of Medicine, University of Toledo, 3120 Glendale Avenue, Toledo, OH 43614, USA; Tel: 419-383-4089; Fax: 419-383-6244; E-mail: sadik.khuder@utoledo.edu

[§]These authors contributed equally to this work.

Considerable worldwide variation in the occurrence of MS according to latitude has been reported with an increasing south to north gradient in the northern hemisphere [11]. In Australia, increased prevalence rates in a southerly direction were observed across the continent [12, 13]. However, significant differences were reported between urban and rural regions within the same latitude and with significantly higher prevalence rates in rural areas [14-16].

In this study, we describe the pattern of hospital admissions for MS patients in selected counties in Ohio and investigate the urban/rural differences.

METHODS

Approval for the study was obtained from University of Toledo Institutional Review Board. We examined Hospital discharge data from 1999-2004 for residents in eight counties in Ohio. These counties are Cuyahoga, Franklin, Hamilton, Lucas, Mahoning, Montgomery, Portage, and Wood.

Data included date of admission, primary (MS-P) and secondary diagnoses (MS-S), length of stay, sex, date of birth, city of residence and zip code. We identified patients diagnosed with MS based on the International Classification of Diseases Ninth Revision, Clinical Modification (ICD-9-CM) codes. To be included in the analysis, a patient had to have the primary diagnosis for admission or any of the 14 diagnoses recorded as ICD-9 code 340. Due to the limited number of MS cases before age 18, we examined only admissions for adults (age ≥18 years). Multiple admissions for the same patient in a given year were identified by

1874-2971/09 2009 Bentham Open

matching the patient's birth date, gender and zip code for that particular year.

Population data for cities in the selected counties was obtained from the 2000 census (Bureau of the Census). Data on the number of MS patients living in northern Ohio was obtained from the National Multiple Sclerosis Society (Northwestern Ohio Chapter, Ohio Buckeye Chapter).

We used the Bureau of the Census Urban and Rural Classification system to classify cities into urban and rural areas. Accordingly, rural areas were defined as territory, population, and housing units located outside of urbanized areas or urban clusters. Rural areas were defined as those with fewer than 2,500 residents or areas where people live in open country. The 2000 census population data for cities were used as the denominator for rates estimation for the duration included in this study. For each city, demographic data on racial composition, median family income, and level of education were retrieved from the 2000 census.

Data Analysis

Annual admission rates were calculated for 1999-2004, and reported as number of cases per 100,000 populations. We compared the number of admissions, accounting for multiple admissions, to the number of MS patients living in the particular county. Comparisons of the demographic variables and MS were performed using the Chi-square test. Cochran-Armitage Trend Test was used to examine yearly changes in admission rates.

We examined the relation between admission rates and living in rural area using Poisson regression model. The exponent of the estimated parameter (β) obtained from the model was taken as an estimate of the admission rate ratio (ARR). Adjusted ARR was calculated for age group, gender and rural residence. All statistical analyses were performed with SAS 9.1 (SAS Institute, Inc., Cary, NC). Values of $p \leq 0.05$ were considered significant.

RESULTS

Between 1999 and 2004, a diagnosis of MS was recorded for 15,389 admissions (Table **1**). Of these admissions, 3,467 had MS as the primary diagnosis. An upward trend in the total number of admissions is obvious in the table. The number of admissions have increased from 2228 in 1999 to 2805 in 2004 (p=0.001). Admission rates for MS as a primary diagnosis ranged from 17 per 100,000 to 20 per 100,000 and with an average rate of 19 per 100,000. Estimates for total admissions ranged from 70 per 100,000 to 90 per 100,000. The average rate was 82 per 100,000.

Table 1. Number of Hospital Admissions for MS Patients from 1999 to 2004

Year	Number of Admissions		Rate per 100,000	
	Primary	Total	Primary	All
1999	581	2228	19	70
2000	576	2373	17	80
2001	591	2651	20	80
2002	563	2644	19	80
2003	594	2688	18	90
2004	562	2805	18	90
Total	3467	15389	19	82

The distributions of admissions by demographic variables are presented in Table **2**. The admission rate was higher in females (110 per 100,000 compared to 50 per 100,000 in males, p=0.0001). Admission rate for the older age group (≥ 45 years) was significantly higher than the younger age group (18-44 years). The rate for rural residence was significantly higher than urban residence.

Table 2. Characteristics of the MS Subjects Included in the Analysis

	Number	Rate Per 100,000	P-Value
Gender			
Male	4124	50	0.0001
Female	11265	110	
Age Group			
18-44	4849	50	0.0001
≥ 45	10540	120	
Residence			
Urban	14276	80	0.0001
Rural	1113	160	

Table **3** shows the results of the Poisson regression. A small but significant increase was noted in the ARRs after year 2001 (ARR=1.12, 95% CI, 1.09-1.16). The ARR for female was 2.44 (95% CI 2.36-2.53). The ARR for older age group was 2.45. Finally, the ARR for rural residence was 1.23 (95% CI 1.17-1.35).

Table 3. Poisson Regression Model for Predictors of MS Related Admissions

	ARR	95% CI
Year		
1999-2001	1	
2002-2004	1.12	1.09-1.16
Gender		
Male	1	
Female	2.44	2.36-2.53
Age Group		
18-44	1	
≥ 45	2.45	2.37-2.54
Residence		
Urban	1	
Rural	1.23	1.17-1.35

To estimate the number of MS patients in a particular year, we removed multiple admissions for the same patients in that year. In 1999, 1756 MS patients were admitted to hospitals in the selected counties. The largest number was from Cuyahoga County (34.6%). Over the years, there was an increase in the number of MS patients and for all the counties (Table **4**).

DISCUSSION

In our analysis of data from eight counties in Ohio, the estimated rate of admission for MS patients was 66 per 100,000. This estimate is within the range of rates reported

from similar regions in the United States [17] and European countries [18, 19] using population-based ascertainment. However, the estimate is lower than MS prevalence rates reported in the literature for similar region in the United States [20], Canada [21], and United Kingdom [22]. The number of MS patients identified in this study is lower than the patients registered at the local Multiple Sclerosis Society. Hospital admissions often underestimate the actual number of MS cases in the community as it excludes patients who are treated at the outpatient facilities. Moreover, the likelihood of hospital admission for patient on disease-modifying therapies is low during the relapse and progression free observation period.

Table 4. Number of Admissions with MS* for Selected Counties in Ohio

County	Number of Admissions with MS					
	1999	2000	2001	2002	2003	2004
Cuyahoga	608	654	767	719	791	768
Franklin	328	374	328	330	359	366
Hamilton	274	286	295	288	298	336
Lucas	188	158	199	212	228	224
Mahoning	76	105	135	137	145	134
Montgomery	181	177	186	205	245	202
Portage	53	48	54	53	61	55
Wood	48	41	42	46	57	65
Total	1756	1843	2006	1990	2184	2150
Rate per 100,000	57	60	66	65	71	70

*After eliminating multiple admissions for the same patient.

We found a higher hospital admission rate for MS in females compared to males. This is similar to the findings of other studies in the literature [4]. The higher rate in female may reflect better survival with the disease [23] or some risk factor specific to the female gender [24]. Although, the exact mechanism for the gender influence on the susceptibility and course of MS is largely unknown, increasing evidence suggests that sex hormones play an important role in susceptibility and progression of the disease [25-27].

The findings of our study suggest an association between admission rates and residency in rural region. Higher admission rates in rural areas may be due to higher comorbid conditions, differential survival rates, confounding variables or possibly risk factors associated with rural environment. It is also possible that patients in the rural and urban areas differ from each other in seeking medical care. There is some evidence from the literature that patients tend to migrate from rural area to city after the onset of the disease to be near specialist clinics, and other supportive facilities [13]. One study [28] reported a significantly larger proportion of people with MS in urban areas had a neurologist as their primary care physician. Moreover, a significantly lower probability of seeing a neurologist was reported for people who lacked health insurance, were poor, or lived in rural areas [29]. Rural residents travel significantly greater distances to receive MS-focused care than their urban counterparts do. Limited access to specialized care in rural areas may result in restricted access to disease modifying treatment. Thus, disease activity and course may be more severe in patients in rural areas, which may cause higher admission rates (e.g. for steroid treatment) or any secondary reason due to more severe cases of the disease. Limited availability of specialized care in rural areas, and greater travel time and distance required to receive care from specialists, may lead to higher admission rates in nearby hospitals.

The aetiology of MS remains unknown. The leading hypothesis is that MS occurs as the result of viral infection in susceptible individuals [30]. Susceptibility could be related to the route of transmission or to other age-related covariates, or it may be hormonally mediated [31]. Recent studies suggest that viral or bacterial infections or reactivations may trigger clinical exacerbations in relapsing-remitting MS [6, 32]. It is not clear whether infection(s) triggers MS or whether elevated markers of infection are secondary to the underlying inflammatory processes of the disease. The possibility of infections stemming from animals is higher in rural areas as the opportunity for contact with a farm or raw farm products is increased. This is in line with the mathematical models of MS proposed for communities reporting high prevalence [33]. In a twin study [34], contact with farm animals was found to be a significant environmental variable contributing to MS. Higher prevalence rate was reported when childhood is spent in rural areas [35]. Moreover, higher prevalence of MS in farmers and agricultural workers from the Northern Ireland register of MS has been reported [36]. Therefore, the high admission rates of MS in rural areas could be related to risk factors, possibly infectious agents common in the rural environment.

Our study has several limitations that need to be taken into consideration. The data only includes people who were admitted to hospital and thus may not be representative of all those with MS in that particular city or county. Only approximately 30% of patients were admitted for MS as a principal diagnosis and this may cause a bias to calculate any prevalence rate. We focused on admission according to the place of residence at the time of admission to the hospital. However, this residence may not be the same residence at younger age especially at the time when disease was likely acquired. We did not have residential history for the subjects. Finally, other confounding variables (such as race, socioeconomic status, smoking, diet, vitamin D level, ultraviolet light or other exposures etc.) cannot be excluded.

CONCLUSIONS

Our findings suggest that hospital admission rates for MS patients are higher among women and in rural areas. Estimate of MS prevalence based on hospital discharge data underestimates the actual prevalence rate. The association between hospital admission rates and residence in rural areas warrant further study to improve care for MS patients.

ACKNOWLEDGEMENTS

The authors wish to thank the National Multiple Sclerosis Society (Northwestern Ohio Chapter, Ohio Buckeye Chapter) for providing data for this study. Also thanks to

Maureen Gilmor for her assistance in proofreading the manuscript.

REFERENCES

[1] van Oosten BW, Truyen L, Barkhof F, Polman CH. Multiple sclerosis therapy: a practical guide. Drugs 1995; 49: 200-12.

[2] Noseworthy JH, Lucchinetti C, Rodriguez M, Weinshenker BG. Multiple sclerosis. N Engl J Med 2000; 343: 938-52.

[3] National Institute of Neurological Disorders and Stroke (NINDS). National Institute of Health (NIH). Multiple Sclerosis: Hope through Research. [Accessed 12 Nov 2008]. Available from: http://www.ninds.nih.gov/disor ders/multiple_sclerosis/detail_multiple_sclerosis.htm

[4] Noonan CW, Kathman SJ, White MC. Prevalence estimates for MS in the United States and evidence of an increasing trend for women. Neurology 2002; 58: 136-8.

[5] Hirtz D, Thurman DJ, Gwinn-Hardy K, Mohamed M, Chaudhuri AR, Zalutsky R. How common are the "common" neurologic disorders? Neurology 2007; 68: 326-37.

[6] Granieri E, Casetta I, Tola MR, Ferrante P. Multiple sclerosis. infectious hypothesis. Neurol Sci 2001; 22: 179-85.

[7] Axelson O, Landtblom AM, Flodin U. Multiple sclerosis and ionizing radiation. Neuroepidemiology 2001; 20: 175-8.

[8] Landtblom AM. Exposure to organic solvents and multiple sclerosis. Neurology 1997; 49: S70-4.

[9] Lauer K. Diet and multiple sclerosis. Neurology 1997; 49: S55-61.

[10] Riise T, Nortvedt MW, Ascherio A. Smoking is a risk factor for multiple sclerosis. Neurology 2003; 61: 1122-4.

[11] Kurtzke JF. Geography in multiple sclerosis. J Neurol 1977; 215: 1-26.

[12] Hammond SR, de Wytt C, Maxwell IC, *et al.* The epidemiology of multiple sclerosis in Queensland, Australia. J Neurol Sci 1987; 80: 185-204.

[13] Hammond SR, McLeod JG, Millingen KS, *et al.* The epidemiology of multiple sclerosis in three Australian cities: Perth, Newcastle and Hobart Brain 1988; 111: 1-25.

[14] Sotgiu S, Pugliatti M, Sotgiu A, Sanna A, Rosati G. Does the "hygiene hypothesis" provide an explanation for the high prevalence of multiple sclerosis in Sardinia? Autoimmunity 2003; 36: 257-60.

[15] Murray TJ. An unusual occurrence of multiple sclerosis in a small rural community. Can J Neurol Sci 1976; 3: 163-6.

[16] Lauer K, Firnhaber W. Epidemiological investigations into multiple sclerosis in Southern Hesse. IV: the influence of urban and rural environment on disease risk. Acta Neurol Scand 1985; 72: 403-6.

[17] Williamson DM, Henry JP, Schiffer R, Wagner L. Prevalence of multiple sclerosis in Texas counties, 1998-2000. J Environ Health 2007; 69: 41-5.

[18] Hirtz D, Thurman DJ, Gwinn-Hardy K, Mohamed M, Chaudhuri AR, Zalutsky R. How common are the "common" neurologic disorders? Neurology 2007; 68: 326-37.

[19] Vukusic S, Bockstael VV, Gosselin S, Confavreux C. Regional variations in the prevalence of multiple sclerosis in French farmers. J Neurol Neurosurg Psychiatry 2007; 78: 707-9.

[20] Mayr WT, Pittock SJ, McClelland RL, Jorgensen NW, Noseworthy JH, Rodriguez M. Incidence and prevalence of multiple sclerosis in Olmsted County, Minnesota, 1985-2000. Neurology 2003; 61: 1373-7.

[21] Warren S, Warren KG. Prevalence, incidence, and characteristics of multiple sclerosis in Westlock County, Alberta, Canada. Neurology 1993; 43: 1760-3.

[22] Murray S, Bashir K, Penrice G, Womersley SJ. Epidemiology of multiple sclerosis in Glasgow. Scott Med J 2004; 49: 100-4.

[23] Wallin MT, Page WF, Kurtzke JF. Epidemiology of multiple sclerosis in US veterans. VIII: Long-term survival after onset of multiple sclerosis. Brain 2000; 123(Pt 8): 1677-87.

[24] Confavreux C, Vukusic S, Adeleine P. Early clinical predictors and progression of irreversible disability in multiple sclerosis: an amnesic process. Brain 2003; 126: 770-82.

[25] Zorgdrager A, De Keyser J. Premenstrual exacerbations of multiple sclerosis. J Neurol Neurosurg Psychiatry 1998; 65: 279-80.

[26] Smith R, Studd JW. A pilot study of the effect upon multiple sclerosis of the menopause, hormone replacement therapy and the menstrual cycle. J R Soc Med 1992; 85: 612-3.

[27] Dalal M, Kim S, Voskuhl RR. Testosterone therapy ameliorates experimental autoimmune encephalomyelitis and induces a T helper 2 bias in the autoantigen-specific T lymphocyte response. J Immunol 1997; 159: 3-6.

[28] Buchanan RJ, Wang S, Stuifbergen A, Chakravorty BJ, Zhu L, Kim M. Urban/rural differences in the use of physician services by people with multiple sclerosis. Neurorehabilitation 2006; 21: 177-87.

[29] Minden SL, Hoaglin DC, Hadden L, Frankel D, Robbins T, Perloff J. Access to and utilization of neurologists by people with multiple sclerosis. Neurology 2008; 70: 1141-9.

[30] McMichael AJ, Hall AJ. Does immunosuppressive ultraviolet radiation explain the latitude gradient for multiple sclerosis? Epidemiology 1997; 8: 642-5.

[31] Riise T, Gronning M, Klauber MR, Barrett-Connor E, Nyland H, Albrektsen G. Clustering of residence of multiple sclerosis patients at age 13 to 20 years in Hordaland, Norway. Am J Epidemiol 1991; 133: 932-9.

[32] Vollmer T. The natural history of relapses in multiple sclerosis. J Neurol Sci 2007; 256(Suppl 1): 5-13.

[33] Murrell TG, Harbige LS, Robinson IC. A review of the aetiology of multiple sclerosis: an ecological approach. Ann Hum Biol 1991; 18: 95-112.

[34] Bobowick AR, Kurtzke JF, Brody JA, Hrubec Z, Gillespie M. Twin study of multiple sclerosis: an epidemiologic inquiry. Neurology 1978; 28: 978-87.

[35] Murrell TG, O'Donoghue PJ, Ellis T. A review of the sheep-multiple sclerosis connection. Med Hypotheses 1986; 19: 27-39.

[36] Kurtzke JF. Epidemiologic contributions to multiple sclerosis: an overview. Neurology 1980; 30: 61-79.

Received: November 19, 2008 Revised: March 2, 2009 Accepted: March 5, 2009