Giovanni Savettieri Giuseppe Salemi Paolo Ragonese Paolo Aridon Giovanni Scola Giovanna Randisi

Prevalence and incidence of multiple sclerosis in the city of Monreale, Italy

Received: 25 March 1997 Received in revised form: 30 June 1997 Accepted: 10 July 1997

G. Savettieri (⊠) Department of Neurological Sciences, University of Naples "Federico II", Via Sergio Pansini, 5, I-80131 Naples, Italy Tel.: +39-81-7462660, Fax: +39-81-7462667

G. Salemi · P. Ragonese · P. Aridon · G. Scola · G. Randisi Institute of Neuropsychiatry, University of Palermo, Via Gaetano La Loggia, 1, I-90129 Palermo, Italy Abstract The prevalence and incidence of multiple sclerosis (MS) in the city of Monreale, southern Italy were ascertained 10 years after a preliminary study in the same area. The study was undertaken in a population of 26,256 people. The patients were classified according to Poser's criteria. The prevalence of MS on 31 December 1991 was 72.4 per 100,000 population. The incidence of MS for the period 1981-1991 was 3.3/100,000 per year. The mean period between onset and diagnosis of MS was 4.9 years for those patients found during this survey and 9.2 years for those in the first study. This study shows an increase of MS

prevalence in Monreale city and a high incidence. The findings parallel the reduction of the lag time between onset and diagnosis.

Key words Multiple sclerosis · Epidemiology · Prevalence · Incidence · Italy

Introduction

The interest in southern Europe in epidemiological research on multiple sclerosis (MS) began in 1976 as a result of studies in greater London and the West Midlands in which the prevalence among Italian immigrants was shown to be similar to that found in the general English population, but no Maltese MS patients were found, although ten cases were expected [2]. This prompted studies in Malta [21], nearby Sicily [3, 4, 17,18] and in other parts of Italy [7, 8, 10, 14, 20]. MS prevalence on the islands of Sicily and Sardinia has been the topic of a number of investigations.

In Sicily, four surveys conducted in four different communities have shown MS prevalence rates of between 32 and 51 cases per 100,000 population [3, 4, 17, 18]. The city of Monreale (Palermo province) was one of four cities that were investigated in the preliminary surveys in Sicily. In Monreale, the prevalence of MS on 30 June 1980 was 43 per 100,000 population [17].

We undertook a further study in Monreale to ascertain whether there had been any change in prevalence or incidence rates.

Methods

Monreale is a city situated 9 km from Palermo. The total area is 529 km² and the population on 31 December 1991 was 26,256 (12,874 men, 13,382 women). In 1980 the population was 25,403.

We searched for patients affected by MS who were resident in the study area. The 1980 study formed the basis of this second survey. Two MS patients from the first study had since died. A formal diagnostic reappraisal was made of all patients surviving from the 1980 study. The new patients were identified from the following sources: archives of the Neurological Clinic of the University Hospital of Palermo, of the neurological divisions of the hospitals of Palermo and of the Office for Handicapped Persons of Monreale. All of the general practitioners in Monreale collaborated in the study. The social workers and pharmacists of Monreale were asked if they knew of anyone with symptoms that might be attributable to MS. The records of public and private centres equipped for magnetic resonance imaging (MRI) located in Palermo were studied. Patients were classified according to Poser's criteria [11].

Crude and age- and sex-adjusted prevalence rates were calculated on 31 December 1991. The incidence rate was computed for the period 1 January 1981–31 December 1991. The onset-adjusted-prevalence rate (OAPR) was also estimated by including patients for whom the onset of MS was before the prevalence day, but who were diagnosed subsequently [12]. We also calculated the mean period between the onset of the disease and diagnosis in both the 1980 and 1991 series of patients.

Results

Prevalence

Table 1 Age and sex distribu-tion of the population of Mon-reale in 1981 and 1991

Nine patients (five men and four women) remained of the 11 patients found in the 1980 study, since two patients (a men and a women) had died. Ten new MS patients (three men and seven women) were found during the second study, making a total of 19. One of the ten new patients was a women who experienced the first symptoms of MS in 1976, but was not found in the first study.

Table 1 shows the age and sex distribution of the population of Monreale in 1981 and 1991. Table 2 shows the age- and sex-specific prevalence rates per 100,000 population in 1991. The overall prevalence was 72.4 per 100,000 [95% confidence interval (C.I.) 43.6–113.1], 62.1 for men and 82.2 for women. Age-specific prevalence showed a peak at age 50 years. Prevalence increased with age up to 40 years in men, and up to 50 years in women.

All of the patients were classified as clinically definite multiple sclerosis (CDMS) patients according to the Poser classification [11]. The course of the disease was relapsing-remitting or relapsing-progressive.

The mean age at onset was 30.5 years (range 16–42); 30.3 for men and 30.6 for women. The mean age on 31 December 1991, was 45.3 years (range 23–73); 44.3 for men and 46.1 for women. The mean period between onset of the disease and diagnosis for all 19 patients was 7.3 years (range 1–21); it was higher in women (9.4 years) than in men (4.4 years). Details of lag time between onset and diagnosis for the 19 prevalent patients are shown in Table 3. The average duration of MS from onset to prevalence days was 14.9 years (range 0.5–37); 14.1 for men and 15.5 for women.

The lag time between the onset and the diagnosis of MS for the 11 patients investigated during the first survey was 9.2 years, compared with 4.9 years for the 10 new patients found during the present study. There was a shift to a peak of highest prevalence from 40 years in the 1980

Age (years)	Men		Women		Both sexes	
	Population 1981	Population 1991	Population 1981	Population 1991	Population 1981	Population 1991
0–14	3,200	3,050	3,042	2,844	6.242	5,894
15-24	2,122	2,329	2,060	2,240	4,182	4,569
25-34	1,599	2,128	1,659	2,178	3,258	4,306
35–44	1,275	1,650	1,404	1,722	2,679	3,372
45-54	1,259	1,264	1,338	1,402	2,597	2,666
55-64	924	1,176	1,177	1,258	2,101	2,434
65–74	846	741	942	963	1,788	1,704
75+	414	536	613	775	1,027	1,311
Total	11,639	12,874	12,235	13,382	23,874	26,256

Age (years)	Men			Women			Both sexes		
	Population	Cases	Prevalence (× 100,000)	Population	Cases	Prevalence (× 100,000)	Population	Cases	Prevalence (× 100,000)
0–24	5,379	0	_	5,084	1	19.7	10,463	1	9.6
25-34	2,128	1	47.0	2,178	1	45.9	4,306	2	46.4
35–44	1,650	4	242.4	1,722	2	58.1	3,372	6	118.6
45-54	1,264	1	79.1	1,402	5	356.6	2,666	6	187.5
55-74	1,917	2	104.3	2,221	2	90.0	4,138	4	96.7
75+	536	0	_	775	0	_	1,311	0	-
Total	12,874	8	62.1	13,382	11	82.2	26,256	19	72.4

Patient no.	Sex	Year of onset	Year of diagnosis	Interval (years)	
1	F	1954	1974	20	
2	F	1956	1970	14	
3	F	1958	1979	21	
4	F	1971	1974	3	
5	F	1976	1988	12	
6	F	1983	1987	4	
7	F	1983	1994	11	
8	F	1986	1992	6	
9	F	1987	1989	2	
10	F	1988	1995	7	
11	F	1989	1992	3	
12	М	1962	1966	4	
13	М	1968	1977	9	
14	М	1971	1980	9	
15	М	1973	1975	2	
16	М	1975	1980	5	
17	М	1982	1984	2	
18	М	1991	1992	1	
19	М	1991	1992	1	

Table 3Interval between onset and diagnosis of multiple sclerosis for the 1991 prevalent cases



Fig.1 Age-specific prevalence of multiple sclerosis in Monreale in 1980 and 1991

study to 50 years in the 1991 study (Fig. 1). The OAPR calculated for the 1980 study was 47.2.

Incidence

Between 1981 and 1991, nine subjects (three men and six women) living in the study area experienced their first symptoms of MS. Therefore, the average annual incidence rate was 3.3 per 100,000 population. The age-specific incidence rates of MS in Monreale are shown in

 Table 4
 Average annual incidence rates of multiple sclerosis in Monreale (1 January 1981–31 December 1991)

Age (years)	Population (person-years ^a)	Cases	Incidence (per 100,000)
0–24	114,878	2	1.7
25-34	41,602	1	2.4
35–44	33,280	6	18.0
45+	85,954	0	_
Total	275,714	9	3.3

^aThe person-year count was calculated by taking the mean population figure for 1981 and 1991 and multiplying by 11

Table 4. The highest rate was observed in the age group 35–44 years. Sex-specific incidence was not computed because of the small numbers.

Discussion

The MS prevalence of 72.4 per 100,000 population found in the present study is higher than has been reported previously [17] and is the highest observed in the Mediterranean area, except for Sardinia.

Prevalence figures often increase in repeated surveys [13, 19]. This may be caused by a real change in MS risk, or may reflect improved diagnosis resulting from greater awareness and new and more sophisticated diagnostic procedures. On the other hand, it may also be related to longer survival. That diagnostic accuracy and, as a consequence, earlier diagnosis are partially responsible for the increase in prevalence rate is shown in the reduction in the length of time between onset and diagnosis. There is a remarkable difference in the period of time between clinical onset and diagnosis when the 1980 series is compared with the new series of patients. Although this difference may partly account for the increasing prevalence, we cannot rule out the possibility that other elements have also contributed and that the numbers are not large enough to make the difference statistically significant after correcting for earlier diagnosis.

The incidence rate of MS observed in Monreale was 3.3 per 100,000 population per year. A multicentre study carried out in Italy [1] reported a mean incidence of 1.9 per 100,000 population. The two surveys are not comparable because of differences in study design.

The results of this second survey on MS in Monreale confirm that the disease has a high frequency in Sicily. This is corroborated by the high incidence rate. Other surveys confirm that Sicily is a high-risk area [5–7, 9, 14, 16]. Sicily contrasts with Malta where a low prevalence has been found [21]. All of these studies are methodolog-ically similar, and the populations under investigation were small, making an intensive search for patients possible.

An increasing frequency of MS in Sardinia is reported by Rosati et al. [15]. A similar increase cannot be shown at present in Sicily. Perhaps a later follow-up study of prevalence and incidence of MS in Monreale and other cities in Sicily will answer the question of whether there has been a true change in the incidence of MS on the island. Acknowledgements We are particularly grateful to Dr. Geoffrey Dean, Emeritus Director of the Medico-Social Research Board, Dublin, Ireland for helpful comments on the manuscript. We would also like to thank all of the people and institutions that helped us in this study.

References

- Comi G, Martinelli V, Giuliani G, Tola MR, Prencipe M, Jandolo B, Mamoli A, Rosati G, Aiello I, De Fanti CR, Fratiglioni L, Fera L, Savettieri G (1989) Incidence of multiple sclerosis in Italy: a multicenter study. In: Battaglia MA (ed) Multiple sclerosis research. Elsevier, Amsterdam, pp 159–163
- Dean G, McLoughlin H, Brady R, Adelstein AM, Tallet-Williams J (1976) Multiple sclerosis among immigrants to Greater London. BMJ i: 861–864
- 3. Dean G, Grimaldi G, Kelly R, Karhausen L (1979) Multiple sclerosis in southern Europe. I. Prevalence in Sicily in 1975. J Epidemiol Community Health 33:107–110
- 4. Dean G, Savettieri G, Giordano D, Butera C, Taibi G, Morreale S, Karhausen L (1981) The prevalence of multiple sclerosis in Sicily. II. Agrigento city. J Epidemiol Community Health 35:118–122
- Dean G, Aksoy A, Akalin T, Middleton L, Kyriallis K (1997) Multiple sclerosis in the Turkish- and Greekspeaking communities of Cyprus. A United Nations (UNHCR) Bicommunal Project. J Neurol Sci 145:163–168
- 6. Fernadez O, Luque G, San Roman, Bravo M, Dean G (1994) The prevalence of multiple sclerosis in the sanitary district of Velez-Malaga, southern Spain. Neurology 44:425–429

- 7. Granieri E, Rosati G (1982) Italy: a medium or high risk area for multiple sclerosis? An epidemiological study in Barbagia, Sardinia. Neurology 32: 466–472
- Granieri E, Tola R, Paolino E, Rosati G, Carreras M, Monetti VC (1985) The frequency of multiple sclerosis in Italy: a descriptive study in Ferrara. Ann Neurol 17:80–84
- Middleton LT, Dean G (1991) Multiple sclerosis in Cyprus. J Neurol Sci 103: 29–36
- 10. Morganti G, Naccarato S, Elian M, Ferrari P, Kelly R, Karhausen L, Dean G (1984) Multiple sclerosis in the Republic of San Marino. J Epidemiol Community Health 38:23–28
- 11. Poser CM, Paty DW, Scheinberg L, McDonald WI, Davis FA, Ebers GC, Johnson KP, Sibley WA, Silberberg DH, Tourtellotte WW (1983) New diagnostic criteria for multiple sclerosis: guidelines for research protocols. Ann Neurol 13:227–231
- 12. Poser C, Benedikz J, Hibberd P (1992) The epidemiology of multiple sclerosis. The Iceland model. J Neurol Sci 111:143–152
- Rosati G (1989) The infectious hypothesis of multiple sclerosis in epidemiology. The time trend of the disease in Sardinia, Italy. In: Battaglia MA (ed) Multiple sclerosis research. Elsevier, Amsterdam, pp 137–146
- 14. Rosati G, Aiello I, Pirastru MI, Mannu L, Demontis G, Becciu S, Sau G, Zoccheddu A (1987) Sardinia. A high risk area for multiple sclerosis. A prevalence and incidence study in the district of Alghero. Ann Neurol 21: 190–194

- 15. Rosati G, Aiello I, Mannu L (1988) Incidence of multiple sclerosis in the town of Sassari, Sardinia 1965 to 1985: evidence for increasing occurrence of the disease. Neurology 38:384–388
- 16. Rosati G, Aiello I, Pirastru MI, Mannu L, Sanna G, Sau GF, Sotgiu S (1996) Epidemiology of multiple sclerosis in northwestern Sardinia: further evidence for higher frequency in Sardinians compared to other Italians. Neuroepidemiology 15:10–19
- 17. Savettieri G, Daricello B, Giordano D, Karhausen L, Dean G (1981) The prevalence of multiple sclerosis in Sicily. I. Monreale city. J Epidemol Community Health 35:114–117
- 18. Savettieri G, Elian M, Giordano D, Grimaldi G, Ventura A, Dean G (1986) A further study on the prevalence of multiple sclerosis in Sicily: Caltanissetta city. Acta Neurol Scand 73: 71–75
- 19. Shepherd DI, Downie AW (1980) A further study of multiple sclerosis in north-east Scotland. J Neurol Neurosurg Psychiatry 43:310–315
- 20. Sironi L, Mamoli A, D'Alessandro G, Camerlingo M, Bottacchi E (1991) Frequency of multiple sclerosis in Valle d'Aosta, 1971–1985. Neuroepidemiology 10:66–69
- Vassallo L, Elian M, Dean G (1979) Multiple sclerosis in southern Europe. II. Prevalence in Malta in 1978. J Epidemiol Community Health 33: 111–113