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Survival in multiple sclerosis correlates to the level of hygiene and mortality

Przeżycie w stwardnieniu rozsianym koreluje z poziomem higieny i umieralnością

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Abstract

Introduction: Survival of patients with multiple sclerosis is a complex variable determined by several factors. **Objective of the study** was to ascertain the association between the level of hygiene well as regional mortality and survival of patients with multiple sclerosis. **Study design:** The study of relation between variables included 14,200 multiple sclerosis patients (male – 6,025, female – 8,175) who died in the period 1981–2010 in Poland. The average survival of male and female patients with multiple sclerosis correlated to the marker of hygiene level (the late mortality in infants rate per 1,000 live births) and average, annual, sex-adjusted mortality rates for multiple sclerosis in towns and in the countryside of Poland (1981–2010). All demographic data were obtained from the Central Statistical Office in Warsaw. **Results:** A longer survival of male and female patients with multiple sclerosis showed a significant correlation to a higher hygiene level in Poland: $r = -0.867$, $r = -0.902$, $p = 0.0001$. Sex-adjusted mortality rates for women with multiple sclerosis in towns and villages were much higher than the analogous rates for men with multiple sclerosis; $p = 0.0001$, $p = 0.019$. A longer duration of life in male and female patients with multiple sclerosis demonstrated a strong, inverse correlation to a lower mortality in the countryside: $r = -0.803$, $r = -0.630$, $p = 0.0001$. The survival of women with multiple sclerosis did not show correlation to sex-adjusted mortality rates in towns: $r = -0.126$, $p = 0.90$. **Conclusions:** The higher level of hygiene was associated with the longer survival of multiple sclerosis patients. The survival of male and female patients with multiple sclerosis showed an inverse correlation to the lower mortality in rural regions. The duration of life in women did not correlate to the higher mortality in towns.

Key words: multiple sclerosis, survival, hygiene level, mortality

Streszczenie

Wprowadzenie: Przeżycie chorych na stwardnienie rozsiane jest złożoną zmienną zależną od licznych czynników. **Celem badania** było stwierdzenie asocjacji między poziomem higieny oraz regionalną umieralnością i przeżyciem chorych na stwardnienie rozsiane. **Metoda:** Badanie relacji między zmiennymi objęło 14 200 chorych na stwardnienie rozsiane (mężczyźni – 6025, kobiety – 8175), którzy zmarli w latach 1981–2010 w Polsce. Przeciętne przeżycie mężczyzn i kobiet ze stwardnieniem rozsianym skorelowano z miernikiem poziomu higieny (współczynnikiem późnej umieralności niemowląt na 1000 żywych urodzeń) oraz z przeciętnymi, rocznymi, dostosowanymi do płci współczynnikami umieralności na stwardnienie rozsiane w miastach i na wsi Polski (1981–2010). Wszystkie dane demograficzne uzyskano z Głównego Urzędu Statystycznego w Warszawie. **Wyniki:** Dłuższe przeżycie mężczyzn i kobiet ze stwardnieniem rozsianym wykazało istotną korelację z wyższym poziomem higieny w Polsce: $r = -0{,}867$, $r = -0{,}901$, $p = 0{,}0001$. Dostosowane do płci współczynniki umieralności kobiet ze stwardnieniem rozsianym w miastach i na wsi były znamiennie wyższe niż analogiczne współczynniki u mężczyzn: $p = 0{,}0001$, $p = 0{,}019$. Dłuższe przeżycie mężczyzn i kobiet ze stwardnieniem rozsianym cechowało się mocną, odwróconą korelacją z niższą umieralnością na wsi: $r = -0{,}803$, $r = -0{,}630$, $p = 0{,}0001$. Długość życia kobiet nie korelowała z wyższą umieralnością w miastach: $r = -0{,}126$, $p = 0{,}90$. **Wnioski:** Im wyższy był poziom higieny, tym dłuższe było przeżycie chorych na stwardnienie rozsiane. Przeżycie mężczyzn i kobiet ze stwardnieniem rozsianym wykazało odwróconą korelację z niższą umieralnością na wsi. Długość życia kobiet nie korelowała z wyższą umieralnością w miastach.

Słowa kluczowe: stwardnienie rozsiane, przeżycie, poziom higieny, umieralność

INTRODUCTION

Survival in multiple sclerosis (MS) in an important demographic and clinical variable that results from the interaction between several differential factors (Poser *et al.*, 1989). Retrospective, population-based and case-control studies demonstrated the effect of positive determinants on the life duration in MS (Wallin *et al.*, 2000). The studies showed that an early age at onset, remittent course, less frequent comorbidities, slight disability, healthy lifestyle and better medical care contributed to a longer survival (Ascherio and Munger, 2007; Brønnum-Hansen *et al.*, 2004; Confavreux *et al.*, 2003; Leibowitz *et al.*, 1969; Wallin *et al.*, 2000). Contemporary analysis revealed the correlation of survival to socioeconomic status and a higher level of education, yet the relationship with the hygiene level and residential location was only scantily investigated (Wallin *et al.*, 2000). The previous epidemiological study in Poland showed an increased life duration in MS (Cendrowski, 2011). However, a detailed analysis of the relation between environmental factors and survival was not carried out.

The present study ascertains the relation between the hygiene level as well as regional mortality and survival in the large cohort of deceased MS patients in Poland. The retrospective, long-term examination was based on the correlation test of the average survival in MS related to the hygiene level and to the sex-specific MS mortality rates in urban and rural areas. The outcome of this study may add new data concerning the relation between the hygiene level and residential location and survival in MS.

MATERIAL AND METHOD

The study of relation between the average survival and environmental factors included 14,200 MS patients (male, M – 6,025, female, F – 8,175) deceased in the period between 1981 and 2010 in Poland. The description of the cohort under investigation (except the years 2008–2010) is presented in the previous article on the topic (Cendrowski, 2011). The objective of the study was to ascertain the association between the level of hygiene and survival in MS as well as to consider the correlation between the duration of live of patients and the sex-adjusted mortality rates (SAMR) in urban and rural areas of Poland. The analysis concerned all deaths of patients diagnosed with MS according to the ICD (International Classification of the Diseases) codes 6/7–10, 340, 345, G35. All demographic and diagnostic data for this study were obtained from the Central Statistical Office in Warsaw. Attributes of the material comprised the annual number of deceased MS patients, their sex, age and place of residence at death and the number of urban and rural population in Poland (1981–2010). In the first part of the analysis, the relation between the average, annually registered life duration of MS individuals and the marker of hygiene level was laid down. The annual late mortality rate in infants (LMI) per 1,000 live birth in Poland (1981–2010) was used as the marker of the hygiene level. The LMI rates were calculated in the cohort of 56,780 infants who have died between the 28th day and the first year of life over three decades. The second part of analysis described the relation of the average life duration in MS to the annual, average SAMR in MS. The SAMR for men and women with MS were calculated in accordance with the following formula:

$$\frac{\text{The annual number of men or women with MS deceased in urban or rural areas}}{\text{The annual number of men or women from the general population residing in urban or rural areas}} \times 100{,}000$$

The correlation between variables was carried out using the test by Pearson. The linear regression test was employed in the evaluation of the relationship between long-term average survival in MS patients and the calendar years or the annual SAMR in Poland (1981–2010).

RESULTS

The entire cohort under investigation featured 6,025 men and 8,175 women with MS who died in Poland in the years 1981–2010. Tab. 1 shows that the F:M ratio was 1,35:1.0. The average life duration in men and women was 53.4 (*SD* 2.1) years and 53.9 (*SD* 2.5) years. The difference between the number of male and female patients survival was not significant; $p = 0.417$. The median of the life duration was 53.4 and 53.9 years.

The linear regression test proved that the life duration of MS individuals significantly increased in the years 1981–2010. The correlation coefficient between the average survival and the calendar years was high: $r = 0.890$ (men) and $r = 0.919$ (women), $p < 0.0001$. The maximal lengthening of the average survival in men reached 7.8 years and in women 10.0 years (Tab. 1). It is worth mentioning that patients who deceased in the years 2001–2010 had lived longer than patients who had died in the years 1981–1990. The difference in male survival was 4.0 (55.6 *vs.* 51.6) years and in female survival – 5.2 (56.6 *vs.* 51.4) years. The outcome supports the hypothesis that contemporary lifestyle, socioeconomic status and medical care including rehabilitation contributed to a longer survival.

The main objective of this study was to ascertain whether survival in MS individuals correlates to the hygiene level in the general population and to the sex-specific mortality for patients with the said disease in towns and in the countryside. The annual mean LMI rate as the marker of hygiene level decreased from 6.4 to 1.5 per 1,000 live births in the years 1981–2010 (Tab. 1). The correlation between the annual survival in men and women with MS and the LMI rate showed a strong inverse relationship: $r = -0.867$ (men), $r = -0.902$ (women), $p = 0.0001$. The schematic relation of these variables is presented in Fig. 1.

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Year	The general number of deceased MS patients yearly		The SAMR for MS in towns per 100,000 residents		The SAMR for MS in the countryside per 100,000 inhabitants		The LMI rate per 1,000 live birth yearly	The average survival of MS patients	
	Men	Women	Men	Women	Men	Women		Men	Women
1981	267	290	1.32	1.43	1.76	1.74	6.4	49.4	49.2
1982	243	273	1.26	1.42	1.51	1.52	6.2	52.0	49.6
1983	284	319	1.42	1.50	1.81	1.98	6.0	50.8	50.0
1984	229	308	1.18	1.64	1.39	1.58	5.9	50.0	49.9
1985	251	291	1.32	1.45	1.45	1.62	5.4	51.1	51.5
1986	238	304	1.01	1.36	1.71	1.92	5.2	52.2	54.0
1987	201	283	1.08	1.37	1.09	1.60	5.0	53.2	52.0
1988	232	293	1.10	1.32	1.48	1.80	4.6	51.3	51.1
1989	231	275	1.25	1.36	1.23	1.49	4.4	52.6	52.5
1990	261	312	1.28	1.64	1.60	1.52	4.4	53.9	53.8
1991	235	309	1.18	1.57	1.39	1.56	4.2	51.0	53.4
1992	206	272	1.01	1.57	1.24	1.36	4.3	50.7	51.8
1993	216	276	1.10	1.39	1.24	1.43	3.8	51.5	52.9
1994	194	291	1.02	1.56	1.06	1.22	3.8	53.2	54.4
1995	200	275	1.04	1.43	1.12	1.34	3.5	53.8	53.9
1996	223	273	1.15	1.42	1.26	1.34	3.3	53.0	54.5
1997	168	190	0.63	0.92	1.24	1.04	2.8	52.5	56.2
1998	144	184	0.77	0.97	0.76	0.86	2.6	53.9	53.8
1999	204	256	1.14	1.49	1.03	0.97	2.5	53.7	53.6
2000	171	264	0.95	1.58	0.86	0.92	2.5	56.5	54.6
2001	186	271	1.04	1.49	0.94	1.17	2.3	55.3	56.1
2002	183	264	1.03	1.44	0.91	1.16	2.2	53.7	56.0
2003	156	270	0.84	1.48	0.76	1.18	2.0	54.7	56.2
2004	158	218	0.82	1.16	0.90	1.01	1.9	54.7	55.0
2005	184	267	0.89	1.41	0.87	1.22	1.9	55.2	55.2
2006	169	272	0.94	1.47	0.87	1.22	1.6	56.4	55.2
2007	171	265	1.05	1.40	0.70	1.14	1.7	55.8	56.4
2008	174	268	0.91	1.50	0.98	1.11	1.7	56.7	58.2
2009	162	290	0.91	1.50	0.82	1.41	1.6	57.0	59.2
2010	165	253	0.96	1.38	0.78	1.08	1.5	57.2	57.9
1981–2010	6025	8175							
Mean *SD*			1.05 (0.18)	1.42 (0.16)	1.16 (0.32)	1.35 (0.29)	3.51 (1.57)	55.5 (1.15)	56.5 (1.42)

Tab. 1. The average survival of patients in relation to the sex-adjusted mortality rate (SAMR) in multiple sclerosis (MS) and to the rate of late mortality in infants (LMI) in Poland (1981–2010)

The outcome indicates that a higher level of hygiene (HLH) was related to a longer survival in Polish patients. It is obvious that the level of hygiene has improved in towns and villages and it may be conceived that the duration of life became longer in both urban and rural MS residents.

Another part of the analysis considered the relation between survival and the SAMR for MS in urban and rural areas. There were generally 8,717 deaths in towns (M – 3544, F – 5173) and 5483 in the countryside (M – 2481, F – 3002). Tab. 1 shows that the average SAMR for MS women was higher than the SAMR for MS men in Polish towns and villages. The preponderance of female mortality in urban and rural areas was statistically significant: $p = 0.0001$ (towns), $p = 0.019$ (villages). The average life duration in men and women with MS was investigated with regard to the SAMR in towns and in the countryside. A significant inverse correlation was found for men who resided in towns and in the countryside: $r = -0.564$, $p = 0.001$ and $r = -0.803$, $p = 0.0001$. These accordant outcomes demonstrated that the longer the survival of MS men in urban and rural areas, the lower the SAMR for male residents. The relationship between male survival and sex-specific rural male mortality is presented in Fig. 2.

In accordance with the former findings, the average survival in women with MS showed a significant inverse correlation to the SAMR in the countryside: $r = -0.630$, $p = 0.0002$. However, in contrast to that outcome, the average survival in women with MS did not correlate to the SAMR in Polish towns. The low inverse correlation

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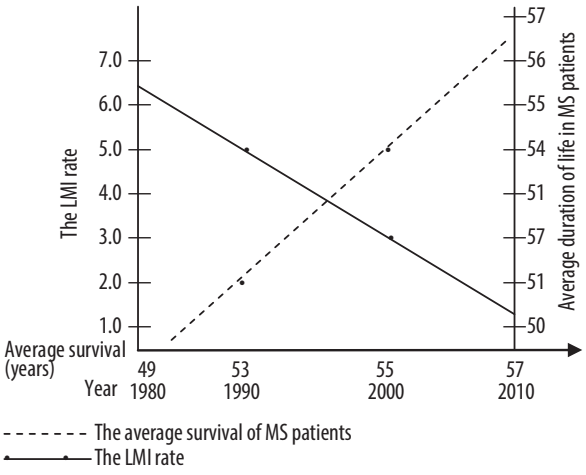

Fig. 1. Schematic presentation of an inverse relationship between an increasing level of hygiene (descending LMI rate) and a longer duration of life in MS patients in Poland 1981–2010

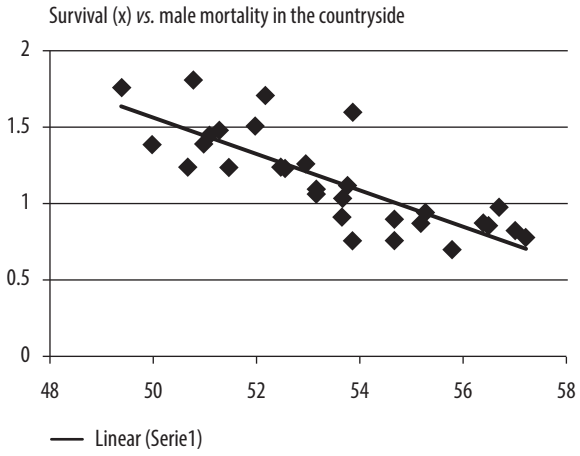

Fig. 2. Diagram of the linear regression test of the relationship between MS male survival (x axis) and the SAMR for men in the countryside (y axis). The correlation coefficient was: r = *–0.803,* p < *0.0001*

coefficient was calculated: $r = -0.126$, $p = 0.90$. A possible hypothesis is that there was a disproportionally high number of women with MS in urban areas considered in the SAMR to the average survival of all MS female patients. Instead, the lower number of countrywomen with MS in the SAMR corresponded to the average survival in the whole MS female population.

DISCUSSION

The current study shows an increase of survival in MS patients over three decades in Poland. The result is in line with previous findings in the whole country and in West Pomerania (Cendrowski, 2011; Potemkowski, 1999). A marked extension of survival was observed in the Danes with MS who lived about 10 years longer (1949–1988) (Brønnum-Hansen *et al.*, 2004). Attention was drawn to the fact that patients deceased in Poland in the years 2001–2010 had had the survival of 5 years longer than those who had died in the years 1981–1990. A similar finding was ascertained in an epidemiological study in Norway. The length of life in the Norwegian patients deceased in the years 1983–2000 was longer than the duration of life in patients who died in the years 1953–1957; $p = 0.001$ (Grytten Torkildsen *et al.*, 2008). The outcomes indicate that environmental, socioeconomic and medical care factors affected survival in MS (Marrie *et al.*, 2008). The longevity in MS is the result of a complex interaction between several factors, one of them being the level of hygiene in the general population. The LMI rate was used in the MS prevalence study in Europe and in the Middle East (Leibowitz *et al.*, 1967). That investigation showed a strong association between the HLH and the higher prevalence particularly in Western Europe. A more recent analysis proved that the HLH raises the risk of MS, but on the other hand, it defends the health status, improves the quality of life and contributes to a longer survival (Cendrowski, 2014). The association of the HLH with a longer survival in Polish MS patients is consistent with the data from the recent international review. Mean age at death in seven countries of Europe and North America in terms of the HLH was 65 years (Scalfari *et al.*, 2013). In contrast, mean age at death in five Asian countries with a lower level of hygiene was only 35 years (Wasay *et al.*, 2006).

The length of life in MS residents passing away either in towns or in the countryside was the object of this analysis. The previous study taking into account the area of West Pomerania documented very similar duration of life in MS inhabitants who lived in urban or rural areas: 55 *vs.* 54 years in the years 1960–1995 (Potemkowski, 1999). Mortality decreased in men and women with MS who died in the Polish villages, but not in MS women who ended their life in towns (1981–2010). The outcome is in agreement with epidemiological findings in Italy (1974–1993) showing variation in MS female mortality (Tassinari *et al.*, 2001). The question remains why the SAMR for urban MS women did not correlate to their duration of life. There is an overwhelming view that incidence, prevalence and mortality for MS is higher in women than in men (Acheson, 1985; Darmstädter *et al.*, 2008; Warren *at al.*, 2011). In addition, the MS incidence in the Greek urban cohort of females was much more pronounced than in the urban group of male patients (Kotzamani *et al.*, 2012). The higher SAMR in urban MS residents is a natural consequence of more frequent deaths caused by the basic disease and comorbidities. The preponderance of MS women, particularly in towns, confounds the outcome of correlation between the SAMR for urban females with that disease and the average survival. The reason of a more prevalent MS occurrence in women is complex, still partly enigmatic and not fully understood. Infections, immunological regulation, sex hormones and genes come at the top of powerful factors determining the etiology of MS in women.

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Epstein–Barr virus (EBV) was more prevalent in girls at the age of 15–19 years than in boys (Ström, 1960). Female patients have much stronger Th1 immune response mediated by interferon gamma as compared with male patients (Dunn and Steinman, 2013). MS women are more frequently the carriers of HLA-DRB1*15 allele and the transmission of the susceptibility genes is more probable in female-female pairs than in female-male pairs (Chao *et al.*, 2011; Hensiek *et al.*, 2002). Furthermore, urban lifestyle, deficient ultraviolet B radiation in towns, modern, sedentary and stressful work seem to be more hazardous for citified women than for men (Cendrowski, 2015; Kotzamani *et al.*, 2012). Summing up, the present study showed that survival in MS patients correlated to the level of hygiene and for urban as well as rural mortality except for female death rate in the Polish towns.

CONCLUSIONS

A significant positive association was found between the HLH and the average survival of men and women with MS in Poland (1981–2010). An inverse correlation was ascertained between the male survival and the SAMR in all areas of the country. Female survival was inversely correlated to the SAMR in the countryside, but was not associated with the sex-adjusted death rate in towns.

Conflict of interest

The author does not report any financial or personal affiliations to persons or organizations that could negatively affect the content of this publication or claim to have rights to this publication.

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