

Environmental risk factors in the aetiology of multiple sclerosis in Kayseri: a case control study

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ABSTRACT

BACKGROUND: our purpose is to evaluate the possible relationship between multiple sclerosis (MS) and environmental factors in Kayseri.

METHODS: this case control study was conducted on 100 patients with MS and 100 sex-aged and residential area matched control. Data was collected by using face to face interviews. Questionnaire consisted of two parts. The first part was comprised of items related with the participants' socio-demographic features. The second part was related with factors thought to be involved in the occurrence or aggravation of the disease. The Chi-square test and logistic regression were used for analysis.

RESULTS: logistic regression analysis revealed the following as possible risk factors in MS cases: economic status (Odds Ratio (OR): 0.14 adjusted 7.19; Confidence Interval 95% (CI): 0.05-0.43), having a sensitive personality (OR:4.51; 95% CI: 1.10-18.45), familial history of MS (OR:3.28; 95% CI: 1.3-8.27), history of cranial and spinal injury (OR: 2.99; 95% CI: 1.11-8.08), cooking oil consumption (OR:0.07 adjusted 13.5; 95% CI: 0.03-0.20), consumption of legumes and grains (OR: 0.11 adjusted 8.9; 95% CI: 0.03-0.41), and living in dwellings within a distance of 500 meters from transformer base-stations (OR: 6.5; 95% CI: 1.54-28.21).

CONCLUSIONS: we believe that it is necessary to inform the individuals about the risk of MS and their relatives of the results of large-scale joint studies and to offer suggestions based on the data obtained.

Key words: Multiple sclerosis; Environmental risk factors

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INTRODUCTION

Characterized by widespread demyelinating lesions of the central nervous system, and often

affecting young adults, multiple sclerosis (MS) is a chronic and disabling disease. Though its etiology is not precisely known, genetic and environmental factors are implicated [1-5]. The

incidence of MS in women is twice as great as in men [6], varies from region to region in the world and increases in countries nearer to the poles. Studies on immigrants demonstrate that MS is less common among those who have migrated from a region with high incidence of MS, especially in those under 15 years of age [1].

Individuals who have first degree relatives with MS in their family have a 10-25 times greater risk of MS than the normal population, and this risk is closely associated with the degree of the relationship and the sex of the relative [2, 4, 7, 8]. Although genes are effective in the development of MS, genetic and epidemiologic studies indicate that environmental factors also play an important role in determining MS risk [4, 7, 8].

Some studies have suggested that a multitude of viruses, such as Epstein-Barr, may be the cause of MS [1, 4, 9]. Among environmental factors contributing to MS development are nutrition [10, 11], infections [9], trauma [5], surgical operations [5, 12], vaccines [1, 5, 13], chemical agents and metals [1, 14, 15], smoking [16], sunlight [1, 2, 17], keeping pets [7, 18], and stress [19, 20].

The European total mean MS prevalence rate is estimated to be 83 cases per 100 000/year [21]. Although one local study was conducted by Türk Börü et al. on MS in the regions of Marmara and the Black Sea, there is no study in the literature on the incidence and prevalence of MS in Turkey. In that study, the prevalence of MS was found to be 101.4/100 000 for Maltepe in Istanbul, and 51/100 000 on average for 3 coastal cities on the Black Sea [22, 23]. These findings have increased our sensitivity to MS. Our objective in this study is to detect what joint environmental risk factors affect MS patients in the province of Kayseri.

METHODS

Geographical characteristics of the field

This is a case-control study performed in Kayseri. Kayseri, one of the major industrial and commercial centers in Turkey, is located in the Central Anatolian Region between the northern latitudes of 38° 18', and the eastern altitudes of 36° 58' (Figure 1). Its elevation is 1094 m. A continental climate is prevalent in the province.

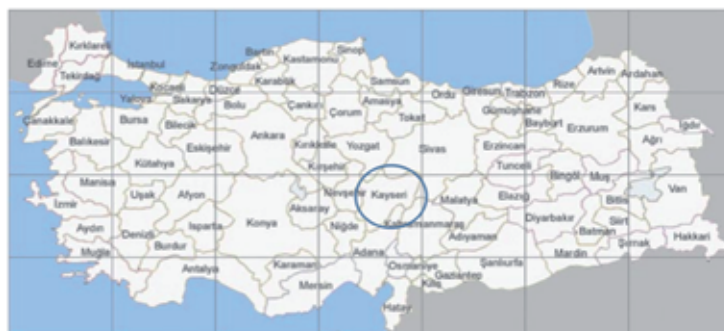
Study participants

Most of the patients in Kayseri were followed up in the university hospital while some went to other hospitals in Kayseri or other cities.

The study was conducted on 100 patients enrolled at the Neurology Policlinic of the Erciyes University Medical Faculty Hospital, all with a definitive diagnosis of MS, between February and December 2010. Patients were followed-up routinely at the MS Policlinic. During the period of this study, there were 310 registered patients attending this Policlinic. It was planned to include all these MS patients in the study. However, some patients refused to participate on the grounds that they would feel uncomfortable about their identities being publicized, or that they did not believe that their participation would provide any contribution to their recovery. As a result, only one in every three patients agreed and these were included in the study.

FIGURE 1

THE MAP OF TURKEY (CITY OF KAYSERI IS CIRCLED)



Control ascertainment

The control group was selected from among 100 health personnel and their relatives with special attention to their being matched by age, gender and residential area.

Ethical approval

Ethical approval for the study was obtained from the Health Sciences Research Ethics Committee of the Medical Faculty of Erciyes University.

Questionnaire

The questionnaire was administered to all the participants, following a preliminary trial, by the same physician using the face-to-face technique. It consisted of 2 parts.

The first part consisted of items related to the participants' socio-demographic features such as age, gender, birthplace, residence during the first 15 years of life, the order of the child in the family, blood type, economical-marital status, social security, schooling level, duration of breastfeeding, employment, smoking, sleep regulation, and dwelling.

The second part was related to factors thought to be involved in the occurrence or aggravation of the disease, such as parental kinship, history of MS in the relatives, cranial or spinal injury, pets, dental fillings, radiation, personality type, infections and viral disorders during childhood, vaccines, drugs, operation, stress and nutritional habits.

The items related with nutritional habits in the questionnaire were prepared in consultation with Erciyes University's Nutrition and Dietetics Department.

After a review of literature [24], the participants' dwellings were divided into 2 groups, depending on the distance from the transformer base stations or power lines (≤ 500 m, and >500 m).

Statistical analysis

The data were recorded in the SPSS packet program (SPSS, version 16.0) for analysis, which was performed in 2 stages. In the first stage,

the Chi-square test and, where necessary, the Chi-square Fisher's exact test were used for the comparison of the proportional differences between the groups. In the second stage, a logistic regression analysis was used to evaluate which possible environmental risk factors were associated with MS. However, since the quantitative levels of some data in the study (such as employment, vaccinations, history of paediatric diseases, consumption of dairy products, fruit and water, blood types and dwellings) were less than desired (i.e. those at the level of 10 and below in the table), they were not included in logistic regression analysis. OR (Odds Ratio) was calculated within the confidence interval of 95% for each risk factor. The patients' ages were presented as mean \pm SD (Standard Deviation). For the assessment of differences between the age groups, t-test was used. $P < 0.05$ values were taken as statistically significant.

RESULTS

The socio-economic status of the study group is presented in Table 1. Intergroup comparisons revealed no statistically significant difference in age, sex, the order of the child in the family and social security status. However, smoking ($p=0.001$), marital status ($p=0.037$), employment status ($p < 0.001$), blood types ($p=0.007$), sleep regularity ($p=0.047$), educational status ($p=0.041$) and economic status ($p < 0.001$) were found to be statistically significant. Although both groups had been breastfed, we determined that the subjects in the control group had been breastfed for a longer period ($p=0.001$).

We observed that the dwellings of the participants in the control group were outside the city centers ($p=0.001$), away from the transformer base-stations ($p < 0.001$).

The comparison of the MS patients with the controls showed that MS patients are usually those who are easily upset and have sensitive personality traits ($p=0.019$), have relatives with MS ($p < 0.001$), history of more head traumas ($p=0.001$) and keep pets ($p=0.029$).

We found (Table 2) that MS patients had paediatric diseases like chickenpox ($p=0.021$), infections during their childhood more acute (especially upper respiratory tract infections) ($p=0.001$), and other disorders like dermal and hormonal diseases more often than their

TABLE 1

SOCIO-DEMOGRAPHIC FEATURES OF THE PARTICIPANTS			
FACTORS	PATIENT GROUP (N=100)	CONTROL GROUP (N=100)	P VALUE
AGE	* 37±9.7	37.6±10.2	0.989
SEX (FEMALE/MALE)	74/26	83/17	0.084
MARITAL STATUS			
MARRIED	85	71	
SINGLE	14	24	0.037
SEPARATED/DIVORCED/ WIDOW(ER)	1	5	
EDUCATIONAL STATUS			
ELEMENTARY	44	40	
MIDDLE SCHOOL	17	11	
SENIOR HIGH SCHOOL	21	19	0.041
UNIVERSITY/GRADUATE	15	30	
ILLITERATE	3	0	
EMPLOYMENT			
HOUSEWIFE	52	53	
UNEMPLOYED	16	0	
CIVIL SERVANT	7	26	
FREELANCE	4	6	<0.001
RETIRED	13	2	
LABORER	4	6	
STUDENT	4	7	

counterparts in the control group. We also determined that MS patients were vaccinated less, except for vaccines against diphtheria, whooping-cough, and tetanus (DWT) ($p < 0.001$). Parental kinship ($p = 0.012$) was found to be statistically significant.

Table 3 shows the nutritional features of the study groups. We found that MS patients consumed more fizzy drinks, like cola, ($p = 0.002$), more saturated fat ($p < 0.001$), more red meat ($p = 0.001$), more food like sausages and processed meats ($P < 0.001$), less vegetables ($p < 0.001$), less fruit ($P = 0.001$), less white meat ($p = 0.005$), less milk ($p = 0.000$), less yoghurt ($p < 0.001$), and less legumes and wholegrain products, like chick-peas, lentils, and cracked wheat ($p < 0.001$), than the controls. The water ($p = 0.012$) and sort of oil they used ($p = 0.002$) were found to be statistically significant. Eight patients reported that they used the water from their own wells in their villages.

The results of logistic regression analysis are

given in Table 4. We observed that MS patients' economic status (OR: 0.14 adjusted 7.19; 95% CI: 0.05-0.43) was 7 times inferior to that of the control group. Having a sensitive personality (OR: 4.51; 95% CI: 1.10-18.45) was found to be 4 times greater, familial history of MS (OR: 3.28; 95% CI: 1.3-8.27), and the history of cranial and spinal injury (OR: 2.99; 95% CI: 1.11-8.08) 3 times greater in the patient group than in the control group. It was also observed that the consumption of unsaturated fat was 13 times greater than that of the subjects in the control group (OR: 0.07 adjusted 13.5; 95% CI: 0.03-0.20), while the consumption of legumes and wholegrain products (OR: 0.11 adjusted 8.9; 95% CI: 0.03-0.41) was approximately 9 times greater than in MS patients. The dwellings or workplaces of the MS patients were found to be located 6 times nearer to transformer base-stations than those of the controls (OR: 6.5; 95% CI: 1.54-28.21). In addition, it was detected that the MS patients used mobile phones more ($p < 0.001$).

TABLE 1 (CONTINUED)

SOCIO-DEMOGRAPHIC FEATURES OF THE PARTICIPANTS			
ECONOMIC STATUS			
GOOD	12	48	<0.001
FAIR	88	52	
SMOKING			
1-10 CIGARETTES DAILY	22	30	
20 AND OVER DAILY	25	6	0.001
NON-SMOKER	53	64	
DURATION OF BREASTFEEDING			
≤ 6 MONTHS	46	22	
12 MONTHS AND OVER	54	78	
SLEEP			
REGULAR, 7-8 HOURS	70	82	0.047
IRREGULAR	30	18	
DWELLING			
CITY CENTER	65	19	
OUT OF THE CITY	24	81	0.001
VILLAGE	11	0	
BLOOD TYPE			
A RH+/A RH-	31/1	45/0	
B RH+/B RH-	9/2	10/0	
AB RH+/AB RH-	3/1	9/0	0.007
O RH+/O RH-	20/6	23/3	
UNKNOWN TO THE SUBJECT	27	10	

X² tests and Fisher's exact method, where necessary, have been used.

* t-test was used

Of the MS patients, 87% reported that they had suffered excessive stress and economic problems prior to the onset of their disease, such as the loss of a parent, sibling or a child, severe illness, imprisonment, divorce, abuse and loss of employment.

DISCUSSION

It is known that MS is a disease affected by a diversity of genetic and environmental factors [25]. In the present study, we observed that 46% of the MS patients had relatives of the first degree with MS. It has been reported in recent genetic studies that the main susceptible allele in MS is HLADRBI 1501 but it is not the

only risk factor [3].

Studies indicate that MS occurs mostly in well-educated individuals with favorable socio-economic status [26]. In our study, however, MS was found in individuals whose education and economic status were both of average level. The number of jobless and retired people among MS patients was significantly high compared to the controls, but the number of state employees was extremely low. Unemployment per se is a chronic risk factor which is known to have an inhibitory effect on the immune system [27]. To be a state employee assures a regular salary and a secure future, factors which we believe prevent stress. We observed that advanced age was a risk factor for MS. However, this needs to be clarified in further studies including larger study groups.

TABLE 2

PRESENCE OF ENVIRONMENTAL RISK FACTORS ASSOCIATED WITH MS IN PARTICIPANTS			
FACTOR	PATIENT GROUP (N=100)	CONTROL GROUP (N=100)	P VALUE
HISTORY OF MS IN THE FIRST-DEGREE RELATIVES			
YES	46	17	<0.001
NO	54	83	
PARENTAL KINSHIP			
YES	27	12	
NO	73	88	
CRANIAL OR SPINAL INJURY			
YES	52	15	0.001
NO	48	85	
PET-KEEPING			
YES	30	16	0.029
NO	70	84	
DENTAL FILLING			
YES	49	59	0.101
NO	51	41	
EXPOSURE TO MOBILE TRANSFORMER BASE STATIONS			
NO	33	63	
YES, MOBILE OR CORDLESS PHONE	27	10	<0.001
YES, BASE STATION (≤ 500 M)	40	27	

We observed that MS patients reported that they had suffered severe stress and unfortunate events in relations with their close environment before the onset of their disease, therefore, they seem to have a frail and sensitive disposition. Other studies also corroborate these findings [1, 19].

Head or spinal injuries facilitate the entry into the central nervous system of the cells responsible for immunity by increasing the permeability of the blood-brain barrier. These cells can be activated against certain myelin antigens and produce demyelinated lesions. There are studies reporting that injuries are risk factors in MS [5, 12]. Our findings were also consistent with the findings of those studies.

One of the causes of MS is the magnetic field of the earth. The study of the earth's magnetic field has indicated a strong relationship between the structure of the field and the number of MS cases. It has been observed that the intensity level of the atmospheric electrical field is higher, in particular, in people who live in cloudy places at a high altitude. In addition, electromagnetic pollution, which technology has brought about,

is one of the factors that threaten human health. Base stations, lines of high electrical current, mobile phone, radio and TV waves, electromagnetic waves transmitted by computers and other electrical appliances in houses and work places cause pollution, thus creating an unhealthy atmosphere. Since this magnetic pollution raises blood temperature, it may cause a rise in the permeability of the blood-brain barrier. It has been observed in a experiments on rats that even a period of 60 minutes' exposure to radiation with a frequency of 2800 MHz and an intensity of 15mW/cm² raised cerebral blood flow [28, 29]. Individual variability of the pernicious effects of electromagnetic radiation is an interesting research finding [30]. Moreover, it can impair the immune system of the body by preventing the signals transmitted by the brain to the cells [31, 32]. We observed that MS patients' dwellings were found to be closer to transformer base stations and the patients' usage of cellular or cordless phones was greater than that of the controls.

In a number of studies it has been proposed

TABLE 2 (CONTINUED)

PRESENCE OF ENVIRONMENTAL RISK FACTORS ASSOCIATED WITH MS IN PARTICIPANTS			
FACTOR	PATIENT GROUP (N=100)	CONTROL GROUP (N=100)	P VALUE
SELF-DESCRIPTION			
EASILY UPSET, SENSITIVE	91	78	0.019
COMFORTABLE, CAREFREE	9	22	
HISTORY OF PEDIATRIC DISEASES			
HISTORY OF PEDIATRIC DISEASES	8	9	
CHICKEN-POX	14	9	
MUMPS	9	6	
MEASLES-CHICKEN POX	7	20	
MEASLES-MUMPS	4	2	0.021
CHICKEN POX-MUMPS	1	26	
MEASLES- CHICKEN POX-MUMPS	11	18	
NOT REMEMBERED	46	10	
INFECTIOUS DISEASES			
YES	19	4	
NO	58	79	0.001
UNKNOWN TO THE SUBJECT	23	17	
PEDIATRIC VACCINES			
DWT-POLIO	70	39	
MEASLES-RUBELLA-MUMPS (MRM)	4	13	
DWT-POLIO-MRM	2	32	<0.001
DWT-POLIO-HEPATITIS	1	1	
DWT-POLIO-MRM-HEPATITIS	3	14	
NOT REMEMBERED	20	1	

that the consumption, especially in childhood, of animal fats, dairy products, smoked and nitrate-containing processed meats results in MS development at advanced ages, and that the consumption of vegetable oil and fish has a prophylactic effect [10, 11]. In another study, however, no correlation was found between the consumption of milk, red meat, poultry and MS [33]. Studies on this subject have not yielded consistent results. There are differences depending on the region and individual. Studies on the consumption of vegetables, fruits, legumes, and grains have not been completed yet. The dietary suggestions we have offered are generally desired in many diseases like coronary heart disease and diabetes. It is interesting that in our patient group the frequency of fruit and vegetable consumption

is low while the consumption of fizzy drinks is high. In the present study, we observed that MS patients consumed 9 times less legumes and whole grains than the control group did. It is known that legumes and whole grains are recommended in such diseases as diabetes for the fiber, carbohydrate, B complex vitamin, and vegetable proteins they contain [34].

Both omega-6 and omega-3 essential fatty acids are the structural components of brain tissue and the myelin sheath. Seventy-percent of the myelin sheath is made up of lipids, and one-third of this consists of polyunsaturated fatty acids [10]. It has been observed in studies on the erythrocyte cell membrane that membrane essential fatty acids are reduced in MS patients [35]. However, in another study, it is reported that the lack of post-natal

TABLE 3

NUTRITION-RELATED RISK FACTORS AMONG MS PATIENTS AND CONTROLS			
FACTOR	PATIENT GROUP (N=100)	CONTROL GROUP (N=100)	P VALUE
CONSUMPTION OF FIZZY DRINKS			
1 CAN PER DAY	10	18	
3-5 CANS PER WEEK	21	12	
1-3 CANS PER WEEK	33	15	0.002
RARE	20	22	
NONE	16	33	
TYPE OF THE COOKING OIL USED			
LIQUID OIL	17	71	
MIXED (LIQUID + SOLID)	83	29	<0.001
VARIETY OF THE OIL USED			
OLIVE OIL	11	28	
CORN OIL, SUNFLOWER OIL	89	72	0.002
CONSUMPTION OF FRUIT JUICE			
1 SMALL PACKET, 3-5 TIMES A WEEK	20	34	
1 SMALL PACKET, 1-3 TIMES A WEEK	39	25	0.035
NONE	41	41	
TYPE OF THE WATER CONSUMED			
BOTTLED WATER	10	14	
SPRING WATER	8	0	0.012
TAP WATER (FROM A RESERVOIR)	82	86	

essential fatty acids have reduced the specific oligodendrocyte myelin protein mRNA in the brain of rats [36]. It is also reported that omega-3 fatty acid, which is present in sea fish and vegetable oil, with its capacity to produce auto-immune response, is immunomodulatory and anti-inflammatory [10, 35]. In the present study, consistent with other studies, we found that the consumption of unsaturated fats, olive oil in particular, by MS patients is 13 times less, and the consumption of processed sausage and meat varieties rich in nitrate is greater than that of the control group.

In other studies it has been reported that the consumption of dairy products plays a role in MS development [7, 11]. It has been demonstrated that in children fed on cow's milk, both the cellular and humoral immune response to cow' milk is provoked, but this diminishes with increasing age [37, 38]. In one study it is reported that the incidence of MS increases as breast milk intake decreases [39]. In our study

findings also showed that MS patients were breastfed for shorter periods than the controls. However, the consumption of such products is recommended after 12 or more months of age [38]. It is known that calcium is necessary for the development, structure, and stability of myelin [40]. Failure to get enough sunlight and insufficient dietary intake of vitamin D lead to vitamin D deficiency, which, in turn, manifests itself in various problems, such as inadequacy of antiviral and antibacterial defense, and impairment of HLA-DRBI-1501 [41]. Moreover, it has been demonstrated that vitamin D reduces MS risk [40]. It is known that milk, yoghurt, and the products of cereal grains contain calcium and vitamin D [41]. In the present study we observed that MS patients consumed less dairy products, notably milk and yoghurt.

It is reported that following a vaccination with a viral peptide activates cross-reactive T cells that recognize myelin antigen. After this activation, they passage through the blood-

TABLE 3 (CONTINUED)

NUTRITION-RELATED RISK FACTORS AMONG MS PATIENTS AND CONTROLS			
FACTOR	PATIENT GROUP (N=100)	CONTROL GROUP (N=100)	P VALUE
VEGETABLE CONSUMPTION			
1 PORTION PER DAY	12	40	
1 PORTION 3-5 TIMES PER WEEK	18	27	<0.001
1 PORTION 1-3 TIMES PER WEEK	48	20	
RARE	22	13	
FRUIT CONSUMPTION			
1 PORTION PER DAY	38	56	
1 PORTION 3-5 TIMES PER WEEK	7	16	
1 PORTION 1-3 TIMES PER WEEK	36	20	0.001
RARE	19	8	
CONSUMPTION OF RED MEAT			
1 PORTION PER DAY	10	10	
1 PORTION 3-5 TIMES PER WEEK	34	29	
1 PORTION 1-3 TIMES PER WEEK	43	23	0.001
RARE	13	38	
CONSUMPTION OF WHITE MEAT			
1 PORTION 3-5 TIMES PER WEEK	20	40	
1 PORTION 1-3 TIMES PER WEEK	59	49	
RARE	21	11	0.005
CONSUMPTION OF SAUSAGE, SALAMI HOT DOG AND SIMILAR FOODS			
YES	84	53	<0.001
NO	16	47	
CONSUMPTION OF LEGUME AND WHOLE GRAIN PRODUCTS			
1 PORTION, 3-5 TIMES A WEEK	16	63	
1 PORTION, 1-3 TIMES A WEEK	59	27	<0.001
1 PORTION, RARELY	25	10	
MILK CONSUMPTION			
2 GLASSES PER DAY	8	24	
1 GLASS, 3-5 TIMES PER WEEK	10	20	
1 GLASS, 1-3 TIMES PER WEEK	26	10	<0.001
RARE, 1 GLASS	26	17	
NONE	30	29	
YOGHURT CONSUMPTION			
1 BOWL, DAILY	18	55	
1 BOWL 3-5 TIMES PER WEEK	27	25	
1 BOWL 1-3 TIMES PER WEEK	25	7	<0.001
RARE	30	13	

χ^2 tests and Fisher's exact method, where necessary, have been used

TABLE 4

FACTORS ACTING ON THE RESULTS OF LOGISTIC REGRESSION OF THE STUDY GROUPS					
VARIABLE	B	WALD	SIG	OR	(CL95%)
DWELLING WITHIN 500 M OF TRANSFORMER BASE STATIONS	1.89	6.47	.011	6.59	1.54-28.21
FAMILIAL HISTORY OF MS	1.19	6.31	.012	3.28	1.3-8.27
FAVORABLE ECONOMIC STATUS	-1.98	11.75	.001	0.14	0.05-0.43
OIL CONSUMPTION	-2.61	25.75	<0.001	0.07	0.03-0.20
SENSITIVE PERSONALITY FEATURES	1.51	4.40	.036	4.51	1.10-18.45
CONSUMING LEGUME-WHOLE GRAIN PRODUCTS 3-5 TIMES A WEEK	-2.19	11.04	.001	0.11	0.03-0.41
CRANIAL OR SPINAL INJURY	1.09	4.67	.031	2.99	1.11-8.08

brain barrier and recognize myelin antigens, which triggers an autoimmune reaction. Genetic disposition is thought to play a key role in the development of an autoimmune reaction after vaccination [8]. In this study we observed that MS patients mostly had DWT-polio vaccines, and that they hardly had any other vaccines. The insufficiency of participant numbers, and the failure of 20% of the patients to remember whether or not they had vaccines prevented us from collecting adequate and reliable data. We found that the majority of the MS cohort in the present study had a history of chickenpox. However, 46% of patients failing to remember what diseases they had suffered from was a great disadvantage. It was determined, however, that they had a history of diseases other than pediatric diseases, which is consistent with the findings in other studies [7, 9]. It is reported that MS patients have, at later ages, had at least one pediatric disease [1]. In this study, we showed that a multitude of factors are involved at the same time in the development of MS.

It is known that, in parallel to scientific development, man has distanced himself from his natural life and biological rhythm and become isolated as a result of industrial developments. Such a lifestyle, while offering numerous technological opportunities, forces him to live with the pollution it entails. The impairment of sleep rhythm in addition to a

rapid tempo of life has necessitated mostly processed food. As a result of such a lifestyle in this industrialized world children are now used to being protected with drugs without waiting for their bodies to produce antibodies against disease. This occurs as a result of being weaned too early off breast milk, which is essential both physically and emotionally, or as a result of the early start of supplementary foods. We are of the opinion that the reaction of the body to this situation differs from person to person due to changes in lifestyle.

The frequency of MS is increasing in our city. It was our intention to find the common environmental characteristics of MS, our aim being to help reduce the increase of the disease by providing life-style changes.

The most important limitation of this retrospective study design is that related with the definition of past events. It is not always easy to ascertain exactly the presence or absence of exposure to any risk factor. Another limitation of this study is that we were unable to include all patients (i.e those in our hospital and those in nearby hospitals). We think that we could have obtained more significant and reliable results by including a greater number of patients in the study, and by considering the data subject to logistic regression analyses.

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References

- [1] Marrie RA. Environmental risk factors in multiple sclerosis aetiology. *Lancet Neurol* 2004; 3(12): 709-18
- [2] Ebers GC. Environmental factors and multiple sclerosis. *Lancet Neurol* 2008; 7(3): 268-77
- [3] Hoppenbrouwers IA, Hintzen RQ. Genetics of multiple sclerosis. *Biochim Biophys Acta* 2011; 1812(2): 194-201
- [4] Ramagopalan VS, Dobson R, Meier UC, Giovannoni G. Multiple sclerosis: risk factors, prodromes, and potential causal pathways. *Lancet Neurol* 2010; 9(7): 727-39
- [5] Granieri E. Exogenous factors in the aetiology of multiple sclerosis. *J Neurovirol* 2000; 6(Suppl 2): 141-6
- [6] Tintoré M, Arrambide G. Early onset multiple sclerosis: The role of gender. *J Neurol Sci* 2009; 286(1-2): 31-4
- [7] Khadilkar SV, Sahni AO, Agarwal SA. A case control study of environmental risk factors in Indians with multiple sclerosis. *Neurol Asia* 2005; 10: 47-52
- [8] Zorzon M, Zivadinov R, Nasuelli D, et al. Risk factors of multiple sclerosis: a case-control study. *Neurol Sci* 2003; 24(4): 242-7
- [9] Kakalacheva K, Münz C, Lünemann JD. Viral triggers of multiple sclerosis. *Biochim Biophys Acta* 2011; 1812(2): 132-40
- [10] Payne A. Nutrition and diet in the clinical management of multiple sclerosis. *J Hum Nutr Diet* 2001; 14(5): 349-57
- [11] Schwarz S, Leweling H. Multiple sclerosis and nutrition. *Mult Scler* 2005; 11(1): 24-32
- [12] Goodin DS, Ebers GC, Johnson KP, et al. The relationship of MS to physical trauma and psychological stress. *Neurology* 1999; 52(9): 1737-45
- [13] Hernán MA, Jick SS, Olek MJ, Jick H. Recombinant hepatitis B vaccine and the risk of multiple sclerosis: A prospective study. *Neurology* 2004; 63(5): 838-42
- [14] Attar AM, Kharkhaneh A, Etemadifar M, et al. Serum mercury level and multiple sclerosis. *Biol Trace Elem Res* 2012; 146(2): 150-3
- [15] Riise T, Moen BE, Kyvik KR. Organic solvents and the risk of multiple sclerosis. *Epidemiology* 2002; 13(6): 718-20
- [16] Riise T, Nortvedt MW, Ascherio A. Smoking is a risk factor for multiple sclerosis. *Neurology* 2003; 61(8): 1122-4
- [17] Van Amerongen BM, Dijkstra CD, Lips P, Polman CH. Multiple sclerosis and vitamin D: an update. *Eur J Clin Nutr* 2004; 58(8): 1-15
- [18] Cook SD, Dowling PC. A possible association between house pets and multiple sclerosis. *Lancet* 1977; 1(8019): 980-2
- [19] Palumbo R, Fontanillas L, Salmaggi A, et al. Stressful life events and multiple sclerosis: a retrospective study. *Ital J Neurol Sci* 1998; 19(4): 259-60
- [20] Artemiadis AK, Anagnostouli MC, Alexopoulos EC. Stress as a risk factor for Multiple Sclerosis onset or relapse: A systematic review. *Neuroepidemiology* 2011; 36(2): 109-20
- [21] Pugliatti M, Rosati G, Carton H, et al. The epidemiology of multiple sclerosis in Europe. *Eur J Neurol* 2006; 13: 700-22
- [22] Türk Börü U, Alp R, Sur H, Gül L. Prevalence of multiple sclerosis door-to-door survey in Maltepe, Istanbul, Turkey. *Neuroepidemiology* 2006; 27: 17-21
- [23] Börü UT, Ta demir M, Güler N, et al. Prevalence of multiple sclerosis: door-to-door survey in three rural areas of coastal Black Sea regions of Turkey. *Neuroepidemiology* 2011; 37: 231-5
- [24] Blettner M, Schlehofer B, Breckenkamp J, et al. Mobile phone base stations and adverse health effects: phase 1 of a population-based, cross-sectional study in Germany. *Occup Environ Med* 2009; 66(2): 118-23
- [25] Compston A, Coles A. Multiple sclerosis. *Lancet* 2008; 372(9648): 1502-17
- [26] Hammond SR, McLeod JG, Macaskill P, English DR. Multiple sclerosis in Australia: socioeconomic factors. *J Neurol Neurosurg Psychiatry* 1996; 61(3): 311-3
- [27] Cohen F, Kemeny ME, Zegans LS, et al. Immune function declines with unemployment and recovers after stressor termination. *Psychosom Med* 2007; 69(3): 225-34
- [28] Co kun Ö. Mechanisms of interaction between RF (Radio Frequency) fields and biological tissue. *SDU Journal of Technical Science* 2011; 1(1): 16-22
- [29] Matthes R. Non-ionizing radiation. *Austria* 1996; ICNIRP: 1-96
- [30] D'Andrea J, Chou C, Johnston S. Microwave effects on the nervous system. *Bioelectromagnetics* 2003; Suppl 6: 107-47
- [31] Hossmann KA, Hermann DM. Effects of electromagnetic radiation of mobile phones on the central nervous system. *Bioelectromagnetics* 2003; 24(1): 49-62
- [32] Canbay C. The essential environmental cause of multiple sclerosis disease. *Progress In Electromagnetics Research (PIER)* 2010; 101: 375-91
- [33] Zhang SM, Willett WC, Hernán MA, et al. Dietary fat in relation to risk of multiple sclerosis among two large cohorts of women. *Am J Epidemiol* 2000; 152(11): 1056-64
- [34] Venn BJ, Mann JI. Cereal grains, legumes and diabetes. *Eur J Clin Nutr* 2004; 58: 1443-61
- [35] Hon GM, Hassan MS, van Rensburg SJ, et al. Membrane saturated fatty acids and disease progression in Multiple Sclerosis patients. *Metab Brain Dis* 2009; 24: 561-8
- [36] van Meeteren ME, Teunissen CE, Dijkstra CD, van Tol EA. Antioxidants and polyunsaturated fatty acids in multiple sclerosis. *Eur J Clin Nutr* 2005; 59(12): 1347-61
- [37] Vaarala O, Saukkonen T, Savilahti E, et al. Development

- of immune response to cow's milk proteins in infants receiving cow's milk or hydrolyzed formula. *J Allergy Clin Immunol* 1995; 96(6 Pt 1): 917-23
- [38] Davis MK. Breastfeeding and chronic disease in childhood and adolescence. *Pediatr Clin North Am* 2001; 48(1): 125-41
- [39] Tarrats R, Ordonez G, Rios C, Sotelo J. Varicella, ephemeral breastfeeding and eczema as risk factors for multiple sclerosis in Mexican. *Acta Neurol Scand* 2002; 105(2): 88-94
- [40] Goldberg P, Fleming MC, Picard EH. Multiple sclerosis: Decreased relapse rate through dietary supplementation with calcium, magnesium and vitamin D. *Med Hypotheses* 1986; 21(2): 193-200
- [41] Hanwell HE, Banwell B. Assessment of evidence for a protective role of vitamin D in multiple sclerosis. *Biochim Biophysica Acta* 2011; 1812(2): 202-12

