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Factors Associated with Brain Multiple Sclerosis Lesions Detected by Magnetic Resonance Imaging

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ABSTRACT

Multiple sclerosis (MS) is a demyelinating disease that mainly impacts the central nervous system (CNS) and spinal cord. Several factors may affect the risk of MS lesions. Hence, this study was carried out to determine factors associated with brain MS lesions detected by Magnetic Resonance Imaging (MRI). A prospective cross-sectional survey was carried out in this study. An unenhanced T1, T2, Fluid Attenuated Inversion Recovery (FLAIR) with axial, sagittal, and coronal sections were performed. The respondents who had exposed to radiotherapy or chemotherapy had previous brain pathology or surgery, and brain congenital anomalies were excluded from this survey. A *P*-value of < 0.05 was considered significant. A total of 71 subjects underwent MRI and included in the statistical analysis. The mean age of the subjects was 31.5 ± 11.5 years, with predominance for females (59.2%) among this study population. Moreover, the findings reported that the family history of MS was highly significantly associated with MS (*P* = 0.001). Besides, there was no significant association found between gender (*P* = 0.682), smoking (*P* = 0.272), alcohol intake (*P* = 0.986), hypertension (*P* = 0.792), diabetes mellitus (DM) (*P* = 0.198), and body mass index (BMI) (*P* = 0.650). From this study, the family history of MS is found to develop the risk of MS.

INTRODUCTION

Multiple Sclerosis (MS) is an autoimmune demyelinating, inflammatory, and neurodegenerative disease of the central nervous system (CNS)[1]. A histopathological study carried out in 1838 by Carswell, in which

the underlying pathological mechanism of MS lesions was described[2]. Then, in 1868, Charcot has named the disease as "la sclerose en plaques" and confirmed an association between the histopathological and clinical aspects of MS lesions[3]. Besides, Charcot has also described the MS disease as "plaques" and focal demyelination lesion, gliosis, inflammation, and various degrees of axonal loss as well as distribution and the histopathological manifestation of these plaques in the CNS. The diagnosis of MS is based on evidence of the dissemination of white matter lesions[4]. In the early stages of the MS, evidence of plaques, demyelination, and inflammation are abundant, while in the later stages, neuronal loss and axonal damage are predominant[3]. This characterization of the MS lesions is still valid as a gold reference nowadays.

In 2010, McDonald criteria for MS indicated that dissemination in space (DIS) could be observed on T2 at least one lesion in 2 out of 4 locations characteristics for MS (juxtacortical, periventricular, infratentorial, and spinal cord). In the same context, dissemination in time can be noted at least on one new T2 and/or contrast-enhancing lesion on follow-up MRI. Furthermore, the simultaneous presence of asymptomatic contrast and non-contrast enhancing lesions could be at any time[5].

There are several environmental and genetic factors associated with MS progression[6]. Evidence is increasing with environmental factors, including vitamin D deficiency, smoking, altered lipid metabolism, and Epstein-Barr virus are related to the development of MS[7 – 15]. MRI usually reveals several lesions in many individuals at the clinical onset of MS[16].

A recent study showed that there are other risk factors, including underlying comorbidities associated with the progression of MS[17]. Patients who have more than one cardiovascular (CV) risk factors such as hyperlipidaemia, hypertension, and heart disease are more likely to increase the risk of MS[18]. A histopathological mechanism of CV disease associated with the progression of MS is resulting in hyperplasia of brain white matter and hypotrophy of grey matter, leading to damaging the myelin sheath[19 – 21]. Moreover, several previous studies reported a positive association between smoking and dyslipidaemia with MS lesions[12, 15, 22, 23].

MS lesions cannot be diagnosed by a single test, including MRI. However, MRI is a more accurate and sensitive tool for diagnosis of MS than other diagnostic modalities such as biochemical tests[4]. This study was designed to determine factors associated with brain MS lesions detected by MRI.

MATERIALS AND METHODS

A prospective cross-sectional survey was carried out over two months from March 2019 to May 2019. All subjects who have clinical symptoms of MS lesions underwent MR imaging and were eligible for this study. A total of 71 subjects were selected based on a systematic random sampling method. Inclusion criteria included age ranging from 16 years and above, Iraqis (no other races/ethnicities), both genders, and subjects who could complete their questionnaire. The study was conducted in four provinces in the middle and south of Iraq, including Baghdad, Diyala, Babil, and Al-Najaf. Firstly, the respondents were informed verbally about the nature and aims of the study. Secondly, all respondents were given an informed consent form before the information was taken. A structured self-administered questionnaire was used as an instrument to collect information from the respondents. The subjects with an age range from 16 years and above, Iraqis, the respondents who had exposed to radiotherapy or chemotherapy, had previous brain pathology or surgery, and brain congenital anomalies were excluded from this survey. Ethical approval was obtained from

the scientific committee in the Radiological Techniques Department, College of Health and Medical Technology, Middle Technical University, Baghdad.

After the weight and height of the respondents have been measured, Body Mass Index (BMI) was calculated. BMI is weight in kilogram (kg) divided by metre square (m^2). It was classified according to World Health Organization guidelines for the Asia-Pacific region[24]. BMI of less than 18.5 kg/m^2 was classified as underweight, 18.5 – 24.9 kg/m^2 were classified as normal, ≥ 25.0 – 29.9 kg/m^2 were classified as overweight, and 30.0 kg/m^2 and above were classified as obese. A respondent was considered having hypertensive if he/ she has been taking antihypertensive medication(s), if he/ she has a self-reported history of hypertension, or if he/ she had systolic blood pressure (SBP) ≥ 130 mmHg or diastolic blood pressure (DBP) ≥ 85 mmHg[25].

Conventional MRI (SEIMENS and PHILIPS with 3 Tesla) with an 8-channel head and neck coil have been used for diagnosis MS lesions. Sagittal, axial, and coronal sections have been taken for each case. T1-weighted, T2-weighted, Fluid Attenuated Inversion Recovery (FLAIR) sequences have been imaged. A contrast agent has not been given to the patients because it is not available in the imaging screening centres while the study was conducting. MRI diagnosis was blinded to the respondent's physical and neurological pathology.

Data Analysis

Data analysis was performed using Statistical Package for Social Science (SPSS) program version 22.0. First, descriptive analysis was carried out to calculate the percentages of each factor among our study population. A Chi-square test was performed to determine the association between categorical variables. Then, an independent samples *t*-test was used to compare a mean between two groups with normally distributed data. A *p*-value of less than 0.05 was considered statistically significant.

RESULTS

The distribution of the study population is shown in Table 1. The mean age of the subject was 31.5 ± 11.5 years. Females were predominant (59.2%) in the study population. A higher percentage was reported for non-hypertensive subjects (56.3%) than hypertensive subjects (43.7%). Likewise, a percentage of non-diabetic subjects was higher (64.8%) than diabetic subjects (35.2%). Moreover, the normal BMI subjects had the highest percentage (40.8%), whereas underweight subjects had the lowest (9.9%). Besides, 35.2% of the subjects tend to be overweight, whereas only 14.1% of the subjects were obese. Out of 71 subjects, there were 24 subjects (33.8%) were reported to have MS lesions.

Table 1 Characteristics of the study population (*n* = 71)

Variables	*n* (%)	Mean ±SD
Age	–	31.5 ± 11.5
Gender		
Male	29 (40.8)	
Female	42 (59.2)	
Smoking		
Yes	27 (38.0)	
No	44 (62.0)	
Alcohol consumed		
Yes	3 (4.2)	
No	68 (95.8)	
Hypertension		
Yes	31 (43.7)	
No	40 (56.3)	
DM		
Yes	25 (35.2)	
No	46 (64.8)	
BMI categories		
Underweight	7 (9.9)	
Normal	29 (40.8)	
Overweight	25 (35.2)	
Obese	10 (14.1)	
Family history of MS		
Yes	15 (21.1)	
No	56 (78.9)	
MS		
Yes	24 (33.8)	
No	47 (66.2)	

n = Sample size

According to an independent samples *t*-test, our results revealed that differences of mean age between subjects with and without MS were not found to be significant ($P = 0.877$) (Table 2). Furthermore, A Chi-square test showed that the prevalence of MS between males and females was close to each other (31.0 % and 35.7%, respectively). This indicates that gender was not significantly associated with MS ($P = 0.682$). Regarding smoking and alcohol intake, this study showed an association between smoking and alcohol intake with MS was not found to be significant ($P = 0.272$ and $P = 0.986$, respectively). According to the medical history of the disease, the study findings confirmed that hypertension and diabetes mellitus (DM) were also not significantly associated with MS ($P = 0.792$ and $P = 0.198$, respectively). Nevertheless, the prevalence of MS was significantly higher among subjects who had a family history of MS than those without ($P = 0.001$). In terms of BMI, although half of the MS patients were obese, an association between MS and BMI was not noted to be significant ($P = 0.650$).

Table 2 Factors associated with MS lesions

Variables	MS findings		*p*-value
	Yes	No	
Age	31.8 ± 11.9	31.4 ±11.4	0.877
Gender			0.682
Male	9 (31.0)	20 (69.0)	
Female	15 (35.7)	27 (46.3)	
Smoking			0.272
Yes	7 (25.9)	17 (38.6)	
No	20 (74.1)	27 (61.4)	
Alcohol consumed			0.986
Yes	1 (33.3)	2 (66.7)	
No	23 (33.8)	45 (66.2)	
Hypertension			0.792
Yes	11 (35.5)	20 (64.5)	
No	13 (32.5)	27 (67.5)	
DM			0.198
Yes	6 (24.0)	19 (76.0)	
No	18 (39.1)	28 (60.9)	
Family history of MS			0.001*
Yes	13 (86.7)	2 (13.3)	
No	11 (19.6)	45 (80.4)	
BMI categories			0.650
Underweight	2 (28.6)	5 (71.4)	
Normal	10 (34.5)	19 (65.5)	
Overweight	7 (28.0)	18 (72.0)	
Obese	5 (50.0)	5 (50.0)	

* Significant as $p < 0.05$

DISCUSSION

MS is a complex idiopathic inflammatory disease that mainly affects the myelin sheath of the CNS or spinal cord. It is essential to know that no specific markers to diagnose MS lesions, where it primarily depends on neurological investigation and medical history. Thus, MS lesions attack should be defined precisely and correctly. The neurologists define MS lesions attack as a neurological defect that persists more than one day and can be correlated with an anatomical localization with no evidence of any infection or fever. The neurological defect always evolves from 2 – 4 weeks, and it entirely or partially recovers between 6 and 8 weeks, either spontaneously or with corticosteroid medication[26, 27]. However, patients with presenting an attack, MRI is the most accurate and vital diagnostic modality to confirm the diagnosis, especially with intravenous contrast agent given. This can serve to monitor the characteristics of lesion (demyelinating and inflammatory) as well as distribution and localization of the lesions within CNS[28]. Moreover, on the MR imaging, one anatomical region is presented by monofocal attack or more than one anatomical CNS region concurrently, such seen by multifocal attacks[26, 27].

In terms of sociodemographic factors such as age and gender, the previous studies stated that female gender and individuals

over 11 years old are more likely to have MS[29]. Besides, 2–10% of all patients with MS lesions have clinical onset before 18 years of age[30]. Simpson et al. demonstrated that females were predominant in the most prevalent studies[31]. Otherwise and surprisingly, we did not find an association between age and gender with MS lesions. The lifestyle and environmental factors, including exposure to smoking, high BMI, and vitamin D deficiency, increase the risk of MS disease, whereas alcohol consumption has potentially reduced the risk of MS[16, 32].

In contrast, Kappus et al. revealed that the prevalence of overweight/obesity among MS subjects did not differ from that in healthy controls[33]. This indicates that the association of overweight/ obesity was not significantly associated with MS lesions. Similarly, the researchers also have identified that smokers or hypertensive subjects are more likely to have MS lesions as compared to their counterparts who are non-smokers or having normal blood pressure. Nevertheless, our study showed that smoking was not significantly associated with MS. Based on BMI status, our findings showed that an association between BMI and MS was not noted to be significant although there is a higher prevalence of MS (50%) was found among obese patients compared to those who were underweight, normal or overweight. Regarding the family history of MS, a study by Montgomery et al. suggested increased the risk of MS in offspring was probably associated with the older father's age[34]. This finding was consistent with findings from our study, where the latter demonstrated that the prevalence of MS lesions in subjects with a family history of the disease itself was significantly higher than in those without a family history of the disease.

Description of MS by MRI is based on the presence of focal lesions in the white matter of CNS. These focal lesions are considered as typical criteria for this disease in terms of distribution, morphology, evolution, and signal changes on MRI sequences (T2-weighted image, T2- FLAIR, pre- and post-contrast T1- weight images)[35]. However, evidence of hypointense lesions on non-enhancing T1-weighted image it is not likely to consider a criterion for detecting MS lesions[36].

The limitation of this study is a small sample size due to a preliminary study to determine factors associated with MS lesions diagnosed by MRI. Hence, we recommended future studies to carry out a cross-sectional-based population study and increased the sample size to determine the overall prevalence of MS among the whole Iraqi population as well as studying other affecting factors. Importantly, a contrast-enhanced T1-weighted image is also highly recommended for future work as an additional sequence to assess and monitor the number and dissemination of MS lesions.

CONCLUSION

The family history of MS lesions is noted to increase the risk of MS lesions. Otherwise, other factors such as age, gender, smoking, alcohol consumed, hypertension, DM, and BMI were not associated with MS lesions.

CONFLICT OF INTEREST

The authors declare that they have no competing interests in publishing this article.

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