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Original article

Study of (IL17A) Genetic Variant (rs 2275913) and its Association with Reduced Risk of Multiple Sclerosis Disease in Egyptian Patients

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Abstract

Background: The autoimmune disease multiple sclerosis (MS) typically strikes middle-aged and younger adults. Genetic biomarkers linked to multiple sclerosis include single nucleotide polymorphisms (SNPs). **Aim of the work:** aim of the work guided to study the role of interleukin IL17A genetic variant (rs 2275913) and its association with reduced risk of MS disease in Egyptian patients. **Subjects & Methods:** This cross-sectional study included 50 participants; 30 patients diagnosed with MS attended MS Unit of Department of Neuropsychiatry and outpatient clinic of Benha University Hospitals and 20 apparently healthy control candidates. This study aimed to determine whether there is a correlation between the IL17A gene variation rs2275913 A/G and the MS risk. Genetic material were extracted from EDTA blood and genotyping was carried out using the PCR-RFLP method for rs2275913. Then, we looked at how the frequency of different genotypes and alleles correlated with disease risk. **Results**: revealed that the IL17A (rs2275913) gene polymorphism has significant genotype variation between MS cases and controls, notably for the AA genotype (p = 0.027), which appears to be related with a low risk of MS (OR = 0.29). The A allele is also considerably less prevalent in MS patients.

Conclusion: The IL17A (rs2275913) gene polymorphism has been linked to MS. The IL17A GG genotype is associated with higher disability levels while the AA genotype may offer some protection against severe disability.

Keywords: IL17A gene, Genetic Variant, single nucleotide polymorphisms SNP, Multiple Sclerosis Disease.

Introduction

An autoimmune disease commonly affecting middle-aged and younger adults is multiple sclerosis (MS). A hallmark of this disorder is the disordered conduction of nerve impulses caused by demyelination of the nerve axons within the central nervous system (CNS). Among middle-aged and younger adults, multiple sclerosis (MS) ranks high as a non-traumatic disability cause, leading to a decline in productivity [1-2]. The complex aetiology of multiple sclerosis, which also entails environmental variables, is primarily determined by human leukocyte antigen genes. The Epstein-Barr virus (EBV), a deficiency of vitamin D, nicotine, obesity, and stress are among the environmental factors that may contribute to the disease [3]. The revised McDonald criteria 2017 establish the diagnostic criteria for multiple sclerosis (MS) as neurological symptoms and signs, and evidence of spatial and temporal dissemination of CNS lesions. Recognizing MS lesions is now possible with the help of modern, ground breaking techniques like MRI and immunohistochemistry. These lesions manifest as localized areas of inflammation, demyelination, and glial reaction all over the CNS [4]. One of the most important pro-inflammatory cytokines is interleukin 17 (IL-17), which is also called cytotoxic T-lymphocyte-associated protein 8 (CTLA 8). It has recently emerged as a critical element of the immune response and is secreted by a diversity of cells, such as Th17, gamma delta T, Type 17 CD8+ T, and natural killer cells. IL-17A to IL-17F are the six members of the IL-17 family. IL-17A, also known as IL-17, is the most extensively researched member of the family [5].

A significant amount of evidence suggests that CD4+ TH cells, particularly TH1 cells which secrete IFNγ and TH17 cells which secrete IL-17, are pivotal in the progression of MS within the CNS [6]. In addition to their principal function in infection protection, TH cells has an important role in MS by targeting astrocytes, a type of glial cell that resides in the central nervous system, and by activating and maturing microglia that reside in the CNS and monocytes that invade the CNS. In particular, TH17 cells have the ability to compromise the blood-brain barrier [7].IL-17A is associated with the breakdown of the BBB in relapsing remitting multiple sclerosis[8].

Subjects and Methods:

This cross-sectional case control study was conducted on 30 MS cases aged (20-45 years) of both sexes recruited from MS Unit of Department of Neuropsychiatry and outpatient clinic of Benha University Hospitals and 20 apparently healthy candidates during the period from September 2023 to September 2024. An informed consent was obtained from the patients. The study was performed after approval from the Ethics Committee of the Faculty of Medicine, Benha University Hospitals, and Approval code: (MS 5-7-2023).

The laboratory work was done in the Specialized Medical Analysis Unit (SMAU), in the Clinical and Chemical Pathology Department in Benha University Hospitals

Inclusion criteria for group I: Both sexes are affected, and the McDonald criteria 2017 are

used to diagnose multiple sclerosis. The age range is 20 to 45 years.

Exclusion criteria for group I were subjects with other inflammatory disease, other autoimmune disease affecting CNS and subjects who failed to meet the McDonald criteria 2017 and who were not validated by the neurologist.

All participants were categorized into 2 groups:

Group I (n=30): MS patients diagnosed as MS according to the McDonald criteria 2017 [9].

Group II (n=20): included apparently healthy candidates selected from general population.

All participants in MS group were subjected to full history taking including (age, residence, onset, course and duration of MS, other associated symptoms, family history of MS) and clinical examination including (full neurological examination, assessment of functional disability using EDSS score at the time of sample withdrawal) and in the control group including complete medical history.

Laboratory investigations:

1-Vitamin D measurement: Quantitative determination of 25-hydroxy vitamin D was performed using Human 25-hydroxy vitamin D ELISA Kit (Catalog No: E1981Hu, Bioassay technology laboratory, China.) ELISA was performed using auto washer (Tecan, Japan) and micro plate reader (Infinite F 50, Tecan, Japan) set to 450 nm. Detection range was 0.5- 150 ng/ml. Serum levels of vit D3 were interpreted as follows: Deficiency (a 25-OH vit D3 serum concentration less than 20 ng/mL), insufficiency (a 25-OH vit D3 concentrations between 21-29 ng/mL) and sufficiency (a 25-OH vit D3 concentrations between 30−100 ng/ml [10].

2-Cerebrospinal fluid (CSF) analysis: Intrathecal immunoglobulin G (IgG) synthesis, according to present diagnostic criteria, shows that the disease is inflammatory, increases diagnostic certainty, and stands in for time-dependent dissemination. The gold standard for intrathecal IgG synthesis is the detection of CSF-restricted oligoclonal bands (OCBs). For intrathecal IgG synthesis, the detection of CSF-restricted oligoclonal bands (OCBs) is the gold standard [11]. (Results were obtained from patients medical files)

3-Molecular assessment of IL17A gene polymorphism (rs2275913):

The patient and control groups' peripheral blood were withdrawn using tubes that contained EDTA, an anticoagulant. The DNAs were subsequently extracted from the whole blood samples following the manufacturer's protocol using a DNA extraction Kit (NJD Scientific DNA/RNA Extraction Kit 96T, Lot No.NJ021002-M01). We used a NanoDrop micro-volume spectrophotometer (Nanodrop 2000, Thermo Scientific, USA) to verify the DNA's quality. DNA amplification using conventional PCR using FIREPol Master Mix (Cat .,04-12-00125 Lot.,04121251020.4) The utilized primers (Eurofins , Europe) for the polymerase chain reaction have the following sequence : Forward ; 5′-GCATAACTCTTCTGGCAGCTGTA-3′ Reverse: 5′-TGCCCACGGTCCAGAAATAC-3′. A 445-bp fragment was amplified by the

aforementioned specific PCR primers, which contained a specific restriction site that was used to identify the individual alleles of the rs2275913 SNP. The following conditions were utilized to conduct the PCR on a thermal cycler (Life Touch Thermal Cycler, Serial No. BYQ6.0.98E1901-427, China): The temperature was maintained at 95°C for 5 minutes, followed by 30 cycles of 30 seconds at 95°C, 30 seconds at 60°C, 45 seconds at 72°C, and a terminal extension of 5 minutes at 72°C. Then PCR amplified products were detected using 2% agarose gel electrophoresis with ethidium bromide, then visualized using ultraviolet light trans-illumination **(Fig. 1).** The researchers employed (PCR-RFLP) to carry out the genotyping process. The next step was to break down the PCR products using the XagI restriction enzyme. After only one hour of incubation at 37°C, Xagl restriction enzyme partitioned the 445 bp PCR product into two parts, each measuring 148 and 297 bp. A 2% agarose gel was utilized for electrophoresis in order to observe the end products. There was one 445 bp fragment which pointed to a mutant homozygous AA genotype, two smaller ones measuring 297 bp and 148 bp, respectively, which pointed to a non-mutated homozygous GG genotype and three segments measuring 297 bp, 148 bp, and 445 bp were used to indicate the heterozygous AG genotype **(Fig. 2).**

Statistical analysis:

IBM Corp. released the Statistical Package for Social Science in 2017. The data that was collected was revised, coded, and tabulated. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp., and Handbook of Medical Statistics) [12]. Numerical data were analysed using the mean, standard deviation (± SD), median, and range. Non-numerical data was analysed using frequency and percentage. Chi-Square (χ^2) tests are among the analytical statistics. Student T Test, Mann Whitney Test, One Way ANOVA test was used to assess the statistical significance of the difference between more than two study group parametric variables. Logistic regression analysis was used for the prediction of risk factors when the variable is categorical, specific odds ratios (ORs), p-value is considered significant if <0.05 at confidence interval 95%.

Results

The studied SNP rs2275913 is composed of G and A alleles, G is the reference, and A is the alternative allele. It is located within IL17A gene, on chromosome 6. The Hardy-Weinberg equilibrium analysis for the IL17A (rs2275913) gene polymorphism in both MS patients and controls shows that the observed genotype frequencies are consistent with the expected frequencies, as evidenced by the non-significant p-values (p = 0.714 for MS patients and p = 0.371 for controls). This implies that the genetic polymorphism does not deviate considerly from equilibrium in either group

Table 1: Assessment of Hardy Weinberg equilibrium for genetic polymorphism

The statistical analysis of MS patients and controls shows no significant variations in sex distribution, residence family history and smoking. MS patients are statistically significantly deficient in vitamin D. The findings demonstrate that the IL17A (rs2275913) gene polymorphism reveals

significant genotype variation between MS cases and controls, notably for the AA genotype (p = 0.027), which appears to be related with a low risk of MS (OR = 0.29) indicating that this genetic variant may have a protective effect against the development of MS.

Table 2: Comparison of patients with MS and the control group regarding baseline parameters, Vitamin D and IL17A (rs2275913) gene polymorphism

Table 3: MS features among patients' group

The examination of family history, smoking status, demographic data, disease history, number of attacks among patients, MS types, the incidence of optic neuritis and EDSS score and relationship between IL17A genotypes is not significantly different. The examination of the association between IL17A (rs2275913) genotypes and the number of plaques identified on MRI shows significant variations across the groups (p < 0.001). The examination of Vitamin D levels in association with IL17A genotypes revealed significant differences (p = 0.001).

Table 4: Association between IL17A (rs2275913) and risk factors, disease features, EDSS, MRI (number of plaques) and vitamin D among patients with MS

The logistic regression analysis shows that Vitamin D level is a significant predictor of MS susceptibility in both univariate (p = 0.001) and multivariate (p = 0.003) models, with an OR<1, showing that lower Vitamin D levels are linked with an increased risk of MS. In addition, the IL17A rs2275913 polymorphism is significant in the univariate analysis (p = 0.034), as well as in the multivariate model (p = 0.034), with OR<1, indicating that AA genotype is associated with protective effect against MS. Other characteristics, such as gender, age, residency, family history, and smoking, do not have a statistically significant connection with MS

Table 5: Logistic regression analysis for prediction of MS susceptibility

Table 3: Assessment of Hardy Weinberg equilibrium for genetic polymorphism

		MS patients n = 30		Control n = 20	
		Observed	**Expected**	**Observed**	**Expected**
IL17A (rs2275913) gene polymorphism	**GG**	15	15.4	6	5.0
	AG	13	12.2	8	10.0
	AA	2	2.4	6	5.0
	$\chi 2$	0.135		0.800	
	p-value	0.714		0.371	

χ^2, Pearson's goodness-of-fit test. (P-value)

Table 4: Comparison of patients with MS and the control group regarding baseline parameters, Vitamin D and IL17A (rs2275913) gene polymorphism

			MS patients (n = 30)	Control (n = 20)	p-value	OR (95 % CI)
Baseline parameters	**Sex**	**Male**	11 (36.7%)	8 (40.0%)	0.812	----
		Female	19 (63.3%)	12 (60.0%)		----
	Age (years)		32.83 ± 7.92	29.80 ± 7.08	0.197	----
	Residence	**Rural**	14 (46.7%)	9 (45.0%)	0.908	----
		Urban	16 (53.3%)	11 (55.0%)		----
	Family history		2 (6.7%)	1 (5.0%)	1.0	----
	Smoking		7 (23.3%)	2 (10.0)	0.285	----
	Vitamin D (ng/mL)		21.50 ± 6.51	38.15 ± 5.94	**<0.001***	----
IL17A (rs2275913) gene polymorphism	**Genotypes**	**GG**	15 (50.0%)	6 (30.0%)	---	Reference
		AG	13 (43.3%)	8 (40.0%)	0.513	0.77(0.35–1.69)
		AA	2 (6.7%)	6 (30.0%)	**0.027***	0.29(0.10–0.87)
	Dominant model	**GG**	15 (50.0%)	6 (30.0%)	---	Reference
		AG+AA	15 (50.0%)	14 (70.0%)	0.160	0.59(0.29–1.23)
	Recessive model	**GG+AG**	28 (93.3%)	14 (70.0%)	---	Reference
		AA	2 (6.7%0	6 (30.0%)	**0.034***	0.33(0.12–0.92)
	Alleles	**G**	43 (71.7%)	20 (50.0%)	**---**	Reference
		A	17 (28.3%)	20 (50.0%)	**0.029***	0.56(0.33–0.94)

P: Comparing MS and control group. ; OR, odds ratio; CI, confidence interval; Reference genotype and allele based on NCBI database; G, guanine; A, alanine; OR<1 is considered protective; OR>1 is considered risky. *, p<0.05 is considered significant.

Table 3: MS features among patients' group

	MS patients , n=30
Duration (years)	6.50 ± 4.92
Age of onset (years)	26.30 ± 7.18
Number of attack during disease course	3.23 ± 2.84
Type of MS	
RRMS	n=24 (80%)
SPMS	n=6 (20%)
EDSS	2.28 ± 1.51
CSF analysis (OCBS)	
Done	n = 21
Positive , > 2 bands	21 (100%)
MRI (Number of plaques)	15.23 ± 7.39

Data presents as mean ± SD or frequency (%). RRMS: relapsing remitting multiple sclerosis. SPMS: secondary progressive multiple sclerosis . EDSS: expanded disability standard score. OCBS: oligoclonal bands. MRI: magnetic resonance imaging

Table 4: Association between IL17A (rs2275913) and risk factors, disease features, EDSS, MRI (number of plaques) and vitamin D among patients with MS

		IL17A (rs2275913)			P-Value
		GG (N = 15)	**AG (N = 13)**	**AA (N = 2)**	
			Risk factors		
Family history		1 (6.7%)	1 (7.7%)	0 (0.0%)	MC 1.0
Smoking		3 (20.0%)	3 (23.1%)	(50.0%)	MC 0.649
			demographic data		
Sex	**Male**	3 (20.0%)	7 (53.8%)	1 (50.0%)	MC 0.127
	Female	12 (80.0%)	6 (46.2%)	1 (50.0%)	
Age (years)		34.13 ± 8.0	32.62 ± 7.82	24.50 ± 4.95	0.309
Residence	**Rural**	7 (46.7%)	6 (46.2%)	1 (50.0%)	MC 1.0
	Urban	8 (53.3%)	7 (53.8%)	1 (50.0%)	
			Disease features		
Duration (years)		7.60 ± 5.95	5.38 ± 3.48	5.50 ± 4.95	0.711
Age of onset (years)		26.47 ± 6.78	27.23 ± 7.82	19.0 ± 0.0	0.177
Number of attacks		3.87 ± 3.74	2.77 ± 1.36	1.50 ± 0.71	0.432
Type of MS	**RRMS**	10 (66.7%)	12 (92.3%)	2 (100.0%)	MC 0.255
	SPMS	5 (33.3%)	1 (7.7%)	0 (0.0%)	
EDSS		3.13 ± 1.70	1.50 ± 0.58	1.0 ± 0.0	**p1=0.010*, p2=0.012*, p3=0.025, p4=0.331**
MRI (Number of plaques)		19.13 ± 6.73	12.77 ± 4.92	2.0 ± 1.41	**p1=0.001*, p2=0.021, p3=0.002, p4=0.057**
Vitamin D (ng/mL)		17.87 ± 5.29	24.0 ± 5.12	32.50 ± 0.71	**P1=0.001*, p2=0.010*, p3=0.002, p4=0.091**

Data presents as mean ± SD or frequency (%). p: Comparing the different IL17A genotypes. SD. Standard deviation, H: Kruskal–Wallis test, MC: Monte Carlo. p1: Comparing the different IL17A genotypes, p2: Comparing GG and AG, p3: Comparing GG and AA, p4: Comparing AG and AA,

Table 5: Logistic regression analysis for prediction of multiple sclerosis susceptibility

	Univariate			Multivariate		
	p	**OR**	**95% CI**	**p**	**OR**	**95% CI**
Sex	0.812	1.092	0.530–2.250	---	---	---
Age	0.166	1.034	0.986–1.085	---	---	---
Rural vs. urban	0.908	1.043	0.515–2.111	---	---	---
Family history	0.807	1.207	0.266–5.471	---	---	---
Smoking	0.226	1.843	0.685–4.960	---	---	---
IL17A rs2275913 (AA vs. GG+GA)	**0.034***	0.331	0.119–0.921	**0.034***	0.104	0.013–0.844
Vitamin D	**0.001***	0.905	0.855–0.958	**0.003***	0.912	0.859–0.969

Data presents as numbers. OR, odds ratio; CI, confidence interval; OR<1, protective; OR>1, risky; *: Significant when p value <0.05.

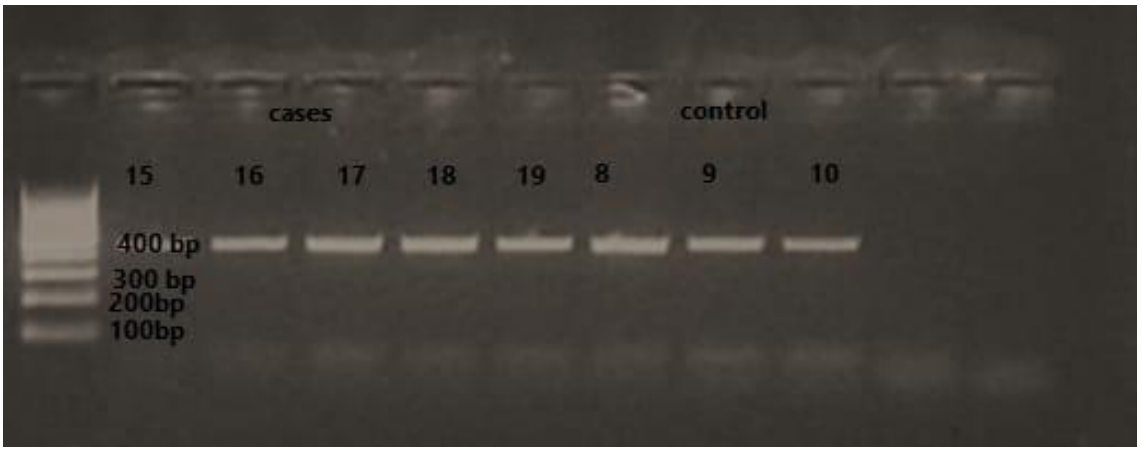

Figure 1 : PCR product of (IL 17 A)gene polymorphism (rs 2275913) with 445 bp length using 2%agarose gel electrophoresis. Left lane is PCR Marker(100 -1000 bp) .

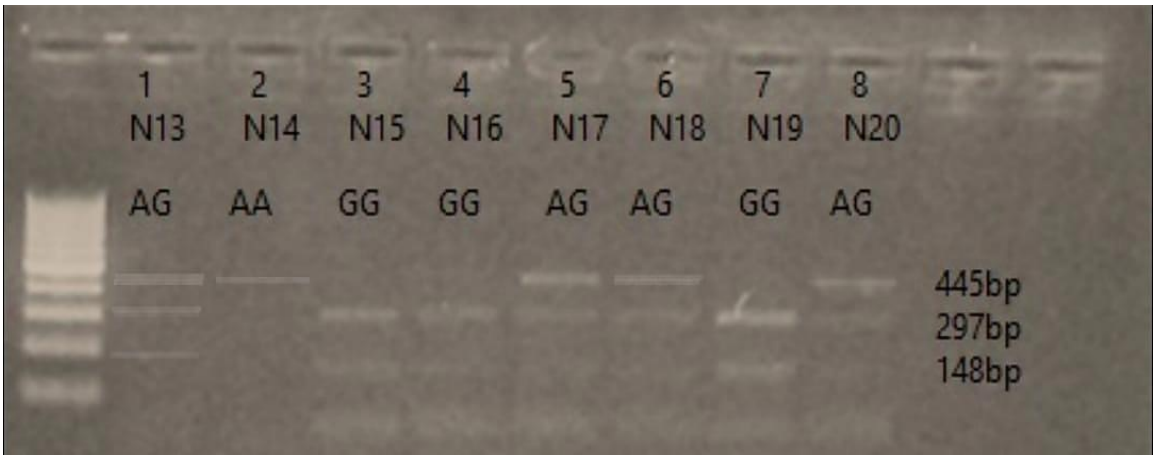

Figure 2 : Enzyme digestion for samples genotyping using 2 %agarose gel electrophoresis .

Discussion

MS is a chronic autoimmune disorder marked by damage to myelin sheath within the CNS. MS manifests with a diversity of clinical features as motor dysfunction, sensory disturbances, and autonomic irregularities. These dysfunctions are attributed to the disruption of white matter connections and the atrophy of gray matter in people with MS [13]. Also, the incidence and progression of MS are entirely associated with Th17 cells and the cytokines they produce, including IL-17 [14] . Given the importance of IL-17A and IL-17F cytokines in the development and progression of inflammatory and autoimmune diseases [15] . The target of this work guided to study the role of IL17A genetic variant (rs2275913) and its association with lower risk of MS disease in Egyptian patients

The present study showed female predominance among MS group (63.3%) **Table (2).** This is in accordance with a

previous Egyptian study that reported female: male ratio to be 2.03:1[16]. This was higher than that in some Middle East countries as in Iraq (1.2:1), Kingdom of Saudi Arabia (1.32:1) [17], and Qatar (1.33:1) [18].

The residence of MS patients was rural in 46.7% and urban in 53.3% **Table (2)** with no significant differences were found versus control group.

A study conducted in Bavaria, Germany, found similar results, indicating that urban areas had a higher incidence and prevalence compared to rural areas [19]. On the other hand, a study conducted in Moldavia found that rural areas had a higher prevalence than urban areas [20].

The investigation of family history reveals that the majority of MS patients (93.3%) had no family history of the MS **Table (2).** Family history in our study was comparable to that of the other Egyptian studies as **Zakaria and colleagues**. [21] found that 6% of patients had positive family history , and **Alemany-Rodríguez and colleagues** [22] found that 5.9% of Patients of MS have a 1^{ST}- and/or 2^{nd}-degree relative with MS.

The smoking status comparison shows that a greater percentage of controls (90.0%) do not smoke than MS patients (76.7%) **Table (2).** This difference has no significance statistically. Smoking considered as a major environmental risk factor for MS, influencing both the disease onset and progression [23] . Data from a prior study revealed that the proportion of smokers in MS groups is different statistically. There were 71.4% smokers in the MS group and 28.6% in the control group [24] **.**

MS cases had a mean illness period of 6.50 years **Table (3).** This was comparable to previous study in Kuwait mean illness period was 7.21 years [25]. But the mean disease duration observed in **Eva and researchers** [26] was 3.2 years.

The average age of onset is 26.30 years Table (3). This was comparable to previous study as **Hamdy and colleagues** [27] observed that age at diagnosis was 26.61years but younger than other study observed that age at MS onset was 33 years [28].

The average number of attacks per MS patient is 3.23 **Table (3)**. This was comparable to previous study by **Jamalian et al**. [29] who observed that frequency of attacks was equal to 3.37 with a variance of 0.43

The most prevalent form of MS in our study was RRMS (80%), followed by SPMS (20%)

Table (3). The aggregate estimate for RRMS, SPMS, and PPMS was 71%, 12%, and 8%, respectively, according to a meta-analysis [30].

The present study showed that average EDSS of 2.28 with range from 1 to 6 in our patients **Table (3). Eva and researches**. [26] Observed that baseline EDSS (SD) was 1.8 (1.4).

The MRI data indicate a mean of 15.23 plaques per patient , ranging from 1 to 31 attacks **Table (3)** .This was comparable to previous study [31] indicating that the average number of license plates increased from 8.7 ± 5.68 at the commencement of the period to 15.14 ± 8.83 at the conclusion of the period (1 year follow-up). The CSF analysis in 21 patients **Table (3)**, shows that

all patients examined (100%) had more than two oligoclonal bands, which is a typical finding in MS and confirms the diagnosis.

The findings in our study demonstrate that the IL17A (rs2275913) gene polymorphism reveals significant genotype differences between controls and MS patients **Table (2),** notably for the AA genotype (p = 0.027), which appears to be related with a lower risk of MS (OR = 0.29). The A allele is also considerably less prevalent in MS patients. In line with our findings, **Khouzani et al**. [32] discovered that Because the A allele is more common , the incidence of GG + AG genotypes if it compared with AA had a strong correlation with MS . Alle A also significantly decreased the risk of MS illness development , although only slightly (OR =0.702 , P=0.051). **Al-Naseri and colleagues** [33] found that IL17A (rs2275913) SNP may not play a considerable role in the predisposition to MS in a sample of the Iraqi population.

It was found that cells with the A allele secreted more IL-17A than cells without the A allele**.** Hence, the IL-17A rs2275913 polymorphism results in more efficient secretion of IL-17A [34]. The finding that the IL-17A (rs2275913) AA genotype is associated with reduced MS risk , despite higher IL-17A secretion confirms the complicated nature of immune regulation in complex diseases as MS that often modulated by gene-gene interactions, gene-environment interactions and functional variation in the type of IL-17A response (e.g. ., its timing , cellular source , or downstream signaling pathway) could be qualitatively different or more controlled in individuals with AA genotype , leading to a net protective effect.

The relationship between IL17A genotypes other variables shows no significant variations in demographic data , family history, smoking status, the number of attacks, disease duration, age of onset, MS types or incidence of ocular neuritis among patients across the genotype groups **Table (4).**

The relationship between IL17A genotypes and EDSS scores is strong, with the GG genotype being associated with a higher mean EDSS score (3.13) than the AG (1.5) and AA (1) genotypes **Table (4)**. The examination of the association between IL17A (rs2275913) genotypes and the amount of plaques identified on MRI shows significant variations across the groups. Patients with the GG genotype had a mean of (19.13) plaques, which is considerably higher than those with the AG (12.77) and AA (2) genotypes, suggesting that the GG genotype is linked with a higher disease burden as evaluated by MRI. While AA genotype is associated with better outcome **Table (4).** The current study showed that MS patients had a significantly lower mean Vitamin D level (21.50 ng/mL) than controls (38.15 ng/mL).

In line with our findings, many epidemiological researches have reported a correlation between low Vitamin D levels and a raised risk of MS [35] [36].

Contrarily to our study, other researchers observed that the level of vitamin D between the MS cases and the control group had no variation in a statistically point of view [37] [38] .

The current study found that the examination of Vitamin D levels in association with IL17A genotypes revealed significant differences (p = 0.001), with the GG genotype having the lowest mean Vitamin D level (17.87 ng/mL) compared to the AG (24.0 ng/mL) and AA (32.50 ng/mL) **Table (4).** This implies that the GG genotype may be related with Vitamin D insufficiency.

Some researchers found that the elevation in serum vitamin D level was related with a reduced incidence of MS relapse. The majority of the individuals in their research were receiving immunomodulatory treatment and concluded that boosting 25(OH)D levels could reduce the risk of relapse [39].

In the current work **Table (5),** the IL17A rs2275913 polymorphism was found to be significant in the univariate model (p = 0.034), as well as in the multivariate model (p = 0.034), with OR<1, indicating that AA genotype is associated with protective effect against MS. Other characteristics, such as gender, age, residency, family history, and smoking, do not have a significant connection with MS susceptibility, indicating that vitamin D and the IL17A polymorphism may be more important in understanding the genetic and environmental interactions in MS pathogenesis.

Smolders et al. [40] observed a negative correlation between vitamin D and EDSS.

Conclusions

The IL17A (rs2275913) gene polymorphism has been linked to MS but the A allele may have a protective effect , So the IL17A GG genotype is associated with higher disability levels while the AA genotype may offer some protection against severe disability.

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