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Magnetic resonance imaging markers of disability in Egyptian multiple sclerosis patients

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ABSTRACT

Background: The aim of this work was to identify the magnetic resonance imaging (MRI) markers of disability in Egyptian multiple sclerosis (MS) patients.

Subjects and methods: This retrospective observational study included 673 patients recruited from the registry of the MS unit at Ain Shams University hospitals. At the time when the MRI scans of the brain and spinal cord were done (with and without gadolinium enhancement), clinical disability was rated using the Expanded Disability Status Scale (EDSS) during the patient's first visit.

Results: Females represented 72.5%, all types of MS were included, the mean age of onset was 26.1 ± 7.7(SD) years, mean duration of illness was 8.3 ± 5.5(SD) years. The mean EDSS of the patients was 3.5 ± 2.1. The study population was divided into three groups according to the EDSS score; mild from 0–3 (56.6%), moderate from 3.5–6 (34.9%) and severe more than 6 (8.5%). The number and types of MRI lesions (T2, T1 black holes, T1 contrast and confluent lesions) in the different anatomical locations (periventricular, juxtacortical, infratentorial and spinal) were correlated with the clinical and demographic data of the patients as well as with the EDSS score. The presence of confluent brain lesions ($P < 0.001$), brain T1 hypointense lesions ($P = 0.009$), and infratentorial T2 lesions (from 1 to 3 lesions ($P = 0.04$), from 4 to 10 ($P < 0.001$) and more than 10 ($P < 0.001$)), were significantly correlated to high EDSS scores after linear regression analysis.

Conclusion: This is the first Egyptian study to show that infratentorial lesions, confluent brain lesions and T1 hypointense lesions are conventional MRI parameters that correlate with the degree of disability in Egyptian MS patients.

1. Introduction

Magnetic resonance imaging (MRI) techniques are a cornerstone in the diagnosis and management of multiple sclerosis (MS) (Barkhof, 2002). The conventional MRI parameters such as the number and distribution of T2 lesions and contrast enhancing lesions have been included in the outcome measures of the pivotal clinical trials and they remain the main available imaging tool in the everyday MS practice (Polman et al., 2011; Zivadinov and Bakshi, 2004). MRI imaging data are lacking from Egypt. Clinical characteristics of Egyptian MS patients have been previously published (Zakaria, 2016). The aim of this study was to describe the MRI characteristics of Egyptian MS patients and to correlate these MRI findings with the degree of disability, as measured by the EDSS in order to identify the MRI markers of disability in Egyptian MS patients.

2. Patients and methods

This was a retrospective observational study from the patients' records of the database of the Ain Shams university MS unit registry, which is the largest MS registry in Egypt, established in 2013. Patients were included only if an informed consent, by themselves or their guardians, was obtained at their first visit to use the demographic, clinical and radiological data in clinical research.

This study included 673 patients with the diagnosis of MS or clinically isolated syndrome (CIS), based on the 2010 McDonald's criteria (Schreiber et al., 2001). All clinical types of MS were included. The Expanded Disability Status Scale (EDSS) score was recorded at the

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patient's first visit to assess disability.

MRI scans of the brain, cervical and dorsal cord, with gadolinium enhancement (GAD), were performed at the patient's first visit using a Philips superconductive magnet system 1.5 Tesla machine. All patients underwent examination by our MRI protocol tailored specifically for multiple sclerosis patients. The various MR sequences for brain and spine imaging and their acquisition parameters are listed in two supplementary tables.

These scans were assessed by three of the co-authors who are neuroradiology consultants in the department of Radiology, faculty of medicine, Ain Shams University. They were working in consensus to evaluate the MRI's of the patients. The total number of T2 lesions, their distribution (periventricular, juxtacortical, infratentorial and spinal cord) and evidence of GAD enhancement were reported. Confluent lesions were defined as a single T2 lesion larger than 20 mm, typically located in the periventricular region, or as two or more T2 lesions connected at one or more margins (Schreiber et al., 2001).

3. Statistical methods

The collected data were coded, tabulated, and statistically analyzed using IBM SPSS statistics (Statistical Package for Social Sciences) software version 22.0, IBM Corp., Chicago, USA, 2013.

Descriptive statistics were done for quantitative data as minimum and maximum of the range as well as mean ± SD (standard deviation) for quantitative normally distributed data. Median and 1st and 3rd inter-quartile range for quantitative non-normally distributed data, while it was done for qualitative data as number and percentage.

Inferential analyses were done for quantitative variables using ANOVA test with post hoc Tukey test for more than two independent groups with normally distributed data and Kruskal Wallis test with post hoc Dunn's test for more than two independent groups with non-normally distributed data. In qualitative data, inferential analyses for independent variables were done using Chi square test for differences between proportions and Fisher's Exact test for variables with small expected numbers with post hoc Bonferroni test. While correlations were done using Pearson correlation for numerical normally distributed data, and using spearman rho test for qualitative data. Linear and logistic regressions were used to find out independent factors affecting certain conditions. The level of significance was taken at *P*value < 0.05 being significant, otherwise non-significant.

4. Results

Analysis of the demographics and clinical characteristics of the study population (Table 1) showed that the majority of patients were females (72.5%) with a female to male ratio of 2.6:1. The age of the patients at the onset ranged from 12 to 54 years with mean of 26.1 ± 7.7(SD) years. The mean duration of illness among the patients was 8.3 ± 5.5(SD) years.

The clinical presentations were: RRMS (78.7%), SPMS (15.5%), PPMS (2.8%), and CIS (3%).

The median and IQR EDSS score of all the study population as well as the different MS subtypes are shown in Table 1. The study population was divided into 3 groups according to the EDSS score; patients with mild disability (EDSS score ranging from 0–3) included 56.6%, patients with moderate disability (EDSS score ranging from 3.5–6) included 34.9%, and patients with severe disability (EDSS score more than 6) included 8.5%.

As regard the MRI findings of the study population (Table 2), the total number of brain T2 lesions was more than 10 in 73.4% of the patients, while 23.0% had from 4 to 10 lesions, and 3.6% had from 1 to 3 lesions. It was noticed that 90.4% of SPMS patients had more than 10 brain T2 lesions, compared to 71.9% of RRMS patients, 57.9% of PPMS patients and 45.0% of CIS patients ($P < 0.001$).

The number of T2 lesions and their distribution in relation to the periventricular, juxtacortical and infratentorial regions are shown in Table 2. It was observed that 55.8% of SPMS patients had more than 10 periventricular lesions, compared to 35.7% of RRMS patients, 31.6% of PPMS patients and 20.0% of CIS patients ($P < 0.001$). Also, 32.7% of SPMS patients had more than 10 juxtacortical lesions, compared to 16.2% of RRMS patients, 5.3% of PPMS patients and 5.0% of CIS patients ($P < 0.001$). While infratentorial lesions showed non statistical difference among the different MS subtypes.

Confluent brain lesions were present in 46.8% of the patients. It was more prevalent in SPMS (67.3%), compared to 44.5% of RRMS, 31.6% of PPMS and 15.0% of CIS patients ($P < 0.001$).

Brain T1 hypointense lesions were present in 51.3% of patients. It was detected in 74.0% of SPMS, compared to 48.3% of RRMS, 42.1% of PPMS and 20.0% of CIS patients ($P < 0.001$).

Spinal cord lesions were present in 71.3% of the patients. There was no statistical difference between the different MS subtypes.

Brain enhancing lesions were present in 29.3% of the patients and spinal cord enhancing lesions were present in 9.7%, with no statistical differences among the different subtypes.

The comparison of demographics and clinical characteristics of the patients based on their grade of disability (Table 3) showed that patients with mild disability were significantly younger (mean age of 32.6 ± 8.4 years) compared to patients with moderate disability (mean age of 36.3 ± 8.8 years) and severe disability (mean age of 37.9 ± 8.2 years) ($P < 0.001$). Also patients with mild disability had shorter duration of illness (mean of 6.9 ± 4.6 years) compared to patients with moderate disability (mean of 9.6 ± 6.1 years) and severe disability (mean of 11.3 ± 5.1 years) ($P < 0.001$). There were no significant differences between the groups as regards smoking ($P = 0.786$) or relapses ($P = 0.239$).

The correlation between the MRI characteristics and the degree of disability is seen in Table 4 which showed a significant positive correlation between the total number of brain T2 lesions and degree of disability ($P < 0.001$).

Table 1
Demographics and clinical characteristics of study population.

Characteristics		All patients	RRMS	SPMS	PPMS	CIS
Number of patients (%)		673	530 (78.7%)	104 (15.5%)	19 (2.8%)	20 (3%)
Gender	Male	185 (27.5%)	398 (75.1%)	72 (69.2%)	8 (42.1%)	11 (55.0%)
	Female	488 (72.5%)	132 (24.9%)	32 (30.8%)	11 (57.9%)	9 (45.0%)
Smoking status	Smoker	92 (13.7%)	65 (12.3%)	16 (15.4%)	5 (26.3%)	6 (30.0%)
	Non smoker	581 (86.3%)	465 (87.7%)	88 (84.6%)	14 (73.7%)	14 (70.0%)
Age of patient (years) (mean ± SD)		34.4 ± 8.8	33.3 ± 8.3	39.6 ± 8.3	39.5 ± 10.2	27.4 ± 8.6
Age of patient at onset of disease (years) (mean ± SD)		26.1 ± 7.7	25.8 ± 7.5	26.7 ± 7.7	29.2 ± 9.4	26.8 ± 8.5
Duration of illness (years) (mean ± SD)		8.3 ± 5.5	7.4 ± 4.8	12.8 ± 6.1	10.3 ± 6.4	1.1 ± 0.5
EDSS [range, median (IQR)]		0–8, 3 (2–6)	1–6, 2 (2–4)	5.5–8, 6 (4.5–6.5)	3–7, 6 (4–7)	0–2, 2 (1–2)
EDSS grading	Mild disability (0–3)	381 (56.6%)	359 (67.7%)	0 (0.0%)	4 (21.1%)	18 (90.0%)
	Moderate disability (3.5–6)	235 (34.9%)	169 (31.9%)	54 (51.9%)	10 (52.6%)	2 (10.0%)
	Severe disability (> 6)	57 (8.5%)	2 (0.4%)	50 (48.1%)	5 (26.3%)	0 (0.0%)

Table 2
MRI characteristics of study population.

Characteristics		All patients (n = 673)	RRMS (n = 530)	SPMS (n = 104)	PPMS (n = 19)	CIS (n = 20)	P
Total number of brain T2 lesions	1–3	24 (3.6%)	21 (4.0%)	0 (0.0%)	0 (0.0%)	3 (15.0%)	< 0.001[a]
	4–10	155 (23.0%)	128 (24.1%)	10 (9.6%)	8 (42.1%)	8 (40.0%)	
	> 10	494 (73.4%)	381 (71.9%)	93 (90.4%)	11 (57.9%)	9 (45.0%)	
Number of periventricular lesions	Zero	7 (1.0%)	6 (1.1%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	< 0.001[b]
	1–3	130 (19.3%)	111 (20.9%)	5 (4.8%)	6 (31.6%)	8 (40.0%)	
	4–10	279 (41.5%)	224 (42.3%)	41 (39.4%)	7 (36.8%)	7 (35.0%)	
	> 10	257 (38.2%)	189 (35.7%)	58 (55.8%)	6 (31.6%)	4 (20.0%)	
Number of juxtacortical lesions	Zero	109 (16.2%)	87 (16.4%)	8 (7.7%)	6 (31.6%)	8 (40.0%)	< 0.001[b]
	1–3	232 (34.5%)	189 (35.7%)	30 (28.8%)	7 (36.8%)	7 (35.0%)	
	4–10	207 (30.7%)	168 (31.7%)	32 (30.8%)	5 (26.3%)	4 (20.0%)	
	> 10	125 (18.6%)	86 (16.2%)	34 (32.7%)	1 (5.3%)	1 (5.0%)	
Number of infratentorial lesions	Zero	209 (31.0%)	170 (32.0%)	20 (19.2%)	7 (36.8%)	10 (50.0%)	0.054[b]
	1–3	306 (45.5%)	241 (45.5%)	47 (45.2%)	7 (36.8%)	7 (35.0%)	
	4–10	137 (20.4%)	101 (19.1%)	31 (29.8%)	4 (21.1%)	3 (15.0%)	
	> 10	21 (3.1%)	18 (3.4%)	6 (5.8%)	1 (5.3%)	0 (0.0%)	
Presence of confluent brain lesions		315 (46.8%)	236 (44.5%)	70 (67.3%)	6 (31.6%)	3 (15.0%)	< 0.001[b]
Presence of brain T1 hypointense lesions		345 (51.2%)	256 (48.3%)	77 (74.0%)	8 (42.1%)	4 (20.0%)	< 0.001[b]
Presence of spinal cord lesions		480 (71.3%)	372 (70.2%)	80 (76.9%)	15 (78.9%)	13 (65.0%)	0.370[a]
Presence of brain GAD		197 (29.3%)	164 (30.9%)	21 (20.2%)	4 (21.1%)	8 (40.0%)	0.143[a]
Presence of spinal cord enhancing lesions		65 (9.7%)	53 (10.0%)	8 (7.7%)	2 (10.5%)	2 (10.0%)	0.642[b]

[a] Chi square test with post hoc Bonferroni test.
[b] Fisher's Exact test with post hoc Bonferroni test.

Also there was a significant positive correlation between the number of T2 lesion in the different brain regions and the degree of disability (periventricular $P < 0.001$, juxtacortical $P < 0.001$ and infratentorial $P < 0.001$). However, infratentorial lesions were absent in 39.1% of patients with mild disability, compared to 21.3% of the patients with moderate disability and 17.6% of the patients with severe disability.

Confluent brain lesions were significantly more prevalent among patients with severe disability (68.4%) compared to patients with mild disability (34.1% of patients) ($P < 0.001$). Also brain T1 hypointense lesions were significantly more among patients with severe disability (78.9%) compared to those with mild disability (39.4% of patients) ($P < 0.001$). There were no significant differences between the three groups as regards the presence of spinal cord lesions ($P = 0.185$), brain enhancing lesions ($P = 0.271$) or spinal cord enhancing lesions ($P = 0.291$).

Correlation between different variables and the EDSS score are shown in Table 5, which showed a positive correlation with the age, age of onset, duration of illness and the different MRI parameters. There was no correlation between the EDSS score and relapses ($P = 0.688$).

However, when Linear regression analysis was done for the factors affecting the EDSS score (Table 6) it showed that the MRI parameters that were significantly correlated to high EDSS scores were the presence of confluent brain lesions ($P = 0.005$, 95% CI: 0.140–0.772), brain T1 hypointense lesions ($P = 0.009$, 95% CI: 0.107–0.761), the number of infratentorial lesions ranging from 1 to 3 lesions ($P = 0.04$, 95% CI: 0.016–0.676), 4 to 10 lesions ($P = 0.001$, 95% CI: 0.314–1.223) and more than 10 infratentorial lesions ($P < 0.001$, 95% CI: 1.047–2.791). Also, the age at onset and the duration of illness were significantly correlated to high EDSS scores.

The demographics and clinical characteristics of the study population were compared and correlated to the total number of brain T2 lesions (Tables 7 and 8) showing that the total number of brain T2 lesions was positively correlated to the age of patient ($P < 0.001$, $r = 0.106$), the duration of illness ($P < 0.001$, $r = 0.216$) and EDSS score ($P < 0.001$, $r = 0.164$).

The patients who had 1–3 T2 lesions were significantly younger ($P = 0.014$), had lesser duration of illness ($P < 0.001$) and lower EDSS scores ($P < 0.001$).

Logistic regression analysis was done for the factors predicting the presence of more than 10 brain T2 lesions (Table 9) showed that the duration of illness [$P < 0.001$, 95% CI: 1.124 (1.098–1.151)] and male gender [$P = 0.017$, 95% CI: 1.603 (1.087–2.364)] were the significant factors.

5. Discussion

The correlation between the MRI findings and the degree of clinical disability in MS patients has been previously assessed in numerous studies. However, to our knowledge, this is the first study from Egypt. Previous studies showed inconsistent results. This was another reason for attempting to validate this data among Egyptian MS patients.

Table 3
Demographics and clinical characteristics of study population based of grading of disability.

Characteristics		Mild disability (EDSS 0–3) (n = 381)	Moderate disability (EDSS 3.5–6) (n = 235)	Severe disability (EDSS > 6) (n = 57)	P
Gender	Male	278 (72.8%)	183 (75.0%)	41 (61.2%)	0.079[b]
	Female	104 (27.2%)	61 (25.0%)	26 (38.8%)	
Smoking status	Smoker	53 (13.9%)	32 (13.6%)	9 (15.8%)	0.786[b]
	Non smoker	328 (86.1%)	203 (86.4%)	48 (84.2%)	
Age of patient (years) (mean ± SD)		32.6 ± 8.4	36.3 ± 8.8	37.9 ± 8.2	< 0.001[a]
Age of patient at onset of disease (years) (mean ± SD)		25.7 ± 7.8	26.7 ± 7.6	26.6 ± 7.1	0.288[a]
Duration of illness (years) (mean ± SD)		6.9 ± 4.6	9.6 ± 6.1	11.3 ± 5.1	< 0.001[a]
Relapses [median (IQR)]		3.0 (2.0–5.0)	3.0 (2.0–5.0)	4.0 (3.0–6.0)	0.239[c]

[a] ANOVA test with post hoc Tukey HSD test.
[b] Chi square test with post hoc Bonferroni test.
[c] Kruskal Wallis test.

Table 4
Correlation between MRI characteristics and grades of disability.

Characteristics		Mild disability (EDSS 0–3) (n = 381)	Moderate disability (EDSS 3.5–6) (n = 235)	Severe disability (EDSS > 6) (n = 57)	P
Total number of brain T2 lesions	1–3	21 (5.5%)	3 (1.3%)	0 (0.0%)	< 0.001[a]
	4–10	110 (28.9%)	38 (16.2%)	7 (12.3%)	
	> 10	250 (65.6%)	194 (82.6%)	50 (87.7%)	
Number of periventricular lesions	Zero	6 (1.6%)	1 (0.4%)	0 (0.0%)	< 0.001[b]
	1–3	98 (25.7%)	30 (12.8%)	2 (3.5%)	
	4–10	160 (42.0%)	90 (38.3%)	29 (50.9%)	
	> 10	117 (30.7%)	114 (48.5%)	26 (45.6%)	
Number of juxtacortical lesions	Zero	71 (18.6%)	30 (12.8%)	8 (14.0%)	< 0.001[a]
	1–3	145 (38.1%)	64 (27.2%)	23 (40.4%)	
	4–10	108 (28.3%)	86 (36.6%)	13 (22.8%)	
	> 10	57 (15.0%)	55 (23.4%)	13 (22.8%)	
Number of infratentorial lesions	Zero	149 (39.1%)	50 (21.3%)	10 (17.6%)	< 0.001[a]
	1–3	165 (43.3%)	113 (48.1%)	28 (49.1%)	
	4–10	63 (15.6%)	59 (25.1%)	15 (26.3%)	
	> 10	4 (1.0%)	13 (5.5%)	4 (7.0%)	
Presence of confluent brain lesions		130 (34.1%)	146 (62.1%)	39 (68.4%)	< 0.001[a]
Presence of brain T1 hypointense lesions		150 (39.4%)	150 (63.8%)	45 (78.9%)	< 0.001[a]
Presence of spinal cord lesions		268 (70.3%)	167 (71.1%)	45 (78.9%)	0.185[a]
Presence of brain enhancing lesions		119 (31.2%)	65 (27.7%)	13 (22.8%)	0.271[a]
Presence of spinal cord enhancing lesions		40 (10.5%)	22 (9.0%)	3 (4.5%)	0.291[a]

[a] Chi square test with post hoc Bonferroni test,.
[b] Fisher's Exact test with post hoc Bonferroni test.

Table 5
Correlations between EDSS score and different variables.

Variables	r	P
Age of patient	0.306	< 0.001*
Age at onset of disease	0.1118	0.002*
Duration of illness	0.348	< 0.001*
Total number of T2 lesion	0.164	< 0.001*
Periventricular	0.214	< 0.001*
Juxtra cortical	0.151	< 0.001*
Infratentorial	0.196	< 0.001*
Relapses	0.033	0.688

Spearman correlation.
* Significant.

The total number of brain T2 lesions was significantly associated with disability; more than 80% of the patients with either moderate or severe disability had more than 10 brain T2 lesions compared to patients with mild disability, and the total number of brain T2 lesions was positively correlated with the EDSS score ($P < 0.001$).

This was previously corroborated in cross sectional (Zakaria, 2016; Schreiber et al., 2001; Mammi et al., 1996) and prospective studies (Filippi et al., 1995; Weiner et al., 2000; Grimaud et al., 1999). Data from those prospective studies showed that increased disability was significantly associated with the number of new T2 lesions, a fact that established the number of lesions as a useful marker of disease activity. Definitely, the T2 lesion volume determined by computerized analysis is more accurate than manual counting of lesions, but the unavailability of the software at most of MRI centers of our country made us rely on counting the number of lesions. However, counting the number of lesions is still useful in assessment of treatment response (Sormani et al., 2013).

Although the total number of T2 lesions was significantly associated with disability, yet, after linear regression analysis, the total number of T2 lesions was not significantly a factor determining the EDSS score. In one study, the number of T2 lesions had a small predictive value for progression of disability in RRMS (Mostert et al., 2010). Even some studies reported that the predictive value of T2 lesions for disability progression is modest and not absolute (Filippi, 2002; Fisniku et al., 2008). This may be attributed to the fact that T2 lesions represent a diverse pathological substrate, ranging from blood–brain barrier breakdown and inflammatory demyelination to astrocytosis and remyelination (Guttmann et al., 1995).

Also the logistic regression analysis did not prove EDSS score or EDSS grading as predictors for the presence of more than 10 brain T2 lesions. However, the duration of illness was a predictive factor for the presence of more than 10 brain T2 lesions, which hypothesize that the number of brain T2 lesions is a reflection of the duration of illness rather than the degree of disability. One fact that may support this assumption is the patients with radiologically isolated syndrome who are prone to evolve to MS; these patients have white matter lesions

Table 6
Linear regression for the factors affecting EDSS score.

Factor	B	SE	P	95% CI	R^2
Gender	0.078	0.163	0.633	−0.242–0.397	0.783
Age of patient at onset of disease	0.060	0.008	< 0.001	0.044–0.075	
Duration of illness	0.122	0.014	< 0.001	0.095–0.149	
Confluent brain lesions	0.456	0.161	0.005	0.140–0.772	
Brain T1 hypointense lesions	0.434	0.167	0.009	0.107–0.761	
Infratentorial lesions ranging from 1 to 3 lesions	0.346	0.168	0.04	0.016–0.676	
Infratentorial lesions ranging from 4 to 10 lesions	0.768	0.231	0.001	0.314–1.223	
More than 10 infratentorial lesions	1.919	0.444	< 0.001	1.047–2.791	
Total number of T2 lesions	−0.039	0.143	0.783	−0.320–0.242	
Periventricular lesions	0.151	0.136	0.267	−0.116–0.419	
Juxtacortical lesions	−0.089	0.094	0.342	−0.274–0.095	

β: Regression coefficient, SE: Standard error, CI: Confidence interval, R^2: Coefficient of determination.

Table 7
Comparison between Total T2 lesions regarding demographic and clinical characteristics.

Variables		1–3 (*N* = 24)	4–10 (*N* = 155)	> 10 (*N* = 494)	*P*
Age (years)		31.0 ± 7.6	33.3 ± 8.8	34.9 ± 8.7	0.014[a]
Onset age (years)(mean ± SD)		26.3 ± 7.3	26.4 ± 7.6	26.1 ± 7.8	0.878[a]
Duration (years) (mean ± SD)		4.6 ± 2.6	6.9 ± 4.5	8.9 ± 5.7	< 0.001[a,*]
EDSS score, Median(IQR)		2.0 (2.0–4.3)	2.0 (1.5–4.5)	3.0 (2.0–6.0)	< 0.001[b,*]
Sex	Female	20 (83.3%)	121 (78.1%)	361 (73.1%)	0.159[c]
	Male	4 (16.7%)	34 (21.9%)	151 (30.6%)	
Smoking		5 (20.8%)	21 (13.5%)	70 (14.2%)	0.720[c]
EDSS grade	Mild disability (0–3)	21 (87.5%)	110 (71.0%)	250 (50.6%)	< 0.001[c]
	Moderate disability (3.5–6)	3 (12.5%)	38 (24.5%)	194 (39.3%)	
	Severe disability (> 6)	0 (0.0%)	7 (4.5%)	50 (10.1%)	
Relapses, Median (IQR)		3.0 (2.0–4.0)	3.0 (2.0–5.0)	4.0 (3.0–6.0)	0.917[b]

[a] ANOVA test with post hoc Tukey HSD test.
[b] Kruskal Wallis test with post hoc Dunn's test.
[c] Chi square test with post hoc Bonferroni test.

Table 8
Correlation between total number of brain T2 lesions and demographics and clinical characteristics of study population.

Variables	*r*[a]	*P*
Age	0.106	< 0.001*
Onset age	−0.027	0.476
Duration	0.216	< 0.001*
EDSS score	0.164	< 0.001*
Relapses	0.008	0.830

Total = 673.
[a] Spearman correlation.
* Significant.

Table 9
Logistic regression for factors predicting the presence of more than 10 brain T2 lesions.

Factors	β	SE	P	95% CI
Male gender	0.472	0.198	0.017	1.603 (1.087–2.364)
Duration of illness	0.117	0.012	< 0.001	1.124 (1.098–1.151)

β: Regression coefficient, SE: Standard error, CI: Confidence interval.

fulfilling the radiological criteria of MS that may have temporal dissemination with no obvious neurological symptoms suggestive of MS and normal neurological examination (Okuda et al., 2009).

The results showed significant correlation between the presence of infratentorial lesions and disability; more than 80% of patients with severe disability had at least one infratentorial lesion while 40% of patients with mild disability did not have any infratentorial lesions. The presence of infratentorial lesions was strongly correlated with disability after linear regression analysis regardless of the number of infratentorial lesions. Similar results were previously reported; in one study two or more infratentorial lesions predicted long-term disability representing an effective tool to identify patients at high risk for earlier occurrence of disability (Minneboo et al., 2004). Even one study reported that the presence of at least one brainstem lesion reflected an increased risk of disability (Tintore et al., 2010).

In this study the presence of confluent brain lesions (brain T2 lesions larger than 20 mm, or two or more T2 lesions connected at one or more margins) were significantly correlated to disability; approximately two thirds of the patients with EDSS score ≥ 3.5 had confluent brain lesions compared to one third only of the patients with EDSS score ≤ 3. This correlation was highly significant after linear regression analysis. This seems concordant with one study observation that patients with SPMS tended to have more extensive and confluent lesions compared to RRMS patients (Kidd et al., 1996). The latter observation was noted in our study where 67% of patients with SPMS had confluent brain lesions compared to 44% of RRMS patients.

The presence of brain T1 hypointense lesions, known also as black holes, was significantly associated with disability, and this correlation remained significant after linear regression analysis. The hypointense T1 lesions represent considerable irreversible structural brain changes (van Waesberghe et al., 1998). Data from previous studies showed diversity; some supported the correlation between disability and total lesion load on T1 weighted sequence (Grimaud et al., 1999; Parry et al., 2002), while others did not (Minneboo et al., 2004).

In this study there were no significant association between disability and enhancing lesions (either brain or spinal cord). Gadolinium enhancement in MRI denotes disturbance of the blood-brain barrier occurring with active inflammation during relapses, however, it is not a strong predictor of disability (Minneboo et al., 2004; Kappos et al., 1999).

Although the aim of this work was to study the MRI parameters of disability, yet, the clinical and demographic characteristics showed a significant correlation (Linear regression) between the age of onset of the disease and the duration of illness with increased disability. Relapses and smoking were not statistically significant to disability in this study.

The relationship between the presence of spinal cord lesions and disability has been reported in some studies (D'Amico et al., 2016; Kearney et al., 2015), this was not validated in this study. However, this relationship will be explored in a prospective study at our center that we are planning for.

The study has several limitations; first, it is a cross sectional study and hence causal relations could not be assessed properly. Second, all types of MS were studied collectively and the inclusion of PPMS cases (although less than 3% of the cases) and CIS cases (3%) might cause bias in the results as PPMS cases may have marked disability with a low lesion load and the opposite may occur in CIS cases. Third, assessment of brain volumetric changes and brain atrophy was not performed. Fourth, using a 1.5 T MRI machine may not enable advanced spinal cord imaging.

Nevertheless, the study power is in the detailed description and analysis of a large number of patients (673).

The results of this study highlighted the correlation between infratentorial lesions, confluent brain lesions, T1 hypointense lesions and disability in Egyptian MS patients. Although these findings are not novel, yet, the validity of these MRI parameters of disability in Egyptian MS patients has not been previously established. The presence of such MRI parameters in a patient's scan may help to identify patients at high risk for disability and should draw the attention of neurologists to strict monitoring of the response to disease modifying therapies and consideration of escalation to different therapeutic options.

Conclusion

The presence of infratentorial lesions, confluent brain lesions and brain T1 hypointense lesions are conventional MRI parameters that are significantly correlated with disability in Egyptian MS patients.

Declaration of Competing Interest

The authors declare that they have no conflict of interest in relation to this article.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.msard.2019.101417.

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