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# Expanded disability status scale in Multiple Sclerosis: Relationship to visual evoked potential

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**Abstract:**

**Background:** Multiple sclerosis (MS) prevalence in Iraq is 11.73/100,000 it causes disability in younger adults. Expanded Disability Status Scale (EDSS) can monitor MS disability while Visually Evoked Potentials (VEP) serves as a marker of myelination.

**Objectives:** To explore the relationship between EDSS and VEPs in multiple sclerosis patients.

**Patients and Methods:** A cross-sectional study was conducted in Ghazi Al- Hariri Hospital from first of Nov 2021 till the end of Jan 2022. Fifty patients with multiple sclerosis were compared to 50 healthy individuals. EDSS Data were collected using a structured questionnaire, P100 latency were measured using VEP. The Correlation was used to investigate the relationship between P100- latencies and EDSS. P value ≤0.05 was considered significant.

**Results:** The average age of MS cases was 33.5±8.01 years, and the mean EDSS was 2.8±2.86. A significant difference in the latency period was reported. The study showed a significant positive correlation between EDSS and P100 latency period.

**Conclusions:** Using non-invasive procedures like VEPs can help to monitor and detect deterioration and improvement in MS patients.

**Keywords**: EDSS; MS; VEPS; evoked potentials

## Introduction:

Multiple Sclerosis (MS) is one of the most recorded common reasons of young adults' disability involving the central nervous system. It affects about 2.1 million individuals every year.**[1]**The prevalence of MS varies from 5 to 300/100,000 people and usually tends to upsurge at higher latitudes. MS has a significantly increasing incidence in Iraq, the incidence was 0.05 in the year 2000 and reached up to 1.5 in the year 2017. The prevalence was found to be 11.73/100,000 which is low compared to neighboring countries.[2]
The overall life expectancy of MS patients, is lower than that of the general population and it more commonly affects women, with the female to male ratio being nearly 3:1.[3] This higher prevalence among women had led to extensive education and training to explore the differences in the immune system and/or the nervous system between women and men, which might be related to gonadal hormones, genetic differences, or even different environmental exposures and modern lifestyle in men and women including some behavioral patterns like smoking, sun exposure, and occupational risks.[4]
One of the most popular and widely used instruments in monitoring the disability and progress of disease activity is the expanded disability status score (EDSS). It remained unchanged since it was first introduced and this by itself is considered beneficial for researches and comparison purposes.
Even though there had been some reported variations in EDSS calculation between doctors and/or users of EDSS, yet this score/scale has been in use for over thirty years and can be used as a monitoring scale for the clinical status of the patients. [5] EDSS ranges from zero (normal neurological status) up to 10 (death due to MS). The lower the value of EDSS scale measure disability and impairments based on the neurological examination, while the upper range of the scale (> EDSS 6) measures the ability of walking and the degree of handicaps of patients with MS.[6]
Visually evoked potential (VEP) is uniquely placed to serve as a biological identifier and a tracer of the myelination along the visual pathway[7], so based on this foundation the VEP timing ("latency") are affected by pathological changes in multiple sclerosis lesions along the entire visual trail.[8] The current study aims to explore the relationship between EDSS and VEPs in a sample of multiple sclerosis diagnosed patients.

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**Patients and Methods:**

A cross-sectional study with a comparative element was conducted in Ghazi Al Hariri Hospital during the period from the first of November 2021 to the end of January 2022. All eligible participants were interviewed and examined for VEP and visual acuity in the electrophysiology unit in the outpatient clinic of Ghazi Al Hariri Hospital. Fifty patients diagnosed with multiple sclerosis who were referred from MS clinic in Baghdad Teaching Hospitals were approached and compared to 50 healthy individuals who were selected from the same hospital. (control).

**Exclusion criteria:** Patient who had been diagnosed as multiple sclerosis but complained from other conditions including chronic meningitis, vasculitis, sarcoidosis, Behçet's disease, tuberculosis, Lyme disease, Sjögren's syndrome, antiphospholipid or anticardiolipin antibody syndromes.

**Inclusion criteria:** All patients with a documented multiple sclerosis diagnosis referred to the Nerve conduction velocity studies and Electromyogram outpatient clinic were enrolled.

The method in the current study included two main steps, the first was collecting data using a structured questionnaire to measure EDSS score, then calculating P100 latency using VEP test. The tool of the study was a well-structured questionnaire adapted from the new MS-patient questions of the Neurology Department in South Florida University ]9[.

The following data were recorded: Social history: Age (in years), gender, ethnicity, marital status: (single, married, divorced with or without children), employment history (employed, unemployed, on disability leave), use of alcohol, tobacco or recreational drugs. Medical and surgical history including the history of vaccinations and any medical or surgical history.

**EDSS calculation:** In EDSS, the score increases corresponding to the deterioration in MS and the score next to 0 is 1. After 1, the score upsurges with an increment of 0.5 to express the clinical deterioration. The score depends on the functional system (FS) ranging between 1.0–4.0 scores and added to that the ambulation between 4.0–8.0 scores. The EDSS score cannot be lower than the score of a single FS (except for visual, mental, and bladder-bowel) [4].

**Visual (optic):** visual acuity

**Cerebral function:** Depression, euphoria, mentation status, and fatigue can be documented. Because fatigue is difficult to evaluate objectively, it does not contribute to the cerebral FS score or EDSS step.

**Brain stem questionnaire**: If there is numbness, facial pain, weakness, hearing loss, difficulty in speech, swallowing foods or liquids.

**Pyramidal function questionnaire:** Site of weakness, spasms, and if the spasms occur during walking, fatigue and the ability to exercise.

**Cerebellar function questionnaire:** If there is balance difficulty, the ability to sit without assistance, tremors, standing with closed eyes, clumsy feeling, or if there is an unsteady walk, in addition to questions about falls, vertigo and dizziness.

**Sensory function:** A selective range of sensory problems (pain, numbness, tingling, itching, painful cold, burning sensation, shock like sensation, increased sense to touch)

**Bowel and Bladder function**: If there is a difficulty in emptying the bladder, urinary tract infections, urinary incontinence, constipation, measures used to evacuate the bowel (enema or manual), if the patient is using pads for urinary or bowel incontinence and whether they have been seen by a urologist or gastroenterologist

**Mobility questionnaire:** Were checked regarding the ability to walk (no restrictions, walk without assistance one block, walk without assistance less than one block, use assistive device on one side and the range of walk, also if the patient uses wheelchair and if he/she was able to walk a few steps or not.

**VEP**: All patients and controls were submitted to visual acuity and VEP. VEP are used to assess the visual conduction pathways through the optic nerves and brain. To measure VEP, visual fields are stimulated, usually with a checkerboard visual stimulus, and the evoked response is recorded using surface recording electrodes over the occipital lobe. The patient is asked to sit comfortably in front of the screen (that will provide the visual stimuli). Electrodes are glued and wires are attached on the patient's skull accordingly. The electrodes used for recording are positioned on the person's scalp, classically over the midline occiput (Oz), vertex (Cz), and forehead (Epz) according to the International 10-20 System. Additional electrodes are placed to the sides of the midline occipital electrode laterally, if partial-field stimulation is performed. The eye which was not undergoing the VEP test was covered and patched accordingly. Verbal consent was obtained from all interviewed participants after carefully explaining the aim and the expected results of the study.

**Statistical Analysis:**

All data were refined and entered into the Statistical Package for Social Sciences, version 20 worksheet. Numerical data were presented by means and standard deviations (M ± SD) while for categorical data, numbers and percentages were calculated. Correlation was calculated to investigate the type of relationship between P100 latencies and EDSS. In all statistical tests a p-value less than or equal to 0.05 was considered significant.

**Results:**

The average age of MS cases was 33.5±8.01 years, ranging between 18-53 years of age, compared to 31.3±6.10 years ranging between 21-44 years for controls. Among the cases there were 32 (64%) females and 18 (36%) males compared to 30 (60%) females and 20 (40%) males among controls. EDSS scores of multiple sclerosis patients average was

2.5±2.32 ranging from 1- 8. While a significant difference in latency period of both eyes VEPs was reported between the two groups (p value <0.001) prolonged waves were noticed among MS cases. Table (1) demonstrate the demographic and test features of the study groups.

**Table (1): Demographic and test results of the study groups**

| Demographic and test variables | | Groups | | P value |
|---|---|---|---|---|
| | | MS Cases (n=50) | Controls (n=50) | |
| | | Mean ± SD | Mean ± SD | |
| Age (years) | | 33.5±8.01 | 31.3±6.10 | 0.129* |
| Gender | Males | 18 (36%) | 20 (40%) | 0.680** |
| | Females | 32 (64%) | 30 (60%) | |
| Disease duration | | 4.1±3.05 | | |
| EDSS score | | 2.5±2.32 | | |
| RP 100 latency | | 183.8±51.69 | 94.5±4.5 | <0.001 |
| LP 100 latency | | 186.7±42.05 | 94.5±5.6 | <0.001 |

***Independent t student test, ** Chi-square test***

Figure (1) Illustrates the EDSS score of MS-cases. Just more than half 26 (52%) had an EDSS score between 0-1, of whom 7 (14%) scored zero and 19 (38%) scored one.

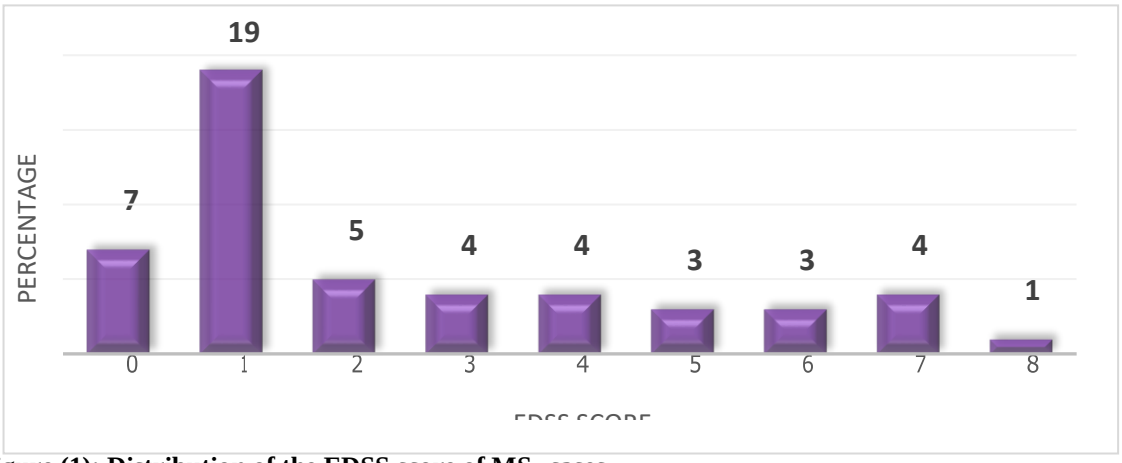


**Figure (1): Distribution of the EDSS score of MS- cases**

Figure (2) shows the correlation of EDSS score of the studied MS group to disease duration in years. With increased disease duration the EDSS score increased. There was a positive and significant correlation between EDSS and disease duration (r=0.577; p value < 0.001)

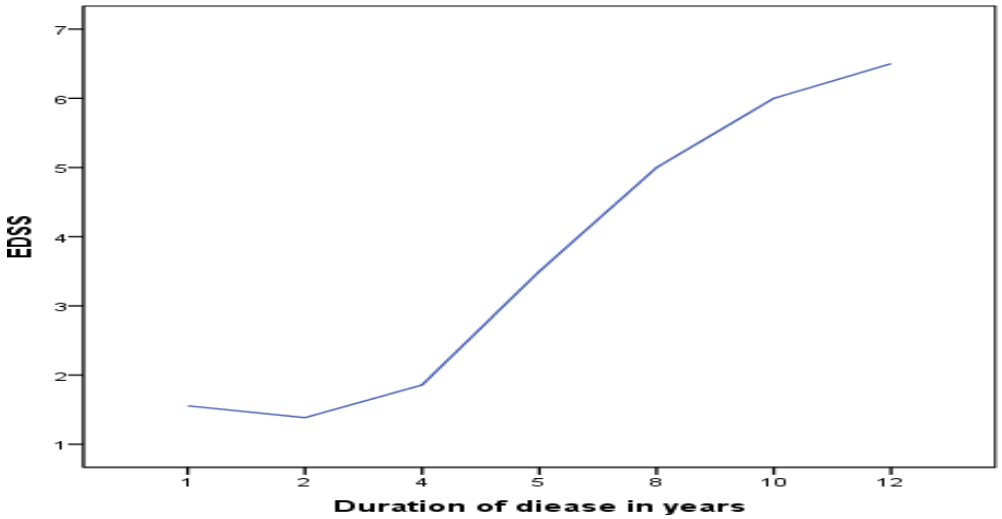


**Figure (2): Distribution of the sample EDSS to the disease duration (n=50)**

The current study showed a positive significant correlation between EDSS scores and P100 latency period. Table (2) illustrates the Pearson coefficient r and p values.

**Table (2): Correlation between EDSS and P 100 latency period**

| Variables | | MS Cases |
|---|---|---|
| LP 100 latency | Pearson Correlation | 0.455** |
| | P value | 0.001 |
| RP 100 latency | Pearson Correlation | 0.433** |
| | P value | 0.002 |

***Correlation is significant at the 0.01 level*

**Discussion:**

The gender distribution in our cases agrees with a recent Iraqi study which found that 68.5% of MS cases were females [2], and compares to an Iranian study[10] where the majority (70.1%) were females. Female predominance is clear and the risk strikes three times higher in women compared to men, although some evidence describes a worst clinical course among men[11]. Research on sex hormone had lengthily been scrutinized mainly because of the effect of hormones on immune cells12]. Estrogen, progesterone, and testosterone are the incriminated hormones in causing an alteration in the immune system and thus had been studied in a detailed manner among MS cases as almost all of these hormones have been proved to significantly affect not only the clinical outcome but also the probability of being susceptible to MS[13, 14]. Studies assessing sexual dimorphism in regard to the immune system and the autoimmune responses focus on the relationships and interdependence of these factors, as well as their independent contributions[15]. The mean age of MS cases and their age range in our study agrees with the results of another Iraqi study where the mean age was 32.3±9.8 years[2], with the results of an Iranian study where the mean age was 33.14 years[10] and it compares to results of a wide review of literature by McGinley et al[3], which reported that MS typically begins in young adults aged 20 to 30 years. Although the current result shows a lower mean age which might indicate a shift in MS trend through involving younger generations, as the previous Iraqi mean age reported in 2011 was 45.6 years[16]. It might also shed the light on better advances and development of diagnostic criteria in addition to better awareness among physicians.

The mean EDSS scores of MS patients was 2.5±2.32, which is in alignment with a study in Germany[17]. More than half of our cases had an EDSS score between 0-1. This may be related to the early diagnosis of the cases as it had been reported that around 67% of MS cases were diagnosed within weeks or months from the beginning of symptoms.[2]

Although EDSS had witnessed some changes over the years, yet it is still the most stable tool to evaluate disability in MS patients, and had correlated positively with trace elements deficiency in MS cases[18]. It is significantly associated with risk factors for upper urinary tract damage and it even allows classifying the patients based on their risk to identify MS patients who are in need for further neuro- urological assessment, treatment and follow up[19]. Interestingly, it had been stated that the disability builds up from EDSS score 4 to 6 took a shorter time compared to the disability interval of 0 to 3 or the interval of 6 to 8. For EDSS of 1 or 1.5, sensory, cerebellar, bowel function, pyramidal, bladder and mental system scores were connected with advanced consequent EDSS scores[20, 21]. As each episode of relapse would leave a lesion with some sort of disability, it is only natural to expect a positive correlation between EDSS and disease duration which was clearly illustrated in the current study. The current study showed a significant positive correlation between EDSS scores and prolonged P 100 latency period, in agreement with the results of a published study [22] in which the authors suggested that the most reliable VEP parameter in the diagnosis of MS, is the prolonged P100 latency values. As the VEP tests are useful in discovering abnormalities in patients with MS and monitoring the worsening and progression of the lesions through demyelination or the regression of lesions and initiation of remyelination [23]. The current result are in concordance with other published studies from Switzerland [24], Spain [25] and Croatia[26] in which a significant correlation between VEP and disease severity, as measured by EDSS score had been established, which confirms the role of VEPs as a functional marker for MS severity and progress. VEP has been shown to be predictive of the disease course, and might even be considered in defining the high-risk patients in need to be enrolled in clinical trials or at higher risk for progression as VEP can detect deterioration, as well as enhancement of impulse dissemination, independent from the main cause that is triggering that change.

**Conclusions:**

MS is an incapacitating chronic disease with a high burden. Using non-invasive procedure like VEPs were linked to disease activity and thus it can help to monitor and detect deterioration and improvement in MS patients.

**Authors' contributions:**

**Rand S. Jassim : students**

**Hanan L. Al-Omary: supervisor**

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# مقياس الإعاقة الموسع في تصلب الاعصاب المتعدد: وعلاقته بفحص فسيولوجيا كهربائية العين

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**الخلاصة:**
**خلفية البحث:** إن معدل إنتشار مرض تصلب الاعصاب المتعدد في العراق هو 11.73 لكل 100.000 شخص وهو يسبب الإعاقة لدى المصابين في عمر الشباب. يمكن لـ مقياس الإعاقة الموسع مراقبة درجة الإعاقة لدى المرضى بينما يعمل فحص فسيولوجيا كهربائية العين كعلامة على تكوّن غمد المايلين
**الأهداف:** تهدف هذه الدراسة إلى إستكشاف العلاقة بين مقياس الإعاقة الموسع وفحص فسيولوجيا كهربائية العين لدى مرضى تصلب الأعصاب المتعدد.
**المرضى والمنهجية:** دراسة مقطعية أجريت في مستشفى غازي الحريري لمدة ثلاثة أشهر. تم مقارنة خمسين مريضا يعانون من مرض تصلب الأعصاب المتعدد مع 50 من الأفراد الأصحاء. تم جمع بيانات مقياس الإعاقة الموسع باستخدام إستبيان منظم، وتم قياس زمن إنتقال P100 باستخدام فحص فسلوجيا كهربائية العين. تم استخدام مقياس الأرتباط للتحقيق في العلاقة بين زمن انتقال P100 ومقياس الإعاقة. تعتبر قيمة $P \leq 0.05$ معتدة إحصائياً.
**النتائج:** كان متوسط عمر حالات تصلب الأعصاب المتعدد 33.5 ± 8.01 سنة. كان متوسط مقياس الإعاقة هو 2.8 ± 2.86. تبين وجود إختلاف معتد إحصائياً بين زمن فحص فسيولوجيا كهربائية العين. أظهرت الدراسة وجود علاقة إرتباط موجبة معتدة إحصائياً بين زمن الإنتقال ومقياس الإعاقة لمرضى تصلب الأعصاب المتعدد.
**الإستنتاجات:** يمكن أن يساعد استخدام الإجراءات غير الجراحية مثل فحص فسيولوجيا كهربائية العين في مراقبة واكتشاف التدهور والتحسن لدى مرضى التصلب المتعدد اذ انه يرتبط ارتباطا معنويا مع نشاط المرض وفعاليته.
**مفتاح الكلمات**: مقياس الإعاقة، فحص فسلوجيا كهربائية العين، تصلب الأعصاب المتعدد، فحوصات الجهود المحرَّض