The association between clinical defects and ventilatory functions parameters in patients with multiple sclerosis

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ABSTRACT

Background: The respiratory motor pathways may be involved in multiple sclerosis because of the multi-focal nature of central nervous system affection in such disease, leading to respiratory muscle weakness (predominately expiratory muscles involvement), producing a restrictive ventilatory defect. Materials & Methods: Clinical pulmonary dysfunction index, Kurtzke MS rating scales, fatigue severity scale (FSS), fatigue descriptive scale (FDS) and Pulmonary function tests evaluated by means of a battery of measures, (including maximal voluntary ventilation (MVV), forced vital capacity (FVC), forced expiratory volume (FEV1) were used in 28 Egyptian patients with definite MS. Result: The clinical pulmonary dysfunction index was positive (abnormal) in 16 (57.1%) subjects [10 subjects (35.7%) with secondary progressive type and 6 subjects (21.4%) with relapsing remitting type]. Statistically significant positive correlations were found between the index and EDSS scores; FSS scores; and FDS scores. Statistically significant positive correlations were also found between cerebellum, brain stem, bladder and cerebral dysfunctions and pulmonary dysfunction index. Mean values of MVV (58.75% ±16.77), FVC (72 percent ± 20.17) and FEV1 (77 percent ± 20.64), were lower than normal in our patients. The Respiratory function tests (MVV, FEV1, FVC) were significantly lower in secondary progressive MS than relapsing MS patients (33±0 vs. 67.33±6.3, p=0.001; 46±0 vs. 87.33±9.1, p=0.001; 42±0 vs. 82±9.4, p=0.001 respectively). Statistically significant negative correlations were found between the Respiratory function tests and; EDSS scores; FSS scores; and FDS scores. Statistically significant negative correlations were found between pyramidal and sensory dysfunctions and respiratory function tests (FVC, FEV1, and MVV). Statistically significant negative correlation was found between brainstem dysfunction and FVC. Statistically highly significant negative correlation was found between cerebellum dysfunction and FEV1/FVC. There was also a trend wise significant negative correlation was found between bladder dysfunction and FVC. Also trend wise significant negative correlations were found between brainstem, cerebral dysfunctions and MVV. Pulmonary function tests (FVC, FEV1, and MVV) were negatively correlated with FSS and FDS scores; and this may establish a physiological basis to multiple sclerosis-related fatigue. Those patients with medullary lesions (n=6, 21.4%); showed positive correlation with clinical pulmonary dysfunction index (ρ=0.04); and negative correlation with MVV (P=-0.04), FEV1(P=-0.04)and FVC (P=-0.04). Also, those with pontine lesion (n=4, 14.3%) showed trend wise positive correlation with pulmonary dysfunction index (ρ=0.06); and negative correlation with FEV1/FVC (P=-0.04).Those with periventricular lesions (n=22, 78.6%) showed negative correlation with FEV1/FVC (P<-0.01). Conclusion: It is concluded that impaired respiration in some MS patients is related to central defects, bladder dysfunction is associated with disturbed pulmonary function, almost certainly because the micturition and pneumotaxic center are closely related and severe cerebellar signs in patients with MS were related to a risk of occurrence of respiratory impairment. MS lesions in the brain stem can also interrupt the motor pathway to phrenic, intercostal and accessory respiratory muscle nerves. Therefore, respiratory dysfunctions were linked to brain stem disorder. Pyramidal dysfunction is associated with disturbed pulmonary function, because pathology in the corticospinal cord may produce not only paralysis of the limbs, but also weakness of the respiratory truncal muscles. Pulmonary function tests (FVC, FEV1, and MVV) were negatively correlated with FSS and FDS scores; and this may establish a physiological basis to multiple sclerosis-related fatigue. This necessitates inclusion of respiratory function evaluation in clinical examination protocols of patients with MS to guide early intervention efforts. (Egypt J. Neurol. Psychiat. Neurosurg., 2007, 44(2): 449-459)
INTRODUCTION

Multiple Sclerosis (MS) can produce a diversity of different respiratory abnormalities because of the multi-focal nature of central nervous system involvement in the disease.

When respiratory motor pathways are involved, respiratory muscle weakness frequently occurs, producing a restrictive ventilatory defect. Expiratory muscle weakness is more prominent than inspiratory muscle weakness and may impair performance of coughing.

Subsequently, in addition to bulbar dysfunction, respiratory muscle weakness may contribute to ineffective coughing, pneumonia, and sometimes even acute ventilatory failure may ensue.

Respiratory muscle weakness may also occur early in the course of the disease, mostly due to reversible neuromuscular failure. Recent studies suggest that the respiratory muscles can be trained for both strength and endurance in multiple sclerosis patients. Respiratory muscle training delays the development of respiratory dysfunction and subsequently improves exercise capacity and cough efficacy, prevents pulmonary complications or prolongs survival in the long-term.

Fatigue is the most common symptom of MS, affecting at least two thirds of patients and one of the most disabling aspects of the disease. Fatigue associated with MS is an abnormal, generalized lack of energy that significantly limits physical and/or mental ability regardless of the degree of effort or level of neurological disability. The pathogenesis of MS fatigue is poorly understood. MS fatigue is not adequately explained by disease duration, gender, psychosomatic mechanisms, physical disability, or sleep dysfunction.

However, few data are available concerning the relationship between the neurological dysfunctions of MS and the lung function abnormalities.

Aim of work: to assess respiratory functions in multiple sclerosis (MS) to investigate whether the localization of multiple sclerosis (MS), the duration of the disease, and the degree of neurological dysfunctions in patients with MS can be associated with respiratory impairment, to identify the neurological defects that predispose MS patients to develop impaired breathing, and to test the hypothesis whether there is any correlation between respiratory dysfunction and fatigue in multiple sclerosis.

PATIENTS AND METHODS

Patients:

Twenty-eight subjects (22 females and 6 males) were included in this study. They were with definite diagnosis of multiple sclerosis, according to Poser et al., supported by clinical examination, MRI brain and/or cervical and; evoked potentials.

Methods:

1. Clinical assessment:
   1. Through neurological clinical examination.
   2. Kurtzke MS rating scales:
      They are subdivided into:
      a) Functional system scales: Each functional system is independent of others, yet together they reflect all neurological impairment in MS.
      b) Expanded disability status scales (EDSS): The findings on neurological examination were scored on a set of subscales: function system scales, which were used as guides for scoring the EDSS.
   3. Fatigue Severity Scale:
      Fatigue severity scale (FSS) consists of 9 statements. The subject is asked to read each statement and circle a number from 1 to 7, depending on how appropriate they felt the statement applied to them over the preceding week. A low value indicates that the statement is not very appropriate whereas a high value indicates agreement. The scoring is done by calculating the average response to the
questions (adding up all the answers and dividing by nine). People with depression alone score about 4.5. But people with fatigue related to MS average about 6.5.

4. Fatigue Descriptive Scale\textsuperscript{17}:
Fatigue descriptive scale (FDS)\textsuperscript{17} is a tool developed to evaluate the periodicity, severity, and quality of fatigue caused by MS. Based on the subject's responses, a score of 0 to 3 is assigned to each of the categories of initiative, modality, frequency, severity, and fatigue associated with heat.

5. Pulmonary Dysfunction Index:
Pulmonary dysfunction index (PDI)\textsuperscript{18} comprised of four clinical components: the patient's report of difficulty in clearing pulmonary secretions and his report of a weakened cough, the examiner's observation of the patient's cough, and ability to count on a single exhalation (a patient with normal vital capacity is able to count to 20 in a single exhalation) was devised for clinical assessment of expiratory muscle weakness in MS\textsuperscript{19}. The index has an acceptable validity and reliability for use in clinical practice to identify those neurological patients with respiratory muscle weakness\textsuperscript{19}. In this study, the index is considered as positive (abnormal) or negative (normal) & the count in a single exhalation is also considered as a separate item.

II. Neurophysiological assessment by the different evoked potentials.

III. Radiological investigations:
MRI brain and/or spinal cord: T1, T2 weighted images, proton density pulse sequences and Flaire images were taken in different planes of the brain and the spinal cord.

IV. Pulmonary function tests:
Pulmonary function tests performed in the occupational medicine department, Cairo University for the studied patients in a sitting position using 2200 computerized sensor medics. The pulmonary function tests were evaluated by flow volume loop. The following data were obtained: forced vital capacity" (FVC) as % predicted, forced expiratory volume in first second (FEV1) as % predicted, FEV1/ FVC and MVV as % predicted. The normal values are >85% of predicted values.

Statistical methods:
Quantitative data were summarized as means and standard deviations, number and percentage. Group means were compared by (student t. test). Analysis of variance (ANOVA) was also used to compare the means and standard deviations of dependent variables when the cases are divided into groups based on their values for categorical variables. Pearson correlation coefficient (r) was done for all continuous data and the probability (p) was obtained from the tables according to the degree of freedom and so significance was calculated. Non parametric correlation was used for non parametric values. A P-value < 0.05 was considered significant. All has been performed using SPSS ver.9.

RESULTS

1. Demographic and clinical result:
Included patients were 6 males (21.4%) and 22 females (78.6%), ranging in age between 17-53 years with a mean age of 30.78 ±10.02 years. They were with diagnosis of definite multiple sclerosis, in stable condition. The disease duration ranged from 1 year to 10 years with a mean of 3.46±2.7 years. The course was relapsing remitting in 16 patients (57.1%), secondary progressive in 10 (35.7%) and primary progressive in 2 (7.2%).

2. EDSS scores:
Across all subjects, EDSS scores ranged between 2 to 8.5 (mean=4.36±2.08). Functional system scales, were: (pyramidal 2.93±1.1; brain stem 0.64±0.9; cerebral 0.2±0.4; cerebellar 1±1.49; sphincter 1±1.08; visual 1.14±1.38; and sensory 1.07±1.18).

3. **FSS scores:**
The scores of the FSS ranged from 4.5 to 7 with a mean of 6.1±1.07.

4. **FDS scores:**
The scores of the FDS scores ranged from 2 to 17 with a mean of 6.57±5.8.

5. **Clinical pulmonary dysfunction index:**
The clinical pulmonary dysfunction index was positive (abnormal) in 16 (57.1%) subjects [10 subjects (35.7%) with secondary progressive type and 6 subjects (21.4%) with relapsing remitting type]. In those subjects during quiet breathing, the physical examination of the respiratory muscles was normal, while during cough there was impairment in abdominal muscle performance; one of these patients recovered from unilateral diaphragmatic paralysis one year ago, before this study. The range of count in a single exhalation was 10-25 with a mean of 18.2±5.9.

6. **Evoked potential results:**
Abnormalities of the VEP were detected in 10 patients (35.7%), abnormalities of the BAEP were detected in 12 patients (42.85%) and abnormalities of the SSEP were detected in 8 patients (28.57%). Combined evoked potential abnormalities were seen in 10 patients (35.7%).

7. **MRI results:**
a) MRI brain: Four subjects (14.29%) had normal MRI of the brain. MS plaques were detected in 24 subjects (85.7%), most of which were periventricular in location (78.6%). Other plaques were in medulla (21.4%), pons (14.3%), cerebellum (7.1%) and parietal (7.1%).

b) MRI cervical: MS plaques in cervical spine were detected in 20 subjects (71.4%) by MRI cervical. Sixteen patients (57.1%) had MS plaques in both MRI brain and cervical spine.

8. **Pulmonary function test:**
Mean values of FEV1 (77 percent ± 20.64), FVC (72 percent ± 20.17) and MVV (58.75 percent ± 16.77) were lower than normal in our patients, however, FEV1/FVC (85.25 percent ±1.58) was normal (Table 1).

**Correlations**

1) **Of the EDSS scores:**
No statistically significant correlation was found between EDSS scores with age, sex, duration of illness (p>0.05). However a tendency towards significant correlation was found between the mean EDSS scores with the number of attacks (p=0.08). Moreover, the severity was significantly greater in secondary progressive MS (mean=6.7±1) than relapsing MS patients (mean=2.68±0.44) (p=0.01) (Table 2).

**Correlation of functional system scales:**
Statistically highly significant positive correlations were found between cerebellum, brain stem, bladder dysfunctions and respiratory dysfunction index. A statistically significant positive correlation was also found between cerebral dysfunction and respiratory dysfunction index. More to the point, statistically significant negative correlations were found between cerebellum, brain stem, visual dysfunctions and the count in a single exhalation. Highly significant negative correlations were found between sensory, sphincter and cerebral dysfunctions and the count in a single exhalation. There was also a trend wise significant negative correlation between pyramidal dysfunction and the count in a single exhalation.

Statistically significant positive correlation was found between cerebellum, bladder, brainstem, visual and cerebral dysfunctions and both FDS scores and FSS scores.

Statistically highly significant positive correlation was found between pyramidal, sensory dysfunctions and FDS scores. There was also a
trend wise significant correlation was found between pyramidal dysfunction and FSS scores (Table 3).

(2) Of the FSS scores:
No statistically significant correlation was found between FSS scores with either number of attacks and duration of illness (p>0.05). Moreover, the severity of fatigue was significantly greater in secondary progressive MS (mean=7±0) than relapsing MS patients (mean=5.75±1.03) (p=0.01).

Also, significant correlation was found between FSS scores with EDSS scores (p=0.02) (Table 2).

(3) Of the FDS scores:
No statistically significant correlation was found between FDS scores with either sex or duration of illness (p>0.05). However, a statistically significant positive correlation was found between FDS scores with number of attacks and EDSS scores (p=0.01, 0.05 respectively). The mean score was significantly greater in secondary progressive MS (mean=13.4±4.35) than relapsing MS patients (mean=2.87±1.3) (p=0.001) (Table 2).

(4) Of clinical pulmonary dysfunction index:
Statistically highly significant positive correlations were found between the index and EDSS scores; FSS scores; and FDS scores (p=0.008, 0.001, 0.004 respectively).

No statistically significant correlation was found between index with sex; duration of illness; type of MS; or number of attacks (p>0.05).

Statistically significant negative correlations were found between the count in a single exhalation and number of attacks; EDSS scores; FSS scores; and FDS scores (p=-0.02, -0.001, -0.005, -0.001 respectively). No statistically significant correlation was found between the count in a single exhalation and sex; duration of illness; or type of MS (p>0.05) (Table 2).

(5) Of evoked potentials:
No significant correlation was found between evoked potentials abnormalities with either clinical data or scales.

(6) Of MRI brain results:
Those patients with medullary lesions (n=6, (21.4%)); showed positive correlation with clinical pulmonary dysfunction index (p=0.01); and trend wise significant correlation with EDSS (p=0.08). Also, those with pontine lesion (n=4, (14.3%)) showed trend wise positive correlation with pulmonary dysfunction index (p=0.06).

However, those with other lesions showed no significant correlation with EDSS, FSS, FDS, or pulmonary dysfunction index. Those patients with medullary lesions (n=6, (21.4%)); showed negative correlation with MVV (P=-0.04), FEV1 (P=-0.04) and FVC (P=-0.04), but no with FEV1/FVC P=0.4. Also, those with pontine lesion (n=4, (14.3%)) showed negative correlation only with FEV1/FVC (P=-0.04). Also, those with periventricular lesions (n=22, 78.6%) showed negative correlation with FEV1/FVC (P=-0.01).

(7) Of MRI cervical spine:
Patients with positive MRI cervical showed no significant correlation with EDSS, FSS, FDS, or respiratory index.

(8) Of respiratory function tests:
No statistically significant correlation was found between Respiratory function tests with sex; duration of illness, apart from FEV1/FVC which was negatively correlated, (p=-0.002); or number of attacks (p>0.05). The Respiratory function tests (MVV, FEV1, FVC) were significantly lower in secondary progressive MS than relapsing MS patients {33±0 vs. 67.3±6.3 (p=0.001); 46±0 vs. 87.3±9.1 (p=0.001); 42±0 vs. 82±9.4, (p=-0.001), respectively}.

Statistically significant negative correlations were found between the respiratory function tests (MVV, FEV1, FVC) and pulmonary dysfunction index; EDSS scores; FSS scores; and FDS scores.

Statistically significant positive correlation was found between Respiratory function tests (MVV, FEV1, and FVC) and the count in a single exhalation (Table 4).

Statistically significant negative correlations were found between pyramidal and sensory dysfunctions and the respiratory function tests (MVV, FEV1, and FVC). Statistically significant
negative correlations were found between visual dysfunctions and the respiratory function tests (MVV, FEV1/FVC, and FVC). Statistically significant negative correlations were found between brainstem dysfunctions and FVC. Statistically highly significant negative correlation was found between cerebellum dysfunctions and FEV1/FVC. There was also a trend wise significant correlation was found between bladder dysfunctions and FVC. Trend wise significant negative correlations were found between brainstem and cerebral dysfunctions and MVV (Table 5).

**Table 1.** The mean and SD values of ventilatory functional parameters of the studied MS patients.

<table>
<thead>
<tr>
<th>Ventilatory functional parameters</th>
<th>Range</th>
<th>Mean and SD values</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1</td>
<td>46-96</td>
<td>77±20.64</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>83-87</td>
<td>85.25±1.58</td>
</tr>
<tr>
<td>FVC</td>
<td>42-94</td>
<td>72±20.17</td>
</tr>
<tr>
<td>MVV</td>
<td>33-75</td>
<td>58.75±16.77</td>
</tr>
</tbody>
</table>

**Table 2.** Correlation between clinical data and clinical scales.

<table>
<thead>
<tr>
<th>Clinical indices</th>
<th>Respiratory function index</th>
<th>Respiratory function count in a single exhalation</th>
<th>EDSS</th>
<th>FSS</th>
<th>FDS</th>
<th>sex</th>
<th>duration</th>
<th>Number of attack</th>
<th>Type of MS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory function index</td>
<td>1</td>
<td>0.008**</td>
<td>0.001**</td>
<td>0.004**</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>count in a single exhalation</td>
<td>1</td>
<td>-0.001**</td>
<td>-0.005**</td>
<td>-0.001**</td>
<td>NS</td>
<td>NS</td>
<td>-0.02*</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>EDSS</td>
<td>0.008**</td>
<td>-0.001**</td>
<td>1</td>
<td>0.02*</td>
<td>0.05*</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>0.01*</td>
</tr>
<tr>
<td>FSS</td>
<td>0.001**</td>
<td>-0.005**</td>
<td>0.02*</td>
<td>1</td>
<td></td>
<td>0.002**</td>
<td>NS</td>
<td>NS</td>
<td>0.01*</td>
</tr>
<tr>
<td>FDS</td>
<td>0.004**</td>
<td>-0.001**</td>
<td>0.05*</td>
<td>1</td>
<td></td>
<td></td>
<td>NS</td>
<td>0.01*</td>
<td>0.001**</td>
</tr>
</tbody>
</table>

NS: non significant, *significant, **highly significant

**Table 3.** Correlation of functional system scales and clinical instruments.

<table>
<thead>
<tr>
<th>Functional system scales</th>
<th>FDS</th>
<th>FSS</th>
<th>Respiratory dysfunction index</th>
<th>The count in a single exhalation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyramidal dysfunction</td>
<td>0.001**</td>
<td>0.07~</td>
<td>NS</td>
<td>-0.08~</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>0.002**</td>
<td>0.05*</td>
<td>0.007**</td>
<td>-0.02*</td>
</tr>
<tr>
<td>Brainstem</td>
<td>0.05*</td>
<td>0.02*</td>
<td>0.001**</td>
<td>-0.03*</td>
</tr>
<tr>
<td>sensory</td>
<td>0.002**</td>
<td>NS</td>
<td>NS</td>
<td>-0.001**</td>
</tr>
<tr>
<td>Bladder</td>
<td>0.001**</td>
<td>0.03*</td>
<td>0.001**</td>
<td>-0.002**</td>
</tr>
<tr>
<td>visual</td>
<td>0.001**</td>
<td>0.005*</td>
<td>NS</td>
<td>-0.04*</td>
</tr>
<tr>
<td>Cerebral</td>
<td>0.001**</td>
<td>0.01*</td>
<td>0.01*</td>
<td>-0.001**</td>
</tr>
</tbody>
</table>

~Trend wise significant, *significant, **highly significant

**Table 4.** Correlation between clinical data and respiratory function tests.
Multiple sclerosis (MS) can produce a variety of different respiratory abnormalities. Respiratory complaints are common in the terminal stage of multiple sclerosis (MS), and death is often due to bulbar weakness leading to aspiration and pneumonia.

In this study, the clinical pulmonary dysfunction index was positive (abnormal) in 16 (57.1%) subjects. In our study, we found no significant correlation between both the index and lung function tests (FVC, MVV, FEV1) and the duration of illness (p>0.05). This is in harmony with Rasova et al., Mutluay et al., and van Klaveren et al., who established that the pulmonary dysfunction has no relationship with the duration of the MS disease; which can be explained by the variable course of MS itself with variable respiratory and muscular involvement. On the other hand, Grasso et al., found significant negative correlation with long disease duration (>15 years).

Statistically significant positive correlations were found between the index and EDSS scores, FSS scores; and FDS scores. Statistically significant negative correlations were also found between both the count in a single exhalation and pulmonary function tests (FVC, FEV1, and MVV) and EDSS scores; FSS scores and FDS scores. This is in agreement with Grasso et al., Mutluay et al., and Smeltzer et al., who instituted that pulmonary impairment increases with multiple sclerosis-induced disability level.
Likewise, Wiens et al.\textsuperscript{25} reported that respiratory muscle weakness, predominantly of the expiratory muscles, is characteristic of individuals with advanced multiple sclerosis and can result in difficulty in clearing secretions and repeated episodes of pneumonia.

As well, Gosselink et al.\textsuperscript{26} and Buyse et al.\textsuperscript{27} stated that in patients with advanced MS, expiratory muscle strength was significantly reduced and related to FVC, pulmonary dysfunction index (cough efficacy), and EDSS. Quite the opposite, Rasova et al.\textsuperscript{20} stated that it is not possible to prove any correlation between pulmonary impairment parameters and neurological impairment in multiple sclerosis. Furthermore, in the study by Foglio et al.\textsuperscript{28} found no significant relationship between pulmonary function tests and EDSS.

In this research, statistically highly significant positive correlation was found between cerebellum dysfunction and pulmonary dysfunction index. Statistically significant negative correlation was also found between cerebellum dysfunction and the count in a single exhalation. In addition, cerebellum dysfunction negatively correlated with pulmonary function test (FEV1/FVC).

Grasso et al.\textsuperscript{23} and Amal et al.\textsuperscript{29} concluded that the presence of severe cerebellar signs in patients with MS was associated with a very high risk of occurrence of respiratory impairment.

In this research, statistically highly significant positive correlation was found between brain stem dysfunction and pulmonary dysfunction index. Statistically significant negative correlation was also found between brain stem dysfunction and the count in a single exhalation. In addition, brain stem dysfunction negatively correlated with pulmonary function tests (FVC, FEV1, and MVV).

Buyse et al.\textsuperscript{27} affirmed that MS lesions in the brain stem can also interrupt the motor (reticulospinal) pathway to phrenic, intercostal and accessory respiratory muscle nerves. Therefore, it is not unexpected that pulmonary functions were more disturbed in those with a severe brain stem disorder than in those without.

In this research, statistically highly significant positive correlation was found between bladder dysfunction and pulmonary dysfunction index. A statistically significant negative correlation was also found between bladder dysfunction and the count in a single exhalation.

Van Klaveren et al.\textsuperscript{22} found that Detrusor-sphincter dyssynergia (DSD) is the most important predictor of disturbed respiration in MS patients, presumably because the micturition and pneumotaxic center are closely related and located in the rostral pons.

What's more, a statistically significant positive correlation was found between cerebral dysfunction and pulmonary dysfunction index. Highly significant negative correlation was found between the count in a single exhalation and cerebral dysfunctions.

This is in concurrence with van Klaveren et al.\textsuperscript{22}, who concluded that impaired control of breathing in some MS patients is related mainly to central defects.

Furthermore, Grasso et al.\textsuperscript{23} found that mental impairment in patients with MS was significantly associated with pulmonary dysfunction. In this study, statistically significant negative correlation was also determined between Visual dysfunction and the respiratory function tests (MVV, FEV1/FVC, and FVC). The better respiratory function in those with less mental disturbance and the better respiratory function in those with less visual disturbance can be explained by better collaboration and coordination.

In this research, pyramidal dysfunction negatively correlated with pulmonary function tests (FVC, FEV1, and MVV). There was also a trend wise significant negative correlation between pyramidal dysfunction and the count in a single exhalation. Smeltzer et al.\textsuperscript{24} demonstrated marked expiratory weakness in MS patients with severe pyramidal dysfunction. Pathology in the corticospinal cord may produce not only paralysis
of the limbs, but also weakness of the respiratory truncal muscles.

The pathogenesis of MS fatigue is poorly understood, but the phenomenon appears to be multifactorial and directly related to the underlying MS disease process. MS fatigue is not adequately explained by disease duration, gender, psychosomatic mechanisms, physical disability, or sleep dysfunction.  

Statistically significant positive correlation was established between the pulmonary dysfunction index and both FSS scores and FDS scores. Pulmonary function tests (FVC, FEV1, and MVV) were negatively correlated with FSS and FDS scores; this may establish a physiological basis to multiple sclerosis-related fatigue. Conversely, Rasova et al. stated that it is not possible to prove any correlation between pulmonary impairment parameters and fatigue in multiple sclerosis.

In this research, those with periventricular lesions (n=22, 78.6%) showed negative correlation with FEV1/FVC, to our knowledge, there is no published data as regard such finding.

In this research, those patients with medullary lesions showed positive correlation with clinical pulmonary dysfunction index and negative correlation with pulmonary function tests (MVV, FEV1 and FVC). Also, those with pontine lesions showed trend wise significant positive correlation with pulmonary dysfunction index and negative correlation with pulmonary function test (FEV1/FVC). The involvement of respiratory nuclei of medullary and pontine respiratory centres and airways of corticonuclear routes of caudal cranial nerves due to the presence of a demyelinating plaque in the brainstem fibres causes the development of respiratory dysfunction and decreased sensitivity of respiratory centre to CO₂.

It is concluded that impaired respiration in some MS patients is related to the stage of neurological disability; bladder dysfunction is usually linked to disturbed pulmonary function, presumably because the micturition and pneumotaxic centers are closely related and severe cerebellar signs in patients with MS were associated with a very high risk of occurrence of respiratory impairment. Disturbed pulmonary functions also correlated with the stage of pyramidal and brain stem dysfunctions, There is no correlation between pulmonary dysfunction and duration of disease, due to the variable course of the disease. The spontaneous respiratory complaints are quite rare, that is because the fatigability is so pronounced in MS; so fatigue rather than dyspnoea appears to be the limiting factor and due to the impairment innervations of the upper airway which result in a diminished awareness of coughing. However, systematic clinical assessment can uncover subtle respiratory dysfunction in patients with MS.

This warrants inclusion of respiratory function evaluation in clinical examination protocols of patients with MS to guide early intervention efforts.

**REFERENCES**

الملخص العربي

دراسة العلاقة بين الأعراض الإكلينيكية وقياسات الوظائف التنفسية في مرضى التصلب المتعدد

يعتبر مرض التصلب المتعدد من الأمراض العصبية التي قد تسبب مسارات الأعصاب المتحركة في التنفس مما يؤدي إلى التأثير في عملية التنفس وعملية خاصة تشكل تأثيرات وظيفية على الجهاز. في هذا البحث تم تقييم 28 مريضاً بالتصلب المتعدد بواسطة:
- معدل علاج التنفس الإكلينيكي،
- مقياس شدة المرضى،
- مقياس الرئة.

كما تم قياس الوظائف التنفسية (التيو هده الإكلينيكية) للجهاز الرئيسي في ثانية واحدة: السعة الهوائية القصيرة (التيو). معدل الحجم الرئيسي القصري في ثانية واحدة: السعة الحيوية القصيرة (التيو). وقد وجد أن معدل حجم الحجم الإكلينيكي (التيو) ايجابياً في 57.1% من المرضى.

كما وجدت علاقة إيجابية ذات دالة إحصائية بين هذا المعدل ومقياس شدة المريض والخصائص الوظيفية لل📢 التصلب المتعدد، مؤشرات شدة الرئة ومقياس الرئة التصويري. هذا بالإضافة إلى وجود علاقات إيجابية ذات دالة إحصائية بين هذا المعدل وبين عدم الانتزاع الحركي نتيجة الخنقة، وأيضاً مع حمل وظيفة جراحية وخلال التحكم في المريض.

فقي قياسات الوظائف التنفسية (التيو الإكلينيكية) (75.77±7.75)، الحجم الرئيسي القصري في ثانية واحدة (77%±20.17)، السعة الحيوية القصيرة (التيو) (72%±17.20). أقل من مثيلاتها في الناس الطبيعيين. كما أن القصور في الوظائف التنفسية كان أشد في النوع الثاني المفقود بالنوع الارتجاعي التنفسي.

كما وجدت علاقة تجاهية ذات دالة إحصائية بين قياسات وظائف التنفس ومقياس شدة المريض والخصائص الوظيفية لل📢 التصلب المتعدد. كما وجدت علاقة تجاهية ذات دالة إحصائية بين قياسات وظائف التنفس (التيو الإكلينيكية) للجهاز الرئيسي في ثانية واحدة: السعة الحيوية القصيرة (التيو) والخصائص الوظيفية بين السعة الحيوية القصيرة (التيو) ومقدار جذع الدم بالمريض. كما وجدت علاقة تجاهية ذات دالة إحصائية بين السعة الحيوية القصيرة (التيو) والخصائص الوظيفية بين.

وظائف التنفس ومقياس شدة الرئة ومقياس الرئة التصويري ما قد يوفر أسس فسيولوجية لهذا الانتزاع الحركي لمرضى التصلب المتعدد. المرضى الذين كتبوا إصابات لديهم في التدخل المستطيل والجسر كانوا أكثر أقل في بعض التحصين.

ينص المرضى في مرضى التصلب المتعدد من سمنة التصلب المميتة. أكثرن قشرة فان الفحص الإكلينيكية مع قياسات الوظائف التنفسية غالباً ما يظهر قصوراً في الجهاز التنفسي خاصة أولئك الذين يعانون من إصابة في جذع الدم، عند تحكم في المريض، عند الانتزاع حركي لإصابة المخ، أو حتى إصابة في الجهاز الهلني، مما يظهر أهمية أن يدرج تقييم هذا الجانب في مرضى الالتهاب المتعدد مع الفحص المكثف حتى يتمكن تدارك القصور في بداية منها يتبع.

لـ، فيصل، ونفسيو.