

Original Article**Serum Homocysteine level in patients with Multiple Sclerosis***F. Ashtari MD\*, Sh. Salehi Abari MD, V. ShayganNejad, MD\****ABSTRACT**

**Background:** The etiology of multiple sclerosis (MS), a chronic demyelinating disease-is unknown. The damage of blood-brain barrier (BBB) vasculature is a characteristic of MS and Homocystein (Hcy) can damage BBB, then increase in total Hcy may be important in MS pathogenesis. The aim of this study was to compare the serum level of total Hcy in MS patients with control group.

**Methods:** In a case control study, serum level of total Hcy measured in 35 MS patient and compared with 30 healthy matched controls. All patients had definitive MS according to Poser criteria, without history of myocardial infarction, stroke, neuropathy, transient ischemic attack, homocystinuria or renal failure.

**Results:** The serum concentration of total homocystein was significantly higher in multiple sclerosis patients than healthy controls. The mean total Hcy level was  $17.92 \pm 6.9$  mmol/lit in cases and  $14.6 \pm 2.92$  mmol/lit in controls ( $P=0.013$ ).

**Conclusion:** Serum total Homocystein may have a role in MS pathogenesis and reduction of it should be studied moreover.

**Key words:** Multiple Sclerosis, Homocystein, Serum level

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**M**ultiple sclerosis (MS) is a chronic inflammatory demyelinating disease of central nervous system (CNS), with an onset typically between 20 and 40 years of age and more prevalent in women<sup>1,2</sup>.

Definite clinical diagnosis of MS requires the presence of at least two neurological events consistent with demyelination, separated anatomically in central nervous system. Its clinical manifestation is variable, determined by varied location and extent of demyelinating foci<sup>3</sup>.

Its distribution is geographically worldwide. In general, the disease increases in frequency with latitude in both northern and southern hemispheres, although the rates tend to decrease above 65 degrees north or south.

Its prevalence differs from 5-10 up to 50-100 degrees based on geographic attitudes of coun-

tries and its prevalence is increasing in recent years<sup>4,5</sup>.

The etiology of MS is still unknown and considered to be multifactor, genetic, and infectious or an autoimmune process that triggered by environmental factors leading to its clinical manifestation later in life<sup>6,7</sup>. In recent years, many studies are performed to determine the etiologic factors in the pathogenesis of MS.

Homocystein may has a neurotoxin that activates N-methyl-D -aspartate receptor which leads to cell death. It may be converted into homocysteic acid which also has a toxic effect on the neurons of cerebral cortex. So increased plasma level of total homocystein (tHcy) has a neurodegenerative effect and may be a risk factor for progression of disability in MS<sup>8,9</sup>.

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In the present study, the plasma level of tHcy measured in MS patients compared with healthy subjects.

### Subjects and Methods

This case-control study was performed in Al-Zahra university hospital, Isfahan, Iran. Serum tHcy level was measured in 35 MS patients (case group) and 30 healthy persons (control group), matched for age and sex.

All patients had definite MS according to Poser criteria. According to course of disease, the patients divided to secondary progressive (sp) and relapsing remitting (RR), and their disabilities was detected by EDSS score.

None of subjects in case or control groups had past history of Myocardial infarction, Transient ischemic attack (TIA), stroke, neuropathy, homocystinuria or Renal failure. None of control subjects had a family history of MS<sup>10,12</sup>.

In every subject, 2 milliliter of coagulated blood were drawn from antecubital vein and centrifuged immediately or until maximum up to 20 minute at 2500 rpm for 10 minute and then its serum was separated.

In order to decrease bias, the separated serum samples were stored at -20° centigrade and assayed at the same time with same laboratory kits. Total plasma homocystein (tHcy) including the sum of protein band and free homocystein was assayed by Elisa test with Axis homocystein EIA Kit (iBl ELISA kit, 96 wells Germany). The data were statistically analyzed by SPSS software using independent t-test.

### Results

In this study, 35 MS patients (24 women and 11 men) and 30 normal persons with same demographic feature (21 women and 9 men) were enrolled. All subjects were 18-50 years-old.

The mean age in both groups was 27.9±9.09 years. Serum homocystein was 8 to 30.2 mmol/lit with mean of 17.92±6.9 in the case group and 7.6 to 19 with a mean of 14.6 ±2.92 mmol/lit in the control group. The mean se-

rum tHcy level in MS patients was significantly higher than control (P=0.013).

In the case group, the mean of serum tHcy was 19.39±6.72 mmol/lit in men and 17.25±7.1 mmol/lit in women. In the control group, they were 15.71±2.3 mmol/lit and 14.12±3.07 mmol/lit, respectively (p>0.05). The mean tHcy of men was not significantly different in both groups (p=0.136).

In both group, the mean tHcy of women was significantly different (p=0.069). The patients divided in two groups according to disability: EDSS <3 in 24 patients with mean tHcy 16.4±6.4 mmol/lit, and EDSS ≥3 in 11 patients with mean tHcy 21.2±7.27 mmol/lit (p=0.059). The mean tHcy was 18.93±8.8 in SP and 17.33±5.7 in RR patients (p=0.52).

### Discussion

The results of this study significantly demonstrate higher level of tHcy in MS patients than controls (p=0.013). This finding suggests that serum tHcy can be important in the pathogenesis of MS.

Few studies have assessed tHcy level in MS patients. Our results are in line with some previous findings as the recent study of Vrethem et al that assessed tHcy in 72 MS patients and 23 healthy persons, and showed that the mean serum level of tHcy was significantly higher in MS patient (11.4 mmol/lit) than control group (7.4 mmol/lit)<sup>12</sup>. But another similar study performed by Rio et al could not show any significant association between MS and tHcy<sup>13</sup>.

In Besler study, lipoprotein oxidation and homocystein level were assessed and found that significantly higher tHcy level in MS patients with low plasma vitamin B12 and folate levels but this difference was not statistically significant<sup>14</sup>. Of course, vitamin B12 have an important role in myelin synthesis and integrity of it<sup>15</sup>.

According to our study, high serum tHcy is more in MS patients than healthy controls and significantly higher in the patients with sever disability (EDSS≥3). So, serum tHcy may have a positive effect on pathophysiology of MS.

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