Volume : 2 | Issue : 5 | May 2013 • ISSN No 2277 - 8160

Research Paper | Medical Science

# A Relative Screening of Blood Lipids, Total Homocysteine, Uric Acid and Vitamin Concentration in Subjects with Multiple Sclerosis Against Healthy Controls

**Dr.Sarah Afaq** — Assistant Professor, Department of Clinical Biochemistry, College of Medicine, King Khalid University, Abha, Kingdom of Saudi Arabia

**ABSTRACT**

*Retrospective studies have shown Multiple Sclerosis (MS) patients present a decrease in antioxidant and immunoregulatory vitamins along with increase in total Homocysteine (tHcy), cholesterol (CHL), HDL-cholesterol, and cellular stress markers, variably associated with the different phases of the disease. It has also been shown that Vitamin D levels are inversely related with the progression of the disease. Thus, a combined study was done where the blood levels of uric acid (UA), vitamin E, vitamin D, along with tHcy and HDL-Cholesterol were monitored in thirty MS patients during a phase of clinical inactivity along with those of sixty healthy controls, matched for age and sex. We found higher levels of tHcy (p = 0.032) and HDL-cholesterol (p = 0.001) and lower levels of vitamin E (p = 0.001) and uric acid (p = 0.019) with no change in vitamin D levels in MS patients.*

**KEYWORDS: Multiple sclerosis, immunoregulatory vitamins, uric acid, total**

**Introduction:**

A decrease of antioxidants [1], and neuroprotective [2,3] and immunoregulatory vitamins [3,4] and an increase of total homocysteine (t-Hcy) [5], cholesterol (CHL), HDLcholesterol [6], and of cellular stress markers [7,8] were reported in patients affected by multiple sclerosis (MS).These changes are regarded as markers of autoimmunity or neurodegeneration. However some papers have refuted the role of uric acid in MS patients with clinical inactivity .Along with this, there have been the hygiene hypothesis and the vitamin D hypothesis that predicts inverse relationship of vitamin D plasma levels and multiple sclerosis. Therefore, we assessed the biochemical status of MS during a phase of clinical inactivity and compared the blood levels of UA, vitamins E and D along with t-Hcy, CHL, HDL-cholesterol with those of healthy controls.

**Results and conclusions:**

Thirty consecutive MS patients with relapsing-remitting or secondary-progressive courses and in a phase of clinical inactivity participated in the study. They had been free of steroids for at least one month and of immunomodulatory or immunosuppressive drugs along with any Vitamin D/Calcium supplementations for at least two months. Use of certain medicines, including phenytoin, phenobarbital, and rifampin, which can decrease Vitamin D levels were excluded. History for any liver or kidney disease along with Parathyroid status which can decrease Vitamin D levels was taken as well. The study protocol was approved by the local Ethics Committee. Formal written consent was obtained from each patient. Two venous blood samples were obtained from patient with a time lag of one month in between. A number of healthy individuals were enrolled after their formal written consent. Controls were matched for age (+2 years) and gender to the patients in the ratio of two controls for each case. A venous blood sample was obtained from each control. Pregnant women, habitual smokers, alcohol drinkers, and consumers of vitamins-rich products were excluded. Among the cases, individuals with other disorders in addition to MS were also excluded. Venipuncture, using masked materials, was performed in fasting subjects who on the two previous days had avoided certain habits (alcohol consumption, cigarettes, cigars, and pipe smoking) and foods (red meat, liver, kidney, spleen, fish and sea food, salted food and fat cheese, sweets, grapes, bananas, figs, persimmons, cherry, nuts, and the like) which could have modified the concentration of the molecules to be detected. The Ubbink method was used was used to establish plasma levels of tHcy [9]. High performance liquid chromatography and fluorimetry were used for vitamin A and vitamin E assays. The radioimmunoassay (RIA) method for measuring total vitamin D levels (Diasorin) was used to measure 25-hydroxyvitamin D. Commercially available enzymatic colorimetric tests were used for UA, CHL and HDL-cholesterol (Roche Diagnostics GmbH, Mannheim). Mean differences in normally distributed data between cases and controls were analysed by Student's t test. As tHcy, UA, vitamin D, and vitamin E concentrations were not uniformly distributed, median values and the Mann-Whitney U test were then used for comparison of the patient and control groups. To increase dosage reliability; patients had two different venipunctures and their mean value was used for calculations.

We included 30 MS patients and 60 healthy controls .The patient's median age was 42 years (range 16 - 58); twelve were male (M/F1:2.5; mean MS duration was 7years (SD, 7.1; range 0.5–21 years); median EDSS was 3.0 (range 1.0 - 6.0); mean MSSS was 3.95 ± 1.95; 20 patients had a relapsing remitting course and 10 had a secondary-progressive course. Because of the matching criteria, the control group had the same distribution for age (median age: 42 years; range 16 -58) and gender. Table 1 shows the results obtained for each compound comparing the cases and the control groups. The concentration of UA and vitamin E was low in patients as compared with controls, which reached statistical significance. CHL concentration was higher in MS patients, but the difference between the two groups did not reach statistical significance. The concentration of HDL-cholesterol and tHcy was higher in the MS group, these differences were statistically significant. While the concentration of vitamin D was found more or less similar between MS group and control, which didn't achieved statistical significance. This study shows that the MS patients in a phase of clinical inactivity presented modifications of some biochemical markers of cell damage. The study's main weakness is its limited sample size and it must therefore be regarded as preliminary to larger investigations. We found that the MS patients in a phase of clinical stability had higher blood levels of tHcy and HDL-cholesterol as reported in other papers[5,11] but lower blood levels of vitamin E and uric acid. The meaning of high tHcy increase, could be related to the damage in the folding of the proteins by increasing the cleavage of disulphide bridges and was targeted to generate free radicals, which is again consistent with previous paper, although it requires further study. The increased concentration of HDL-cholesterol in a stable phase of the disease could counteract the increased concentration of cholesterol that occurs in the course of a relapse and ensure that it reaches the liver [10]. Increased values of total and HDL - cholesterol were reported in a study aimed at assessing the correlation between blood CHL and MRI activity after a clinical episode suggesting MS [6]. The decrease in the concentration of vitamin E, the major hydrophobic chain-breaking antioxidant, confirms the possible involvement of this vitamin in MS pathology: vitamin E levels are decreased in the demyelination plaques of MS brains, and vitamin E levels and E/CHL ratios are lower in the serum of MS patients [2]. However, serum vitamin E is not a marker of clinical activity because similar low concentration in the CSF or by a reduction of the [vitamin ECSF]/ [vitamin E serum] ratio does not happen. The data could indicate that vitamin E was consumed to counterbalance MS chronic neurodegeneration. Uric acid levels were found to be significantly low as well which was not reported in a similar study[11]. Lowered serum UA concentrations in MS patients might be due to both intrinsically reduced antioxidant capacity and increased consumption of UA in MS. Uric acid (UA) can scavenge not only peroxynitrite, but other free radicals [12, 13].UA is the final product of purine metabolism and accounts for 60% free radical scavenging activity in human blood [12].Although the role of uric acid in etiopathogenesis of MS is controversial with some papers denying any association with MS ; others found an increase of UA ,like this study, both in serum and in cerebrospinal fluid (CSF) [1,7,11].

These conflicting results could be explained by differences in the pop-

ulations studied or by different detection methods and they require further investigation for a better understanding of the role of UA in the biochemical changes occurring in the course of MS. However, we observed no difference as regards with Vitamin D levels between MS patients and healthy controls, which means that it is unlikely to be involved in the biochemical processes taking place during this phase of MS. But the role of Vitamin D by increasing (bone health) intakes and the potential positive effects of vitamin D on MS disease development cannot be ruled out.

The above studies ,definitely requires 'Ad hoc' studies but invariably, multiple sclerosis is proving to be an autoimmune disease where oxidative stress markers/free radicals are important in its etiopathogenesis as much as the role of antioxidants (Vitamin E and uric acid) in the progress and possibly treatment of the disease.

**Table 1 Comparison of Blood Lipids, total Homocysteine, Uric Acid and Vitamins concentration in subjects with a Multiple Sclerosis and in healthy controls**

| Compounds * | Patients | Controls | P° |
|---|---|---|---|
| Uric acid | 267.2±70.2 | 294.5 ± 55.13 | 0.019 |
| Homocysteine | 10.3 (4.0, 86.5) | 7.3 (3.2, 15.0) | 0.032 |
| Vitamin D | 80 (75, 190) | 81 (76, 220) | 0.149 |
| Vitamin E | 13.0 (5.4, 26.5) | 23.5 (1.9, 70.2) | 0.001 |
| Cholesterol | 189.70 ± 40.30 | 171.07 ± 35.18 | 0.071 |
| HDL-cholesterol | 63.42 ± 14.85 | 52.05 ± 10.81 | 0.001 |

## REFERENCES

1. Kutzing, M.K. and Firestein, B.L.2008. Altered Uric Acid Levels and Disease States. Journal of Pharmacology and Experimental Therapy, 324:1-7. | | 2. Jimenez-Jimenez, F.J., de Bustos, F., Molina, J.A., de Andrés, C., Gasalla, T., Ortí-Pareja, M., Zurdo, M., Porta, J., Castellano-Millán, F., Arenas, J. and Enríquez de Salamanca, R.1998. Cerebrospinal fluid levels of alpha-tocopherol in patients with multiple sclerosis. Neuroscience Letters, 249:65-67. | | 3. Besler, H.T., Comoglu, S. and Okcu, Z.2002. Serum levels of antioxidant vitamins and lipid peroxidation in multiple sclerosis. Nutritional Neuroscience, 5:215-220. | | 4. Vrethem, M., Mattsson, E., Hebelka, H., Leerbeck, K., Osterberg, A., Landtblom, A.M., Balla, B., Nilsson, H., Hultgren, M., Brattström, L.and Kågedal, B.2003. Increased plasma homocysteine levels without signs of vitamin B12 deficiency in patients with multiple sclerosis assessed by blood and cerebrospinal fluid homocysteine and methylmalonic acid. Multiple Sclerosis, 9:239-245. | | 5. Giubilei, F., Antonini, G., Di Legge, S., Sormani, M.P., Pantano, P., Antonini, R., Sepe-Monti, M., Caramia, F. and Pozzilli, C.2002. Blood cholesterol and MRI activity in first clinical episode suggestive of multiple sclerosis. Acta Neurologica Scandinavica, 106:109-112. | | 6. Mostert, J.P., Ramsaransing, G.S., Heersema, D.J., Heerings, M., Wilczak, N. and De Keyser, J.2005. Serum uric acid levels and leukocyte nitric oxide production in multiple sclerosis patients outside relapses. Journal of Neurological Sciences, 231:41-44. | | 7. Rejdak, K., Petzold, A., Stelmasiak, Z. and Giovannoni, G.2008. Cerebrospinal fluid brain specific proteins in relation to nitric oxide metabolites during relapse of multiple sclerosis. Mult Scler, 14:59-66. | | 8. Ubbink, J.B., Hayward, V.W. and Bissbort, S. 1991. Rapid high-performance liquid chromatographic assay for total homocysteine levels in human serum. Journal of Chromatography, 565:441-446. | | 9. Ginsberg, H.N. 1998. Lipoprotein physiology. Endocrinology Metabolism Clinical of North America, 27:503-519. | | 10. Salemi, G., Gueli, M.C., Vitale, F., Battaglieri, F., Guglielmini, E., Ragonese. P., Trentacosti, A., Massenti, M.F., Savettieri, G. and Bono, A. 2010. Blood lipids, homocysteine, stress factors,and vitamins in clinically stable multiple sclerosis patients. Lipids in Health and Disease, 9:19-21. | | 11.Ames, B.N., Cathcart, R., Schwiers, E.and Hochstein, P.1981. Uric acid provides an antioxidant defense in humans against oxidant-and radical-caused aging and cancer: a hypothesis. Proc Natl Acad Sci USA,78:6858–62. | | 12. Davies, K.J., Sevanian, A., Muakkassah-Kelly, S.F. and Hochstein, P.1986. Uric acid-iron ion complexes. A new aspect of the antioxidant functions of uric acid. Biochem J, 235:747–54. |