Correlation between vitamin D and lipid profile in multiple sclerosis patients

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ABSTRACT

Background: Studies have suggested that vitamin D and lipid profile have been linked to the etiology of multiple sclerosis and have an impact on the activity and progression of the disease.

Objectives: The aim of the present study was to determine correlation between vitamin D level and lipid profile in multiple sclerosis (MS) patients and their effect on disease activity and progression for better management and control of risk factors.

Patients and Methods: It is a cross-sectional hospital based study carried on clinically definite 111 Relapsing Remitting MS (RRMS) patients according to McDonald criteria 2010 recruited from Multiple sclerosis unit at Ain Shams University Hospitals, both genders included and aged from 18 to 50 years old. All subjects were assessed regarding their basic demographic data, serum vitamin D level and lipid profile and correlated these data with their state of disease activity and degree of disability.

Results: The mean level of serum vitamin D was 18.93 ± 9.85 ng/mL. Serum vitamin D level was insufficient (< 30 ng/mL) in 81.08% of patients and sufficient (≥ 30 ng/mL) in 18.92% of patients. The mean level of total cholesterol (TC) was 204.9 ± 50.9 mg/dL, of tri-glycerides (TG) was 105.4 ± 44.6 mg/dL, of low density lipoprotein (LDL) was 122.2 ± 38.8 mg/dL and of high density lipoprotein (HDL) level was 56.2 ± 16.6 mg/dL**.** High relapse frequency was found to be significantly related to low serum vitamin D level with P-value 0.005. Near all lipid related variables were positively correlated to disease duration. TC and TG were positively related to EDSS while HDL was negatively related with it. Number of brain T2 lesions was significantly correlated with TC and TG levels with P-value 0.001 and 0.002 respectively. Fingolimod was found to be associated with dyslipidemia. We found that each 1 ng/mL increase in vitamin D was associated with decrease in TC of 1.48 mg/dL (95% CI: -2.42 to -0.54, P-value 0.002) and increase in HDL of 0.35 mg/dL (95% CI: 0.04 to -0.66, P-value 0.028).

Conclusion: Vitamin D deficiency is predominant among Egyptian MS patients. Patients with insufficient vitamin D were found to have higher annualized relapse rate (ARR). Patients with dyslipidemia found to have longer duration, more disability and higher brain T2 lesion load. Vitamin D was correlated positively with HDL and negatively with TC.

Keywords: Vitamin D, Lipids, Multiple sclerosis, Egyptian.

INTRODUCTION

Multiple sclerosis (MS) is a chronic immune-mediated demyelinating disease of the central nervous system (CNS) that is characterized pathologically by inflammation, demyelination, and, ultimately axonal loss. Its diagnosis is based on the concept of the disease's dissemination in both space and time (***Frohman et al., 2006 and Compston and Coles, 2008).*** It is a leading cause of non-traumatic disability in young adults in many countries ***(Heydarpour, 2015).***

In general, the researchers found that MS prevalence has increased dramatically in that 5 year span, by 10% and now affecting 2.3 million people worldwide. Whether this is due to a true intrinsic increase in prevalence or whether the condition is being better diagnosed and reported ***(Multiple Sclerosis International Federation, 2013).***

A single door to door survey in Alkosier and Alkharga Oasis, Egypt reported MS prevalence of 13.7/100,000 ***(Tallawy et al., 2013).*** It is not clear why MS develops in some people and not others. The most accepted theory is that MS is caused by an environmental trigger (or triggers) in a genetically susceptible individual ***(Verhey, 2013).***

MS has been characterized by demyelinating plaques of the central nervous system. While these inflammatory lesions have now been well studied, there is still much debate surrounding the etiology and early pathogenesis of the disease. The blood-brain barrier has long been thought to play a key role in this by regulating leucocyte movement into the CNS. Also recent developments in MS drug therapies have emphasized leukocyte passage across the BBB as being of paramount importance for disease pathophysiology ***(Spencer et al., 2017).***

These factors may increase the risk of developing multiple sclerosis including age, sex, family history, certain infections like Epstein-Barr virus, race, climate, certain autoimmune diseases, obesity, vitamin D deficiency and vascular risk factors like dyslipidemia, smoking ***(Wingerchuk, 2014).***

Increased body mass index (BMI) at the age of 18 is associated with a two-fold increase in the risk of MS ***(Munger et al., 2009).*** Obesity has been associated with a chronic inflammatory state, due to the secretion of pro-inflammatory proteins in the blood ***(Ouchi et al., 2012).***

The breakdown of the blood-brain-barrier vascular endothelium is critical for entry of immune cells into the MS brain. Vascular co-morbidities are associated with increased

risk of progression. A single-center, retrospective, longitudinal study at State University of New York reported results indicating that lipid profile variables such as increased LDL, triglycerides and total cholesterol levels are associated with increased disability progression in MS. Higher HDL levels and lower levels of triglycerides were associated with decreased contrast enhancing lesions activity ***(Weinstock-Guttman et al., 2011).***

An early recognized indication for vitamin D being a risk factor for MS development is the geographical distribution of MS, which is highest near the poles and lowest near the equator. Ultraviolet exposure is the most decisive factor for vitamin D status. The association between Ultraviolet radiation and MS risk has been confirmed in several countries including the UK, France and the USA ***(Holmoy et al., 2012).***

During the second half of the 20th century, researchers started to recognize the potential non-skeletal effects of vitamin D. Studies have shown that vitamin D modulates the immune system by decreasing the proliferation of pro-inflammatory lymphocytes and regulating the production of cytokines. Since both of these mechanisms contribute to the pathogenesis of multiple sclerosis (MS), the role of vitamin D in MS has been studied.

Several studies reported that most MS patients have low serum levels of vitamin D. More recent study reported that patients, who were having MS exacerbations requiring hospital admissions, had lowest vitamin D levels 3 months prior to these events. Low vitamin D serum levels were also negatively correlated with the degree of disability measured by the Expanded Disability Status Scale (EDSS) ***(Mesliniene et al., 2013).***

Vitamin D is known as a nutrient that can play an important role in lipid metabolism. Studies have shown a positive relationship between vitamin D deficiency and lipid metabolism. Lower levels of vitamin D are associated with obesity. Those who are obese will accumulate vitamin D in their fatty tissue, rather than converting it into 1, 25 (OH) D3. A cross-sectional study in Tehran, Iran reported that there is 77% reduction in the chances of developing metabolic dyslipidemia in sufficient status of vitamin D in compare to deficiency. Cholesterol and serum LDL levels have also been shown to improve vitamin D status ***(Rashidbeygi et al., 2018).***

THE AIM OF STUDY

The aim of the study is to determine correlation between vitamin D level and lipid profile in multiple sclerosis (MS) patients and their effect on disease activity and progression for better management and control of risk factors.

Definition of Multiple Sclerosis

Multiple Sclerosis (MS) is a chronic neurological disorder affecting central nervous system. However the etiology is not well understood, but most probably multifactorial involvement is the most convenient theory till now ***(McKay et al., 2017)***.

It is characterized by inflammation, demyelination, axonal loss and degeneration. There is a debate about neurodegenerative character of the disease, whether inflammation initiates neurodegeneration or neurodegeneration occurs independent of inflammation ***(Losy, 2013).***

Phenotypes of MS

Several clinical courses are described in MS*;* 85% of patients are diagnosed with relapsing remittent MS (RRMS). Seventy five percent of RRMS patients will develop secondary progressive MS (SPMS) within 10-15 years of the initial diagnosis. Ten to fifteen percent of MS patients, develop progressive disability from the start, so-called primary progressive MS (PPMS) ***(Leray et al., 2010).*** An international panel in 2013 added clinically isolated

syndrome (CIS) and radiologically isolated syndrome (RIS) as MS phenotypes ***(Lublin et al., 2014)*** **(Figure 1).**

In Egypt, RRMS was the most common presentation (74.6%), SPMS was presenting (16%), with about 2–4% having PPMS or CIS ***(Zakaria et al., 2016).***

Clinically isolated syndrome (CIS) is "the first clinical presentation of a disease that shows characteristics of inflammatory demyelination that could be MS, but has yet to fulfill criteria of dissemination in time ***(Lublin et al., 2014***).

RIS is a syndrome where incidental imaging findings suggest inflammatory demyelination without clinical signs or symptoms. RIS patient should be followed prospectively for other positive findings enhancing diagnosis of MS as cerebrospinal fluid findings, enhancing or spinal cord lesions ***(Lebrun et al., 2009).***

RRMS disease course marked by acute exacerbations (relapses) from which they typically completely or incompletely recover, with periods of relative clinical stability in between ***(Lublin et al., 2014).*** A relapse is a patient-reported or objectively observed events typical of an acute inflammatory demyelinating event in the CNS,