Serum Complement Factor H & Tyr4O2 His Gene Polymorphism Among Egyptians with Multiple Sclerosis Background and Objectives:

The complement system is part of the innate immune defense mechanism and is involved in modulating various immune and inflammatory responses. Under normal conditions, the complement system is active at a low level and is tightly regulated by various complement regulatory proteins (CRegs), such as complement factor H (CFH). Disruption in the balance of complement activation and CRegs will result in harmful effects and lead to several immune-related diseases. CFH is one of the most important regulators in the alternative complement pathway and is involved in the pathogenesis of immunological diseases. Multiple sclerosis (MS) is a common inflammatory disease of the central nervous system with a poorly defined and complex immunopathogenesis. A contribution from complement (C) has long been suspected. We aimed to examine whether C Factor H (CFH) Tyr402 His gene polymorphism and serum level might identify or predict specific pathological processes and outcomes in MS.

Methods:

The study subjects were 86 subjects with MS and 74 healthy controls (HC). They were divided into two groups. In group (1) (34 HC compared to 42 MS) we measured serum CFH by an ELISA method. In group (2) (40 HC compared to 44MS) detection of the gene polymorphism was done by a polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP). Subjects were subjected to history taking, neurological examination and magnetic resonance imaging (MRI). The subjects were classified according to the clinical phases of MS.

Results:

In group (1) serum CFH levels was significantly different in the HC compared to MS group ($P < 0.01$) and also when compared to the MS types ($P < 0.05$), with the highest levels in the primary progressive MS and secondary progressive MS.

Within the relapsing remitting MS (RRMS) group, CFH levels in remission & in relapse were higher than HC. The number of brain MRI lesions did not influence CFH levels; CFH level MS subjects with ≥ than 9 MRI brain lesions was not statistically significantly different from MS subjects with < than 9 MRI brain lesions ($P > 0.05$). Similarly there was no statistically significant difference in serum CFH among MS subjects with visual evoked potential affection compared to MS subjects without visual evoked potential affection ($P > 0.05$).

Neither age ($P > 0.05$) nor disease duration ($P > 0.05$) nor EDSS ($P > 0.05$) were correlated with serum complement factor H level. Meanwhile MSSS was positively correlated with serum complement factor H level ($P < 0.01$).

No significant association was found between MS subjects (N = 44) compared to HC (N = 40) in the frequency of CFH Tyr402 His genotypes and alleles ($P > 0.05$).

Conclusions:

There is evidence that serum CFH level might be associated with disease risk providing objective evidence to help guide therapeutic decisions. Serum CFH level does not reflect the nature of the lesion in MS subjects. There was no association in the frequency of CFH Tyr402 His genotypes and MS.

Key words:

Complement factor H Tyr402 His gene polymorphism – serum complement factor H – multiple sclerosis