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ORIGINAL ARTICLES

Association of Serum Ceruloplasmin Level with Parkinson's's Disease

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bstract:

Background: *Parkinson's disease, though a common neurodegenerative disease, is still elusive regarding its pathobiology. Neuronal degeneration in the midbrain substantia nigra by excess oxidative stress may play a role. As ceruloplasmin (Cp), a plasma protein is important to maintain intracellular iron homeostasis and reduce cellular oxidative stress, decreased serum Cp level may be an important factor in the pathogenesis of Parkinson's disease.* ***Methods:*** *This case-control study was conducted in the department of Neurology, BSMMU. Forty-five Parkinson's disease patients and equal number of controls were selected. Serum ceruloplasmin level was measured in the department of Biochemistry and Molecular Biology, BSMMU.* ***Results:*** *Mean serum Cp level was significantly lower (p-value <0.001) in case (27.64 mg/dl) than in control group (33.10 mg/dl).* ***Conclusion:*** *The association of low serum Cp level with Parkinson's disease may indicate a possible iron homeostasis abnormality as a pathogenic factor in Parkinson's disease.*

Keywords: *Parkinson's disease, Ceruloplasmin, Substantia nigra etc.*

Introduction:

Parkinson's disease (PD), a common neurodegenerative disease, is a clinical syndrome with variable combination of tremor, rigidity, bradykinesia and postural instability.PD is the second most common neurodegenerative disorder after Alzheimer disease[1]. Among general population the worldwide prevalence of PD was approximately 0.3 percent in a meta-analysis of 47 studies[2].

Although the majority of cases are sporadic, genetic factors play an important role in the pathogenesis, particularly when symptom appear before the age of 40 years[3].Pathologically PD is characterized by degeneration of dopaminergic neurons in the substantia nigra of the midbrain. An intracytoplasmic neuronal inclusion known as Lewy body, made up mainly of alpha-synuclein and ubiquitin, is the pathologic hallmark[4].Genetic factors along with abnormalities in protein processing, oxidative stress, mitochondrial dysfunction, excitotoxicity and other unknown mechanisms are probably involved in the pathogenic process[5]. Several evidences support disruption of iron metabolism as a key mechanism involved in neuronal death in PD[6]. Excess nigral iron deposition in PD using magnetic resonance based highly sensitive susceptibility weighted imaging was also demonstrated[7].

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Ceruloplasmin (Cp), an alpha-glycoprotein, is mainly synthesized in liver and plays an important role in cellular iron homeostasis. Decreased Cp activity in brain leads to intracellular iron accumulation, increasing oxidative stress which leads to cell death[8]. As Cp readily crosses blood-brain barrier, Cp level in serum is in equilibrium with brain Cp level and serum Cp level reflects the Cp activity in brain. It may be used as a biomarker for diagnosis of early PD when classical motor features have not yet developed[7].

As an indicator of cellular iron dis It may also facilitate the advent of iron chelation therapy as a disease modifying treatment option in PD patients[9]. Direct ceruloplasmin administration is also reported to be helpful in improving PD symptoms in some studies recently in animal models[10].

Methods:

This case-control study aimed to assess the association of serum ceruloplasmin level with Parkinson's disease. It was conducted in the department of Neurology, BSMMU in the time period of June, 18 to September, 19. Ethical clearance was taken from the institutional review board, BSMMU. Calculated 45 cases (Parkinson's disease diagnosed by Movement Disorder Society clinical diagnostic criteria, 2015) and equal number of controls (non-Parkinson'sian age and sex matched subjects) were selected via purposive sampling method. Patients of Wilson disease, chronic liver disease, chronic kidney disease, pregnant women or patients with active infection or inflammation were excluded. Serum ceruloplasmin level was measured by using Beckman Coulter-AU680 automated analyzer in thelaboratory of the department of Biochemistry and Molecular Biology, BSMMU. The mean and standard deviation of serum ceruloplasmin level of both case and control groups were calculated. Quantitative data were analyzed by Student's t-test and qualitative data were analyzed by χ^2 test. P value <0.05 was considered as statistically significant. Statistical analysis was done by SPSS software.

Results and Discussions:

In this study the mean age of case and controlgroups were respectively 57.8 and 58.0 years. Majority of the patients belonged to 50-80 years of age.Among the study population 68.9% were male and 31.1% were female in the case group(male: female = 2.2:1). Rahman et al. (2018) found 2.6 times male predominance in their study in Bangladesh.

Table-I

Demographic characteristics of the study population

Variables	Case (n=45)	Control (n=45)
Mean age (years)	57.8	58
Gender		
Male	31 (68.9%)	29 (64.4%)
Female	14 (31.1%)	16 (35.6%)

Serum ceruloplasmin level was significantly lower in case (27.64 mg/dl) than in control (33.10 mg/dl) group. This finding is similar to the studies by Jin et al.[7], Ling and Bhidayasiri[11], Nikam et al.[12], Song et al.[13] and Torsdottir et al.[14].

As a neurodegenerative disease of unknown etiology, PD has no established disease-modifying treatment option so far. As low serum ceruloplasmin may have a role in the pathogenesis of PD due to disturbance in brain intracellular iron accumulation and consequent oxidative stress, this finding may open a window forinvention of disease-modifying therapy for PD. Intravenous ceruloplasmin infusion and iron chelation therapy have been proposed and are under trial with initial success[15].

Table-II

Serum ceruloplasmin level in the study subjects

Serum ceruloplasmin (mg/dl)	Case (n=45) no. (%)	Control (n=45) no. (%)	p-value
Mean± SD	27.64±6.09	33.10±7.63	<0.001[s]
Range	(17-43) mg/dl	(21-49) mg/dl	

Conclusion:

The mean serum ceruloplasmin (Cp) level in Parkinson's disease (PD) patients was significantly lower than that of the control group. The study was conducted in a single center within a short time. Long term, multicentered, prospective study may further help confirm the association.

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