

Association of Serum Uric Acid and Parkinson's Disease: A Case Control Study

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Abstract:

Aim: Recent studies have provided evidence that uric acid (UA) is supposed to play a neuro-protective role in Parkinson's disease (PD). Uric acid is a natural antioxidant that may reduce oxidative stress, a mechanism thought to play a role in the pathogenesis of PD. This study aimed to evaluate whether the serum UA level was associated with PD in a relatively small population of Bangladeshi patients.

Materials and methods: An observational prospective case control Study was conducted in Neurology department of Sir Salimullah Medical College & Mitford Hospital including both the male and female wards during July 2012 to December 2013. Serum uric acid were determined from 40 PD patients and compared with 70 age and sex matched control; following the uric acid colorimetric method, the serum creatinine (Scr) levels were also measured to reduce the bias caused by possible differences in renal excretion function. Data were analyzed with software SPSS 16 and statistical descriptive methods (mean percentage, SD) and t-test.

Result: In this study, 22 men (55%) and 18 women (45%) with PD were evaluated. The mean serum uric acid in patients was 3.7 ± 0.97 and in the control group was 5.32 ± 0.44 . This difference was statistically significant ($p=0.001$). Also, the mean serum uric acid in both men (3.48 ± 0.98) and women (4.1 ± 1.17) patients group was statistically lower than both men (5.39 ± 0.46) and women (5.17 ± 0.35) in control group ($p=0.001$). **Conclusion:** This present study showed a positive association between low serum UA and PD.

Key Word: Serum Uric Acid, Parkinson's disease

Abbreviation: Uric Acid(UA), Parkinson's disease(PD)

Introduction:

PD is the second commonest neurodegenerative disease, clinically characterized by rest tremor, rigidity, bradykinesia, and gait impairment and pathologically, there are degeneration of dopaminergic neurons in the substantia nigra pars compacta, reduced striatal dopamine, and intracytoplasmic proteinaceous inclusions known as Lewy bodies¹.

UA is the final oxidation product of purine metabolism and is excreted in urine. It is a marker of oxidative stress, and may have a potential therapeutic role as an antioxidant^{2,3}.

It is reported that uric acid could suppress oxidative stress and prevent dopaminergic cell death in animal models of Parkinson's disease. Reduced UA levels have been found not only in the substantia nigra but

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also in the cerebrospinal fluid and serum of PD patients^{4,5,6}

The association between UA and risk of PD has been investigated in several previous prospective studies and higher serum uric acid levels might have been correlated to a significantly reduced risk of PD^{7,8}. There is also evidence that higher uric acid levels could slow the clinical progression of PD^{9,10}.

Some recent studies show that UA can decrease the onset of the disease or its intensity, because of having the antioxidant effects and this effect must be considered in the therapeutic process of the disease¹¹. Some other studies indicate that high uric acid levels lead to the decrease of the free radicals and subsequently the onset of the disease³.

Another 14 years period research in America revealed that the risk of onset of PD in people with higher dietary intake of uric acid index was much lower than others; instead, the onset of Gout and renal stones was higher than other people^{7,12}. Some studies also show that the risk of PD is much lower in patients suffering from Gout^{13,14}.

Despite the above researches, results of the recent researches are not yet adequate for a general conclusion. Yet there are many studies indicating the need for more investigations,^{5,15,16,17}.

Here, with considering the above studies, we would like to embark on measuring the serum UA levels in PD patients in Bangladesh to find out their association, so that the study result might open new era of future research regarding alternative management of PD.

Materials and Methods:

This is a observational prospective case control study, carried out on Parkinson patients in the Department of Neurology of Sir Salimullah Medical College & Mitford Hospital, Dhaka Bangladesh from July 2012 to December 2013. Being manifested with the disease was confirmed through clinical examinations by a neurologist and the Para clinical measures according to Brain Bank clinical criteria for diagnosis of Parkinson's disease. All of the

patients suffering from Gout, blood diseases and vasculitis, those who had a history of using the drugs effective on the uric acid levels (Corticosteroids, Colchicine, Alluporinol), and also the patients taking medications other than the anti – Parkinson drugs were excluded from the study. Then, 40 patients were included in the research. Meanwhile, 70 people of age and sex matched healthy individual from patient's attendants and yet had taken no specific medications were selected as the control group. The ethical committee of the Sir Salimullah Medical College, Dhaka, Bangladesh had approved the research. The serum uric acid levels were measured by milligram per deciliter, and the results were evaluated with 95% confidential interval. The values were registered with the demographic information of the questionnaire and were statistically analyzed by the use of the SPSS-16 software, the descriptive statistics methods (the number of percentage and average) and the analytic statistics (comparing the mean and the T- test and ANOVA).

Results:

In this study, the age distribution of study population in case group 15(37.5%) patients belonged to age 71-80 years and their mean age was found 69.15±10.08 years. In control group, 27(38.6%) patients belonged to 51-60 years and their mean age was 67.14±10.25 years. The mean age difference was not statistically significant ($p>0.05$) between two groups.(Table:I)

The observation of sex distribution of the study was, male 22(55.0%) and female 18(45.0%) in case group. The male were 40(57.1%) and female were 30(42.9%) in control group. Male female ratio was found 1.22:1 & 1.33:1 in case and control group respectively. The difference was not statistically significant ($p>0.05$) between two groups.(Table:II)

In Table III shows serum uric acid of the study population. It was observed that mean serum uric acid was found 3.7±0.97 mg/dl in case group and 5.32±0.44 mg/dl in control group. The mean difference was statistically significant ($p<0.05$) between two groups.

Table-I
Distribution of the study population by age (n=110)

Age (in years)	Case (n=40)		Control (n=70)		P value
	No	%	No	%	
≤50	2	5.0	1	1.4	
51-60	8	20.0	27	38.6	
61-70	13	32.5	24	34.3	
71-80	15	37.5	9	12.9	
>80	2	5.0	9	12.9	
Mean±SD	69.15±10.08		67.14±10.25		0.321ns
Range (min, max)	48,100		50,90		

ns= not significant
P value reached from unpaired t-test

Table-II
Distribution of the study population by sex (n=110)

Sex	Case (n=40)		Control (n=70)		P value
	No	%	No	%	
Male	22	55.0	40	57.1	0.827ns
Female	18	45.0	30	42.9	

ns= not significant
P value reached from chi square test

Table-III
Distribution of the study population by serum uric acid (n=110)

	Case (n=40)		Control (n=70)		P value
	Mean	±SD	Mean	±SD	
Serum uric acid (mg/dl)	3.7	±0.97	5.32	±0.44	0.001s
Range (min,max)	1.8	,5.8	4.5	,6.2	

s= significant
P value reached from unpaired t-test

Discussion:

This observational prospective case control study was carried out with an aim to determine the relation of serum UA level with prevalence of PD and also to find out the correlation of UA with severity of PD.

In this study it was observed that in case group 37.5% patients were in 8th decade and their mean age was 69.15±10.08 years, varied 48 – 100 years. In control, 38.6% patients were in 6th decade and their mean age was 67.14±10.25 years, varied 50 – 90 years. The mean age was almost alike between the two groups. In a recent research showed that the mean age of male patients of the control group

was 64.7±6.4 years and the mean age of the female patients of the control group was 63.2±5.6 years¹⁸. There were no statistical differences between the mean ages of the estimated groups. 20 % of patients were under 60, 18% between 61–65, 28% were between 66–70 and 34% were more than 70 years old, which is consistent with the current study¹⁸. Another researcher mentioned in his study that one in seven patients with PD is under the age of 50 years, and there is an increase in prevalence with increasing age¹⁹. In this study only 5% of patients were 50 years or below which is much lower than that of previous study. The prevalence of PD in

industrialized countries is thought to be approximately 0.3%²⁰. This rises to 1.0% in people over the age of 60 and 3% in people over 80 years²¹. In the UK, PD is estimated to affect 100–180 per 100,000 of the population and has an annual incidence of 4–20 per 100,000²². Finding of present study regarding age also consistent with these previous studies.

In this study it was observed that male was 55.0% and 57.1% in case and control group respectively, which indicates that Parkinson's disease is more common in male subjects. Male to female ratio was 1.2:1 in case group and 1.3:1 in control group. The difference was not statistically significant ($p > 0.05$) between two groups. In a recent research showed, 52.0% of the people in both groups of case and control were males and 48.0% were females¹⁸. A similar previous study showed 53.8% were males and 46.2% were females²³. Our present study supports previous studies.

In this present study it was observed that mean \pm SD serum uric acid was 3.7 ± 0.97 mg/dl varied from 1.8 to 5.8 mg/dl in case group and 5.32 ± 0.44 mg/dl varied from 4.5 to 6.2 mg/dl in control group. The mean serum uric acid level was significantly lower in case group ($p < 0.05$). Similarly, it was observed that the mean uric acid levels were 4.79 ± 1.21 mg/dl in the patients group, and it was 5.85 ± 1.14 mg/dl in the control group¹⁸. The serum uric acid levels in the case group was significantly lower than the control group ($p < 0.001$), which also consistent with the current study¹⁸. When compared male and female individually it was observed that serum uric acid was significantly lower in Parkinson's disease patients of both male and female separately. [3.48 ± 0.98 mg/dl Vs 5.39 ± 0.46 mg/dl ($p < 0.05$) in male and 4.1 ± 1.17 mg/dl Vs 5.17 ± 0.35 mg/dl ($p < 0.05$) in female]. A recent study observed that the mean uric acid levels were significantly lower when compared male and female separately (4.87 ± 1.2 mg/dl and 4.70 ± 1.23 mg/dl in male and female cases respectively Vs 5.42 ± 1.25 mg/dl and 5.91 ± 1.62 mg/dl in male and female controls respectively) which is supported by this study¹⁸.

Evaluation of serum uric acid level with disease severity observed that though it is not statistically

significant; mean serum uric acid level was steadily lower with disease severity in stage II to IV but in stage V there was a slight raise of serum uric acid level than that of stage IV. Schwarzschild et al. did a large prospective study among subjects in the early stages of PD enrolled in a randomized clinical trial and found that the rate of progression declined with increasing level of serum urate level¹⁰. Another study had observed among subjects with early PD participating in a large randomized trial, that both serum and CSF urate concentrations measured at baseline were inversely related to clinical progression of PD⁶. But a discriminating report was found in the study by Hau and Eugene, who observed that there was no significant correlation serum uric acid level and staging of PD except a trend of lower uric acid level in stage 5 patients²⁴.

There was no relationship between the uric acid and the duration of illness (Table II), and this was in line with other studies. More researches still deem necessary in this area²⁵⁻²⁷. The main limitation of the research was the lack of comparison between the serum uric acid levels and the severity of illness which has to be considered in future studies²⁸⁻³⁰.

Conclusion:

This present study showed that the uric acid levels in the Parkinson's patients were lower than healthy people. This means that the decrease of the uric acid levels lead to more outbreak of Parkinson both in men and women. This finding confirms the previous studies, emphasizes on the role of uric acid levels on the PD, and also indicates the necessity of more studies specially the cohort studies to achieve a final result and to clarify a part of the treatment process.

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Authors' Contributions:

All authors had equal role in design, work, statistical analysis and manuscript writing.

Conflict of Interest:

The authors declare no conflict of interest.

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