

# Association between Serum Uric Acid Level and the Severity of Parkinsons Disease: A cross sectional study

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## Abstract:

**Background:** Parkinson's disease is a chronic, progressive, neurodegenerative disease. Various factors have been attributed to the development and progression of the disease over the years. Uric acid is the final oxidation product of purine metabolism with potent antioxidant properties, which could play an important role in reducing the risk of development of Parkinson's disease (PD) as well as it could have a role in delaying the progression of Parkinson's disease (PD).

**Aim:** This study aims at evaluating the role of serum uric acid level in clinical progression of Parkinson's disease.

**Methods:** This cross-sectional study was conducted among 70 patients of Parkinson's disease attending the outpatient department and meeting the inclusion criteria. All the clinical and biochemical data were collected and analyzed by SPSS. Mean serum uric acid levels were compared between different stages of Parkinson's disease. A p value of less than 0.05 was considered as significant.

**Result:** Mean age of the patients with Parkinson's disease was  $62.25 \pm 8.56$  years with a male to female ratio of 1.12:1. Regarding the clinical presentation of the patients, it was observed that 16 (22.9%) patients had combination of tremor, hypokinesia, rigidity and postural imbalance, 18 (25.7%) had tremor, hypokinesia & rigidity and 36 (51.4%) had tremor and rigidity. It was observed that 24.3% of the patients had sensory, sleep and cognitive disorder, 21.4% patients had sleep and cognitive disorder, 2.9% patient had disorder in sleep and anosmia, 8.6% patients had only sleep disturbance, 17.1% had only cognitive disturbance but 25.7% had no non-motor symptoms. Majority (61.4%) patient's disease duration was 1-5 years. The mean duration of disease was found  $6.34 \pm 5.53$  years. Majority 34 (48.6%) patients were in stage II, 19 (27.1%) were in stage III, 5 (10.0%) were in stage IV and 12 (17.1%) were in stage V. Mean serum uric acid was found to be  $3.45 \pm 1.26$  mg/dL (2.0-5.8) in male and  $3.36 \pm 0.81$  mg/dL (2.1-5.8) in female patients. Serum uric acid level steadily reduced with the severity of PD which is statistically significant. Advanced stages of parkinson's disease were associated with significantly lower levels of serum uric acid. The difference between the stages were statistically significant ( $p=0.007$ ).

**Conclusion:** This study shows a negative association between serum uric acid level and the severity of Parkinson's disease. The level of serum uric acid decreased with the disease progression. This study added evidence consistent with an association between serum uric acid level and the severity of Parkinson's disease. This finding pushes us to emphasize on the role of uric acid levels on the Parkinson's disease.

**Key words:** Parkinson's disease, Rigidity, Serum uric acid, Tremor.

## Introduction:

Parkinson's disease is the second commonest neurodegenerative disease, clinically characterized by resting 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 bodies.<sup>1</sup>

The prevalence of Parkinson's disease is about 0.3% of the whole population in industrialized countries, it is more common in the elderly and prevalence rises from 1% in those over 60 years of age to 4% of the population over 80.<sup>2</sup> The mean age of onset is around 60 years, although 5- 10% of cases, classified as young onset, begin between the ages of 20 and 50.<sup>3</sup>

Most Parkinson's disease occurs sporadically (85-90%) and are of unknown cause. Some studies suggest that environmental factors play more important role in patients

older than 50 years, with genetic factors being more important in younger patients.

Epidemiologic studies suggest increased risk with exposure to pesticides, rural living, and drinking water from well and reduced risk with cigarette smoking and caffeine.<sup>1</sup> About 10-15% of cases are familial in origin and associated with multiple specific gene mutations among which mutation in Parking gene are associated with 50% of early onset inherited and 20% of sporadic early onset Parkinson's disease.<sup>4</sup>

Factors that have been implicated in the pathogenesis of cell death include oxidative stress, intracellular calcium accumulation with excitotoxicity, inflammation, mitochondrial dysfunction and proteolytic stress.<sup>1</sup>

Uric acid is the final oxidation product of purine metabolism and is excreted in urine. It is a strong reducing agent and potent antioxidants which covers more than half of the antioxidant capacity of blood plasma (Maxwell et al. 2007)<sup>5</sup>. It is a marker of oxidative stress, and may have a potential therapeutic role

as an antioxidant.<sup>6,7</sup>

It is reported that uric acid could suppress oxidative stress and prevent dopaminergic cell death in animal models of Parkinson's disease. Reduced uric acid levels have been found not only in the substantia nigra but also in the cerebrospinal fluid and serum of Parkinson's disease patients.<sup>8,9,10</sup>

The association between uric acid and risk of Parkinson's disease has been investigated in several previous prospective studies and higher serum uric acid levels might have been correlated to a significantly reduced risk of Parkinson's disease.<sup>2,11</sup> There is also evidence that higher uric acid levels could slow the clinical progression of Parkinson's disease.<sup>12,13</sup>

Some recent studies show that uric acid 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 disease.<sup>14</sup> Some other studies indicate that high uric acid levels lead to the decrease of the free radicals and subsequently the onset of the disease.<sup>7</sup>

Another 14 years period research in America revealed that the risk of onset of Parkinson's disease 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.<sup>2,11</sup>

Some studies also show that the risk of Parkinson's disease is much lower in patients suffering from Gout.<sup>15</sup> Despite the above researches, results of the recent researches are not adequate for a general conclusion, as in case serum uric acid level is not free from adverse effects. So, these potential benefits of serum uric acid, however should be weighed against expected adverse effects in risk of gout and other chronic disease.<sup>11</sup>

Here, with considering the above cited instances, this study was conducted to embark on measuring the serum uric acid levels in PD patients and see its relation in different stages of Parkinson's disease patients in Bangladesh. So that the study result might open the door of future research regarding alternative treatment and prevention of Parkinson's disease.

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## Methods

This observational cross-sectional study was carried out in the out-patient department of Neurology and Medicine at Mymensingh Medical College Hospital, Mymensingh from August 2017 to October 2018 for a period of fifteen (15) months. All Parkinson's disease patients who visited out-patient department of Neurology and Medicine at Mymensingh Medical College Hospital & fulfilled the inclusion criteria were included as study population (According to Brain Bank criteria).<sup>16</sup> Purposive consecutive type of sampling technique was applied. Patients who were diagnosed as Parkinson's disease according to Brain Bank clinical criteria<sup>16</sup> for diagnosis of Parkinson's disease and who gave consent to undergo the study procedure were included in the study. Prior to the commencement of this study, the research protocol was approved by the institutional review board of Mymensingh medical college, Mymensingh and was approved by the thesis committee of Mymensingh Medical College and Hospital, Mymensingh. Patients who were suffering from systemic disease that were likely to affect serum uric acid level such as Gout, Hematological malignancies, Renal failure, and Vasculitis were excluded by history, clinical examinations and previous treatment records. Patients who were taking drugs which were established as having effect on serum uric acid level such as Corticosteroids, Colchicine, Pyrazinamide, Aspiring, Allopurinol and thiazide diuretic were also excluded from the study.

Before data collection, informed written consent was taken from patient himself/herself or his/her attendant. All information regarding history including risk factor and physical findings were recorded from hospital records and also by direct examination. All participants were evaluated for their serum uric acid level by Olympus AU680 Random Access Multi batch Chemistry Analyzer, Japan. A semi-structured questionnaire and checklist were prepared for study population. The interview schedule was made in Bangla which included questions related to the variables of the study. After explaining the purpose of the study, data were collected in a semi-structured questionnaire through face to face interview from the out patient department of Neurology and Medicine at Mymensingh Medical College, Mymensingh. Serum uric acid was measured from study population by using chemical analyzer in a private laboratory (Popular diagnostic center limited) due to lack of that facility in the hospital during the study period. After collection, all data were checked for inadequacy, irrelevancy and inconsistency. All irrelevant and inconsistent data were corrected or discarded methodically.

#### Operation definition:

Identification of a Parkinsonian Syndrome: Commonly used criteria are the presence of bradykinesia and at least 1 of the following: muscular rigidity, 4- to 6-Hz resting tremor, and/or postural instability. UK Parkinson's Disease Society Brain Bank (Hughes et., 1992)<sup>16</sup>.

Hoehn and Yahr Stage<sup>17</sup>:

Stage	Disease State
I	Unilateral involvement only, minimal or no functional impairment
II	Bilateral or midline involvement, without impairment of balance
III	First assign of impaired righting reflex, mild to moderate disability
IV	Fully developed, severely disabling disease; patient still able to walk and stand unassisted
V	Confinement to bed or wheelchair unless aided.

Normal Serum uric acid Level: Male 3.0-7.0mg/dL, Female 2.4-5.7mg/dL.

All the data were checked and edited after collection. Then the data were entered into computer and statistical analysis of the result was obtained by using Windows based computer software devised with Statistical Packages for Social Sciences (SPSS-22). The results were presented in tables and figures. The statistical terms include in this study were mean, standard deviation, percentage. Statistical significance was set at  $p < 0.05$ .

**Result:**

This hospital-based Case Control Study was conducted in Mymensingh Medical College Hospital with a view to evaluate the association of serum uric acid level with Parkinson's disease. maximum patients were in age range from 61 – 70 years. Mean age of the patients was  $62.25 \pm 8.56$  year. Males were 37 (52.9%) females were 33 (47.1%). Male female ration was found 1.12:1.

**Table I: Distribution of the study patients by presenting complaints in combinations (n=70)**

Presenting complaint	Frequency (n)	Percentage (%)
Tremor+Hypokinesia+Rigidity+ Postural Imbalance	16	22.9
Tremor+Hypokinesia+Rigidity	18	25.7
Tremor+Rigidity	36	51.4

**Table II: Distribution of the study patients by combinations of non-motor symptoms (n=70).**

Not motor symptoms	Frequency (n)	Percentage (%)
Disorder in sensory+sleep +cognitive	17	24.3
Disorder in sleep+cognitive	15	21.4
Disorder in sleep+anosmia	2	2.9
Disorder in Sleep	6	8.6
Cognitive disturbance	12	17.1
None	18	25.7

**Table III: Distribution of the study patients by Hoehn and Yahr staging (n=70)**

Hoehn and Yahr staging	Frequency (n)	Percentage (%)
II	34	48.6
III	19	27.1
IV	5	7.1
V	12	17.1
Total	70	100

**Table IV: Serum uric acid level at different Hoehn and Yahr staging of PD (n=70)**

Hoehn and Yahr staging	Uric acid (Mean±SD)	p value
Stage II	$3.79 \pm 1.14$	0.007
Stage III	$3.26 \pm 0.63$	
Stage IV	$3.04 \pm 0.08$	
Stage V	$2.67 \pm 1.05$	

P value derived from ANOVA test

Table I shows combinations of presenting complaints of the patients. It was observed that 16 (22.9%) patients had combination of tremor, hypokinesia, rigidity and postural imbalance, 18 (25.7%) had tremor, hypokinesia & rigidity and 36 (51.4%) had tremor and rigidity (Table I).

Table II shows combinations of non-motor symptoms of the patients. It was observed that 24.3% of the patients had sensory, sleep and cognitive disorder, 21.4% patients had sleep and cognitive disorder, 2.9% patient had disorder in sleep and anosmia, 8.6% patients had only sleep disturbance, 17.1% had only cognitive disturbance but 25.7% had no non-motor symptom (Table II). Majority (61.4%) patient's disease duration was 1-5 years. The mean duration of disease was found  $6.34 \pm 5.53$  years.

Table III shows Hoehn and Yahr staging of the patients. It was observed that majority 34 (48.6%) patients were in stage II, 19 (27.1%) were in stage III, 5 (10.0%) were in stage IV and 12 (17.1%) were in stage V (Table III). Mean serum uric acid was found to be  $3.45 \pm 1.26$ mg/dL (2.0-5.8) in male and  $3.36 \pm 0.81$ mg/dL(2.1-5.8) in female patients.

Table IV shows serum uric acid level at different Hoehn and Yahr staging of PD. Serum uric acid level steadily reduced with the severity of PD which is statistically significant. Advanced stages of parkinsons disease were associated with significantly lower levels of serum uric acid. The difference between the stages were statistically significant ( $p=0.007$ )(Table IV).

**Discussion:**

PD is the second most common age related neurodegenerative condition in the US, affecting approximately one percent of the population over the age of 65 in North America and Europe.<sup>18</sup> The symptoms of PD are characterized by loss of

dopaminergic neurons in the substantia nigra. While the cause of this loss is thought to be multifactorial, there is evidence to support oxidative stress as a factor in neurodegeneration.<sup>19</sup> Hyperuricemia is associated with antioxidant effects.<sup>20</sup> Many researchers have proposed that elevated levels of uric acid yield a protective effect against the development and progression of PD.<sup>13,15,21</sup> In addition, it has been suggested that a diet rich in purines may play a role in prevention of PD.<sup>11</sup>

At this point in time, we can only note that there is an association between PD and uric acid. Whether this is a cause or an effect of the disease remains to be proven. There have been several studies supporting the hypothesis that elevated levels of uric acid are associated with a decreased incidence of idiopathic PD.<sup>9,22</sup> In 1996, Davis et al.<sup>9</sup> reported data from the Honolulu Heart Program suggesting that men with uric acid levels above the median level had a 40 percent reduction in the incidence of idiopathic PD.

The Honolulu Heart Program was a prospective study that followed men of 8006 Japanese or Okinawan men for 30 years. The reduction in IPD was only marginally statistically significant (RR=0.6, CI: 0.4-1.0); however, this was one of the first large studies showing a clear relationship between uric acid levels and IPD.<sup>9</sup> In a prospective study of 18,000 men in the Health Professionals Follow-up Study, Weisskopf et al.<sup>22</sup> examined the relationship between uric acid levels and PD. In this study, a statistically significant association was seen between uric acid levels drawn four years prior to the diagnosis of PD and incidence of IPD. The men in the top quartile of plasma urate concentration had a 55 percent lower rate of PD than did men in the bottom quartile, and the decrease in rate of IPD was greater once the data was modified to include only men with blood collected at least four years prior to the diagnosis.

This modification of the data suggested that the decreased levels of uric acid seen in PD patients occurs prior to neurological symptoms and is unlikely a side effect of behavior changes or medication. Following the results of these studies, several authors looked at the relationship between gout, a clear hyperuricemic state, and PD.

Alonso et al.<sup>21</sup> utilized the General Practice Research Database, where they identified 1,052 cases of PD and 6,634 matched controls. They found that patients with a prior diagnosis of gout had a 30 percent reduction in the incidence of PD. This association was significant in men, but not in women.<sup>21</sup> Approximately one year later, de Vera et al.<sup>15</sup> reported similar results using the British Columbia Linked Health Database and PharmaCare data. In this study, the authors identified 11,258 gout patients and 56,199 controls and estimated the relative risk of PD among patients with gout. They found a 30 percent reduction in the risk of PD among individuals with gout. Subgroup analysis did show that the lower rate of PD existed in both men and women.<sup>15</sup>

Taking the relationship of elevated serum urate levels and PD one step further, in 2007, Gao et al.<sup>11</sup> examined the relationship between diets high in urate and the incidence of PD. They worked on 47,406 men from the Health

Professionals Study, and calculated a dietary urate index for all participants. The authors used 14 years of follow up data and documented 248 incident cases of PD. They found that a higher dietary urate index was associated with a lower risk of PD. A greater than twofold reduction in risk of PD was seen between the highest and lowest quintiles of dietary urate. Ingredients such as fructose and ethanol were found to be associated with an increased rate of gout, and led to a higher dietary urate index. Vitamin C was also found to be associated with both a lower incidence of PD and gout, which was the only hypouricemic food to be associated with a lower incidence of PD. Other antiuricemic foods such as dairy proteins were not found to be significant.

Most recently, Schwarzcild et al.<sup>13</sup> used data from the Parkinson's Research Examination of CEP-1347 (PRECEPT) study to assess the relationship between levels of serum urate and the progression of PD, both clinically and radiographically by single photon emission computed tomography (SPECT). In this study, the authors followed 804 subjects with a diagnosis of early PD, prior to dopaminergic therapy. Baseline uric acid levels were used, and the endpoint signifying rate of progression was initiation of dopaminergic therapy. There was a 49 percent reduction in rate of progression among those in the highest quintile of uric acid as compared with those in the lowest quintile, and a 35 percent reduction in the rate among those in the fourth quintile as compared with the lowest quintile. Compared to the lowest quintile, there were 35 percent and 49 percent reductions in rate of progression in the 4th and 5th quintiles respectively. In addition, patients with a higher initial urate concentration had a lower percentage loss of striatal uptake of iodine I 123-labeled B-CIT by (SPECT) imaging. When subgroup analysis was completed, the rate of change in Unified Parkinson's Disease Rating Scale (UPDRS) was inversely associated with urate concentrations in men while this relationship was not significant in women.

Overall, recent research supports an inverse relationship between serum urate levels and the incidence of PD in men. There is also evidence to support the association between high dietary urate and a decreased incidence of PD. It should be noted that there are numerous risks associated with hyperuricemic diets, such as gout, stroke and hypertension. At this point, the data we have suggests an association, but not a causal relationship between low serum urate and the incidence of PD.

Sakuta et al.<sup>23</sup> conducted a cross-sectional study to evaluate the associations between serum UA levels and disease duration, disease severity, and motor function among PD, MSA, and progressive supranuclear palsy (PSP) patients. A total of 100 patients with PD, 42 patients with MSA, 30 patients with PSP, and 100 controls were included in this study. Serum UA levels were determined, and associations among serum UA levels and disease duration, disease severity, and motor function in PD, PSP, and MSA patients were evaluated. Serum UA levels were significantly lower in male PD, MSA, and PSP patients compared with the controls, but not in female patients. Serum UA levels were negatively

correlated with disease duration and severity in MSA and PSP patients, but no correlations were observed in PD patients. The serum UA levels were significantly decreased in the tauopathy group (PSP patients) compared with the synucleinopathy group (PD and MSA patients) after adjusting for age, gender, and body mass index. They found decreased serum UA levels in male patients with PD-related disorders (PD, MSA, and PSP) compared with

male controls, and significant correlations between serum UA levels and disease severity in MSA and PSP patients.

Jesus et al.<sup>24</sup> conducted a case control study among Parkinson's disease patient in Southern Spain where they included 161 patients with PD and 178 controls UA concentration was compared between these two groups. Patients with PD showed lower serum UA concentrations (4.68 1.66mg/dl) than controls (5.37 1.60 mg/dl). The difference was statistically significant even when comparing each sex separately. The multivariate analysis adjusted for age and sex showed that his relationship remained statistically significant. Post hoc analysis showed a significant difference in serum UA concentrations when comparing stage 2 and stages 4 and 5 for both sexes (P=0.028) and for men only (P=0.014), but not for women only (P=1). No significant association was found between serum UA concentration and age at disease onset or disease duration in both sexes. They did not find a significant association between serum UA concentration and levodopa equivalent daily dose in the total group. When analyzing each sex separately, a significant relationship between those factors was found in men. Shen and Ji<sup>25</sup> meta analysed of six studies to see uric acid levels in patients with PD in comparison with controls. The meta-analysis results showed that patients with PD had lower levels of uric acid than healthy controls both in women and men. It was found that patients with PD had lower serum levels of uric acid than healthy controls and this association was more significant in men than in women. More efforts are encouraged to explore the prognostic and therapeutic implications for PD of the present finding.

The risk of Parkinson disease (PD) and its rate of progression may decline with increasing concentration of blood urate, a major antioxidant. Ascherio et al.<sup>10</sup> determined whether serum and cerebrospinal fluid concentrations of urate predict clinical progression in patients with PD. Eight hundred subjects with early PD enrolled in the Deprenyl and Tocopherol Antioxidative therapy of Parkinsonism (DATATOP) trail. The pretreatment urate concentration was measured in serum for 774 subject and in cerebrospinal fluid for 713 subjects.

The Hazard ratio of progressing to the primary end point decreased with increasing serum urate concentrations (Hazard ratio for highest vs lowest quintile= 0.64; 95% confidence interval [CI], 0.44- 0.94; HR for a 1-SD increase =0.82; 95% CI, 0.73-0.93). In analyses stratified by -tocopherol treatment (2000 IU/d), a decrease in the HR for the primary end point was seen only among subjects not treated with -tocopherol (HR for a 1-SD increase = 0.75; 95% CI, 0.62-0.89; vs HR for those treated=0.90; 95% CI, 0.75-1.08). Results were similar for the rate o change in the Unified Parkinson's Disease

Rating Scale score. Cerebrospinal fluid urate concentration was also inversely related to both the primary end point (HR for highest vs lowest quintile=0.65; 95% CI, 0.44-0.96; HR for a 1-SD increase=0.89; 95% CI, 0.79-1.02) and rate of change in the Unified Parkinson's Disease Rating Scale score. As with serum urate concentration, these associations were present only among subjects not related with -tocopherol.

Schwarzschild et al.<sup>13</sup> determined whether concentration of serum urate, a purine metabolite and potent antioxidant that has been linked to a redacted risk of Parkinson's disease (PD), predicts prognosis in PD. Eight hundred four subject with early PD enrolled in the PRECEPT study. The adjusted HR of reaching end point declined with increasing baseline concentrations of urate; subjects in the to quintile reached the end point at only half the rate of subjects in the bottom quintile (HR, 0.51; 95% confidence interval [CI], 0.37-0.72; P<0.001). This association was markedly stronger in men (HR, 0.39; 95% CI, 0.26-0.60;

P<0.01) than in women (HR, 0.77; 95% CI, 0.39-1.50; P>0.50). The percentage of loss in striatal  $\beta$ -CIT uptake also improved with increasing serum urate concentrations (overall P<0.05; men, P<0.001; women, P>0.05). These findings identify serum urate as the first molecular factor directly linked to the progression of topical PD and suggest that targeting urate or its determinants could be an effective disease-modifying therapy in PD.

Goa et al.<sup>11</sup> examined whether a diet that increases plasma urate level is also related to reduce risk of Parkinson's disease (PD). Their study population comprised 47,406 men in the Health Professionals Follow-up Study. The potential effect of diet on plasma urate level was estimated by regressing plasma urate on intakes of selected foods and n nutrients in a sub sample of 1,387 men. Coefficients of this regression model were then used to calculate a dietary urate index for all cohort participants. Multivariate relative risk of PD were estimated by means of Cox proportional hazards odes. After 14 years of follow -up (1986-200), the authors documented 248 incident cases of PD. A higher dietary urate index was associated with a lower risk of PD, after adjustment for age, smoking, caffeine, intake, and other potential confounders. This association remained strong and significant after further adjustment for each component of the index individually (p < 0.02 for each). These data support urate as a potentially protective factor in PD and suggest that dietary changes expected to increase plasma urate level may contribute to lower risk of PD. These potential benefits, however, should be weighted against expected adverse effects on risk of gout and other chronic diseases.<sup>11</sup>This cross sectional study was carried out in the out- patient department of Neurology and Medicine at Mymensingh Medical College Hospital, Mymensingh from August 2017 to October 2018 to determine the association of serum uric acid level with severity of Parkinson's disease. During the study period, a total of 70 patients diagnosed as Parkinson's disease by Brain Bank clinical criteria OPD of Neurology and Medicine department at Mymensingh Medical College Hospital, Mymensingh were included. The following observations and

results were obtained in this study. In this study, mean age of the PD patients was  $62.25 \pm 8.56$  years. Similar age also observed in the study of Andreadou et al.<sup>14</sup> In this study, it was observed that male was 52.9%, Male to female ratio was 1.12:1. Similar finding also found in the study of Andreadou et al.<sup>14</sup>

Regarding the clinical presentation of the patients it was observed in this study that Combination of tremor, hypokinesia, rigidity and postural imbalance were in 16 (22.9%), 18 (25.7%) patients had tremor, hypokinesia & rigidity and 36 (51.4%) had tremor and rigidity. O'sullivan et al.<sup>26</sup> found tremor in 76.3% of cases, rigidity in 78.2% of cases, postural instability in 7.8% cases with "motor symptoms" at presentation, which are not similar to this current study that maybe due to the lack of awareness and scarcity of availability of health care facilities in our community which failed to detect the disease in early stage as well as reluctant to take comprehensive care as much as possible by the patients.

In this present study it was observed that majority (61.4%) of the patient's disease duration was 1- 5 years and the mean duration of disease was  $6.34 \pm 5.53$  years, with a range of 1 to 30 years. Similarly, Chaudhuri et al.<sup>27</sup> found that the mean duration of disease was  $6.4 \pm 6.0$  years. In this present study it was observed that mean serum uric acid was  $3.40 \pm 1.04$  mg/dl with a range of 2.0 to 5.8 mg/dl. Mean serum uric acid in male was  $3.45 \pm 1.26$  (2.0-5.8) and in female was  $3.36 \pm 0.81$  (2.1-5.8). Mean serum uric acid level was  $5.47 \pm 1.40$  mg/dl in PD patients in the study of Andreadou et al.<sup>14</sup> Similarly, Iranmanesh et al.<sup>28</sup> observed the mean uric acid level was  $4.79 \pm 1.21$  mg/dl in the patients. Iranmanesh et al.<sup>28</sup> showed mean serum uric acid male was in  $3.48 \pm 1.12$  (2.1-6.0) and female was in  $3.39 \pm 1.34$  (2.0-5.9). Which was similar to that study. In this study it was observed that Mean serum uric acid level was ( $3.79 \pm 1.14$ ), ( $3.26 \pm 1.14$ ), ( $3.04 \pm 0.08$ ), ( $2.67 \pm 1.05$ ) in stage-II, stage -III, stage-IV, and stage-V respectively. In this study it is observed that mean serum uric acid level was steadily lower with disease severity. Which it is statistically significant ( $p=0.007$ ). Schwarzschild et al.<sup>13</sup> carried out 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 uric acid level. Ascherio et al.<sup>10</sup> 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 PD.

### Conclusion:

This study shows a negative association between serum uric acid level and the severity of Parkinson's disease. The level of serum uric acid decreased with the disease progression. This study added evidence consistent with an association between serum uric acid level and the severity of Parkinson's disease. This finding pushes us to emphasize on the role of uric acid levels on the Parkinson's disease.

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