**How to Cite**:
Kamil, M. A. S. (2022). The state of uric acid in Iraqi patients with Parkinson disease. *International Journal of Health Sciences*, *6*(S2), 10505–10512. https://doi.org/10.53730/ijhs.v6nS2.7754

# The state of uric acid in Iraqi patients with Parkinson disease

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***Abstract*---**Uric acid has recently been proposed as a possible cause of Parkinson's disease (PD). The researchers wanted to see how uric acid levels were in persons with Parkinson's disease compared to an age-matched healthy control group. Researchers employed a case control study and a random comparison of plasma uric acid concentrations of collected samples in a clinical neurology department ward at Baghdad education hospital/Medical City and a Parkinson's disease movement disorder clinic. Participants were enrolled in the study from October 2015 to October 2016. We looked examined blood Uric acid levels in 40 Parkinson's disease patients and 40 age-matched healthy controls after controlling for age, sex, race, and geographic location. The Most Important Outcome Measures: Suboptimal Uric acid concentrations have been seen in Parkinson's patients. The results indicated that patients with PD (65%) had lower uric acid levels than controls (22.5%), and that the mean uric acid concentration in PD was (3.24) considerably (P.05) lower than in controls (4.08). The study's findings show that PD patients had much lower uric acid levels than healthy controls. These findings suggest that uric acid may have a role in Parkinson's disease.

***Keywords*---**central nervous system, Parkinson's disease, uric acid, neurodegenerative disorder.

## Introduction

Parkinson's disease (PD) is the second most prevalent neurodegenerative ailment, behind Alzheimer's disease. It is a central nervous system disorder that primarily affects the motor system [1]. The symptoms usually appear gradually over time. The most prominent clinical signs early in the disease are shaking, stiffness, slowness of movement, and trouble walking, as shown in table 1 [1]. Problems with thinking and conduct are also possible. Dementia becomes more frequent as the disease progresses. Depression and anxiety affect more than a third of

patients with Parkinson's disease [2]. Sensory, sleep, and emotional issues are among the other symptoms [1,2]. The primary motor symptoms are referred to as "parkinsonism" or "parkinsonian syndrome"[3].

**CLINICAL FEATURES OF PARKINSON'S DISEASE**

| CARDINAL FEATURES | OTHER MOTOR FEATURES | NONMOTOR FEATURES |
|---|---|---|
| Bradykinesia | Micrographia | Anosmia |
| Rest tremor | Masked facies (hypomimia) equalize | Sensory disturbances (e.g., pain) |
| Rigidity | Reduced eye blink | Mood disorders (e.g., depression) |
| Gait disturbance/postural instability | Soft voice (hypophonia) | Sleep disturbances |
| | Dysphagia | Autonomic disturbances |
| | Freezing | Orthostatic hypotension |
| | | Gastrointestinal disturbances |
| | | Genitourinal disturbances |
| | | Sexual dysfunction |
| | | Cognitive impairment/dementia |

Table (1): clinical features of Parkinson's disease [4]

The etiology of Parkinson's disease is unclear, however it is thought to be a combination of hereditary and environmental factors. Those who have a family member who has the condition are more likely to get it themselves [3]. People exposed to specific pesticides and those who have had past head traumas are at an elevated risk, but cigarette users and those who consume coffee or tea are at a lower risk [3,5].

Uric acid is a carbon, nitrogen, oxygen, and hydrogen heterocyclic molecule with the formula C5H4N4O3. It produces urates and acid urates, such as ammonium acid urate, as ions and salts. Uric acid is a naturally occurring component of urine that results from the breakdown of purine nucleotides in the body. High uric acid levels in the blood induce gout, which has been linked to diabetes and the production of ammonium acid urate kidney stones. With pKa1 = 5.4 and pKa2 = 10.3 [6, uric acid is a diprotic acid. It creates the dually-charged full urate ion in strong alkali at high pH, but it produces the singly-charged hydrogen urate or acid urate ion at biological pH or in the presence of bicarbonate ions. The complete urate salts hydrolyze back to hydrogen urate salts at pH levels around neutral because their second ionization is so feeble. Because both rings have conjugated pi bonding, it is aromatic [7].

The standard range for uric acid in human blood plasma is 3.4–7.2 mg/dL (200–430 mol/L) in men and 2.4–6.1 mg/dL (140–360 mol/L) in females– one milligram per decilitre (mg/dL) equals 59.48 micromoles/litre (mol/L). Blood test findings, on the other hand, should always be interpreted within the testing institution's recommended range. Hyperuricemia and hypouricemia refer to uric acid concentrations in blood plasma that are either above or below the normal range. Hyperuricosuria and hypouricosuria are conditions in which uric acid levels in the urine are abnormally high or low. Such excessive uric acid concentrations are not medical illnesses, although they are linked to a number of them. Hyperuricemia (high uric acid levels) can lead to gout [8].

Recent research suggests that uric acid may have a role in the genesis and progression of Parkinson's disease. Uric acid is a natural antioxidant that may help to minimize oxidative stress, which is considered to be a factor in the development of Parkinson's disease. Serum urate (SU) levels that are higher may have a neuroprotective impact. High SU levels were linked to a lower likelihood of developing PD and a slower course of the disease. In comparison to controls, SU levels were decreased in PD patients. Manipulation of SU levels has shown potential in the therapy of Parkinson's disease. A high purine diet may help individuals with Parkinson's disease slow down their illness development. Milk and meat diet, as well as exercise, may alter the risk of developing PD by affecting SU levels. The relationship between PD and SU levels and its implications for PD management are discussed in this paper [9]. The purpose of this research is to determine the level of uric acid in Parkinson's patients.

## Methods

### Design and Setting

A case-control study was conducted in the neurology wards, Baghdad teaching hospital, medical city, and movement issue clinic. The patients were seen at the medical facility on a regular basis from October 2015 to October 2016, seeking medical guidance on their Parkinson's disease signs and symptoms.

### Study population

This study performed on 40 patients (24 male and 16 female, with mean age 59.225, 23 urban and 17 rural) diagnosed with Parkinson disease according to bank criteria. Who attended neurology wards / Baghdad teaching hospital/ medical city and movement disorder clinic under supervision of consultant neurologist, their selection follows the following criteria:

1. Idiopathic Parkinson disease diagnosis by UK Parkinson's disease society brain bank clinical diagnostic criteria. [10]
2. Patients having a weight range from (45-85) kg.
3. Patients are aged more than 40 years old.

### Parkinson's Disease Society of Great Britain Clinical Diagnostic Criteria of the Brain Bank [10]

Step 1: Confirm the existence of bradykinesia (slowness of voluntary movement start, reduced speed and amplitude of movements, and/or lack or reduction of automatic movements) and at least one of the following:

- Rigidity
- Postural instability • 4Y6 Hz resting tremor (not otherwise explained by primary visual, vestibular, cerebellar, or proprioceptive dysfunction)

Step 2: Look for excluding criteria for Parkinson's disease diagnosis.

- There is no prior history of:

- Parkinson's disease progression with repeated strokes
- Consistent head trauma
- Encephalitis is confirmed
- Neuroleptic therapy when symptoms first appear
- Multiple relatives are impacted (although this exclusion criterion is no longer commonly used)
- Any sustained remission period
- Oculogyric emergencies
- Severe autonomic involvement early on
- Early severe dementia with memory, language, and praxis problems

Exposure to 1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)

- OR a discovery of:
- After 3 years, the characteristics are strictly unilateral.
- Negative reaction to levodopa at high dosages (if malabsorption is excluded)
- Palsy of the supranuclear gaze
- Cerebellar symptoms
- Babinski's signature
- Cerebral tumor or hydrocephalus with communication

Step 3: Confirm the existence of three or more of the supporting criteria for Parkinson's disease diagnosis:

- Unilateral onset • Resting tremor
- Degenerative disease
- Asymmetry persists, with symptoms worsening on the side of beginning.
- A clear and unequivocal response to levodopa (improvement of 70 to 100 percent on the Unified Parkinson's Disease Rating Scale)
- Levodopa-induced chorea that is severe
- 5 years or more of levodopa response
- 10 years or more of clinical experience

**The severity of the condition can be determined using the Hoehn and Yahr Scales [1]**

1.5 Unilateral and axial involvement 1.0 Unilateral involvement exclusively
2.0 Bilateral involvement with no balance impairment
2.5Mild bilateral disease with pull test recovery
3.0Bilateral illness that is mild to severe; slight postural instability; physically independent
4.0Severe disability; able to walk or stand without assistance
5.0 Requires a wheelchair or is bedridden unless assisted

**Exclusion criteria**

1. Atypical parkinsonian syndromes (e.g. multiple system atrophy, progressive supranuclear palsy, corticobasal syndrome).

2. Secondary Parkinsonism (drug-induced, vascular, structural, infectious, immunologic, toxic, traumatic, metabolic).
3. Chronic renal failure.
4. Patients have other diseases like DM, cardiovascular and CNS diseases.
5. Patients take treatment for gout.

All patients underwent a thorough neurological examination, standardized blood tests, and electrolytes, representing serum calcium and phosphate, magnetic resonance imaging of the brain, and cardiac analysis, which included standard 12-lead electrocardiography and serum Uric acid in all patients.

**Statistical analysis**

Data were analyzed by means of statistical package for social sciences (SPSS) software programs. Values were expressed as mean +\- SD. a comparison of continuous variables was performed by unpaired two-tailed Student's t test. A level of P<.05 (two-sided testing) was considered statistically significant.

**Result**

We was study 40 patients in-group I (PD patients), the Mean age of the patients was (59.225 ± 5.968) years and 40 healthy patient in-group II (control) with mean age (59.750 ± 5.674). In the group I (PD patients), there was 24 Male and 16 female, with mean BMI 21.958 and residency distributed in to 23 urban and 17 rural. In the group II (control), there was 23 male and 17 female, with mean BMI 23.277 and residency distributed in to 28 urban and 12 rural (Table 2). This study, show there is no significant difference between the two groups regarding the age, sex, BMI, or residency (Table 2).

Table 2. general characteristic of data

| GROUP | | N | Mean | Std. Deviation | P |
|---|---|---|---|---|---|
| AGE | I | 40 | 59.225 | 5.968 | 0.685 |
| | II | 40 | 59.750 | 5.674 | |
| SEX | I | 40 | 24 / 16 | 0.4961 | 0.812 |
| | II | 40 | 23 / 17 | 0.5006 | |
| BMI | I | 40 | 21.958 | 3.282 | 0.062 |
| | II | 40 | 23.277 | 4.533 | |
| RSE | I | 40 | 23 / 17 | 0.5006 | 0.281 |
| | II | 40 | 28 / 12 | 0.4641 | |

It is obvious that in Parkinson disease patients (group I), there was lower plasma level of uric acid with mean 3.24 , while in healthy control (group II), the mean was 4.08 so there was significant different between groups with p value 0.025.

Table 3 uric acid level in PD

| GROUP | N | Mean | Std. Deviation | P |
|---|---|---|---|---|

| | | | | | |
|---|---|---|---|---|---|
| Uric acid | I | 40 | 3.24 | 1.29 | 0.025 |
| | II | 40 | 4.08 | 1.94 | |

It is obvious that in Parkinson disease patients (group I), there was 14(35%) patients with normal uric acid and 26(65 %) had low uric acid, while in healthy control (group II), there was 31(77.5%) normal or mildly elevated uric acid and 9 (22.5%) low uric acid.

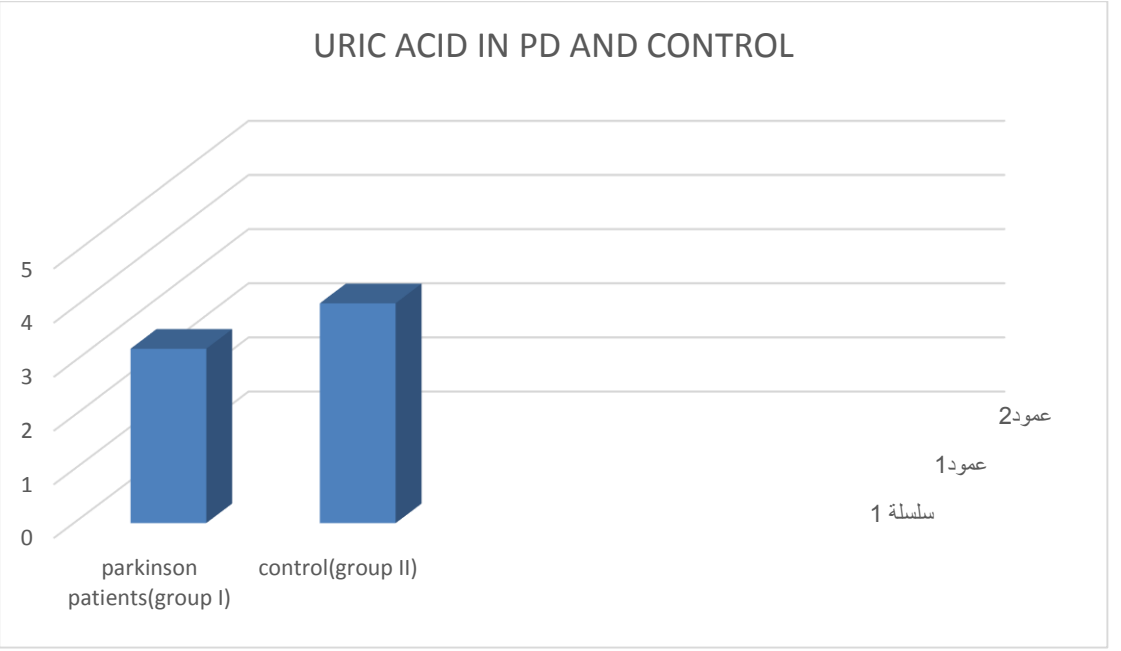


Figure 1 state of Uric acid in PD and control.

In our study, we divided Parkinson patients (group 1) depend on disease severity to two subgroup according to Hoehn and Yahr stages, Subgroup A include stage 1 and 2 and subgroup B, include stages 3 to 5. We find there are significant difference (p value =0.014) between uric acid levels according to disease severity as low reading of uric acid as disease more sever, clarify in (table 4).

Table 4.relation uric acid and PD severity

| | GROUP I | N | Mean | Std. Deviation | P |
|---|---|---|---|---|---|
| Uric acid | subgroup A | 19 | 3.77 | 1.46 | 0.014 |
| | subgroup B | 21 | 2.735 | 0.931 | |

**Discussion**

This is the first research to compare Uric acid levels in Parkinson's disease patients in Iraq to age-matched healthy controls. The etiology of Parkinson's disease may be influenced by oxidative stress (PD). Serum uric acid may aid to

inhibit the beginning of this neurodegenerative disease due to its antioxidant characteristics. Furthermore, a number of literature have shown a strong link between blood uric acid and the occurrence of Parkinson's disease [12]. The results of this study show that (65%) Parkinson patients enrolled in the study having low uric acid level with mean ± SD was significantly lower (3.24 ±1.29 ng/ml) compared to (22.5%) of healthy controls without Parkinson disease with mean ± SD was significantly higher (4.08±1.94 ng/ml) in healthy controls (P = < 0.025). Analyses of substantia nigra tissue specimens from human parkinsonian individuals (PD) and age-matched controls (NC) for uric acid (UA) showed a vital role in normal function due to its antioxidant properties [13-15]. This result agree with study done in 2009 by Andreadou et al establish that patients with Parkinson disease had significantly lower uric acid level [16].

Also, approve in Study by Dr.Winquist that found a High prevalence of low uric acid level in Parkinson's disease [17]. Furthermore this study is compatible with study done In Spain, at 2013 study include 161 patients with Parkinson's disease (PD) and 178 controls were recruited using simple non-random sampling. Patients with PD showed statistically significant lower serum UA concentrations than controls [18]. Serum uric acid (UA) levels in individuals with Parkinson's disease (PD) and multiple system atrophy (MSA) have been found to be lower than in control participants [19, 20]. Reactive oxygen species and oxidative stress may have a role in the development of Parkinson's disease [21]. Increased iron levels as well as altered amounts of other metal ions have been seen in the brains of PD patients [22]. UA has antioxidant properties in neurons via acting as a free radical scavenger and an iron chelator [23].

According to gender in current study, there is no significant difference between male and female with Parkinson patients in uric acid level. This finding reported by Hideki Sakuta in Dokkyo Medical University study 135 patient of PD from 2011 to 2015. The serum uric acid levels were lower in PD patients than in control subjects, but no sex difference in uric acid level [24].

**Conclusions**

Parkinson's disease patients had considerably lower uric acid levels than healthy controls, no different between male and female with PD in level of uric acid, the level of uric acid decrease as disease severity increase, further study need to clarify this relation.

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