



## Uric Acid Levels in Serum in the Assessment of some Psychiatric Disorders in India

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### ABSTRACT

**Background:** *The increasing number of latent and manifest hyperuricemia is important concerning differential diagnosis in neurological and psychiatric diseases. The pathological importance of hyperuricemia in these diseases is particularly unknown. Previous studies have shown that uric acid estimation in cerebrospinal fluid was made with neurological and psychiatric diseases. Monitoring serum uric acid levels, a relatively inexpensive and easily available test, may prove to be a useful adjunct in the assessment of certain indices of certain psychiatric illness. Tranquilizers like 1,4 - benzodiazepine (purinergic) are shown to decrease xanthine oxidase activity initially and may cause fluctuations in serum uric acid levels.*

**Objective:** *In the present study an attempt was made to understand the effect of tranquilizers on serum uric acid levels in different psychiatric conditions.*

**Methods:** *40 cases (22 males and 18 females) of MDP (Maniac depressive psychosis) and Schizophrenia who were undergoing treatment with different tranquilizers from the psychiatric hospital, Patna, India and*

20 healthy controls (12 males and 8 females) not using any tranquilizers were included in the study. Results: The serum uric acid levels were significantly elevated ( $p < 0.05$ ) in these patients receiving treatment with tranquilizers. The levels of uric acid in male patients were significantly higher when compared with females and also over male controls ( $p < 0.01$ ). In female patients uric acids levels are raised but not significant ( $p > 0.05$ ) over control females.

**Conclusion:** This preliminary study does indicate that serum uric acid levels do change with the administration of these drugs. The nature, gender, duration and the type of drugs used and their individual effects on different psychiatric disorders will be discussed.

**Key Words :** Acute psychosis, Affective disorders, Schizophrenia, Tranquilizers, Uric acid

## INTRODUCTION

Uric acid is a constituent of the cell cytosol and also one of the soluble compounds in the blood, whose role in human physiology is controversial.<sup>1</sup> It is mainly synthesized from adenine- and guanine-based purines.<sup>2</sup> Humans lack uricase (urate oxidase) because of an acquired mutation in the urate oxidase gene, which makes the enzyme nonfunctional.<sup>3</sup> Thus, uric acid appears to be an end-product of the purine pathway, and circulating UA levels, which are dependent mainly on the nucleotide catabolism and cell turnover, are higher in humans.<sup>1</sup> According to Ames et al., inactivation of the urate oxidase gene, and thus the nonfunctionality of the corresponding enzyme is an evolutionary strategy to counteract the production of reactive oxygen species associated with the aerobic metabolism.<sup>4</sup> Therefore, uric acid is traditionally considered as a metabolically inert and waste compound without any physiological significance.<sup>2</sup> However, uric acid can be oxidized nonenzymatically, and has proven to be a selective antioxidant, capable of reacting, especially with hydroxyl radicals and hypochlorous acid, itself being converted to

innocuous products (allantoin, allantoate, glyoxylate, urea, oxalate).<sup>5</sup> Uric acid may be found in all tissue compartments except in those of the lipid phase. Uric acid, albumin and ascorbic acid, account for more than 85% of total antioxidant capacity in the plasma.<sup>6,7</sup> Therefore, measuring levels of specific antioxidant molecules, such as plasma uric acid can yield valuable information. Several studies have demonstrated derangement of uric acid levels in various disease states. Uric acid levels have been shown to be positively associated with various markers of systemic inflammation.<sup>8,9</sup> Elevated uric acid level is a risk factor for endothelial dysfunction, hypertension, metabolic syndrome, cardiovascular and cerebrovascular diseases, and all-cause and specific-cause mortality.<sup>10-17</sup> Derangement of uric acid levels has been seen in several neurological and psychiatric conditions. For instance, serum uric acid levels are elevated in epilepsy,<sup>18</sup> and bipolar disorder (especially during the manic phase)<sup>19</sup> while they are decreased in Parkinson's disease,<sup>20</sup> multiple sclerosis,<sup>21</sup> optic neuritis,<sup>22</sup> Alzheimer's disease,<sup>23</sup> and schizophrenia.<sup>24</sup> Reduced levels of uric acid are

seen with a variety of medications like L-Dopa, allopurinol, aspirin, probenacid, coumadin and corticosteroids.<sup>25,26</sup> Several studies have demonstrated that there is a variation in CSF uric acid levels in different neurological and psychiatric disorders.<sup>27,28,29</sup> In conditions like multiple sclerosis, myelopathy, epilepsy, stroke, and viral meningitis, CSF uric acid is increased 2-3-fold compared to controls.<sup>30</sup>

Therefore, since there exists a definite relationship between uric acid levels, and various psychiatric and neurologic conditions, the current study was conducted in order to understand the effect of treatment on serum uric acid levels in different psychiatric conditions.

## MATERIALS AND METHODS

Patients being treated at the psychiatric hospital, Patna, India during the period September 2013 to February 2014 were included as cases in the study. Controls were healthy volunteers. Serum samples were collected from all patients irrespective of their fasting status. Uric acid was measured by using phosphotungstic acid method.

## RESULTS

A total of 40 cases (22 males and 18 females) who were undergoing treatment at the psychiatric hospital, Patna, India for various diagnoses like acute psychosis, schizophrenia, affective disorders, depression and drug addiction; and 20 healthy volunteers (12 males and 8 females) not using any tranquilizers were included as controls. The drugs given included Cogentine, Serenace (Haloperidol), Largactyl (Chlorpromazine)

Depakin, and Inderal (Propranolol). The study findings are shown in Table 1. The serum uric acid levels were significantly elevated ( $p < 0.05$ ) in these patients receiving treatment with tranquilizers. The levels of uric acid in male patients were significantly higher when compared with females and also over male controls ( $p < 0.01$ ). In female patients uric acids levels are raised but not significant ( $p > 0.05$ ) over control females.

**Table 1:** Summary of the Study Findings

	No of Cases	Serum Uric acid		P-value
		Mean	SD	
Total cases	40	6.63	1.16	$\leq 0.05$
Male cases	22	6.98	0.81	$\leq 0.01$
Female cases	18	5.7	1.36	$\geq 0.05$
Total Controls	20	5.6	1.5	
Male Controls	12	5.5	1.4	
Female controls	8	4.5	1.2	

\*Mean±SD SD: Standard Deviation

## DISCUSSION

The findings of the current study showed a positive correlation between uric acid levels and effect of treatment in the patients with psychiatric disorders. Patients who were being treated had significantly higher levels of serum uric acid compared to controls ( $p < 0.05$ ). These findings are in line with those of other studies, which show that uric acid levels are decreased in various psychiatric conditions and improvement in levels

with treatment. In schizophrenia, the levels of uric acid are decreased.<sup>2,24,31,32</sup> Chaudhari et al. Demonstrated that there is a significant decrease in serum uric acid ( $P < 0.0001$ ) was observed in newly diagnosed major depressive disorder subjects when compared to healthy subjects; and this trend was reversed after 6 weeks and more significantly after 12 weeks ( $P < 0.001$ ) of fluoxetine or citalopram treatment with improvement in Hamilton Rating Scale for Depression score.<sup>33</sup> Haloperidol has also shown to decrease uric acid levels in animal models.<sup>34</sup> According to a study by Brunstein et al., in schizophrenic patients, there exists either an altered adenosine (purine) metabolism or is influenced by treatment with antipsychotics, particularly clozapine.<sup>35</sup> Recent studies suggest a dysregulation of the purinergic system in patients with bipolar disorder, especially in the manic phase; and that uric acid is not only a potential marker of treatment response, but its elevated levels may represent a state marker during mania.<sup>19,36</sup>

## CONCLUSIONS

Uric acid is an important antioxidant, derangement of which is observed in several neurological and psychiatric disease states, like Parkinson's disease, Alzheimer's disease, multiple sclerosis, optic neuritis, schizophrenia, bipolar disorder and depression. Treatment has shown to improve the uric acid levels in these patients. Our study also demonstrated an increase in serum uric acid levels with treatment in psychiatric patients. However, the limitation of our study was that the

sample size was small, and larger randomized controlled studies are required to confirm the findings of our study.

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