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Original Research Article

Serum Uric Acid as a Predictive Biomarker in Mania: A Longitudinal Prospective Study in a Tertiary Care Hospital at Kolkata

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Abstract:

Introduction: Bipolar disorder, particularly during manic episodes, has been increasingly linked to abnormalities in purinergic metabolism. Serum uric acid (SUA), a final product of purine degradation, is hypothesized to be elevated during mania and may serve as a state marker or potential predictor of manic episodes.

Aims & Objectives: To evaluate serum uric acid levels in patients during manic episodes and to assess its potential as a predictive biomarker for mania.

Materials & Methods: This prospective study was conducted over a period of one year, from January 2024 to December 2025, in the Outpatient Department (OPD) of Nil Ratan Sircar Medical College & Hospital. A total of 36 patients were included in the study, selected based on predefined inclusion and exclusion criteria to ensure the reliability and validity of the findings.

Result: The study population had a male predominance (54.05%) with a mean age of 31.06 ± 6.78 years. Treatment led to a significant reduction in Young Mania Rating Scale (YMRS) scores (from 43.32 ± 6.29 to 20.92 ± 3.51) and serum uric acid levels (from 6.15 ± 0.85 mg/dL to 5.45 ± 0.72 mg/dL). No significant difference was observed in serum uric acid levels among patients on different mood stabilizers—Lithium Carbonate, Sodium Valproate, and Carbamazepine ($p = 0.779$). However, serum uric acid levels significantly decreased from the manic phase (6.8 ± 1.2 mg/dL) to the remission phase (5.5 ± 1.0 mg/dL; $p = 0.001$). Responders to treatment had significantly lower uric acid levels (5.3 ± 0.9 mg/dL) compared to non-responders (6.4 ± 1.0 mg/dL; $p = 0.004$).

Conclusion: The findings of this study suggest that serum uric acid levels are closely associated with the manic phase of bipolar disorder and may serve as a potential state marker for mania. A significant reduction in both YMRS scores and serum uric acid levels following treatment highlights the therapeutic impact on manic symptoms. Although no significant differences were found in uric acid levels across different mood stabilizers, the marked decline in levels from the manic to the remission phase and the significantly lower levels in responders compared to non-responders underscore the potential utility of serum uric acid as a predictive biomarker for treatment response in mania.

Keywords: Serum uric acid, mania, bipolar disorder, biomarker, purinergic dysfunction, YMRS.

Introduction

Purines, particularly adenosine and adenosine triphosphate (ATP), play crucial roles in central nervous system (CNS) signaling, acting through purinergic receptors to modulate numerous neurophysiological processes. These purinergic receptors are broadly classified into two families: P1 receptors (A1, A2A, A2B, and A3), which are G-protein-coupled receptors responsive to adenosine, and P2 receptors, which include ionotropic P2X and metabotropic P2Y subtypes that are primarily activated by ATP and other nucleotides. These receptors are widely expressed in the brain and influence various neurotransmitter systems, including dopaminergic, glutamatergic, and GABAergic pathways, thereby modulating neuronal excitability, synaptic transmission, and neuroinflammation [Burnstock & Knight, [1], 2017; Fredholm et al. [2], 2011]. In the context of bipolar disorder (BD), growing evidence suggests that dysregulation of adenosinergic signaling may contribute to its pathophysiology, particularly in manic episodes. Adenosine generally exerts inhibitory effects in the CNS, and A1 receptors, in particular, are known to suppress excitatory neurotransmission by inhibiting the release of glutamate and modulating dopamine signaling. It has been hypothesized that reduced

adenosine tone or downregulation of A1 receptor activity may lead to an imbalance in excitatory-inhibitory neurotransmission, contributing to the heightened dopaminergic activity observed in mania [Kaster et al. [3], 2015; Lara et al. [4], 2006]. Furthermore, adenosine has been shown to interact with other neurobiological systems implicated in BD, including circadian regulation and mitochondrial function, suggesting a multifaceted role of purinergic signaling in mood regulation [Elmenhorst et al. [5], 2007; Cunha et al. [6], 2005]. This hypothesis is further supported by pharmacological studies where agents enhancing adenosinergic activity, such as allopurinol (a xanthine oxidase inhibitor that increases adenosine levels), have demonstrated mood-stabilizing and anti-manic properties when used as adjuncts in the treatment of BD [Machado-Vieira et al. [7], 2008]. These findings collectively highlight the significance of purinergic signaling, especially the adenosine-A1 receptor axis, in modulating neurotransmitter systems relevant to bipolar disorder, and they open new avenues for potential therapeutic interventions targeting this pathway. It has been proposed that uric acid, a byproduct of purine metabolism resulting from increased degradation of adenosine, may contribute to the pathophysiology of mania through its association with decreased adenosinergic neurotransmission in the central nervous system (CNS) [Lara et al. [8], 2006]. Adenosine, which exerts inhibitory neuromodulatory effects primarily via A1 receptors, plays a crucial role in maintaining neurochemical balance by regulating the release of excitatory neurotransmitters such as dopamine and glutamate. A reduction in adenosine signaling—whether due to increased metabolic degradation or receptor-level dysregulation—can lead to hyperexcitability in neuronal circuits, a feature characteristic of manic states. Consequently, patients experiencing bipolar mania often exhibit elevated serum uric acid levels, which reflect this underlying purinergic dysfunction. This association supports the hypothesis that hyperuricemia may not simply be a coincidental metabolic finding but rather a biological correlate of purinergic imbalance and manic symptomatology [Machado-Vieira et al. [9], 2001; Kesebir et al. [10], 2009]. Furthermore, studies have shown that uric acid levels tend to normalize with the resolution of manic episodes, reinforcing the potential state-dependence of this marker [Salvadore et al. [11], 2010]. Given these findings, serum uric acid estimation—a cost-effective and widely available laboratory test—holds promise as a potential peripheral biomarker for the detection and monitoring of bipolar mania. Its integration into clinical assessment protocols may enhance early identification, assist in treatment response monitoring, and provide further insight into the biological underpinnings of mood dysregulation.

The present study aims to investigate the socio-demographic characteristics of patients diagnosed with bipolar mania, with particular emphasis on identifying patterns related to age, gender, socio-economic status, and educational background. Additionally, the study seeks to measure serum uric acid levels in these patients to explore potential biochemical alterations associated with manic episodes. By establishing a correlation between elevated uric acid levels and the presence of bipolar mania, the study endeavors to support the role of purinergic system dysfunction in the disorder's pathophysiology. Furthermore, it evaluates the effectiveness of various mood stabilizers in reducing serum uric acid levels, thereby assessing their potential not only as therapeutic agents for mood stabilization but also in normalizing metabolic biomarkers associated with mania.

Materials and Methods

Study Type: Prospective Study

Study Duration: 1 year (January, 2024 – December 2025)

Study Place: OPD of Nil Ratan Sircar Medical College & Hospital

Study Sample Size: 36

Inclusion Criteria:

1. Patients aged more than 18years of age.
2. Newly diagnosed as bipolar disorder, currently mania according to ICD 10.
3. Known case of bipolar disorder but currently in manic state and not receiving pharmacological treatment for last one month.

Exclusion Criteria:

1. Patients diagnosed with metabolic abnormality and renal disease.
2. Patients having congenital purine metabolism pathway dysfunction.
3. Individuals taking probenecid, diuretics were excluded.
4. Patients having history of using any substance within 1 month period were excluded.

Study Tools:

1. Semi structured questionnaire used to assess the socio demographic details.
2. Mini International Neuropsychiatric Interview (MINI).
3. ICD 10
4. Young's Mania Rating Scale(YMRS)

Statistical Analysis: For statistical analysis, data were initially entered into a Microsoft Excel spreadsheet and then analyzed using SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism (version 5). Numerical variables were summarized using means and standard deviations,

while Data were entered into Excel and analyzed using SPSS and GraphPad Prism. Numerical variables were summarized using means and standard deviations, while categorical variables were described with counts and percentages. Two-sample t-tests were used to compare independent groups, while paired t-tests accounted for correlations in paired data.

Chi-square tests (including Fisher's exact test for small sample sizes) were used for categorical data comparisons. P-values ≤ 0.05 were considered statistically significant.

Result

Table 1: Demographic and Clinical Profile Before and After Treatment

N=36		
	Before Treatment	**After Treatment**
Gender	Males (54.05%)	
Age	Mean age 31.06+/-6.78.	
YMRS	43.32+/-6.29	20.92+/-3.51
Serum Uric Acid	6.15+/-0.85	5.45+/-0.72

The decline in serum uric acid is statistically significant with p-0.001.

Table 2: Comparison of Mean Serum Uric Acid Levels among Patients on Different Mood Stabilizers

Mood Stabilizer Used	**Number of Patients**	**Mean Uric Acid**	**P-value**
Lithium Carbonate	15	5.62	0.779
Sodium Valproate	11	5.65	
Carbamazepine	4	5.57	

Table 3: Comparison of Serum Uric Acid between Different Phases of Illness

Phase	**Uric Acid (mg/dL) Mean ± SD**	**p-value (vs baseline)**
Manic Episode	6.8 ± 1.2	-
Remission Phase	5.5 ± 1.0	0.001

Table 4: Uric Acid Levels in Responders vs non-responders after 6 Weeks

Group	**Uric Acid (mg/dL) Mean ± SD**	**p-value**
Responders (n=24)	5.3 ± 0.9	-
Non-responders (n=12)	6.4 ± 1.0	0.004

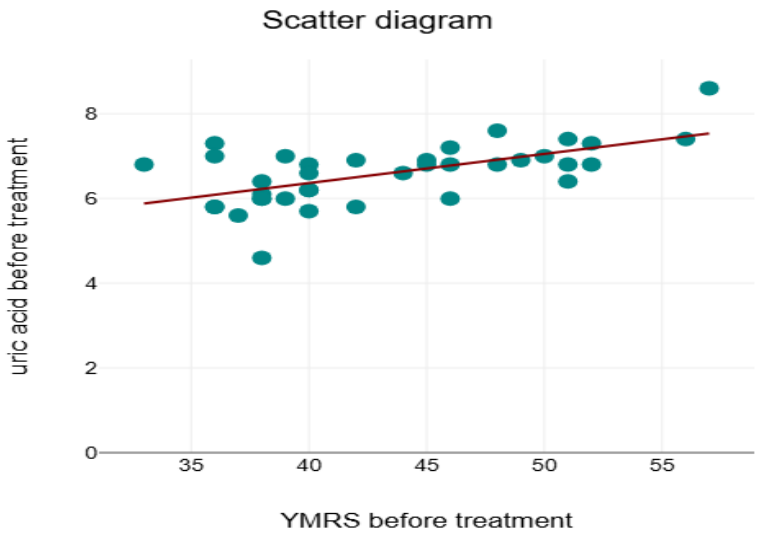

Figure 1: Correlation between YMRS Scores and Uric Acid Levels before Treatment (r=0.6, p<0.01)

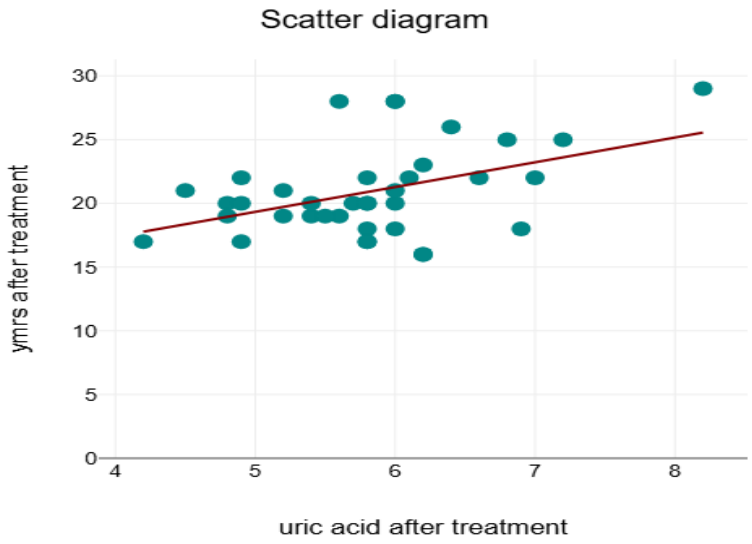

Figure 2: Correlation between Uric Acid Levels and YMRS Scores after Treatment (r=0.55, p=0.006)

The study population consisted predominantly of males (54.05%), with a mean age of 31.06 ± 6.78 years. A significant reduction was observed in Young Mania Rating Scale (YMRS) scores following treatment, with mean scores decreasing from 43.32 ± 6.29 at baseline to 20.92 ± 3.51 post-treatment. Additionally, serum uric acid levels showed a notable decline, from a pre-treatment mean of 6.15 ± 0.85 mg/dL to 5.45 ± 0.72 mg/dL after treatment.

In the present study, the mean serum uric acid levels were compared among patients receiving different mood stabilizers. The mean uric acid level in patients on Lithium Carbonate (n = 15) was 5.62 mg/dL, while those on Sodium Valproate (n = 11) had a mean level of 5.65 mg/dL. Patients on Carbamazepine (n = 4) had a mean uric acid level of 5.57 mg/dL. Statistical analysis revealed no significant difference in mean serum uric acid levels among the three groups, with a p-value of 0.779.

The mean serum uric acid level during the manic episode was 6.8 ± 1.2 mg/dL, which significantly decreased to 5.5 ± 1.0 mg/dL during the remission phase. This reduction in uric acid levels from the manic to the remission phase was found to be statistically significant (p = 0.001).

When comparing treatment outcomes, the mean serum uric acid level among responders (n = 24) was 5.3 ± 0.9 mg/dL, whereas non-responders (n = 12) exhibited significantly higher levels at 6.4 ± 1.0 mg/dL. This difference was statistically significant (p = 0.004).

Discussion

In the present study, we observed a significant reduction in serum uric acid levels following treatment for acute manic episodes, with mean values decreasing from 6.8 ± 1.2 mg/dL during mania to 5.5 ± 1.0 mg/dL during remission (p = 0.001). This aligns well with earlier research, which also reported elevated serum uric acid levels during manic episodes that normalize upon clinical improvement. For instance, Machado-Vieira et al. [12], (2008) demonstrated that hyperuricemia correlates with acute mania and decreases significantly after mood stabilization, supporting the hypothesis that uric acid may serve as a state marker in bipolar disorder (Machado-Vieira et al. [12], 2008).

Further, our findings that responders to treatment had significantly lower uric acid levels (5.3 ± 0.9 mg/dL) compared to non-responders (6.4 ± 1.0 mg/dL) (p = 0.004) are consistent with observations made by Elshahawi et al. [13], (2011), who reported that persistently elevated uric acid levels were associated with poorer clinical outcomes and treatment resistance in bipolar patients (Elshahawi et al. [13], 2011). This suggests that serum uric acid could potentially be explored as a biomarker for treatment response and prognosis in bipolar mania.

Regarding mood stabilizer-specific effects on serum uric acid levels, our study found no statistically significant differences among patients treated with Lithium Carbonate, Sodium Valproate, or Carbamazepine (p = 0.779). The mean uric acid levels were comparable across these groups (5.62, 5.65, and 5.57 mg/dL, respectively). This observation contrasts somewhat with previous studies reporting that certain mood stabilizers, particularly sodium valproate, might influence purine metabolism differently. For example, Kishi et al. [14], (2013) noted that lithium tends to lower uric acid levels, potentially through renal effects, whereas valproate's impact is less clear, and carbamazepine may have negligible effects (Kishi et al. [14], 2013). However, these discrepancies could be due to small sample sizes or differences in study populations and treatment durations.

The mean baseline serum uric acid in our cohort (6.15 ± 0.85 mg/dL) falls within the upper-normal range, corroborating meta-analytical evidence that manic patients tend to exhibit hyperuricemia (Palacios et al. [15], 2018). The pathophysiological basis of uric acid elevation in mania may relate to increased purinergic turnover and oxidative stress, as postulated by Joyce et al. [16], (2012). Elevated uric acid might reflect heightened adenosine triphosphate degradation during acute manic episodes, contributing to neurochemical imbalance (Joyce et al. [16], 2012).

Conclusion

The study demonstrates a significant reduction in both Young Mania Rating Scale scores and serum uric acid levels following treatment in patients with manic episodes. While no significant difference in serum uric acid levels was observed among different mood stabilizer groups, a marked decrease in uric acid was noted from the manic to remission phase. Importantly, lower serum uric acid levels were associated with better treatment response, suggesting that uric acid may serve as a potential biomarker for monitoring treatment efficacy in mania.

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