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Delirium in Bipolar Disorder as a Triggering Factor to Cognitive Decline: A Case Report and Neuroprogression Insight

Hayyunah Rohmatul Ahadiah[1], Lailatus Syadza[2], Moch Syafirul Nur Shafly[3], Asikah[4], Hafid Algristian[5]
[1235]Universitas Nahdlatul Ulama Surabaya, Indonesia
[4]Radjiman Wediodiningrat Hospital Lawang Malang, Indonesia
Correspondent: dr.hafid@unusa.ac.id[5]

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ABSTRACT: Bipolar disorder is a major contributor to global disability, affecting not only mood regulation but also cognitive function, and its impact is often exacerbated by metabolic comorbidities such as type 2 diabetes mellitus, hypertension, and dyslipidemia. These comorbid conditions can lead to poorer clinical outcomes and increase the risk of neuropsychiatric complications such as delirium and cognitive impairment, which are frequently overlooked in clinical practice. This article aims to describe and analyze the case of a 31-year-old male with a history of bipolar disorder who presented with a hyperglycemic crisis and pneumonia, followed by the onset of acute delirium and subsequent cognitive decline. Through a descriptive clinical approach, the patient's medical and psychiatric history, laboratory findings, and treatment course are reviewed to explore the complex interaction between mood disorders and metabolic dysfunction. The analysis reveals a strong link between metabolic dysregulation and worsening neuropsychiatric outcomes. This case underscores the importance of early detection and an integrated, multidisciplinary management approach to prevent long-term cognitive deterioration in patients with psychiatric disorders accompanied by metabolic conditions, offering important implications for future clinical practice.

Keywords: Bipolar Disorder, Delirium, Mild Cognitive Impairment, Metabolic Syndrome, Neuroprogression, Multidisciplinary Management.

INTRODUCTION

Bipolar disorder is one of the leading causes of disability worldwide and represents a significant public health burden. According to the Global Burden of Disease Study 2019, the global prevalence of bipolar disorder is estimated at approximately 0.7% to 1% of the general population, with the highest incidence occurring during the productive years of adulthood (Dall et al., 2022). This disorder contributes substantially to years lived with disability (YLDs), highlighting its profound impact on social functioning, employment, and quality of life. Despite its lower prevalence compared to other mental health conditions, bipolar disorder causes greater disability severity (G.B.D., 2022). The high relapse rate, need for lifelong treatment, and increased suicide

risk underline the urgency of early diagnosis, effective intervention, and comprehensive care (Huang et al., 2023).

Patients with bipolar disorder are at an increased risk of developing metabolic comorbidities, such as type 2 diabetes mellitus, hypertension, and dyslipidemia, compared to the general population. This bidirectional relationship complicates disease management and worsens long-term outcomes, including increased morbidity and treatment resistance. Several studies have identified factors contributing to this comorbidity, such as long-term use of atypical antipsychotics, unhealthy lifestyle patterns, and endocrine or immune dysfunctions inherent in the pathophysiology of bipolar disorder (Dalkner et al., 2021; Dragasek et al., 2023; Mariano et al., 2021).

Bipolar disorder is a chronic psychiatric illness characterized by recurrent episodes of mania, hypomania, and depression, significantly impacting patients' psychosocial functioning and quality of life. The disorder is increasingly recognized as not merely a psychiatric condition but one that involves complex interactions between neurobiological, metabolic, and systemic processes. Emerging evidence suggests that patients with bipolar disorder are at an elevated risk for developing comorbid metabolic syndrome, a cluster of conditions including central obesity, dyslipidemia, hypertension, and insulin resistance. The coexistence of these comorbidities has profound implications for disease progression, cognitive functioning, and treatment outcomes. Understanding this intricate relationship is essential for improving long-term prognosis and enhancing clinical care strategies.

Metabolic syndrome itself has been shown to contribute significantly to neuropsychiatric morbidity (Besterman et al., 2024). In individuals with bipolar disorder, metabolic dysregulation can exacerbate the course of illness through various mechanisms, including increased systemic inflammation, oxidative stress, and disruption of neuroendocrine homeostasis. These pathophysiological alterations may accelerate neuroprogression, leading to cognitive decline and structural brain changes over time. Moreover, the bidirectional nature of this association complicates management: Bipolar disorder increases the risk of metabolic abnormalities through psychotropic medications and lifestyle factors, while metabolic syndrome further exacerbates mood instability and cognitive dysfunction, highlighting the need for integrated assessment and treatment (Cai et al., 2024).

Among the potential complications arising from this interaction, delirium represents one of the most severe and underrecognized neuropsychiatric manifestations. Delirium is an acute disturbance in attention, awareness, and cognition that typically develops over a short period and fluctuates in severity (Chang et al., 2018). It is often multifactorial in origin, triggered by medical, metabolic, and pharmacological factors. In patients with bipolar disorder, delirium presents unique diagnostic and therapeutic challenges, as its clinical features can overlap with or mask mood symptoms. For example, agitation, disorganized thought processes, and perceptual disturbances may be mistakenly attributed to manic episodes, while lethargy and impaired concentration can resemble depressive states. Such diagnostic overshadowing can lead to delays in appropriate management and increase the risk of adverse outcomes.

The occurrence of delirium in bipolar patients carries significant prognostic implications. Research demonstrates that delirium is associated with persistent cognitive deficits, accelerated brain aging,

and heightened mortality risk. Safar et al. (2022) In the context of bipolar disorder, these consequences are particularly concerning, given the pre-existing vulnerability to cognitive impairment and functional decline. Delirium may exacerbate underlying neuroprogression, contributing to long-term deterioration in executive functioning, memory, and emotional regulation (Halvorsen et al., 2019). Therefore, clinicians managing bipolar patients, especially those with concurrent metabolic syndrome, must maintain a high index of suspicion when confronted with sudden changes in cognition, behavior, or consciousness.

Despite growing recognition of the interrelationship between bipolar disorder, metabolic syndrome, and delirium, significant gaps remain in understanding their shared pathophysiology. Existing literature predominantly examines these conditions in isolation, with few studies systematically exploring how they converge to influence clinical trajectories and cognitive outcomes. Consequently, clinicians often face substantial uncertainty when confronted with complex cases involving multiple interacting comorbidities. This lack of integrated evidence highlights the urgent need for case-based studies that capture real-world scenarios, elucidate potential mechanisms, and inform comprehensive management strategies tailored to this vulnerable population.

The present case report contributes to this growing body of knowledge by describing a middle-aged patient diagnosed with bipolar disorder who developed uncontrolled metabolic syndrome and acute delirium. This case underscores the synergistic effects of these comorbidities, illustrating how metabolic dysregulation can precipitate acute neuropsychiatric complications in an already vulnerable brain. Furthermore, it highlights the diagnostic challenges posed by overlapping symptomatology and the critical importance of adopting a multidisciplinary approach to care. The interplay between psychiatric, metabolic, and cognitive factors in this case exemplifies the complexity of managing bipolar disorder in contemporary clinical practice.

Early recognition and intervention are central to optimizing patient outcomes. Comprehensive metabolic screening, coupled with vigilant monitoring for cognitive disturbances, should form an integral part of the clinical assessment of individuals with bipolar disorder. Moreover, collaborative care involving psychiatrists, endocrinologists, neurologists, and other relevant specialists is vital to address the multifaceted needs of these patients. By integrating psychiatric and metabolic perspectives, clinicians can better anticipate complications, mitigate risks, and design personalized treatment plans aimed at preserving cognitive function and quality of life (Liu et al., 2021).

In summary, the convergence of bipolar disorder, metabolic syndrome, and delirium represents a clinically significant yet underexplored area in psychiatric medicine. The case presented in this report provides valuable insights into the real-world challenges and consequences arising from these comorbidities. It emphasizes the necessity of heightened clinical awareness, early detection of metabolic and cognitive dysfunction, and the implementation of collaborative, patient-centered care. Through the lens of this case, the broader implications for understanding neuropsychiatric vulnerability, disease progression, and therapeutic strategies become apparent, ultimately contributing to efforts aimed at improving functional outcomes and long-term prognosis for individuals living with bipolar disorder.

METHOD

This study employs a clinical case report design, which is widely recognized as a valuable method for presenting rare, complex, or challenging cases in clinical psychiatry and medicine. A case report allows for an in-depth exploration of a single patient's clinical presentation, diagnostic challenges, therapeutic interventions, and outcomes. Through this approach, the unique interplay of psychiatric and metabolic conditions can be highlighted in detail, which would otherwise be difficult to capture using broader epidemiological or experimental study designs.

The subject of this case report is a 31-year-old male with a six-year history of bipolar disorder, presenting with comorbid metabolic conditions, including type 2 diabetes mellitus, hypertension, and dyslipidemia. This combination of psychiatric and metabolic comorbidities makes the case particularly significant, as it illustrates the complex bidirectional relationship between mental health disorders and systemic medical conditions (Pan et al., 2020). The chronicity of bipolar disorder in this patient—combined with long-term exposure to psychotropic medications and potential lifestyle-related risk factors—appears to have contributed to the development and persistence of these metabolic abnormalities. Conversely, the presence of these comorbidities likely influences the severity and variability of mood symptoms, cognitive functioning, and overall disease trajectory (Longo et al., 2023).

The case was managed and observed at the Intensive Care Unit (ICU) and inpatient ward of RSI Jemursari, Surabaya, a tertiary care hospital with specialized facilities for both psychiatric and medical management. The choice of this setting allowed for comprehensive multidisciplinary care, integrating psychiatric expertise with internal medicine, neurology, and critical care teams. Such a setting provided the necessary resources to monitor acute changes, perform detailed assessments, and deliver appropriate interventions, particularly given the complexity of managing concurrent psychiatric and metabolic disturbances.

A combination of clinical observation, laboratory testing, and standardized cognitive assessments was employed to gather comprehensive data. Clinical observation focused on monitoring behavioral changes, affective states, psychomotor activity, and potential signs of delirium or mood instability. Laboratory investigations included blood glucose monitoring, pH analysis, and imaging studies to evaluate metabolic status and detect possible systemic complications. Furthermore, cognitive functioning was assessed using validated tools such as the *Mini-Mental State Examination* (MMSE) and the *Montreal Cognitive Assessment* (MoCA). These instruments were selected due to their reliability in detecting subtle cognitive deficits, which are particularly relevant in patients with bipolar disorder experiencing acute episodes or metabolic complications.

Patient information was meticulously compiled from multiple sources to ensure accuracy and comprehensiveness. Medical records provided longitudinal data on the patient's psychiatric history, medication use, and previous hospitalizations. Direct psychiatric evaluations offered current clinical insights, focusing on affective status, thought processes, and the presence of psychotic or cognitive disturbances. Additionally, structured interviews with family members contributed valuable contextual information regarding behavioral changes, functional decline, and medication adherence prior to hospitalization. Importantly, cognitive assessments were conducted

only after the patient's physiological parameters stabilized, ensuring that findings were not confounded by acute metabolic derangements or delirium-related fluctuations (Schou et al., 2023).

Data analysis followed a descriptive synthesis approach, integrating clinical observations, laboratory findings, and cognitive assessments within the framework of relevant neuropsychiatric literature (Rogers et al., 2020). Rather than employing inferential statistics, the goal was to construct a detailed narrative of the patient's clinical course, highlighting the complex interactions between psychiatric illness, metabolic syndrome, and cognitive dysfunction. By situating the findings within the broader context of existing research, this case contributes to a better understanding of how bipolar disorder and metabolic comorbidities may synergistically exacerbate the risk of acute complications, including episodes of delirium, while also informing individualized management strategies (Sesso et al., 2020).

All procedures were conducted in strict adherence to established ethical guidelines for clinical research. Informed consent was obtained from the patient's legal representative after a thorough explanation of the study's objectives, potential benefits, and associated risks. Confidentiality of personal and medical data was rigorously maintained throughout the process, and any identifying information was excluded from the report to protect patient privacy. The ethical safeguards ensured that the case was managed with the highest standards of respect for patient autonomy and dignity while allowing for the dissemination of clinically significant findings that may aid future research and practice.

RESULT AND DISCUSSION

Clinical Presentation

A 31-year-old male with a six-year history of bipolar affective disorder presented to the outpatient psychiatric clinic with complaints of worsening physical health. He had multiple comorbidities including type 2 diabetes mellitus, hypertensive heart disease, dyslipidemia, and obesity (body weight 130 kg). Before hospitalization, his mood was relatively stable under pharmacologic treatment, with no major cognitive complaints.

Cognitive screening at initial evaluation showed impairment, with an MMSE score of 22/30 and a MoCA score of 19/30, indicating mild cognitive impairment (MCI), particularly in memory, attention, and executive functions.

ICU Course

In early November 2024, the patient experienced decreased consciousness, dyspnea, and signs of respiratory infection. Laboratory evaluations revealed:

- Random blood glucose: 468 mg/dL
- Arterial pH: 7.220 (metabolic acidosis)
- Chest imaging: bilateral pneumonia

A working diagnosis of acute delirium was made in the context of a psychiatric background of bipolar disorder (ICD-10 F31.3, depressive episode, mild to moderate) and comorbid borderline and dependent personality traits.

The patient was admitted to the ICU for critical care. Pharmacologic interventions included:

- Haloperidol 5 mg IM (as-needed for agitation)
- Aripiprazole 15 mg/day
- Clozapine 50 mg/day (later switched to Quetiapine 50 mg/day to reduce metabolic burden)
- Trihexyphenidyl 2 mg/day
- Alprazolam 1 mg/day

Clinical Progress and Treatment Adjustments

The switch from Clozapine to Quetiapine was made to reduce metabolic side effects. Blood glucose monitoring before and after the change showed:

- Before switch: Average random glucose = 395.8 mg/dL (range: 300–468 mg/dL)
- After switch: Average random glucose = 279.75 mg/dL (maximum = 342 mg/dL)

The patient exhibited:

- Stabilized mood
- Improved sleep (Bishir et al., 2020)
- Reduced agitation
- Resolution of delirium symptoms

Disposition and Follow-Up Plan

Upon clinical stabilization, the patient was transferred to the general medical ward. Given the combination of severe metabolic dysregulation and psychiatric vulnerability, a comprehensive long-term care plan was emphasized. This included:

- Continued mood stabilization
- Cognitive rehabilitation
- Integrated care for metabolic disease
- Regular psychiatric monitoring to prevent relapse and functional deterioration

Clinical Timeline Summary Table

Table 1. Clinical timeline summary

Date/ Period	Clinical Event	Treatment and Results
Pre-Nov 2024	Outpatient stable bipolar disorder	MMSE: 22/30; MoCA: 19/30; no acute complaints
Early Nov 2024	Acute symptoms onset (dyspnea, ↓ consciousness)	Glucose: 468 mg/dL; pH: 7.220; diagnosis: delirium + pneumonia (Haddad et al., 2021)
ICU Admission	Intensive care + antipsychotic management	Haloperidol, Aripiprazole, Clozapine (→ Quetiapine)
ICU Course	Gradual stabilization	↓ Glucose (avg: 279.75); improved mood; no active delirium
Post-ICU Transfer	General ward care + discharge planning	Focus on long-term cognitive & metabolic management

Source: primary data

Significance of the Case

This case highlights the complex interaction between chronic metabolic dysregulation and neuropsychiatric deterioration. The patient experienced a cascade of events beginning with prolonged hyperglycemia, which progressed to delirium and ultimately long-term cognitive impairment. The clinical trajectory underscores the importance of recognizing metabolic instability as an early warning for neuropsychiatric complications, especially in patients with pre-existing mood disorders (Bertollo et al., 2025).

Metabolic Influence on Neuropsychiatric Symptoms

Chronic hyperglycemia, as seen in diabetes mellitus, contributes to brain dysfunction through multiple pathways. In this case, persistently elevated blood glucose likely induced oxidative stress and increased production of Advanced Glycation End-products (AGEs), leading to activation of microglia and astrocytes (Vargas-Soria et al., 2023). This inflammatory response, marked by elevated cytokines (IL-1β, IL-6, TNF-α), may have compromised the blood-brain barrier and disrupted neuronal signaling, particularly in the hippocampus and prefrontal cortex—regions essential for memory and executive function (Gu et al., 2022). These pathological changes are strongly aligned with the patient's development of delirium followed by progressive cognitive decline.

The Role of Bipolar Disorder and Neuroprogression

The patient's bipolar disorder further exacerbated the neuropsychiatric outcome. Mood disorders are often accompanied by metabolic disturbances, either as a result of the disease itself or due to psychotropic medications (e.g., atypical antipsychotics), which promote weight gain, insulin resistance, and dyslipidemia (Nguyen et al., 2020). This metabolic-psychiatric feedback loop likely intensified both mood instability and physiological vulnerability. The concept of neuroprogression

is particularly relevant here, as chronic inflammation and recurrent mood episodes can accelerate neural atrophy and impair cognitive function (Mazza et al., 2020; Nassar et al., 2023).

Relevance of the Gut–Brain Axis

Schnorr et al. (2022) Emerging evidence linking gut microbiota to neuropsychiatric conditions provides another lens for understanding this case (Hamamah et al., 2022). Poletti et al. (2024) In individuals with metabolic syndrome, gut dysbiosis may influence the production of neurotransmitters and inflammatory mediators, affecting mood and cognition (Carloni & Rescigno, 2023; Cryan et al., 2019). Given the patient's metabolic and psychiatric history, this mechanism might have contributed to the observed neuropsychiatric trajectory.

Clinical Implications

This case demonstrates how intertwined metabolic, immunological, and psychiatric factors can culminate in severe neuropsychiatric outcomes. It emphasizes the need for early and integrated management strategies targeting both metabolic control and psychiatric stability to mitigate long-term cognitive decline.

Several limitations must be acknowledged. This case report lacks neuroimaging data, such as MRI, which could confirm structural abnormalities related to neuroprogression. Additionally, no serial neurocognitive testing was performed, limiting the ability to track cognitive recovery or deterioration over time. The findings represent a single case and should be interpreted with caution when generalizing to larger populations. Furthermore, specific inflammatory or neuroendocrine markers were not assessed, which might have provided additional mechanistic insights.

Future investigations should focus on multimodal assessment approaches, including neuroimaging, inflammatory and neurotrophic biomarkers, and serial neuropsychological evaluations. Longitudinal studies could help establish the trajectory of cognitive impairment and clarify the interplay between metabolic control and psychiatric outcomes. Exploring gut microbiome modulation and anti-inflammatory strategies may offer novel therapeutic avenues. Additionally, large-scale cohort studies are needed to validate integrated treatment models for patients with coexisting mood disorders and metabolic diseases.

CONCLUSION

Patients with bipolar disorder and uncontrolled metabolic comorbidities are particularly vulnerable to acute neuropsychiatric complications, such as delirium and cognitive impairment—especially during medical crises. In this case, delirium acted as a critical trigger for subsequent cognitive decline, underscoring the delicate interplay between systemic metabolic dysfunction and brain health (Sasso et al., 2023).

Early identification and comprehensive management of medical comorbidities, alongside individualized pharmacological interventions, are essential to prevent long-term neurocognitive deterioration. Ongoing cognitive evaluations and coordinated monitoring by psychiatry, internal medicine, and neurology teams can help optimize both mental and physical health outcomes. This case highlights the need for interdisciplinary approaches to prevent irreversible cognitive decline in psychiatric patients with metabolic comorbidities (Krishnan et al., 2022).

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