International Journal of Medicine and Pharmaceutical Research
Home Page: https://pharmaresearchlibrary.org/journals/index.php/ijmpr
CODEN (USA): IJCPNH | ISSN: 2321-2624 | Publisher: Pharma Research Library
DOI: https://doi.org/10.30904/j.ijmpr.2025.4864
Int. J. Med. Pharm. Res., 2025, 13(2): 119-123

Steroid-Induced Psychosis: Advances in Understanding, Diagnosis, and Management

R. Gautham Chakra*, G. Rajeswari[2], Badvel Manvitha[3], Matli Yamuna[3], P. Rathish[3], Dudekula Hasan[3]
[1]Assistant Professor, Department of Pharmacy Practice, Saastra College of Pharmaceutical Education and Research, Totapalli Gudur (M), Varigonda(V), Nellore-524311, Andhra Pradesh, India
[2]Professor and HOD, Department of Pharmacology, Saastra College of Pharmaceutical Education and Research, Totapalli Gudur (M), Varigonda(V), Nellore-524311, Andhra Pradesh, India
[3]IV[th] year B.Pharm, Saastra College of Pharmaceutical Education & Research, Totapalli Gudur (M), Varigonda (V), Nellore-524311, Andhra Pradesh, India

A B S T R A C T

Steroid-induced psychosis is an under recognized but clinically significant complication of systemic corticosteroid therapy, characterized by a spectrum of psychiatric manifestations ranging from mood disturbances to acute psychotic episodes. Its pathophysiology involves multifactorial mechanisms, including dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, altered neurotransmitter signaling (dopamine, serotonin, and glutamate), neuroinflammation, and genetic or epigenetic susceptibility. High-dose and prolonged corticosteroid therapy, advanced age, pre-existing psychiatric conditions, and pharmacokinetic variability are important risk factors, while neuroimaging studies have revealed structural and functional alterations correlating with symptom severity. Diagnosis remains primarily clinical, supported by standardized rating scales, biomarker assessment, and neuroimaging when necessary. Management requires a multifaceted approach encompassing pharmacological interventions (antipsychotics, mood stabilizers, benzodiazepines), non-pharmacological strategies, and careful steroid dose modulation. Emerging personalized medicine strategies, including genetic and epigenetic profiling, offer promise for tailored interventions. Preventive measures such as risk stratification, routine psychiatric screening, patient and caregiver education, and judicious corticosteroid use are critical to minimize morbidity. Future directions involve biomarker discovery, integration of artificial intelligence for risk prediction, and development of standardized clinical guidelines. Early recognition, individualized management, and coordinated multidisciplinary care are essential to optimize patient outcomes and reduce healthcare burden associated with steroid-induced psychosis.

Keywords: Steroid-induced psychosis, Corticosteroids, hypothalamic-pituitary-adrenal axis (HPA), antipsychotics, mood stabilizers, benzodiazepines, Neuroinflammation

A R T I C L E I N F O

Corresponding Author
Dr. R. Gautham Chakra
Assistant Professor, Department of Pharmacy Practice
Saastra College of Pharmaceutical Education &Research
Nellore-524311, Andhra Pradesh, India

Article History:
Received 19 July 2025
Revised 31 Aug 2025
Accepted 30 Sep 2025
Published 09 Oct 2025

E-Mail ID: gauthamrowdhra05@gmail.com | Mobile no: 7674016126 | ORCID: https://orcid.org/0009-0007-7688-1413

Citation: R. Gautham Chakra, *et al*. Steroid-Induced Psychosis: Advances in Understanding, Diagnosis, and Management. Int. J. Med. Pharm. Res., 2025; 13(2): 119-123.

CONTENTS

1. Introduction

Steroid-induced psychosis (SIP) is an important neuropsychiatric complication of corticosteroid therapy, encompassing a spectrum of mental health disturbances from mild mood changes to severe psychotic episodes. Glucocorticoids such as dexamethasone, prednisone, and methylprednisolone are widely used for autoimmune, inflammatory, and oncological conditions due to their potent anti-inflammatory, immunosuppressive properties. Despite their therapeutic efficacy, these agents carry significant neuropsychiatric risks, with reported incidence ranging from 1% to 20%**,** depending on factors such as dose, duration, route of administration, and patient susceptibility. Even though SIP is relatively uncommon, its clinical impact is substantial, affecting patient safety, adherence to therapy, and overall treatment outcomes. The underlying mechanisms of SIP are multifactorial. Corticosteroids act on the hypothalamo-pituitary-adrenal (HPA) **axis** and bind to glucocorticoid, mineralocorticoid receptors in the central nervous system, altering stress responses and emotional regulation. Neurotransmitter imbalances, particularly involving dopamine, serotonin, and glutamate**,** contribute to mood disturbances, cognitive impairments, psychotic features. Prolonged corticosteroid exposure can also induce neuroinflammation through microglial activation and cytokine release, leading to neuronal dysfunction. Additionally, genetic polymorphisms in glucocorticoid receptor genes and epigenetic modifications modulate individual susceptibility, underscoring the need for personalized risk assessment. Clinically, SIP manifests along a broad spectrum. Prodromal symptoms, including irritability, insomnia, and subtle cognitive deficits, may precede full-blown psychiatric episodes. Patients can present with depression, mania, hallucinations, delusions, and paranoia. Symptom onset varies, occurring within hours to days of initiating therapy in some individuals, while others develop delayed presentations over weeks. Severity often correlates with steroid dose, duration of therapy, and patient-specific risk factors, making vigilant monitoring essential.

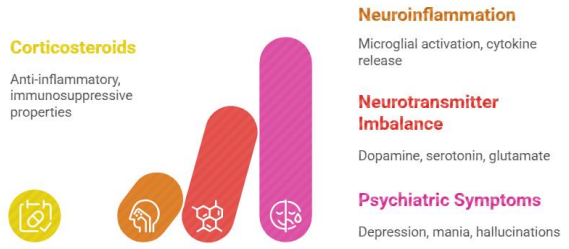

Fig 1: Steroid-induced psychosis impact on patients

SIP also carries significant implications for patient outcomes and healthcare systems. Affected patients frequently require hospitalization, psychiatric consultation, and additional pharmacologic interventions, increasing healthcare utilization and costs. Misdiagnosis or delayed recognition can worsen psychiatric morbidity and complicate management of the primary medical condition. Early identification, patient education, and proactive monitoring are critical to mitigating these risks. Given the widespread use of corticosteroids, understanding the epidemiology, pathophysiology, and clinical consequences of SIP is vital mentioned in fig 2. Clinicians must maintain high vigilance for neuropsychiatric symptoms, implement preventive strategies, and tailor therapy to minimize adverse outcomes, thereby ensuring safe and effective use of corticosteroids across diverse patient populations.

2. Pathophysiology: Modern Insights

2.1 HPA Axis Dysregulation and Corticosteroid Receptors

Glucocorticoids exert their effects primarily through the hypothalamo-pituitary-adrenal (HPA) axis. Corticosteroids can disrupt negative feedback mechanisms, leading to sustained hypercortisolemia. Excessive glucocorticoid receptor activation in the hippocampus, amygdala, and prefrontal cortex affects emotional regulation and cognitive processes, predisposing individuals to psychotic and mood symptoms.

2.2 Neurotransmitter Imbalance: Dopamine, Serotonin, and Glutamate: Corticosteroids influence key neurotransmitters. Dopaminergic hyperactivity has been linked to psychotic symptoms, while serotonergic alterations contribute to mood disorders and anxiety. Additionally, corticosteroid-induced glutamate excitotoxicity can lead to neuronal damage, particularly in the hippocampus, impairing memory and executive function.

2.3 Neuroinflammation and Microglial Activation

Prolonged corticosteroid exposure paradoxically may trigger neuroinflammation. Microglial activation in the CNS releases cytokines (IL-6, TNF-α), which affect neuronal signaling and synaptic plasticity. This neuroinflammatory milieu may contribute to cognitive deficits and emotional dysregulation in SIP.

2.4 Genetic and Epigenetic Factors

Polymorphisms in genes encoding glucocorticoid receptors (NR3C1) and related signaling pathways influence individual susceptibility. Epigenetic modifications such as DNA methylation and histone acetylation further modulate receptor sensitivity and stress response, offering potential markers for risk stratification.

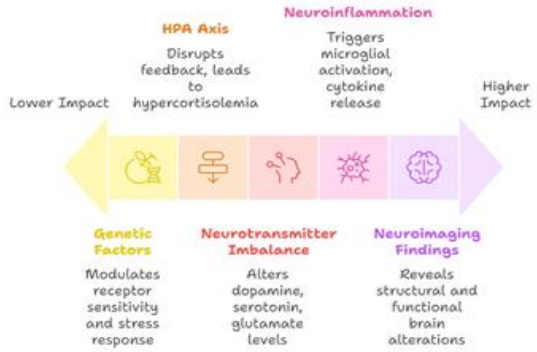

Fig 2: understanding steroid induced psychosis through level of biological impact

2.5 Neuroimaging Findings in Steroid-Induced Psychosis: Advanced neuroimaging studies using fMRI and PET scans have demonstrated corticosteroid-related structural and functional brain alterations. Reduced

hippocampal volume, prefrontal cortex hypoactivity, and altered limbic connectivity correlate with psychiatric symptom severity, supporting a neurobiological basis for SIP. Thus understanding steroid induced psychosis through level of biological impact mention in fig.2.

3. Risk Factors and Vulnerable Populations

3.1 High-Dose and Prolonged Corticosteroid Therapy

Doses exceeding 40 mg/day prednisone equivalent and therapy extending beyond 4 weeks significantly increase SIP risk. Rapid escalation of steroid dose also contributes to acute onset psychiatric symptoms.

3.2 Age, Gender, Pre-existing Psychiatric Conditions: Older adults and females exhibit higher susceptibility, potentially due to hormonal modulation and age-related CNS vulnerability. Patients with prior psychiatric diagnoses, including depression, bipolar disorder, or schizophrenia, are at heightened risk.

3.3 Genetic Predispositions and Biomarkers: Genetic variants affecting glucocorticoid receptor sensitivity, as well as inflammatory biomarkers such as IL-6 and TNF-α, can serve as predictive tools for identifying at-risk individuals before therapy initiation.

3.3.1 Pharmacokinetic Considerations: Different formulations of corticosteroids (oral vs intravenous) and metabolic profiles influence CNS penetration and neuropsychiatric outcomes. High lipophilicity steroids, like dexamethasone, readily cross the blood-brain barrier, increasing the likelihood of CNS effects.

4. Clinical Manifestations

4.1 Early Warning Signs and Prodromal Symptoms

Initial signs may include **insomnia, irritability, and subtle cognitive changes**, often preceding full-blown psychosis. Recognizing these prodromal symptoms is crucial for early intervention.

4.1.1 Spectrum of Psychiatric Symptoms

Mood disturbances: Depression, anxiety, euphoria

Manic features: Hyperactivity, impulsivity, grandiosity

Psychotic symptoms: Delusions, hallucinations, paranoia

Cognitive impairments: Memory deficits, attention disturbances, executive dysfunction

4.2 Duration and Course of Symptoms: Onset can occur **within hours to days** after initiating corticosteroid therapy. Symptoms typically resolve gradually after dose reduction or discontinuation, although prolonged exposure can lead to persistent cognitive impairments.

4.3 Impact on Quality of Life and Functioning: SIP can impair social functioning, occupational performance, and adherence to medical therapy, emphasizing the need for early detection and management.

5. Diagnostic Approach

5.1 Clinical Assessment and Differential Diagnosis

Diagnosis relies on temporal correlation with steroid therapy and exclusion of primary psychiatric disorders. Clinicians must differentiate SIP from metabolic, infectious, or substance-induced psychiatric conditions.

5.2 Role of Neuroimaging and Biomarkers

Functional and structural imaging (fMRI, PET) aids in understanding CNS involvement. Biomarkers like cortisol, cytokine levels**,** and genetic profiles are emerging tools for early detection and risk stratification.

5.3 Standardized Rating Scales and Patient-Reported Outcomes: Use of scales such as PANSS (Positive and Negative Syndrome Scale)**,** YMRS (Young Mania Rating Scale)**,** and patient-reported outcomes facilitates objective monitoring of symptom severity and treatment response.

5.4 Challenges in Diagnosis and Need for Standardization: Lack of specific diagnostic criteria for SIP and overlapping symptoms with other psychiatric disorders necessitate standardized guidelines to improve recognition, management. Thus the diagnostic approches are mentioned in below table.

6. Management Strategies

6.1 Pharmacological Interventions

Antipsychotics: Atypical antipsychotics are preferred due to better tolerability.

Mood Stabilizers: Lithium or valproate for manic or mixed states.

Benzodiazepines: Short-term use for agitation and insomnia.

Electroconvulsive Therapy (ECT): Considered in severe, refractory cases.

6.2 Non-Pharmacological Approaches

Steroid tapering: Gradual dose reduction minimizes psychiatric symptoms.

Substitution strategies: Using less lipophilic or lower-potency corticosteroids.

Psychiatric monitoring: Regular assessments by mental health professionals.

6.3 Personalized Medicine Approaches

Genetic and Epigenetic Profiling: Identification of high-risk patients.

Tailored Treatment Plans: Dose and therapy adjusted based on individual susceptibility.

6.4 Emerging Therapies

NMDA Receptor Modulators: Potential neuroprotective effects.

Anti-inflammatory Agents: Target neuroinflammation to reduce symptom severity.

Neurostimulation: Techniques such as TMS under investigation for resistant cases.

7. Case Studies and Clinical Evidence

7.1 Recent Case Reports and Clinical Observations

Multiple case reports highlight early-onset psychosis within days of high-dose dexamethasone therapy, resolving upon dose reduction.

7.1.1 Insights from Longitudinal Studies

Long-term follow-ups suggest residual cognitive deficits in some patients, emphasizing the need for monitoring post-steroid therapy.

7.1.2 Lessons Learned and Clinical Implications: Proactive risk assessment, early identification of prodromal symptoms, and multidisciplinary management improve patient outcomes.

8. Prevention Strategies

Prevention of steroid-induced psychosis involves risk assessment including psychiatric history and genetic

predisposition, dose minimization or use of alternative therapies, and routine psychiatric monitoring during therapy. Educating patients and caregivers, gradual steroid tapering, a multidisciplinary care approach, and lifestyle interventions such as stress management and adequate sleep further reduce neuropsychiatric complications and enhance patient safety.

1. Risk Assessment and Stratification:

Pre-treatment evaluation should include a detailed psychiatric history, age, sex, comorbidities, and any known genetic predispositions. Identifying high-risk individuals allows clinicians to implement tailored monitoring and early interventions, reducing the likelihood of steroid-induced psychosis (SIP).

2. Dose Minimization and Alternative Therapies:

Whenever possible, clinicians should use the lowest effective corticosteroid dose to achieve therapeutic goals. In patients at high risk for neuropsychiatric complications, consideration should be given to non-steroidal immunomodulatory therapies as alternatives. This strategy reduces neuropsychiatric side effects while maintaining disease control.

3. Routine Psychiatric screening during Steroid Therapy: Regular monitoring of mood, cognition, behavior, and sleep patterns is essential throughout corticosteroid therapy. Standardized psychiatric rating scales such as the PANSS (Positive and Negative Syndrome Scale) or YMRS (Young Mania Rating Scale) can facilitate early detection of prodromal symptoms, enabling prompt management before severe psychiatric manifestations occur.

4. Patient and Caregiver Education: Educating patients and caregivers about potential psychiatric effects, warning signs, and the importance of early reporting enhances adherence to therapy and allows timely intervention. Awareness empowers caregivers to identify subtle changes in behavior or mood that might indicate the onset of SIP.

5. Gradual Steroid Tapering

Abrupt discontinuation of corticosteroids can precipitate neurochemical and hormonal fluctuations, increasing psychiatric risk. Gradual tapering ensures a controlled reduction in steroid exposure, minimizing the likelihood of mood disturbances or psychotic episodes.

6. Multidisciplinary Care Approach

Engaging a multidisciplinary team including psychiatrists, neurologists, and primary care physicians ensures comprehensive patient evaluation, monitoring, and early intervention. Collaborative care is particularly important for high-risk patients or those exhibiting early neuropsychiatric symptoms.

7. Lifestyle and Supportive Interventions

Encouraging adequate sleep, stress management, social support, and regular physical activity can improve resilience against steroid-induced mood changes and cognitive impairments. Supportive interventions complement medical strategies, promoting overall mental well-being during therapy.

8. Future Directions and Policy Implications

A) Advancements in Biomarker Discovery: The search for reliable biomarkers of steroid-induced psychosis (SIP) is gaining momentum. Studies investigating cytokine levels, cortisol dynamics, and genetic variants of glucocorticoid receptors suggest that neuroimmune dysregulation plays a key role in vulnerability. Identifying biomarker signatures before initiating steroid therapy could allow clinicians to stratify patients into low- and high-risk groups. Such predictive capacity would transform SIP management from a reactive to a preventive paradigm, enabling early intervention and dose adjustments tailored to individual biology.

B) Integration of Artificial Intelligence in Diagnosis and Management: Artificial intelligence (AI) is reshaping psychiatric risk assessment. Algorithms trained on electronic health records, neuroimaging, and longitudinal behavioral data can detect subtle cognitive or mood changes preceding overt psychosis. When integrated with biomarker information, AI could provide personalized risk prediction models and suggest individualized therapeutic strategies, including dose modification, adjunctive psychotropics, or closer psychiatric monitoring. AI-driven decision support tools may also reduce diagnostic delays, enhance monitoring precision, and improve overall patient safety during long-term steroid therapy.

C) Global Collaborative Research Initiatives

SIP remains under-recognized partly due to fragmented research efforts. Establishing international registries and multicenter clinical trials will allow standardized data collection, facilitate comparison across populations, and improve the robustness of findings. Global networks could also accelerate translational research, ensuring biomarker discoveries and AI tools are validated across diverse healthcare systems.

Policy Implications and Healthcare Guidelines: Future progress must be anchored by strong policy frameworks. Development of standardized clinical guidelines for prevention, monitoring, and treatment of SIP is urgently needed. These should mandate pre-treatment psychiatric evaluations, dose minimization strategies, routine mental health screening, and clear referral pathways. Health systems must also prioritize patient and caregiver education, ensuring early recognition of psychiatric symptoms. Such policies will harmonize care globally and reduce the morbidity associated with steroid therapy.

9. Conclusion

Steroid-induced psychosis (SIP) remains a clinically significant and often underestimated complication of glucocorticoid therapy. While the therapeutic benefits of agents such as dexamethasone, prednisone, and methylprednisolone are undeniable, their neuropsychiatric risks can compromise both patient safety and treatment adherence. The heterogeneous presentation of SIP ranging from subtle mood fluctuations to severe psychotic episodes underscores the need for vigilance across medical disciplines. Recent advances in understanding SIP have illuminated its multifactorial origins, involving neuroimmune dysregulation, glucocorticoid receptor sensitivity, alterations in dopamine and serotonin pathways, and patient-specific vulnerabilities. These insights are gradually shifting management from a purely reactive

approach toward proactive prevention and early detection. Emerging tools such as biomarker profiling**,** artificial intelligence–driven risk prediction**,** and international collaborative registries promise to refine diagnostic precision and optimize individualized care strategies. The integration of these strategies into standardized clinical guidelines will not only improve outcomes but also reduce the economic and psychosocial burden associated with SIP. Ultimately, addressing SIP requires a multidisciplinary, patient-centered approach that bridges psychiatry, neurology, immunology, and primary care. By combining advances in biomedical research with systematic policy frameworks, healthcare systems can move closer to a model of safe, effective, and personalized steroid use. Continued global collaboration will be key to ensuring that the benefits of glucocorticoids are maximized while minimizing their profound neuropsychiatric risks.

Declaration of Conflicting Interests:

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding: The author(s) received no financial support for the research, authorship, and/or publication of this article.

10. References

[1] Gostoli, S., Carrozzino, D., Raimondi, G., Subach, R., Gigante, G., & Rafanelli, C. Corticosteroid-induced manic and/or psychotic symptoms: A systematic review. Frontiers in Pharmacology, 2025; 16, 1628765.

[2] Canessa-Muñoz S, Yelmo-Cruz S, Hamilton-Lopez A, Baez-Marrero C. Corticosteroid-Induced Psychosis: A Report of Two Cases. Neuropsychiatric Disease and Treatment, 2025; 21, 123–130.

[3] Bhusal, A., Subedi, D., Aryal, S. Steroid induced psychosis in a child with nephrotic syndrome: Case report and review. Pediatric Nephrology, 2022; 37(6), 1425–1431.

[4] Anne-Sophie C A M Koning, Merel van der Meulen, Daphne Schaap, Djaina D Satoer, Christiaan H Vinkers, Elisabeth F C van Rossum 6, Wouter R van Furth, Alberto M Pereira, Onno C Meijer, Olaf M Dekkers. Neuropsychiatric adverse effects of synthetic glucocorticoids: a systematic review. Journal of Clinical Endocrinology & Metabolism, 2024; 109(6), e1442–e1458.

[5] Shimizu, M., Yagi, A., & Matsuoka, H. Incidence and risk factors of psychiatric adverse effects associated with corticosteroid therapy: A prospective study. Neuropsychiatric Disease and Treatment, 2016; 12, 2793–2799.

[6] Lotan, A., Orr-Urtreger, A., Chapnik, L. Methyl prednisolone-induced mania and psychosis: Clinical characteristics and treatment. Journal of Neuropsychiatry, 2016; 28(3), 277–282.

[7] Alturaymi, A. H., Ihunwo, A. O., & Alakeel, A. Psychiatric disorders associated with corticosteroid use: A systematic review. Frontiers in Pharmacology, 2023; 16, 1628765.

[8] Dubovsky, A. N., Arvikar, S., Stern, T. A., & Axelrod, L. The neuropsychiatric complications of glucocorticoid use: steroid psychosis revisited. Psychosomatics, 2012; 53(2), 103–115.

[9] Reinert, J. P., Smith, J. D., & Huynh, G. Pharmacological management of steroid-induced psychosis. Journal of Clinical Psychiatry, 2020; 81(12), e1–e14.

[10] Singh, A., Shrivastava, S. Steroid induced psychiatric adverse effects: An overview of risk factors, clinical features and management. International Journal of Research in Medical Sciences, 2020; 8(6), 2365–2370.

[11] Cross, S., & Lambert, M. Managing steroid-induced psychosis: Practical recommendations. Journal of Psychiatric Practice. 2011; 27(4), 262–270.

[12] Wada, K., & Yoshida, M. Corticosteroid-induced psychotic and mood disorders. Psychosomatics, 2001; 42(6), 531–536.

[13] Lotan, A., Ben-Zvi, A., & Berkovitch, M. High-dose corticosteroids and psychiatric side effects. Journal of Clinical Psychopharmacology. 2018; 38(3), 289–294.

[14] Ward, M., & George, C. (2016). Recognition and treatment of steroid-induced psychosis. CNS Drugs. 2016; 30(5), 437–444.

[15] Gable, R., & Depry, D. Corticosteroid-induced mania and psychosis: Identification and management. Clinical Neuropharmacology. 2015; 38(6), 209–214.

[16] Martinho, F., & Fonseca, A. Steroid-induced psychosis: A comprehensive review. Journal of Psychiatric Research. 2021; 137, 1–7.

[17] Fava, G. A. (2024). Staging method for corticosteroid-induced psychiatric symptoms. Psychotherapy and Psychosomatics, 93(1), 20–27.

[18] Bostwick, J. R., & Cohen, J. A. (2020). Psychiatric side effects of glucocorticoids: Incidence, mechanisms, and management. CNS Drugs, 34(3), 305–319.

[19] Grebelsky-Lichtman, T., & Segal, M. Neurobiological basis of corticosteroid-induced psychiatric manifestations. Frontiers in Neuroscience, 2021; 15, 669163.

[20] Sultana, S., & Chaudhry, I. B. Incidence and management of steroid-induced psychosis in autoimmune disorders. Journal of Clinical Medicine. 2022; 11(23), 7043.

[21] Weller, A., & Halperin, D. M. Psychiatric adverse effects of high-dose corticosteroids: A review. European Neuropsychopharmacology. 2021; 48, 65–73.

[22] Patel, R., & Tripathi, A. Clinical update on steroid-induced psychiatric disorders. Current Psychiatry Reports, 2021; 23(12), 83.