

Ketamine for chronic pain management: Global publication trends and collaboration networks from a 25-year Scopus bibliometric perspective

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Abstract

Objective: To uncover knowledge gaps in terms of ketamine's role in chronic pain management, identify emerging therapeutic directions, and provide a strategic foundation for future research and policy.

Method: The bibliometric study was conducted at Department of Anaesthesiology, Aga Khan University from March 2025 to June 2025 and comprised literature search on Scopus database for English-language original articles published between January 1, 2000, and December 31, 2024. Bibliometric indicators, such as publication trends, citation counts, key word co-occurrence, author collaborations and country-level contributions, were analysed using VOSviewer and Microsoft Excel.

Results: Of the retrieved 2,857 documents initially identified, 244(8.5%) were analysed. Annual publication output showed an overall upward trend, reaching its highest level in 2018 with 20 publications, followed by 19 publications in 2023. The United States was the leading country in the co-authorship analysis, appearing in 102 (42%) publications and accumulating 3,211 citations, with an average normalised citation score of 0.94. Key word analysis revealed three major clusters: clinical-psychiatric applications, perioperative-mechanistic studies, and neuropathic-pharmacological frameworks. Emerging keywords included esketamine (n=5; average publication year 2021.6) and complex regional pain syndrome (n=6; average publication year 2020.8), reflecting recent thematic shifts. Co-authorship analysis showed that 174 (71.3%) papers involved four or more authors, indicating a strong pattern of collaborative research.

Conclusion: Despite growing output and collaboration, critical gaps persist, particularly in standardised dosing protocols, the scarcity of large randomised trials, and limited representation from low- and middle-income countries.

Keywords: Ketamine, Chronic pain, Bibliometric analysis, Scopus, Neuropathic pain, Research trends, Global collaboration. (JPMA 76: 1689; 2026) DOI: <https://doi.org/10.47391/JPMA.32095>

Introduction

Chronic pain is a debilitating condition affecting approximately 20% of the adults, with profound implications for quality of life, mental health and socioeconomic productivity.¹ Despite the availability of multiple pharmacotherapeutic options, a significant proportion of patients do not achieve adequate relief. Conventional treatments, such as opioids, non-steroidal anti-inflammatory drugs (NSAIDs) and adjuvant analgesics, are often constrained by limited efficacy and adverse effects, including the well-documented risks of opioid tolerance, dependence and overdose. Ketamine, a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist, has attracted considerable attention as a novel analgesic, particularly for neuropathic and refractory pain syndromes.² Its unique mechanism, modulating central sensitisation, and glutamatergic transmission sets it apart from traditional analgesics.³ Various formulations and administration routes, including low-dose intravenous (IV) infusions and intranasal delivery, have demonstrated

efficacy in reducing pain and opioid consumption.⁴ However, clinical outcomes remain heterogeneous due to variability in dosing protocols, patient populations and study designs.⁵

In this context, bibliometric analysis offers a valuable macro-level approach to evaluate research output, capturing publication trends, collaboration networks and emerging themes, that complements traditional systematic reviews by revealing high-impact studies and hidden research clusters. It helps to identify knowledge gaps and uncover collaborative networks in a rapidly evolving field.^{6,7} Although reviews have been addressing ketamine's clinical efficacy, a consolidated understanding of global research trends in the use of ketamine for chronic pain remains underexplored.

The current study was planned to fill the gap in literature by mapping the evolution, collaborations and emerging directions of ketamine-related chronic pain research, using established bibliometric methods.⁷

Materials and Methods

The bibliometric study was conducted at Department of Anaesthesiology, Aga Khan University from March 2005 to June 2025 and comprised literature search on Scopus

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database for English-language original articles published between January 1, 2000, and December 31, 2024. Scopus is a widely recognised multidisciplinary citation index that provides comprehensive metadata and citation analysis tools. It was selected as the sole data source as it provides broad coverage of interdisciplinary journals and enables reliable citation and collaboration network analyses.

To retrieve relevant literature on the use of ketamine in chronic pain management, a systematic search was performed using the following query:

(TITLE-ABS-KEY (ketamine) OR TITLE-ABS-KEY (s AND ketamine OR esketamine) OR TITLE-ABS-KEY (r AND ketamine OR arketamine) AND TITLE-ABS-KEY (chronic AND pain)).

This query was constructed as a sensitive first step to capture a broad set of ketamine-related chronic pain records. The initial search results were then narrowed through predefined limits, like publication year, document type and language. Manual screening was done by two independent reviewers. In case of difference of opinion, two additional reviewers were consulted, and their decision was considered final.

The studies included were original research involving primary data, like experimental studies and clinical trials, as well as observational studies, such as those cohort, case-control and cross-sectional designs. Studies were considered relevant only if they focused on ketamine's use in chronic pain. Those addressing acute pain, psychiatric indications without a pain component, or unrelated experimental research were excluded. Articles in the press, conference proceedings, review articles, editorials and book chapters were also excluded. Review articles were excluded specifically because they summarise existing evidence and often receive disproportionately higher citation counts, which may influence citation and publication trend analyses.

The retrieved dataset was exported from Scopus in Comma-Separated Values (CSV) format for further processing. The extracted metadata included title, abstract, key words, authors, affiliations, year of publication, source journal, publisher, and citation count.

The dataset was analysed using VOSviewer and Microsoft Excel. VOSviewer facilitated network analysis, particularly for co-authorship mapping, key word co-occurrence, and citation network visualisation. Microsoft Excel was used for data cleaning, statistical analysis and visualising publication trends.

Several bibliometric indicators were assessed, including

publication trends over time, identification of highly cited publications and influential authors, leading journals and institutions, key word co-occurrence patterns, and collaboration networks among researchers.

The study was approved by the departmental research committee at Department of Anaesthesiology, Aga Khan University. Since it involved no human or identifiable information and was based exclusively on publicly available, anonymised data, formal ethical approval was not required.

Results

Of the retrieved 2,857 documents initially identified, 244(8.5%) were analysed (Figure 1). Publication output increased steadily over the years, with a notable acceleration after 2008 (Figure 2). Citation counts peaked in 2009 (968 citations), reflecting the influence of early foundational studies. Although citation numbers have declined in more recent years, this is likely due to citation lag for newer publications (Figure 2). The annual publication count showed a strong upward slope over the study period ($R^2=0.83$).

The studies analysed had been published across 112 journals, with the top journal carrying 959(%) publications 959 citations per paper (CPP) (Table 1).

Analysis of key word co-occurrence patterns identified three colour-coded clusters (Figure 3), each containing multiple interconnected terms, and each representing a distinct focus within the field. The red cluster reflected clinical and psychiatric applications, including terms related to chronic pain and mental health conditions. The green cluster centred on mechanistic and perioperative contexts, including terms related to perioperative contexts and biological mechanisms. The blue cluster encompassed neuropathic and pharmacological frameworks, focussing on ketamine's molecular targets and its relevance in the treatment of persistent pain syndromes (Figure 3).

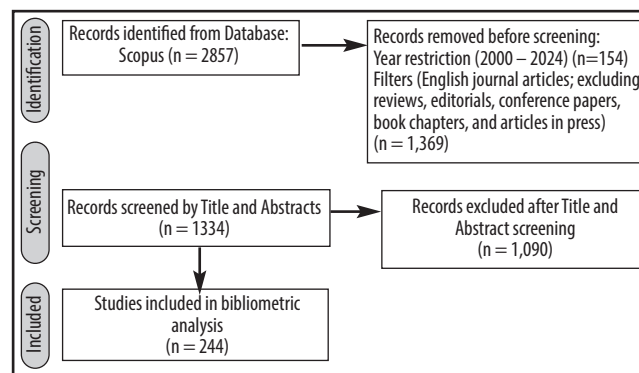


Figure-1: Flow diagram showing the identification, screening and inclusion of studies for bibliometric analysis.

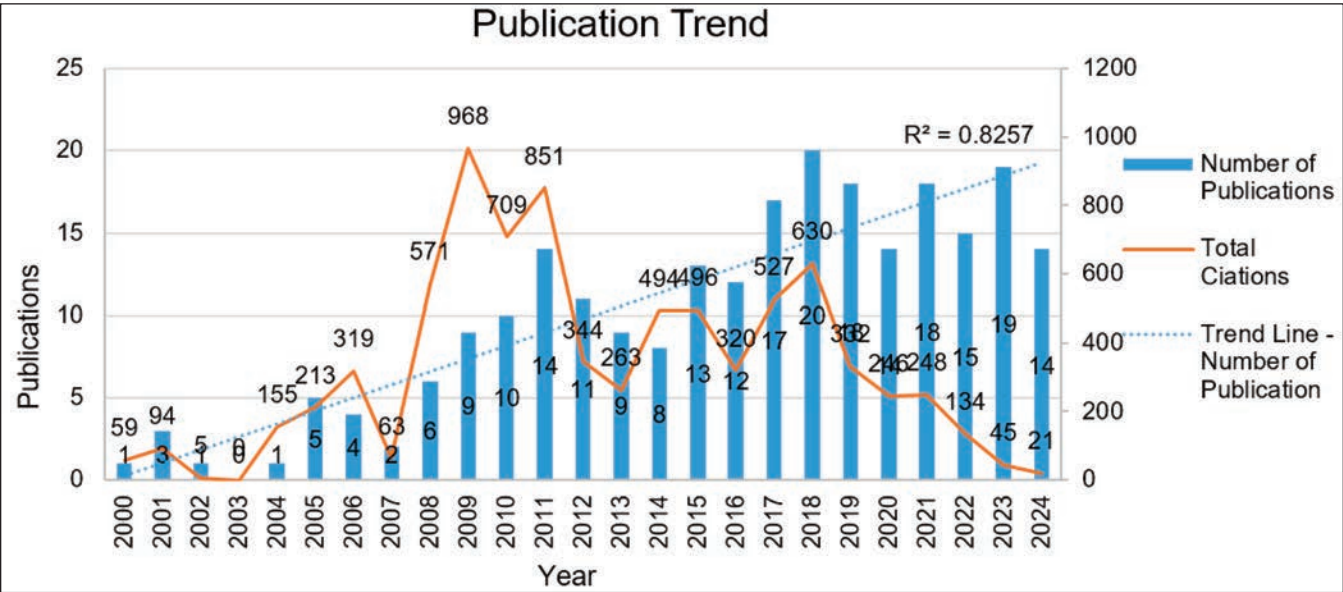


Figure-2:Annual publication output and citation counts for ketamine-related chronic pain research (2000-24).
The dotted line represents a simple linear regression trendline fitted to the annual publication counts ($R^2 = 0.83$).

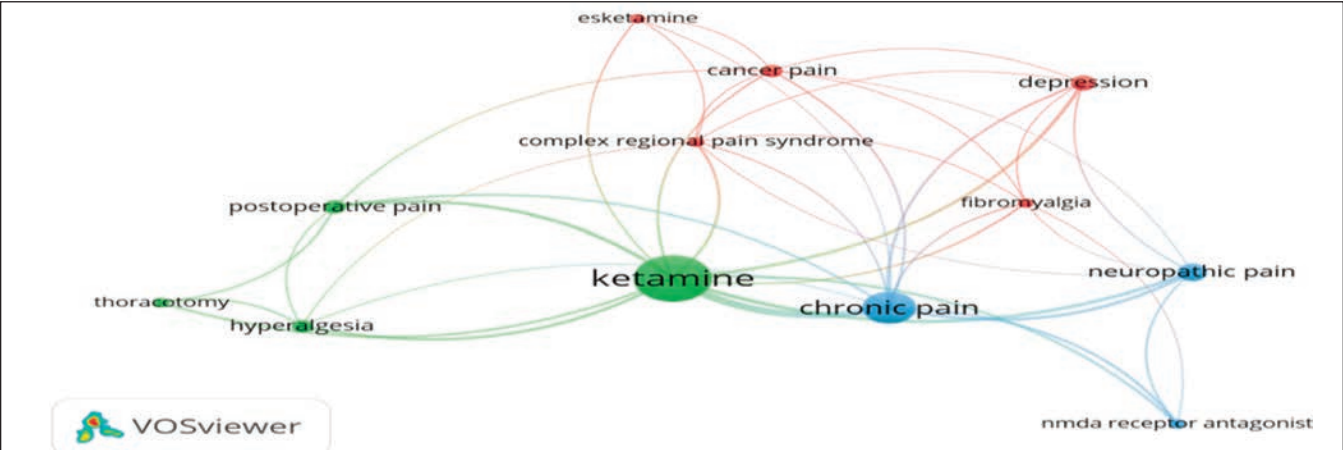


Figure-3: Network of co-occurring key words.
Keyword co-occurrence map showing three colour-coded clusters: red = clinical and psychiatric applications, green = mechanistic and perioperative contexts, and blue = neuropathic and pharmacologic frameworks. Node size reflects key word frequency, and line thickness indicates co-occurrence strength.

Table-1: Top-10 journals publishing research on ketamine and chronic pain.

Journal Name	Number of Publications	Total Citations	CPP
Pain	9	959	106.6
Anaesthesiology	7	874	124.9
Regional Anaesthesia and Pain Medicine	5	422	84.4
Anaesthesia and Analgesia	6	398	66.3
European Journal of Pain	5	388	77.6
British Journal of Clinical Pharmacology	2	368	184.0
Pain Physician	7	333	47.6
Handbook of Experimental Pharmacology	1	323	323.0
Biomedicine and Pharmacotherapy	1	213	213.0
Pain Medicine	4	211	52.8

CPP: Citations per paper.

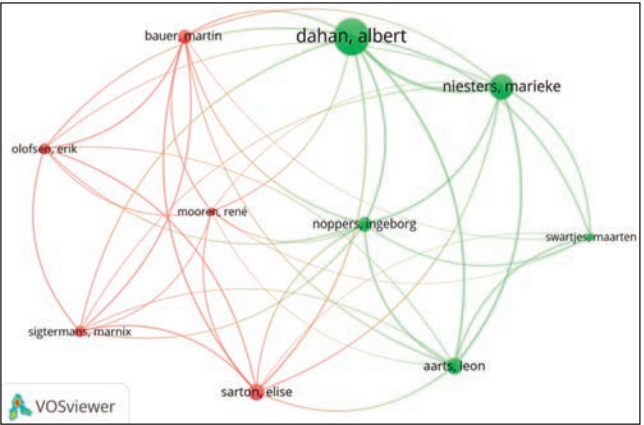


Figure-4: The co-authorship network.

Table-2: Leading countries contributing to research on ketamine and chronic pain.

Label	Total Link Strength	Publications	Citations	ANCS
United States	30	102	3211	0.94
Netherlands	21	22	1424	1.49
Canada	13	17	596	1.10
France	4	17	717	1.24
United Kingdom	16	16	359	1.23
China	7	13	337	1.70
Australia	9	11	462	0.96
Germany	14	9	621	1.30
Brazil	14	6	190	1.19
Finland	5	6	273	1.38
Japan	2	6	184	1.69
Denmark	5	5	361	1.74
Spain	7	5	151	1.01
Colombia	7	4	15	0.21
Switzerland	7	4	83	0.85
Turkey	3	4	172	0.96
Ireland	7	3	36	1.37
Italy	4	3	70	0.97
South Korea	1	3	71	0.97
Sweden	2	3	120	1.02
Chile	7	2	42	0.87
Hong Kong	4	2	14	0.51
Pakistan	7	2	26	0.66
Saudi Arabia	8	2	10	0.36

ANCS: Average normalised citation score.

The overall network structure demonstrated a cohesive and interlinked research field, with ketamine serving as a central bridging concept across all the three clusters. The network structure showed ketamine linking multiple key word groups related to clinical, mechanistic and neuropathic pain research. Keywords such as esketamine, complex regional pain syndrome and depression appeared in more recent publications. (Figure 3).

Authors from 32 countries contributed to ketamine-related chronic pain research, demonstrating both global participation and disparities in impact. The United States accounted for 102(42%) publications and 3,211(41%) of the 7,845 total citations (TCs), with an average normalised citation score (ANC) of 0.94 and total link strength (TLS) of 30, topping the list of 15 countries with respect to publication output (publications ≥ 3) (Table 2).

A small number of countries accounted for a large share of publications and collaboration links, while several other countries also contributed to the research output (Table 2).

The co-authorship network mapped the collaborative relationships among authors (Figure 4). Authors with at least three joint publications were included, revealing two distinct clusters of researchers who frequently collaborated. The largest cluster comprised Albert Dahan,

Marieke Niesters, Ingeborg Noppers, Leon Aarts, and Maarten Swartjes, collectively contributing 36 publications and accruing 2,850 citations, highlighting a highly productive research network. Within this cluster, Dahan led in productivity (13 publications) and total citations (1,062), while Niesters achieved the highest average citations per publication (97.1) and the highest ANCS (1.68). The other cluster comprised Martin Bauer, René Mooren, Erik Olofsen, Marnix Sigtermans and Elise Sarton. Strong collaborative ties were observed, especially between Dahan and Niesters (TLS = 9) and Dahan and Sarton (TLS = 6) (Figure 4).

Discussion

The current bibliometric analysis reveals how research on ketamine for chronic pain has evolved over the past 25 years, reporting significant insights into publication trends, thematic foci, geographic contributions and collaborative networks. A notable increase in publication output began around 2008 and persisted through 2024. The observed surge in publications aligns with growing clinical concerns over opioid-related harms and the pressing need for alternative analgesics. Several authors have explored the ongoing opioid crisis and emphasised the importance of identifying effective alternatives for pain management. Volkow and McLellan, in a review, highlighted the pressing need for reducing opioid reliance, and examined ketamine as a potential adjunct or alternative analgesic.⁶ Similarly, Barrett et al. discussed the utility of ketamine in chronic pain management, underscoring its role as a non-opioid option in specific clinical contexts.⁷ The citation peaked around 2009, which reflects the influential early work, such as Volkow and McLellan's review, on reducing opioid reliance through alternative therapies. As the opioid epidemic gained attention, researchers turned to ketamine's NMDA-receptor antagonism and unique analgesic properties, spurring sustained interest. More recently, the emergence of themes, such as esketamine, complex regional pain syndrome and depression, indicates a shift towards more integrated, biopsychosocial perspectives in pain management. The biopsychosocial model has gained recognition as the most comprehensive framework for addressing chronic pain, as it encompasses the complex interactions involving biological, psychological and social dimensions.^{8,9}

The prominence of journals like *Pain* and *Anaesthesiology*, underscores the interdisciplinary nature of research, bridging clinical pain management, pharmacology and neuroscience. Notably, journals with fewer publications but high citation impact, such as *Handbook of Experimental Pharmacology*, highlight the enduring relevance of mechanistic studies. This suggests that while clinical trials dominate in volume, foundational science continues to

shape the field's trajectory.

The current key word co-occurrence analysis revealed three dominant thematic clusters, each capturing a distinct yet interconnected aspect of ketamine research in chronic pain. These three clusters contained the most frequent key words and strongest co-occurrence links, and corresponded to the main clinically important areas in which the evidence base for ketamine in chronic pain was most developed; other lower-frequency terms visible in the map were treated as extensions of these core themes and were not described separately (Figure 3). The first cluster encompassed clinical and psychiatric applications, reflecting ketamine's expanding role in managing conditions, such as depression, fibromyalgia and complex regional pain syndrome. This focus aligns with a growing body of literature examining ketamine's rapid-acting antidepressant effects. Hunt et al. highlighted its promising psychiatric applications, while Iacobucci et al. and Li and Vlisides explored its neuropharmacological basis, particularly NMDA receptor antagonism and disruption of corticocortical connectivity.¹⁰⁻¹² The appearance of key words like "esketamine" and "depression" in recent years reinforces this evolving emphasis on the biopsychosocial dimensions of chronic pain.

The second cluster was related to perioperative and acute pain contexts. Studies in this domain underscore ketamine's utility in reducing postoperative pain and opioid requirements as well as its efficacy in mitigating opioid tolerance, hyperalgesia and allodynia. Radvansky et al. discussed its integration into perioperative protocols, while Vadivelu et al. emphasised its relevance in managing opioid-induced hyperalgesia and neuropathic pain.^{13,14} However, the evidence remains heterogeneous, with inconsistencies in outcome measures, dosing strategies and patient selection. These gaps highlight the need for methodologically rigorous trials to clarify ketamine's role in perioperative pain management.

The third cluster centred on neuropathic and pharmacological frameworks, particularly studies investigating ketamine's molecular targets and mechanisms of action. Despite a lower volume of publications, this cluster demonstrated the highest average citation impact, suggesting the enduring influence of foundational research in pain neurobiology. Studies focusing on NMDA receptor antagonism and central sensitisation mechanisms continue to provide critical insights that inform both pharmacological theory and clinical applications.

Notably, ketamine functions as a conceptual and therapeutic bridge across these clusters. Its central

positioning in the co-occurrence network illustrates how it connects psychiatric, clinical and mechanistic domains. The emergence of next-generation compounds, such as esketamine, reflects not only a pharmaceutical innovation, but also a shift towards integrating chronic pain management with psychological care. This convergence highlights ketamine's unique capacity to serve as a multimodal agent in addressing the complex, multidimensional nature of chronic pain.

International contributions to the field are both uneven and evolving. While the United States leads in both output and influence, the high ANCS scores of countries like the Netherlands and Denmark demonstrate that smaller, focussed research efforts can yield disproportionately impactful contributions. The growing participation of China and Ireland, with more recent publications and strong ANCS, points to an increasingly globalised research landscape. Consistent with the current findings, Wang et al. reported that although the field is dominated by the United States and China, impactful research also emerges from smaller nations.¹⁵

The co-authorship analysis highlights the influence of closely interconnected research groups in driving progress within ketamine-related chronic pain studies. Researchers, such as Albert Dahan and Marieke Niesters, have significantly contributed to the field through sustained partnerships, consistent scholarly output, and high citation impact. These collaborative networks not only facilitate methodological alignment, but also encourage interdisciplinary exploration. According to Lambiotte and Panzarasa, tightly connected author groups can serve as catalysts for scientific advancement by maintaining thematic coherence and optimising shared intellectual and institutional resources.¹⁶

A recent bibliometric study on (R)-ketamine from 2002 to 2021 identified 922 Web of Science articles, with a predominant focus on antidepressant mechanisms, Kenji Hashimoto from Chiba University as the most productive author, and the United States as the leading contributor to overall output.¹⁷ In contrast, our Scopus-based analysis focusses on ketamine's chronic pain applications and included 244 original articles published between 2000 and 2024. Although both studies demonstrate American leadership in ketamine research, their thematic emphasis differs. The earlier study mainly reflects depression-related mechanisms and clinical research, whereas the current analysis highlights ketamine's chronic pain literature, including neuropathic pain and perioperative research. It also demonstrates the important contribution of European research groups, particularly from the Netherlands and Denmark.

The current study has several strengths. First, it performed a fully transparent, reproducible search in the Scopus database, rigorously applying predefined inclusion and exclusion criteria. This approach ensured that the dataset was able to capture all relevant primary studies on ketamine in chronic pain, minimised selection bias, and allowed other researchers to replicate the findings. Second, by leveraging VOSviewer for network analysis, the study was able to visually map collaborative relationships and thematic clusters using objective thresholds. Finally, the study incorporated normalised bibliometric indicators to account for the fact that citation practices varied by publication year and region. By calculating ANCS and CPP, the study could compare the impact across countries and journals on an even playing field, rather than being misled by raw citation counts alone.

The current study also has several limitations. First, citation lag inevitably affects any bibliometric analysis: articles published in 2022-24 have had insufficient time to accrue citations, so their impact may be underrepresented in the current metrics. Second, because the search was confined to Scopus-indexed journals and English-language publications, relevant studies indexed exclusively in other major databases as well as non-English or non-indexed regional journals may have been overlooked, potentially biasing geographical and thematic conclusions. Third, while bibliometric techniques quantify the volume of output and citation impact, they offer no direct assessment of the methodological rigour or risk of bias within individual studies. In other words, a highly cited paper may still have design flaws, and, conversely, a low-citation study may be methodologically robust. Therefore, follow-up systematic reviews and meta-analyses are necessary to evaluate study quality and clinical outcomes in greater detail. Finally, despite careful efforts to standardise author names and institutional affiliations, some co-authorship links, especially those involving common surnames, may have been misattributed or inadvertently merged, potentially distorting the collaborative network structure. Despite these limitations, however, the findings provide a comprehensive, data-driven foundation for understanding global trends in ketamine research for chronic pain.

On the basis of the findings, three priority areas for future ketamine research in chronic pain are recommended. First, clinical trials must adopt standardised protocols: consistent dosing regimens, clear eligibility criteria, uniform outcome measures (e.g., validated pain scales, quality-of-life metrics), and comparable follow-up periods. Longitudinal safety studies are also needed to clarify ketamine's neurocognitive effects, misuse potential, and mood-related outcomes through extended prospective cohorts.

Second, ketamine's known rapid antidepressant effects should be leveraged within biopsychosocial frameworks. Trials combining ketamine with psychotherapies (e.g., cognitive behavioural therapy or mindfulness) could reveal synergistic benefits for patients with depression and chronic pain. Mechanistic work on central sensitisation, neuroinflammation, and neuroplasticity, using biomarkers like functional magnetic resonance imaging (MRI) or cytokine profiles, can identify who will benefit most, enabling precision approaches.

Third, global collaboration and capacity-building are essential. Cross-disciplinary partnerships among basic scientists, clinicians and implementation experts will streamline translational efforts. Establishing international consortia, similar to existing pain research networks, can harmonise protocols and support multicentre trials. Actively involving underrepresented regions via training workshops, joint grants and mentorship will expand the evidence base and promote equitable research.

Conclusion

Ketamine research was found to have progressed from mechanistic foundations to diverse clinical applications. By standardising protocols, integrating biopsychosocial strategies, and fostering inclusive global collaboration, future research can translate fragmented insights into clear, evidence-based guidelines for ketamine's role in chronic pain management.

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List of Abbreviations:

ANCS – Average normalised citation score, CPP – Citations per paper, NMDA – N-methyl-D-aspartate, NSAIDs – Non-steroidal anti-inflammatory drugs, TC – Total citations, TLS – Total link strength

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Author Contribution:

KK: Concept, design, data acquisition, drafting, final approval and agreement to be accountable for all aspects of the work.

SAD: Data quality assurance, analysis, interpretation, literature review, revision and final approval.

AAK: Data collection, entry, cleaning, revision and final approval.

AAKN: Supervision, study design, interpretation, literature review, critical review, final approval and agreement to be accountable for all aspects of the work.