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Research Article

Expert Perspectives on Polmacoxib and Its Combination with Paracetamol in Osteoarthritis: A Nationwide Survey from India

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Abstract

Objective: To assess expert perspectives and the perceived efficacy, safety, and clinical positioning of polmacoxib, both as monotherapy and in combination with paracetamol, in routine osteoarthritis (OA) management across clinical settings in India. Methodology: This cross-sectional, questionnaire-based survey, was conducted among 346 clinicians involved in OA management across diverse Indian clinical settings. A 22-item structured questionnaire captured treatment preferences, perceived safety concerns with traditional non-steroidal anti-inflammatory drugs (NSAIDs), clinician experience with polmacoxib, and usage patterns of the polmacoxib-paracetamol combination. Data were analyzed using descriptive statistics and presented as frequencies and percentages. Results: The survey included 346 clinicians. Approximately 65% reported that OA most commonly affects the knee joints, and 37% identified paracetamol as the most preferred NSAID. Nearly 64% of clinicians indicated that GI, cardiovascular, and renal adverse effects collectively represent the major drawbacks of traditional NSAIDs. A substantial proportion (92%) reported that polmacoxib's dual binding properties potentially offer superior cardiovascular, renal, and GI tolerability compared with traditional NSAIDs or cyclooxygenase-2 (COX-2) inhibitors. Regarding combination therapy, 53% of experts preferred polmacoxib plus paracetamol in 26-50% of their OA patients, while 32% used the combination in 11-25% of patients. Approximately 49% of clinicians stated that the combination provides improved pain control, allows lower dosing, and may reduce adverse effects. Nearly 90% of respondents reported no adverse drug reactions with polmacoxib. Conclusion: The survey findings indicate that polmacoxib is widely regarded as an effective and well-tolerated option for managing OA. Clinicians demonstrated a strong preference for the polmacoxib-paracetamol combination, highlighting its superior pain control and potential safety benefits. The favorable tolerability profile and perceived reduction in NSAID-related adverse effects support the use of polmacoxib, either alone or in combination, as a valuable option in routine clinical practice for OA.

Keywords

Osteoarthritis, Polmacoxib, Paracetamol, NSAIDs, Pain

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1. Introduction

Osteoarthritis (OA) is a chronic, progressive musculoskeletal disorder and a leading cause of pain and disability worldwide, affecting an estimated 595 million people in 2020 (7.6% of the global population), with a projected 60-100% increase by 2050 due to demographic changes and modifiable risk factors [1, 2]. The disease predominantly affects older adults, with nearly 70% of cases in individuals over 55 years, and women comprise about 60% of patients, though younger individuals with prior joint injury or repetitive mechanical stress may also develop OA. The knee is most commonly involved, followed by the hip and hand, leading to progressive pain, stiffness, and functional limitations that impair daily activities and quality of life, with obesity and sedentary lifestyle further exacerbating risk [1, 3]. In India, the burden of OA is substantial and rising, with around 80% of patients presenting with knee pain showing radiological or clinical evidence of OA, approximately 20% experiencing significant limitations in daily activities, and 11% requiring assistance for self-care; prevalence increases with age, reaching nearly 40% in those over 70 years [4, 5].

In clinical practice, OA management focuses on alleviating pain and maintaining functional mobility, with NSAIDs remaining central to symptomatic treatment. Traditional non-selective non-steroidal anti-inflammatory drugs (NSAIDs), however, carry gastrointestinal (GI), renal, and cardiovascular (CV) risks, particularly with long-term use [6]. Selective COX-2 inhibitors preferentially inhibit the COX-2 isoenzyme involved in inflammation while sparing COX-1, which protects the gastric mucosa, providing anti-inflammatory and analgesic effects with lower GI risk [7, 8].

Polmacoxib is a novel NSAID with dual COX-2 and carbonic anhydrase inhibition, offering tissue-selective pharmacodynamics that target inflamed tissues while potentially reducing systemic adverse effects [9, 10]. Studies indicate it provides effective analgesia with a favorable safety profile compared with conventional NSAIDs and selective COX-2 inhibitors [6, 11]. In routine practice, multimodal strategies often combine NSAIDs with paracetamol to enhance analgesic efficacy and minimize dose-related adverse effects [12-15]. Combination therapy with polmacoxib and paracetamol may therefore provide optimized pain control and improved tolerability in OA management.

Although clinical studies have established the efficacy and safety profile of polmacoxib, there is a dearth of studies regarding their perceived benefits among clinicians in clinical practice. This study aimed to assess expert perspectives on efficacy and safety of polmacoxib alone and in combination with paracetamol in the management of OA in Indian settings.

2. Materials and Methods

2.1. Study Settings

A cross-sectional study was carried out among clinicians involved in the management of OA in the major Indian cities from June 2025 to December 2025. The study was performed in accordance with Bangalore Ethics, an Independent Ethics Committee (ECR/355/Indt/KA/2022), which was recognized by the Indian Regulatory Authority, the Drug Controller General of India.

2.2. Study Participants

An invitation was sent to leading clinicians in managing OA in the month of March 2025 for participation in this Indian survey. About 346 clinicians from major cities of all Indian states, representing the geographical distribution, shared their willingness to participate and provide necessary data.

2.3. Study Procedure

The questionnaire booklet titled the ALPHA (Expert Perspective Study on the Assessment of Polmacoxib and Paracetamol in Arthritis management) was sent to the clinicians who were interested in participating in the survey. The study questionnaire comprised 23 questions focusing on the clinical burden of OA, treatment patterns of NSAIDs, preference for polmacoxib, utilization of combination therapy with paracetamol, perceived advantages over conventional NSAIDs and COX-2 inhibitors, global improvement assessment, and safety experiences in routine clinical practice. Reliability, as determined by a split-half test (coefficient alpha), was adequate but should be improved in future versions of the questionnaire. A study of criterion validity was undertaken to test the questionnaire and to develop methods of testing the validity of measures of clinicians' Perspectives. However, the extraneous variables in this include the clinician's experience, usage of the newer drugs, etc. The two criteria used were the doctors' perspectives from the clinical practice and the assessment of an external assessor and statistician. Clinicians had the option to skip questions as desired and were instructed to complete the survey independently, without peer consultation. Before participating in the survey, all respondents provided written informed consent.

2.4. Statistical Analysis

Data were analyzed using descriptive statistical methods. Categorical variables were presented as frequencies and percentages to describe response distributions. The occurrence and relative proportions of each response category were calculated. Graphical representations were generated to visually depict response patterns using Microsoft Excel (version 16.0.18025.20030).

3. Results

The survey included 346 clinicians. Approximately 61% of

respondents reported seeing 11-20 cases of OA per week, while 34% reported managing 21-30 cases weekly. About 43% of clinicians indicated that 31-40% of their OA patients are women. Nearly 47% of respondents stated that 21-40% of their OA patients are obese. More than half (54.62%) of participants reported that 11-20% of patients diagnosed with OA are younger than 45 years. Approximately 65% of clinicians reported that OA most commonly affects the knees (Table 1).

Table 1. *Distribution of responses on the most commonly affected joint in OA.*

Joints	Response rate (n = 346)
Hip	24.28%
Knee	65.32%
Hand	3.18%
Shoulder	0.29%
All of the above	6.94%

Approximately 65% of respondents identified older age as the most common attributing factor for OA. Nearly 38% of respondents identified lack of patient education as a key factor associated with medication non-adherence among patients with OA, while 36% cited the cost of medications as a contributing factor. About 37% of clinicians reported paracetamol as the most commonly preferred NSAID (Figure 1). Nearly 64% of the participants indicated that GI, CV, and renal adverse effects are collectively the drawbacks of traditional NSAIDs (Figure 2).

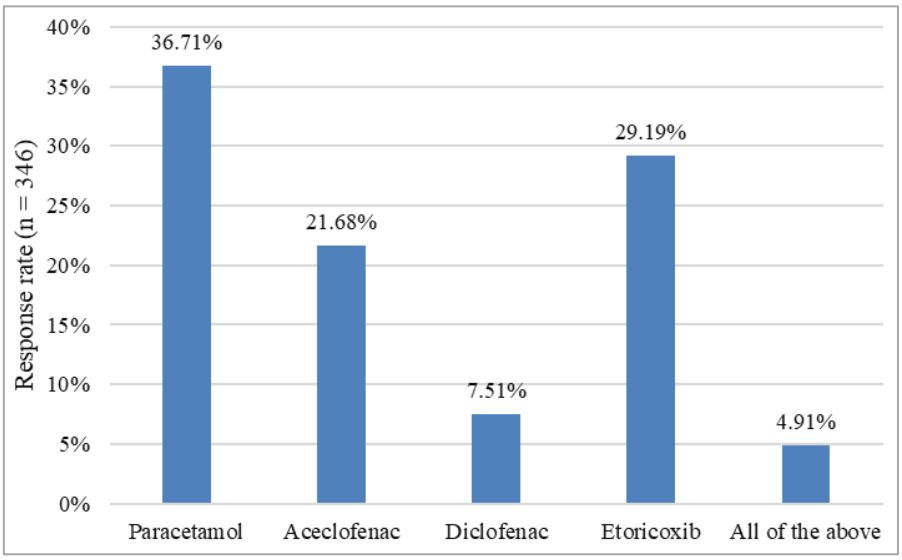

Figure 1. *Distribution of responses on the most commonly preferred NSAIDs.*

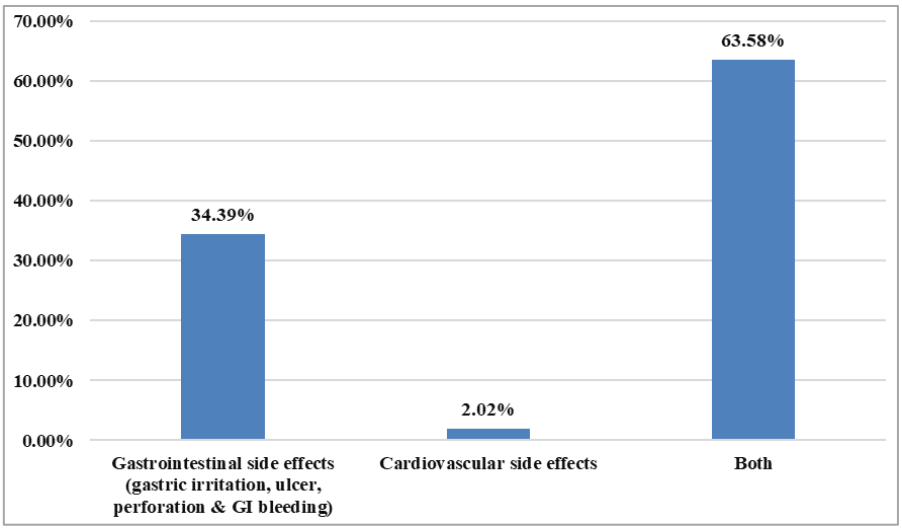

Figure 2. *Distribution of responses on the drawbacks of traditional NSAIDs.*

Around 42% of participants reported that the drawbacks of COX-2-selective NSAIDs include blood pressure elevation and GI-related risks. Approximately 62% of experts opined that the unique properties of polmacoxib, related to dual COX-2 and carbonic anhydrase inhibition, include its ability to inhibit COX-2 in CA-deficient tissues (inflamed joints) while not inhibiting COX-2 in CA-rich tissues (e.g., the CV system). About 54% of clinicians reported that the advantages of polmacoxib include dual inhibition of COX-2 and CA, a novel "tissue-specific" transport mechanism designed to deliver sustained drug levels to inflamed tissues, lack of COX-2 inhibition in CA-rich tissues, and a better tolerability profile. Nearly 92% of respondents reported that polmacoxib's dual COX-2 and carbonic anhydrase binding properties potentially provide superior CV, renal, and GI tolerability compared with traditional NSAIDs or COX-2 inhibitors (Figure 3).

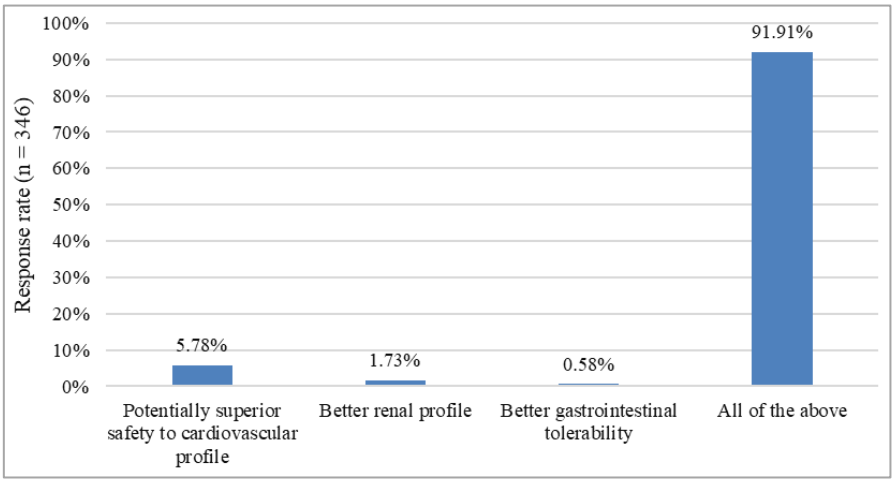

Figure 3. *Distribution of responses on the clinician perspectives on the advantages of polmacoxib's dual COX-2 and carbonic anhydrase binding properties compared with traditional NSAIDs and COX-2 inhibitors.*

Around 45% of participants indicated that the benefits of polmacoxib in OA include improvement in the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC-OA) index, reduced pain and stiffness, and enhanced physical function. Nearly 80% of respondents reported that polmacoxib offers several advantages over etoricoxib, including higher potency at a lower daily dose (2 mg/day of polmacoxib compared with 60-120 mg/day of etoricoxib), a lower risk of GI-related adverse events, and tissue-selective activity, whereas etoricoxib is considered non-tissue selective. About 53% of experts preferred polmacoxib plus paracetamol in 26-50% of their OA patients (Figure 4). Approximately 49% of clinicians stated that the combination of polmacoxib and paracetamol provides improved pain control, allows lower dosing, and may potentially reduce adverse effects (Table 2).

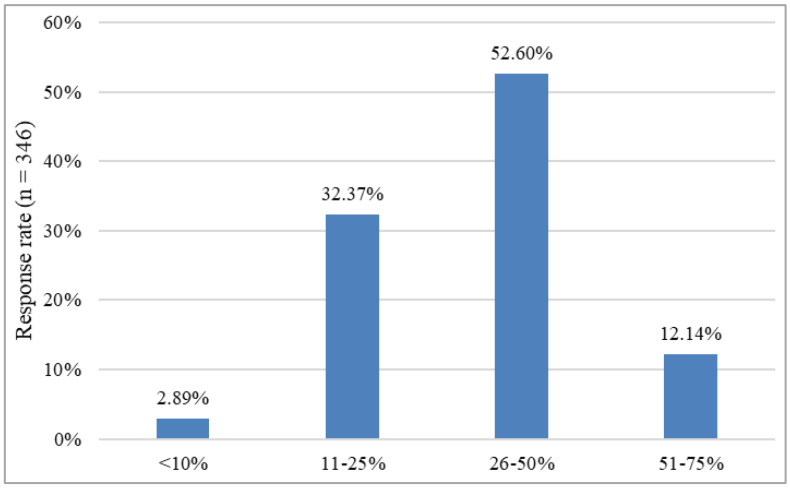

Figure 4. *Distribution of responses on the proportion of patients receiving polmacoxib + paracetamol in OA management.*

Table 2. Distribution of responses on the benefits of polmacoxib + paracetamol combination.

Benefits	Response rate (n = 346)
Improved pain control	34.39%
Lower doses of each medication	8.38%
Potentially reduced risk of adverse effects	8.67%
All of the above	48.55%

Nearly 81% of participants reported that polmacoxib demonstrated several advantages over celecoxib, including greater potency at a lower daily dose (2 mg/day of polmacoxib compared with 200-400 mg/day of celecoxib administered once or twice daily), a higher risk of CV events associated with celecoxib, and improved GI safety with polmacoxib. Approximately 75% of participants reported that polmacoxib has advantages over naproxen, ibuprofen, and diclofenac, including greater tissue selectivity, improved CV safety, and a lower risk of GI adverse events, which are more commonly associated with these conventional NSAIDs.

Approximately 79% of respondents identified several unique features of polmacoxib, including a quicker onset of relief from OA signs and symptoms, a convenient once-daily dosing regimen compared with most other NSAIDs, a low recommended dose of 2 mg/day (among the lowest within the NSAID class), improved GI safety, and tissue-selective COX-2 inhibition perceived to enhance CV safety relative to other NSAIDs. Approximately 90% of clinicians reported not observing any adverse drug reactions with polmacoxib. Nearly 47% of experts opined that, on the 5-point global improvement scale, polmacoxib use in OA patients results in marked improvement, while 42% reported moderate improvement.

4. Discussion

The findings of this survey highlight a substantial burden of OA in routine clinical practice, with most clinicians managing a high weekly case load and identifying the knee as the most commonly affected joint. This observation is consistent with existing literature. Khanna et al. reported that the knee was the most commonly affected joint in OA, as indicated by 95.6% of clinicians [16]. Similarly, Singh et al., in a Global Burden of Disease analysis, identified knee OA as the most prevalent form of OA worldwide [17]. Langworthy et al. also reported that the knee is the joint most frequently affected in OA, accounting for approximately 60% to 85% of all cases [18].

According to the present survey findings, paracetamol is the most commonly preferred NSAID for OA management. This aligns with prior evidence. Rai et al. observed that paracetamol was among the most frequently preferred analgesics for OA patients [19]. Siddiqui et al. similarly reported paracetamol as the most commonly used NSAID in OA management [20]. Conaghan et al. further noted that paracetamol is widely preferred for pain relief in OA [21]. Its widespread use is also supported by clinical practice guidelines, which recommend paracetamol as a first-line agent for the symptomatic management of OA [22, 23]. These findings highlight the continued reliance on paracetamol in routine OA care.

In the current survey, the majority of clinicians indicated that GI, CV, and renal adverse effects collectively represent the major drawbacks of traditional NSAIDs, underscoring the persistent safety concerns associated with their long-term use in OA management. These findings are consistent with existing literature. Chatterjee et al. concluded that the prevalence of GI, cardiac, and renal complications among patients is high due to excessive NSAID use [24]. Similarly, Swathi et al. reported that prolonged NSAID therapy may contribute to chronic kidney disease events leading to hospitalization [25]. Puppala and Reddy further emphasized that NSAIDs are associated with a broad spectrum of adverse effects, primarily involving the GI, renal, and CV systems, with side effects occurring in approximately 1-5% of users [26].

As per the current survey findings, polmacoxib's dual COX-2 and carbonic anhydrase binding properties are perceived to provide superior CV, renal, and GI tolerability compared with traditional NSAIDs or selective COX-2 inhibitors. These observations are consistent with previous evidence. In an earlier survey conducted by the current authors, a large majority of clinicians (86-87%) acknowledged that polmacoxib's dual COX-2 and carbonic anhydrase binding properties may offer an improved safety profile across CV, renal, and GI systems compared with conventional NSAIDs and COX-2 inhibitors [5]. Supporting these perceptions, Madkholkar et al. reported that polmacoxib demonstrated a favorable safety profile, with very low rates of treatment-related adverse events and no serious GI, CV, or renal complications during follow-up [27]. Furthermore, Sinha et al. showed that polmacoxib 2 mg was non-inferior in efficacy to celecoxib over six weeks in Indian patients with OA and exhibited good tolerability, with fewer GI adverse effects compared with traditional NSAIDs [28].

In the current survey, the majority of clinicians preferred the combination of polmacoxib and paracetamol for their OA

patients, reporting that this combination provides improved pain control, allows lower dosing, and may potentially reduce adverse effects. This preference aligns with previous findings. A prior survey conducted by the current authors reported that clinicians commonly favor NSAID-paracetamol combinations for symptomatic relief due to their effectiveness and enhanced tolerability [29]. Lee et al. demonstrated that polmacoxib 2 mg showed non-inferior efficacy to celecoxib, with a favorable tolerability profile in patients with knee OA over six weeks [30]. Furthermore, a meta-analysis by Cao et al., evaluating paracetamol combined with NSAIDs in OA, demonstrated superior short-term pain relief compared with monotherapy, without a significant increase in adverse events [13]. Easwaran et al. concluded that polmacoxib was not associated with clinically significant GI events or blood pressure elevation during therapy [10]. Similarly, Prabhoo and Shrivastava highlighted polmacoxib for its unique mechanism of action and potential safety advantages in OA, suggesting minimal adverse reactions [31]. Consistent with these findings, the present study also observed that the majority of clinicians reported not encountering adverse drug reactions with polmacoxib in clinical practice.

A key strength of the present survey is its large sample size, enhancing the reliability and representativeness of the findings across diverse clinical settings. However, as a questionnaire-based survey, the results rely on self-reported clinician responses and are subject to recall and response bias. The findings reflect perceived clinical benefits rather than patient-level outcomes, and the absence of direct clinical measures limits correlation with effectiveness or safety. Regional practice variations were not specifically analyzed, which may affect generalizability. Additionally, limited published literature on the polmacoxib and paracetamol combination restricts external comparison. Prospective real-world studies are warranted to validate these observations.

5. Conclusions

The survey demonstrates that OA predominantly affects the knee and that paracetamol remains the most commonly preferred analgesic in routine clinical practice. Clinicians widely associate traditional NSAIDs with GI, CV, and renal adverse effects, highlighting ongoing safety concerns with conventional therapies. Polmacoxib is perceived as a well-tolerated treatment option, with most clinicians reporting no observed adverse drug reactions in practice. A substantial proportion of clinicians prefer the combination of polmacoxib and paracetamol, citing improved pain control, the potential for lower dosing, and enhanced safety advantages, suggesting its growing acceptance in OA management.

Abbreviations

ADRs	Adverse Drug Reactions
CA	Carbonic Anhydrase
COX-1	Cyclooxygenase-1
COX-2	Cyclooxygenase-2
CV	Cardiovascular
GI	Gastrointestinal
OA	Osteoarthritis
NSAIDs	Non-Steroidal Anti-Inflammatory Drugs
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

Author Contributions

Manjula Suresh: Conceptualization, Methodology, Project administration, Resources, Supervision, Validation, Writing – review & editing

Krishna Kumar Manjunath: Data curation, Formal Analysis, Investigation, Visualization, Writing – original draft, Writing – review & editing

Conflicts of Interest

The authors declare no conflicts of interest.

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