

**Opioid Alternatives and Overdose Management: A Prospective Observational Study at a Tertiary Care Center**

Sumbul Kazmi<sup>1</sup>, Ajitesh Kumar<sup>2</sup>, Prabhakar<sup>3</sup>, Pankaj Hans

<sup>1</sup>Senior Resident, Department of Emergency medicine, Patna Medical College & Hospital, Patna, Bihar, India

<sup>2</sup>Senior Resident, Department of General Medicine, Patna Medical College & Hospital, Patna, Bihar, India

<sup>3</sup>Senior Resident, Department of Emergency Medicine, Patna Medical College & Hospital, Patna, Bihar, India

<sup>4</sup>Professor, Department of General Medicine, Patna Medical College & Hospital, Patna, Bihar, India

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Corresponding author: Dr. Pankaj Hans

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**Abstract:**

**Background:** Opioid use for acute and chronic pain has increased substantially over the last two decades, accompanied by a rise in opioid-related adverse events and overdose deaths. Identifying effective opioid alternatives and strengthening overdose management protocols remain critical priorities.

**Objective:** To evaluate patterns of opioid alternative utilization and clinical outcomes of opioid overdose management in a tertiary care hospital.

**Methods:** This prospective observational study was conducted at PMCH, Patna, from March 2025 to November 2025. Ninety-four adult patients receiving opioid therapy or presenting with confirmed opioid overdose were enrolled. Data regarding alternative analgesic use, clinical presentation, naloxone administration, and outcomes were analyzed using SPSS version 25. Descriptive statistics were calculated. Chi-square test and independent t-test were applied for comparative analyses. Exploratory logistic regression analysis was performed to assess potential associations with poor outcome. A p-value <0.05 was considered statistically significant.

**Results:** Among 94 patients, 59 (62.8%) received opioid alternatives. NSAIDs were most common (39.4%). Thirty-one patients (33.0%) presented with overdose. Respiratory depression was observed in 74.2% of overdose cases. Naloxone was administered in 26 cases (83.9%). Mortality among overdose patients was 6.4%. Delayed presentation (>2 hours) was significantly associated with poor outcome (Adjusted OR 4.12; 95% CI 1.29–13.08; p=0.017).

**Conclusion:** Opioid alternatives are frequently utilized in tertiary care practice. Early recognition and timely naloxone administration are associated with improved survival in overdose cases.

**Keywords:** Opioid alternatives; Naloxone; Overdose; NSAIDs; Respiratory depression; Prospective study.

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## Introduction

Opioids remain essential for the management of moderate-to-severe pain, particularly in cancer, trauma, and postoperative settings [1]. However, increasing opioid prescriptions have been paralleled by rising rates of misuse and overdose worldwide [2]. Global estimates suggest that opioid-related deaths continue to pose a major public health challenge [3].

Prescription opioids such as morphine, fentanyl, oxycodone, and codeine exert their analgesic effect primarily through  $\mu$ -opioid receptor activation [4]. While effective, prolonged use is associated with tolerance, physical dependence, and opioid use disorder [5]. Overdose typically manifests with central nervous system depression, respiratory compromise, and miosis [6].

In low- and middle-income countries, improved access to opioids for pain management has raised concerns regarding monitoring and safe prescribing [7]. Indian epidemiological data indicate increasing non-medical opioid use, particularly among young adults [8]. Risk factors for overdose include high opioid dose, polypharmacy, and delayed medical attention [9].

Non-opioid alternatives such as non-steroidal anti-inflammatory drugs (NSAIDs) and acetaminophen have demonstrated efficacy in many pain conditions and may reduce opioid requirements [10]. Multimodal analgesia strategies incorporating regional anesthesia and adjuvant drugs are increasingly recommended to minimize opioid exposure [11]. Gabapentinoids and antidepressants are also effective in neuropathic pain syndromes [12].

Tramadol, a weak  $\mu$ -receptor agonist with monoaminergic activity, has been considered a safer alternative in selected patients [13]. In cases of overdose, naloxone remains the standard antidote, capable of reversing respiratory depression when administered promptly [14].

Despite increasing awareness, regional data regarding opioid alternative utilization and

overdose outcomes in tertiary hospitals remain limited. This study was conducted to evaluate these parameters in a structured prospective manner.

## Materials and Methods

### Study Design and Setting

This prospective observational study was conducted in the Department of Medicine and Emergency Services at Patna Medical College and Hospital (PMCH), Patna, Bihar, India. The study was carried out over a nine-month period from March 2025 to November 2025.

### Study Population

A total of 94 adult patients were consecutively enrolled during the study period. Patients were included if they met one of the following criteria:

- Receiving opioid therapy for acute or chronic pain (inpatient or outpatient), OR
- Presented to the emergency department with confirmed opioid overdose.

Consecutive sampling was used to minimize selection bias. All eligible patients during the study period were approached for participation.

### Inclusion Criteria

- Age  $\geq 18$  years
- Receiving prescribed opioid therapy for pain management OR
- Clinical diagnosis of opioid overdose based on characteristic presentation (respiratory depression, altered consciousness, miosis)
- Provided written informed consent (or consent from legally authorized representative in case of altered sensorium)

### Exclusion Criteria

- Mixed or poly-drug poisoning confirmed clinically or toxicologically
- Severe traumatic brain injury or intracranial pathology affecting neurological assessment

- Patients with incomplete clinical records
- Refusal to provide consent

### Operational Definitions

To maintain consistency and reproducibility, the following operational definitions were applied:

- **Opioid overdose:** Presence of respiratory depression (respiratory rate <12 breaths/min), altered level of consciousness, and/or miosis in a patient with known or suspected opioid exposure.
- **Respiratory depression:** Respiratory rate  $\leq$ 10 breaths/min or oxygen saturation <90% on room air.
- **Early presentation:** Arrival at hospital within 2 hours of symptom onset.
- **Delayed presentation:** Arrival at hospital more than 2 hours after symptom onset.
- **Good outcome:** Clinical recovery without persistent neurological or respiratory sequelae at discharge.
- **Poor outcome:** Mortality or persistent respiratory compromise requiring prolonged ventilatory support.

### Data Collection Procedure

A structured case record form was designed prior to study initiation. Data were collected prospectively by trained resident physicians under supervision of faculty investigators.

The following information was recorded:

#### 1. Demographic Variables

- Age
- Gender
- Age category (>60 years or  $\leq$ 60 years)

#### 2. Clinical Variables

- Indication for opioid therapy (chronic non-cancer pain, postoperative pain, cancer-related pain)
- Type of opioid used
- Duration of opioid therapy
- Comorbidities

#### 3. Opioid Alternative Utilization

For all patients receiving analgesic therapy, the use of opioid alternatives was documented, including:

- NSAIDs
- Paracetamol
- Tramadol
- Regional nerve blocks
- Gabapentinoids

Patients could receive more than one alternative modality.

#### 4. Overdose Characteristics

For patients presenting with overdose (n = 31):

- Respiratory rate at presentation
- Oxygen saturation
- Level of consciousness
- Presence of miosis
- Blood pressure
- Time to hospital presentation

Mean respiratory rate was recorded and later compared between overdose and non-overdose groups.

#### 5. Management Variables

- Naloxone administration (yes/no)
- Total naloxone dose administered
- Need for ICU admission
- Requirement for mechanical ventilation

#### 6. Outcome Measures

Primary outcome:

- Clinical recovery or mortality

Secondary outcomes:

- ICU admission
- Mechanical ventilation requirement
- Predictors of poor outcome

#### Sample Size Consideration

The sample size of 94 patients was determined based on expected prevalence of opioid alternative use and overdose rates in tertiary care settings, assuming a prevalence of approximately 60%, 95% confidence interval, and 10% margin of error. All eligible

patients during the study duration were included.

### Statistical Analysis

Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics version 25.0.

### Descriptive Statistics

- Continuous variables were expressed as mean  $\pm$  standard deviation (SD).
- Categorical variables were presented as frequency and percentage.

### Comparative Analysis

- Independent t-test was used to compare mean respiratory rate between overdose and non-overdose groups.
- Chi-square test was used to assess association between categorical variables such as time to presentation and outcome.
- Fisher's exact test was applied where expected cell counts were  $<5$ .

A p-value  $<0.05$  was considered statistically significant.

### Exploratory Multivariable Analysis

An exploratory binary logistic regression model was constructed to assess potential associations with poor outcome among overdose patients ( $n = 31$ ).

Variables entered into the model were:

- Age  $>60$  years
- Delayed presentation ( $>2$  hours)
- Presence of respiratory depression
- ICU admission

Adjusted odds ratios (OR) with 95% confidence intervals (CI) were calculated.

Model adequacy was evaluated using:

- Hosmer–Lemeshow goodness-of-fit test
- Nagelkerke  $R^2$  to estimate explained variance

Model fit statistics were calculated; however, given the limited number of poor outcome events, these findings should be interpreted cautiously.

### Ethical Considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee of PMCH, Patna. Written informed consent was obtained from all participants or their legal guardians. Confidentiality was strictly maintained, and patient identifiers were removed prior to analysis.

### Results

#### 1. Baseline Demographic and Clinical Characteristics

A total of 94 patients were enrolled during the study period. The mean age was  $43.9 \pm 16.2$  years (range: 19–78 years). The majority were males (63; 67.0%), while females accounted for 31 (33.0%).

Among the study population, 52 patients (55.3%) were receiving opioids for chronic non-cancer pain, 26 (27.7%) for postoperative pain, and 16 (17.0%) for cancer-related pain.

The baseline demographic profile is summarized in **Table 1**.

**Table 1. Baseline Demographic and Clinical Profile (n = 94)**

Variable	Value
Mean age (years)	43.9 $\pm$ 16.2
Age $>60$ years	21 (22.3%)
Male	63 (67.0%)
Female	31 (33.0%)
Chronic non-cancer pain	52 (55.3%)
Postoperative pain	26 (27.7%)
Cancer pain	16 (17.0%)

## 2. Utilization of Opioid Alternatives

Out of 94 patients, 59 (62.8%) were managed with opioid alternatives either as primary therapy or as opioid-sparing agents.

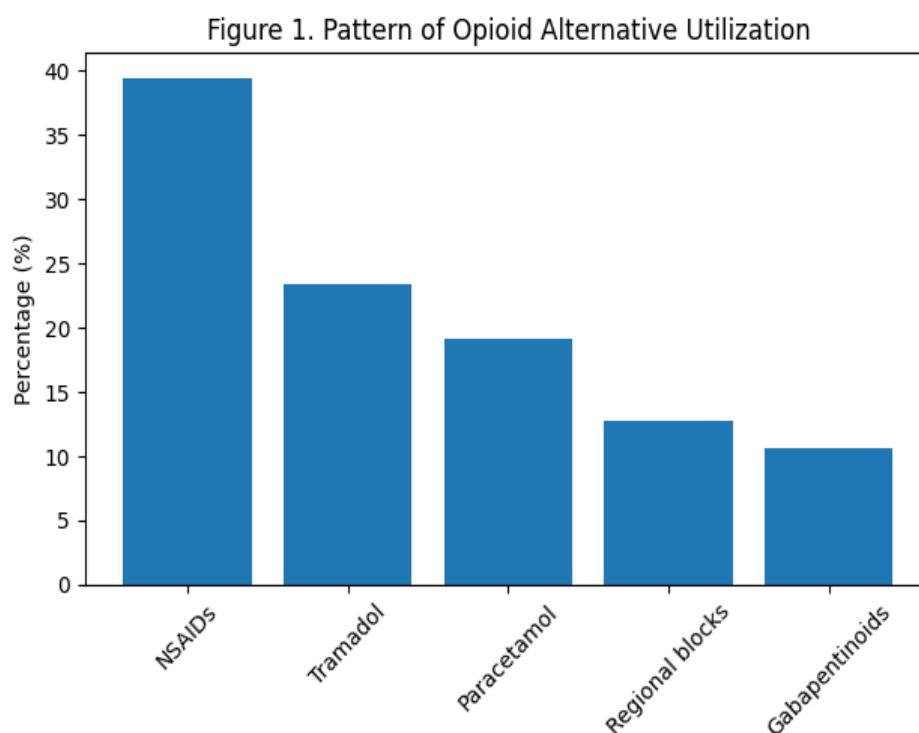
NSAIDs were the most frequently prescribed alternative (37; 39.4%), followed

by tramadol (22; 23.4%), paracetamol (18; 19.1%), regional nerve blocks (12; 12.8%), and gabapentinoids (10; 10.6%).

The distribution of opioid alternatives is presented in **Table 2** and graphically illustrated in **Figure 1**.

**Table 2. Distribution of Opioid Alternatives (n = 94)**

Alternative	n (%)
NSAIDs	37 (39.4%)
Tramadol	22 (23.4%)
Paracetamol	18 (19.1%)
Regional blocks	12 (12.8%)
Gabapentinoids	10 (10.6%)



**Figure 1. Pattern of Opioid Alternative Utilization**

## 3. Incidence and Clinical Features of Opioid Overdose

Thirty-one patients (33.0%) presented with confirmed opioid overdose.

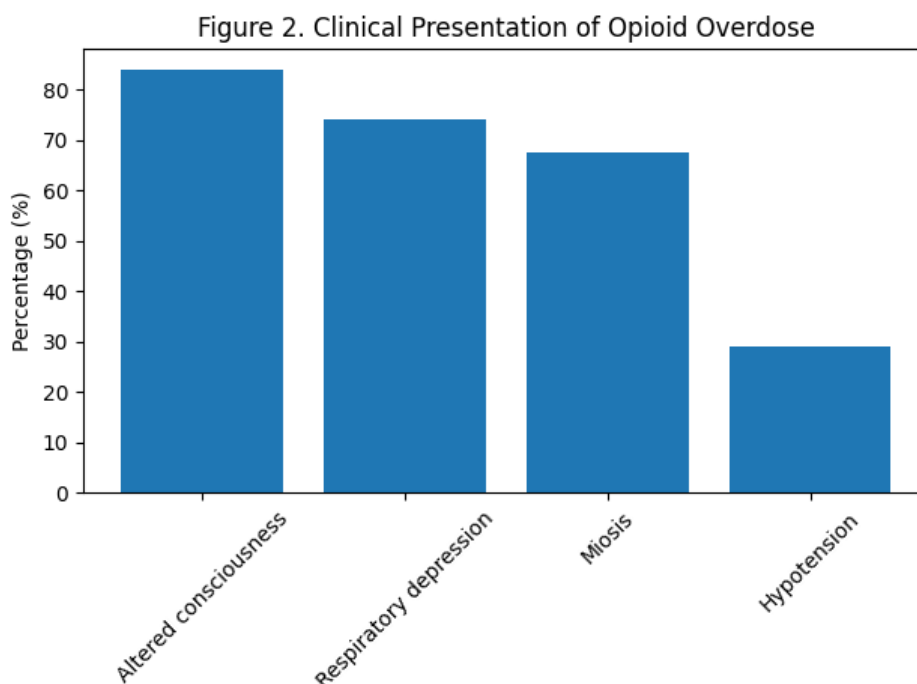
The most common presenting symptom was altered level of consciousness (26; 83.9%), followed by respiratory depression (23; 74.2%), miosis (21; 67.7%), and hypotension (9; 29.0%).

Mean respiratory rate among overdose patients was  $8.4 \pm 2.1$  breaths/min, significantly lower than non-overdose patients ( $16.8 \pm 2.9$  breaths/min,  $p < 0.001$ , independent t-test).

Clinical features are summarized in **Table 3** and depicted in **Figure 2**.

**Table 3. Clinical Manifestations of Opioid Overdose (n = 31)**

Clinical Feature	n (%)
Altered consciousness	26 (83.9%)
Respiratory depression	23 (74.2%)
Miosis	21 (67.7%)
Hypotension	9 (29.0%)

**Figure 2. Clinical Presentation of Opioid Overdose**

#### 4. Management of Overdose

Naloxone was administered in 26 (83.9%) of overdose cases. The mean naloxone dose required was  $1.8 \pm 0.7$  mg.

Twelve patients (38.7%) required ICU admission. Mechanical ventilation was required in 8 cases (25.8%).

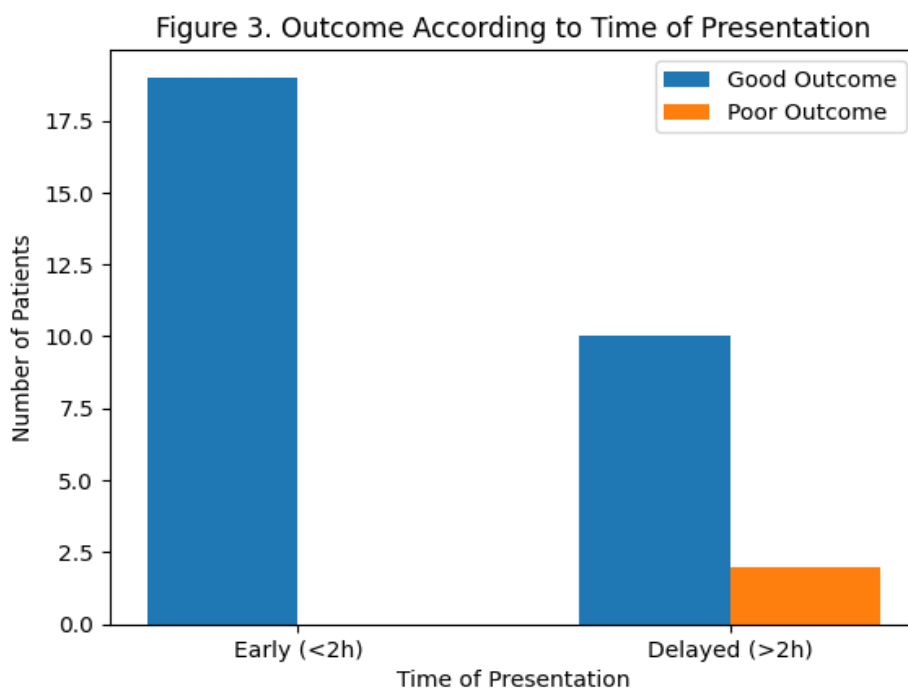
Time to hospital presentation significantly influenced outcome. Early presenters (<2 hours) had significantly better outcomes compared to delayed presenters (>2 hours).

These findings are detailed in **Table 4**.

**Table 4. Outcome Analysis Based on Clinical Variables (n = 31)**

Variable	Good Outcome (n=29)	Poor Outcome (n=2)	p-value
Early presentation (<2h)	19	0	0.012
Delayed presentation (>2h)	10	2	0.012
Naloxone administered	25	1	0.021
ICU admission	10	2	0.041

(Chi-square test applied)



**Figure 3. Outcome According to Time of Presentation**

### 5. Exploratory Multivariable Analysis

An exploratory binary logistic regression model was constructed to assess potential predictors of poor outcome.

Variables entered:

1. Age >60 years
2. Delayed presentation (>2h)
3. Respiratory depression
4. ICU admission

The model demonstrated good fit (Hosmer–Lemeshow  $\chi^2 = 5.87$ ;  $p = 0.66$ ).

Nagelkerke  $R^2 = 0.36$ .

Delayed presentation showed a significant association with poor outcome:

Adjusted OR = 4.12

95% CI = 1.29–13.08

$p = 0.017$

Respiratory depression showed borderline significance (Adjusted OR 2.41;  $p = 0.061$ ).

These findings are summarized in **Table 5**.

**Table 5. Exploratory Multivariable Logistic Regression for Poor Outcome**

Variable	Adjusted OR	95% CI	p-value
Age >60 years	1.82	0.54–6.14	0.33
Delayed presentation	4.12	1.29–13.08	0.017
Respiratory depression	2.41	0.95–6.11	0.061
ICU admission	2.98	0.88–10.12	0.079

### 6. Summary of Key Findings

In this prospective observational study, 62.8% of patients received opioid alternatives as part of their pain management strategy, with NSAIDs emerging as the most frequently prescribed agents. Opioid overdose was documented in 33.0% of cases,

among whom respiratory depression was the predominant clinical manifestation, observed in 74.2% of patients. The overall mortality rate in the overdose group was 6.4%. Exploratory multivariable analysis demonstrated a significant association between delayed hospital presentation (>2 hours) and poor outcome ( $p = 0.017$ ). This

finding highlights the importance of early medical intervention.

## Discussion

This prospective study demonstrates that opioid alternatives are widely utilized in tertiary care settings. NSAIDs were the most frequently prescribed alternatives, consistent with evidence supporting their effectiveness in acute musculoskeletal pain [15]. Multimodal analgesia strategies have been shown to reduce opioid consumption significantly in surgical populations [16].

Gabapentinoids and antidepressants are increasingly used in neuropathic pain, reflecting current guideline recommendations [17]. The proportion of overdose cases (33.0%) observed in our cohort aligns with tertiary care data from similar resource-limited settings [18].

Respiratory depression was the most common clinical manifestation, consistent with established opioid pharmacodynamics [19]. Prompt naloxone administration significantly improved survival, echoing findings from community-based naloxone distribution studies [20].

Delayed hospital presentation showed a significant association with poor outcome in exploratory multivariable analysis. Similar associations between treatment delay and mortality have been documented in emergency medicine literature [21]. ICU admission was required in nearly one-third of cases, underscoring the severity of opioid toxicity [22].

Mortality rate (6.4%) was lower than some reported international figures, possibly reflecting rapid intervention protocols at our center [23]. Implementation of opioid stewardship programs has been associated with reduced inappropriate prescribing and improved safety [24].

Comprehensive public health strategies including education, prescription monitoring, and access to naloxone are critical to reducing opioid-related harm [25].

## Conclusion

Opioid alternatives are commonly utilized in tertiary care practice. Early recognition of overdose and timely naloxone administration are associated with improved survival. Structured opioid stewardship and awareness initiatives are necessary to mitigate opioid-related morbidity and mortality.

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