

# Tramadol for Analgesia in Pediatric Patients at Basra Centre for Hereditary Blood Prospective Observational Study

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## Abstract

**Background:** Tramadol hydrochloride is a centrally acting analgesic widely used in pediatric pain management. Its efficacy and safety in children with hereditary hematological conditions managed at specialist centers in Iraq remain inadequately documented. **Objectives:** This study aimed to evaluate the analgesic efficacy, dose–response relationship, and adverse-reaction profile of tramadol in pediatric patients at the Basra Centre for Hereditary Blood Diseases, as well as to identify clinical variables associated with the degree of analgesic response. **Methods:** A prospective observational study was conducted from September 2024 to January 2026. Thirty-eight pediatric patients aged 4–15 years who received tramadol were enrolled. Pain was quantified using the Numerical Rating Scale (NRS, 0–10) before and after administration. Response was classified as satisfactory (NRS reduction  $\geq 2$  points) or slow ( $< 2$  points). Group comparisons were performed using the Mann–Whitney U test and chi-square test. **Results:** Satisfactory analgesia was achieved in 29 patients (76.3%). The overall mean pain reduction was  $3.03 \pm 2.59$  NRS units:  $4.17 \pm 1.34$  in the satisfactory-response group versus  $-0.67 \pm 2.18$  in the slow-response group ( $p < 0.001$ ). Intravenous (IV) infusion was associated with a significantly higher rate of satisfactory response than intramuscular (IM) injection (92.3% vs. 41.7%;  $\chi^2 = 9.02$ ,  $p = 0.003$ ). Age ( $p = 0.808$ ), sex ( $p = 0.460$ ), and total dose ( $p = 0.397$ ) were not significantly associated with analgesic outcome. Dizziness was the most frequent adverse event ( $n = 9$ , 23.7%); no serious adverse events occurred. **Conclusion:** IV tramadol infusion at approximately 1 mg/kg over 4 hours achieved satisfactory analgesia in the majority of pediatric patients with hereditary blood disorders. The route of administration was the principal determinant of analgesic response. Incorporating IV tramadol infusion into standardized pediatric pain protocols at hematological centers is recommended.

**Keywords:** sickle cell, tramadol, Basra, pediatric analgesia, hereditary blood diseases

## 1. Introduction

Pain is one of the most distressing symptoms experienced by children with hereditary hematological disorders. Patients with sickle cell disease suffer from recurrent vaso-occlusive crises that generate severe acute pain, while those with hemophilia frequently present with hemarthroses. Children with chronic anemias may require repeated invasive procedures, including bone marrow aspirations and venipunctures [1, 2]. Effective analgesic management is therefore central to the quality of care provided at dedicated hematological centers. Tramadol hydrochloride (4-phenyl-1-[2-(dimethylamino)methyl]cyclohexanol; CAS 27203-92-5) is a centrally acting synthetic opioid analgesic with a dual mechanism of action: weak agonism at  $\mu$ -opioid receptors and inhibition of neuronal reuptake of serotonin and noradrenaline [3]. This dual mechanism confers an analgesic potency intermediate between non-steroidal anti-inflammatory drugs (NSAIDs) and strong opioids, with a comparatively favorable respiratory safety profile that makes it particularly attractive for pediatric use [4, 5]. Current pediatric dosing guidelines recommend tramadol at 1–2 mg/kg per dose, with a maximum single dose of 100 mg, administered by oral, intravenous, or intramuscular routes [6]. Pharmacokinetic studies indicate that children older than one year metabolize tramadol more rapidly than adults due to higher hepatic clearance, necessitating weight-adjusted dosing [7]. The drug is extensively metabolized by the cytochrome P450 enzyme CYP2D6 to its active O-desmethyl metabolite (M1), and polymorphisms in this enzyme may contribute to inter-patient variability in analgesic response [8]. Sickle cell disease is highly prevalent in Basra, with sickle cell-related complications and

morbidity accounting for 64.48% of admissions [9]. A large cohort of sickle cell disease patients exists, with more than 6,500 registered cases. In addition, 1,817 patients with different hemoglobinopathies were registered in Basra during the last five years; 27.6% of them were registered during 2019 alone, 39.8% had homozygous sickle cell disease, and heterozygous forms, including sickle/ $\beta^+$  and sickle/ $\beta^0$ , represented 33.0% of all registered cases [10]. Despite widespread clinical use in Iraq and the broader Middle East region, published data on tramadol's efficacy and safety in Iraqi populations, particularly those attending specialist hematological centers, are scarce. The Basra Centre for Hereditary Blood Diseases is the principal tertiary referral unit for inherited hematological conditions in southern Iraq, serving a catchment population in which hereditary anemias, hemoglobinopathies, and coagulopathies carry a substantial disease burden. Documenting tramadol's analgesic response in this specific clinical context may inform the development of evidence-based pain management protocols tailored to the local patient population. The present observational study was therefore designed to highlight and describe the demographic and clinical characteristics of pediatric patients receiving tramadol at the Centre and to evaluate the degree of analgesic response using a validated pain scale.

### 1.1 Objectives

1. To describe the demographic characteristics, including age, sex, and age-group distribution, of pediatric patients receiving tramadol at the Basra Centre for Hereditary Blood Diseases.
2. To assess tramadol's analgesic efficacy using the Numerical Rating Scale (NRS 0–10) before and after administration.
3. To determine the overall rate of satisfactory analgesic response, defined as an NRS reduction of  $\geq 2$  points.
4. To compare key clinical variables, including age, sex, route of administration, and total dose, between patients achieving satisfactory and slow analgesic responses.
5. To document the adverse-reaction profile of tramadol in this pediatric population.
6. To provide locally applicable evidence to support evidence-based pediatric pain management at specialist hematological centers in Iraq.

## 2 Materials and Methods

### 2.1 Study Design and Setting

A prospective, cross-sectional observational study was conducted at the Basra Centre for Hereditary Blood Diseases, Basra Governorate, Iraq, over a 9-month period from March 2025 to January 2026. The Centre is a specialist tertiary referral unit that manages pediatric and adult patients with inherited hematological disorders, including sickle cell disease,  $\beta$ -thalassemia major, hemophilia A and B, hereditary bone marrow failure, and related conditions.

### 2.2 Study Population

All pediatric patients aged 1–15 years who received tramadol hydrochloride for acute pain management during the study period were eligible for inclusion. Patients with incomplete pain-score data, those who received concurrent opioid analgesics, and those with a documented allergy or hypersensitivity to tramadol or any tramadol-containing preparation were excluded. A total of 38 patients who met the inclusion criteria were enrolled consecutively.

### 2.3 Drug Administration Protocol

Tramadol was prescribed and administered by the attending physician at the Centre according to standard pediatric weight-based dosing guidelines, approximately 1 mg/kg per dose. The route of administration was selected by the treating clinician based on clinical presentation and vascular access. Intravenous tramadol was diluted in 50–100 mL of normal saline and infused over 4 hours at a rate of 0.25 mg/kg/hour. Intramuscular injections were administered into the anterolateral thigh or deltoid region at a dose of 1 mg/kg per dose. No standardized rescue analgesia protocol was in place during the study period.

### 2.4 Data Collection

Data were collected prospectively using a structured electronic data-entry form, which was provided through the following link:

<https://docs.google.com/forms/d/1TELtrkFreBBkOhtIPbgGA1DvPISwoS4WWGZvUCbCn>

The following variables were recorded for each patient encounter: date and time of administration, patient age and sex, route of administration (IV infusion or IM injection), total tramadol dose (mg), weight-based dose (mg/kg), number of doses administered, NRS pain score immediately before administration (NRS-before), NRS pain score 30–60 minutes after administration (NRS-after), and any adverse reactions observed within two hours of administration.

### 2.5 Outcome Measures

The primary outcome was the degree of analgesic response, classified as follows:

Satisfactory response: NRS reduction of  $\geq 2$  points from baseline.

Slow response: NRS reduction of  $< 2$  points from baseline, or any increase in NRS score.

Secondary outcomes included the quantitative pain-reduction score (NRS-before minus NRS-after), the proportion of patients reporting each category of adverse reaction, and the association between route of administration and analgesic response.

### 2.6 Statistical Analysis

Data were entered into Microsoft Excel 2019 and analyzed using Python 3.12 with the SciPy (v1.11) and pandas libraries. Continuous variables were summarized as mean  $\pm$  standard deviation (SD) or median with interquartile range (IQR), where appropriate, following assessment for normality. Categorical variables were presented as absolute frequencies and percentages. Between-group comparisons of continuous variables were performed using the two-tailed Mann–Whitney U test, given the non-parametric distribution of most variables and the relatively small sample size. Categorical variables were compared using Pearson's chi-square ( $\chi^2$ ) test; Fisher's exact test was applied where expected cell counts were  $< 5$ . A two-sided p-value of  $< 0.05$  was considered statistically significant for all analyses.

### 2.7 Ethical Considerations

The study was conducted in accordance with the principles of the Declaration of Helsinki (revised 2013) and the International Conference on Harmonisation Good Clinical Practice guidelines. Ethical approval was obtained from the Research Ethics Committee of the Iraqi Association for Medical Research and Studies (IAMRS) (Reference No. 7, dated 4/3/2025), with the approval document provided as a QR code at the bottom. All patient data were anonymized prior to analysis. Written informed consent was obtained from the parent or legal guardian of each participant.

### 3 Results

#### 3.1 Demographic Characteristics

A total of 38 pediatric patients were enrolled during the study period. The cohort comprised 23 males (60.5%) and 15 females (39.5%), with a male-to-female ratio of 1.53:1. The mean age was  $10.6 \pm 3.1$  years (median 12 years; IQR 9–13 years; range 4–15 years). The largest age group was 13–15 years ( $n = 14$ , 36.8%), followed by 10–12 years ( $n = 12$ , 31.6%), 6–9 years ( $n = 8$ , 21.1%), and  $\leq 5$  years ( $n = 4$ , 10.5%). The overall rate of satisfactory analgesic response was 76.3% ( $n = 29$ ). Table 1 and Figure 1 summarize the demographic characteristics and age-group distribution.

Table 1: Demographic and clinical characteristics of the study cohort stratified by analgesic response.

| Variable                     | Overall (n=38) | Satisfactory (n=29) | Slow (n=9)     | p-value |
|------------------------------|----------------|---------------------|----------------|---------|
| Age, mean $\pm$ SD (years)   | 10.6 $\pm$ 3.1 | 10.5 $\pm$ 3.1      | 10.8 $\pm$ 3.4 | 0.808   |
| Age, median (IQR)            | 12 (9–13)      | 12 (9–13)           | 12 (8–13)      | —       |
| Age range (years)            | 4–15           | 5–15                | 4–13           | —       |
| Age group $\leq 5$ yr, n (%) | 4 (10.5%)      | 3 (10.3%)           | 1 (11.1%)      | —       |
| Age group 6–9 yr, n (%)      | 8 (21.1%)      | 6 (20.7%)           | 2 (22.2%)      | —       |
| Age group 10–12 yr, n (%)    | 12 (31.6%)     | 10 (34.5%)          | 2 (22.2%)      | —       |
| Age group 13–15 yr, n (%)    | 14 (36.8%)     | 10 (34.5%)          | 4 (44.4%)      | —       |
| Sex: Male, n (%)             | 23 (60.5%)     | 19 (65.5%)          | 4 (44.4%)      | 0.460   |
| Sex: Female, n (%)           | 15 (39.5%)     | 10 (34.5%)          | 5 (55.6%)      | —       |

Values are n (%) unless otherwise stated. p-values were obtained from the Mann–Whitney U test for age and the chi-square test for sex. IQR = interquartile range.

#### 3.2 Scientific comment

The study cohort was predominantly male (60.5%), consistent with the higher incidence of X-linked hematological disorders, including hemophilia A and B, in male patients attending this center. The predominance of older children (age  $\geq 10$  years, 68.4%) likely reflects the chronic and progressive nature of hematological conditions, with older children accumulating more pain-related episodes. Neither age ( $p = 0.808$ ) nor sex ( $p = 0.460$ ) was significantly associated with analgesic response, suggesting that standard weight-based tramadol dosing provides equitable analgesia across the pediatric age spectrum and across sexes.

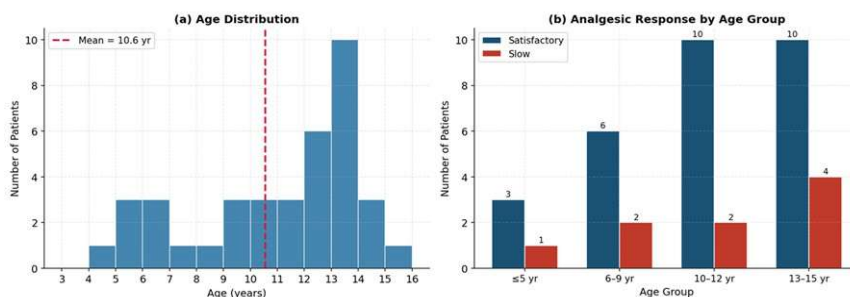


Figure 1: (a) Age distribution of the study cohort ( $n = 38$ ), with the mean age indicated by the dashed red line ( $10.6 \pm 3.1$  years). (b) Frequency of satisfactory versus slow analgesic response across four pediatric age groups.

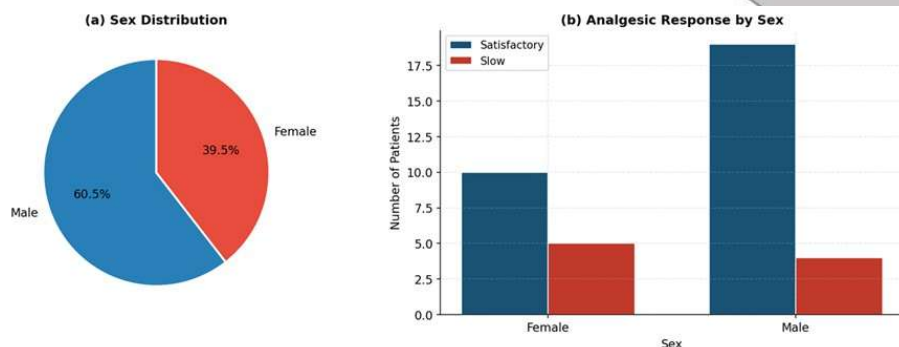


Figure 2: (a) Sex distribution of the study cohort (60.5% male, 39.5% female). (b) Degree of analgesic response stratified by sex.

### 3.3 Route of Administration and Analgesic Response

Intravenous (IV) infusion at a dose of 1 mg/kg/4 hours was the predominant route of tramadol administration, used in 26 patients (68.4%), while 12 patients (31.6%) received intramuscular (IM) injection. Of the 26 patients who received IV tramadol, 24 (92.3%) achieved a satisfactory analgesic response, compared with only 5 of 12 (41.7%) patients who received IM injection ( $\chi^2 = 9.016$ ,  $df = 1$ ,  $p = 0.003$ ). This statistically significant difference identifies the route of administration as the single most important clinical predictor of analgesic outcome identified in this study. Table 2 and Figure 3 present these data.

Table 2: Route of tramadol administration and its association with degree of analgesic response.

| Route        | Total n (%) | Satisfactory n (%) | Slow n (%) | p-value |
|--------------|-------------|--------------------|------------|---------|
| IV Infusion  | 26 (68.4%)  | 24 (92.3%)         | 2 (7.7%)   | 0.003*  |
| IM Injection | 12 (31.6%)  | 5 (41.7%)          | 7 (58.3%)  | —       |
| Total        | 38 (100%)   | 29 (76.3%)         | 9 (23.7%)  | —       |

\* Chi-square test ( $\chi^2 = 9.016$ ,  $df = 1$ ,  $p = 0.003$ ). IV = intravenous; IM = intramuscular.

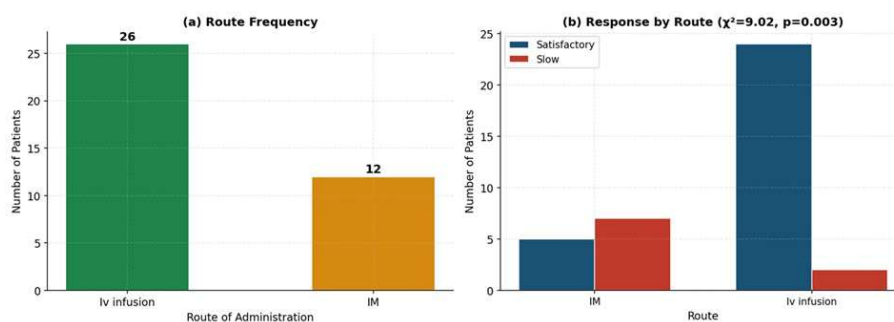


Figure 3: (a) Distribution of routes of tramadol administration: intravenous infusion (68.4%) and intramuscular injection (31.6%). (b) Degree of analgesic response stratified by route.

### 3.3 Scientific comment

The markedly superior analgesic response observed with IV infusion (92.3%) compared with IM injection (41.7%) has a sound pharmacokinetic basis. Intravenous administration delivers the drug directly into the systemic circulation, ensuring rapid and predictable attainment of therapeutic plasma concentrations, with a peak at approximately 10–15 minutes. In contrast, IM absorption is subject to variability influenced by local blood flow, muscle mass, and tissue perfusion, all of which may be compromised in children with chronic anemia, hypovolemia, or malnutrition, which are common in hematological disorders [11, 15]. This finding has direct clinical implications and supports a strong preference for IV tramadol infusion when intravenous access is available.

### 3.4 Pain Scores and Analgesic Efficacy

The overall cohort presented with moderate-to-severe pain prior to tramadol administration, with a mean NRS score of  $7.71 \pm 1.43$ . Following administration, the mean NRS score decreased to  $4.68 \pm 1.82$ , yielding a mean pain reduction of  $3.03 \pm 2.59$  NRS units. In the satisfactory response group ( $n = 29$ ), the mean NRS before administration was  $8.14 \pm 0.74$ , which decreased to  $3.97 \pm 1.21$  after administration, representing a mean pain reduction of  $4.17 \pm 1.34$  NRS units. In contrast, the slow response group ( $n = 9$ ) had a lower mean baseline NRS of  $6.33 \pm 2.18$ , which increased to  $7.00 \pm 1.50$  following administration, yielding a mean change of  $-0.67 \pm 2.18$  NRS units, indicating pain worsening. The difference in pain reduction between the two groups was highly statistically significant (Mann–Whitney U,  $p < 0.001$ ). These data are presented in Table 3 and Figure 4.

Table 3: Pain scores and tramadol dosing characteristics stratified by degree of analgesic response.

| Parameter                      | Overall (n=38)  | Satisfactory (n=29) | Slow (n=9)       | p-value   |
|--------------------------------|-----------------|---------------------|------------------|-----------|
| NRS before, mean $\pm$ SD      | 7.71 $\pm$ 1.43 | 8.14 $\pm$ 0.74     | 6.33 $\pm$ 2.18  | —         |
| NRS after, mean $\pm$ SD       | 4.68 $\pm$ 1.82 | 3.97 $\pm$ 1.21     | 7.00 $\pm$ 1.50  | —         |
| Pain reduction, mean $\pm$ SD  | 3.03 $\pm$ 2.59 | 4.17 $\pm$ 1.34     | -0.67 $\pm$ 2.18 | <0.001*** |
| Total dose (mg), mean $\pm$ SD | 30.7 $\pm$ 13.6 | 31.7 $\pm$ 14.0     | 27.4 $\pm$ 12.2  | 0.397     |
| Dose $\sim$ 1 mg/kg, n (%)     | 30 (78.9%)      | 24 (82.8%)          | 6 (66.7%)        | —         |
| Single dose, n (%)             | 36 (94.7%)      | 27 (93.1%)          | 9 (100%)         | —         |

\*\*\* Mann–Whitney U test,  $p < 0.001$ . NRS = Numerical Rating Scale (0–10). Pain reduction = NRS-before minus NRS-after; negative values indicate worsening.

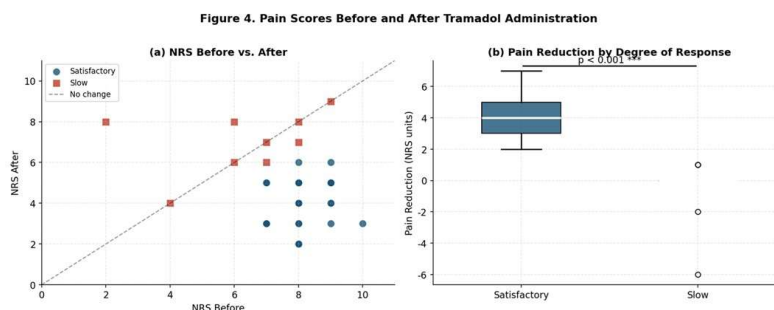


Figure 4: (a) Scatter plot of NRS pain scores before versus after tramadol administration, stratified by degree of analgesic response. (b) Box-and-whisker plots of pain reduction in NRS units in the satisfactory

versus slow response groups.

The highly significant difference in pain reduction between response groups ( $p < 0.001$ ) validates the NRS as a sensitive and clinically meaningful outcome measure in this setting. The negative mean pain change in the slow response group ( $-0.67$  NRS units) is notable and may reflect several mechanisms: pharmacogenomic variation in CYP2D6 activity reducing the conversion of tramadol to its active M1 metabolite; disease-related pain progression during the observation window; or inadequate dose relative to the severity of the acute pain episode [8, 13]. The absence of a significant dose difference between groups ( $p = 0.397$ ) implies that dose alone does not determine the outcome at the 1 mg/kg level, and that the route of administration and individual pharmacokinetics are the dominant determinants of response.

### 3.4 Tramadol Dosing

The mean total tramadol dose administered was  $30.7 \pm 13.6$  mg (range 9.8–60 mg). The majority of patients ( $n = 30$ , 78.9%) received a dose approximating 1 mg/kg body weight, consistent with standard pediatric dosing guidelines [6]. Most patients ( $n = 36$ , 94.7%) received a single dose per encounter; only two patients required two doses.

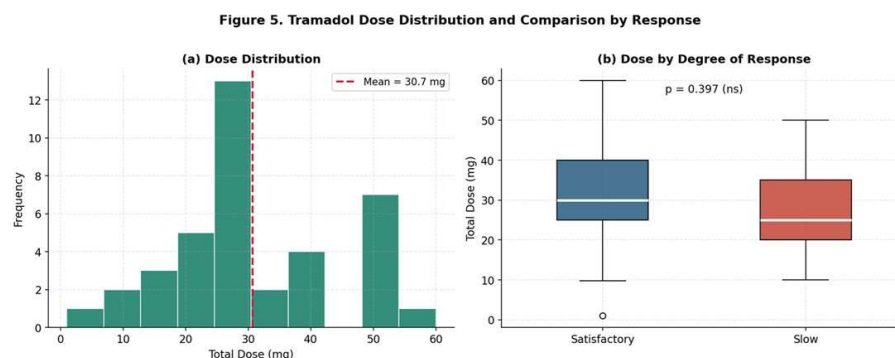


Figure 5: (a) Histogram showing the distribution of total tramadol doses administered in mg, with the mean dose indicated by the dashed red line (30.7 mg). (b) Box plot comparing total tramadol dose between the satisfactory and slow response groups. No statistically significant difference in total dose was observed between the satisfactory and slow response groups ( $31.7 \pm 14.0$  mg vs.  $27.4 \pm 12.2$  mg;  $p = 0.397$ ). The dose distribution and its relationship with analgesic response are illustrated in Figure 5.

#### Scientific comment

The dose distribution reflects adherence to weight-based pediatric guidelines, with most patients receiving approximately 1 mg/kg. The lack of a significant dose–response relationship within this range may indicate a ceiling effect at standard doses or may reflect the overriding pharmacokinetic influence of the route of administration. It is also possible that the small sample size limits the power to detect a modest dose–response effect. Future dose-optimization studies using higher tramadol doses, up to 2 mg/kg with IV administration, may clarify whether increased dosing improves outcomes in non-responders.

### 3.5 Adverse Reactions

Adverse reactions were systematically documented for all 38 patients within two hours of tramadol administration. The most frequently observed adverse event was dizziness ( $n = 9$ , 23.7%), followed by constipation ( $n = 3$ , 7.9%), nausea ( $n = 3$ , 7.9%), and headache ( $n = 1$ , 2.6%). The remaining 22 patients (57.9%) experienced no significant adverse reaction attributable to tramadol. No episodes of respiratory depression, seizure, hypotension, or anaphylaxis were recorded during the study period. Table 4 and Figure 6 detail the adverse-reaction profile.

Table 4: Adverse reactions following tramadol administration, stratified by degree of analgesic response.

| Adverse Reaction                | Overall n (%) | Satisfactory n (%) | Slow n (%) |
|---------------------------------|---------------|--------------------|------------|
| Dizziness                       | 9 (23.7%)     | 8 (27.6%)          | 1 (11.1%)  |
| Constipation                    | 3 (7.9%)      | 3 (10.3%)          | 0 (0%)     |
| Nausea                          | 3 (7.9%)      | 2 (6.9%)           | 1 (11.1%)  |
| Headache                        | 1 (2.6%)      | 1 (3.4%)           | 0 (0%)     |
| No significant adverse reaction | 22 (57.9%)    | 15 (51.7%)         | 7 (77.8%)  |
| Total                           | 38 (100%)     | 29 (100%)          | 9 (100%)   |

No serious adverse events, including respiratory depression, seizure, or anaphylaxis, were recorded in any patient.

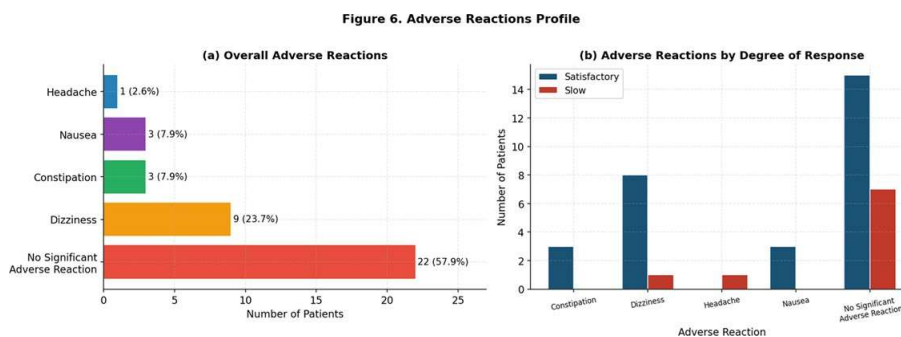


Figure 6: (a) Horizontal bar chart showing the frequency and percentage of adverse reactions following tramadol administration. (b) Adverse reactions stratified by degree of analgesic response.

The adverse-reaction profile observed in this cohort is consistent with tramadol’s known pharmacological effects. Dizziness (23.7%) reflects central nervous system stimulation via serotonergic and noradrenergic pathways and is the most consistently reported side effect across pediatric tramadol studies [14, 20]. Nausea and constipation, each reported in 7.9% of patients, arise from opioid receptor-mediated effects on the gastrointestinal tract. The absence of any serious adverse events, including respiratory depression, in all 38 patients provides reassuring evidence of the drug’s safety at standard 1 mg/kg doses in this age group. This favorable safety profile supports tramadol’s role as a preferred analgesic over stronger opioids in pediatric hematological settings where frequent repeated dosing may be necessary. The high proportion of patients without significant adverse effects (57.9%) further supports the tolerability of tramadol in this population.

## 4 Discussion

This prospective observational study provides original local evidence on the analgesic efficacy and safety of tramadol in pediatric patients with hereditary hematological disorders managed at a specialist center in southern Iraq. The principal findings are as follows: (1) IV tramadol infusion achieves satisfactory analgesia in the majority of patients (76.3%); (2) the route of administration is the single most important predictor of analgesic response; and (3) the adverse-reaction profile is acceptable, with no serious adverse events recorded. The overall satisfactory response rate of 76.3% is broadly consistent with rates reported in comparable pediatric analgesic studies. Finkel et al. reported a response rate of approximately 73% with oral tramadol for post-surgical pain in children aged 7–16 years [5], while Bozkurt’s comprehensive review noted response rates of 70–85% in pediatric populations, depending on the indication and route of administration [17]. The mean pain reduction of  $4.17 \pm 1.34$  NRS units in responders exceeds the minimum clinically important difference (MCID) of 1.5–2.0 NRS points established for pediatric acute pain [21], confirming clinical as well as statistical significance.

The strong association between IV administration and satisfactory response (92.3% vs. 41.7% for IM;  $p = 0.003$ ) is the most clinically important finding of this study. Several mechanisms may explain this observation. First, IV infusion achieves a higher and more consistent peak plasma concentration than IM injection, in which absorption may be delayed or incomplete in patients with impaired peripheral perfusion, a recognized complication of sickle cell disease and chronic anemia [12]. Second, IV tramadol infusion avoids the absorption variability associated with enteral routes, and the controlled infusion rate used in this center over 4 hours minimizes the risk of adverse effects while ensuring therapeutic drug delivery [13]. Based on the 2011 study by El-Hamamsy et al., the study generally indicated that, while both routes provide pain relief, parenteral administration, such as intravenous administration, often yields a faster onset and higher, more consistent plasma levels compared with oral administration [15]. Tramadol has been licensed for use from the age of one year and above, as reported in the published article by Bozkurt [16]. The superiority of opioids and narcotics as painkillers in children has been supported by the Association of Paediatric Anaesthetists of Great Britain and Ireland [17, 18]. These findings are consistent with those of Payne et al., who demonstrated superior bioavailability and more consistent analgesia with parenteral versus oral tramadol in children, aligning with APAGBI guidelines recommending IV administration as the preferred route in hospitalized pediatric patients with established venous access [18]. Age was not a significant predictor of tramadol response ( $p = 0.808$ ) across the age range studied (4–15 years). This finding is consistent with pharmacokinetic data demonstrating relatively stable tramadol clearance per kilogram beyond infancy [7] and supports the use of weight-based dosing across the full pediatric age spectrum at this center. Similarly, sex was not significantly associated with analgesic response ( $p = 0.460$ ), consistent with Stamer et al.'s large-scale retrospective study, which found no clinically significant sex difference in tramadol analgesia [19]. Total tramadol dose was also not significantly different between the response groups ( $p = 0.397$ ), suggesting that, at the standard 1 mg/kg dose, dose titration alone is insufficient to overcome pharmacokinetic variability attributable to route differences or CYP2D6 polymorphisms [8, 13]. The adverse-reaction profile was reassuring. Dizziness (23.7%), nausea (7.9%), and constipation (7.9%) occurred at rates consistent with or below those reported in pediatric tramadol systematic reviews [14, 20]. Critically, no respiratory depression or seizure was observed, supporting tramadol's established safety advantage over morphine and other strong opioids in the pediatric setting [4, 5, 21]. This is particularly relevant in children with chronic hematological conditions, who may require repeated analgesic use over time and in whom the cumulative adverse-effect burden of opioid analgesics is a significant clinical concern. This study has several limitations that should be acknowledged. First, the observational design precludes causal inference, and the absence of a control group or randomization limits conclusions about absolute efficacy. Second, the sample size ( $n = 38$ ) provides limited statistical power for subgroup analyses. Third, pain was assessed at a single post-dose time point, precluding analysis of the duration of analgesia or the requirement for rescue medication. Fourth, pharmacogenomic data regarding CYP2D6 metabolizer status were not available, limiting the mechanistic interpretation of the slow response group. Fifth, the underlying hematological diagnosis was not systematically recorded for all patients, which precludes disease-specific subgroup analyses. Finally, the retrospective completion of some data fields introduced minor inconsistencies in dose recording that required standardization before analysis. Notwithstanding these limitations, this study constitutes the first systematic documentation of tramadol analgesia outcomes in a pediatric hematological population in southern Iraq. The findings provide a locally applicable evidence base for the development of pain management guidelines at similar centers. Future research priorities should include prospective randomized controlled trials comparing IV and IM tramadol, pharmacogenomic profiling of CYP2D6 status in non-responders, evaluation of tramadol combined with NSAIDs for multimodal analgesia, and assessment of repeated-dose safety over prolonged treatment periods.

## 5 Conclusion

Tramadol administered at approximately 1 mg/kg achieves satisfactory analgesia in 76.3% of pediatric patients with hereditary blood diseases at the Basra Centre for Hereditary Blood Diseases. Intravenous infusion is significantly superior to intramuscular injection in achieving a satisfactory analgesic response (92.3% vs. 41.7%;  $p = 0.003$ ) and should be the preferred route of administration whenever intravenous access is es-

tablished. Age, sex, and total dose at the 1 mg/kg level do not significantly predict analgesic outcome. The adverse-reaction profile of tramadol at standard pediatric doses is acceptable, with dizziness being the most commonly observed side effect and no serious adverse events occurring in this cohort. These findings support the incorporation of intravenous tramadol into standardized evidence-based pediatric pain management protocols at hematological disease centers in Iraq and similar resource-constrained settings.

## Acknowledgements

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## Data Availability

The anonymized dataset supporting the findings of this study is available from the corresponding author upon reasonable request.

## Ethical Approval



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