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Authors

Vastola, Marie

Mumma, Bryn

Fine, Jeffrey

et al.

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Analgesia Administration by Sex Among Pediatric Emergency Department Patients with Abdominal Pain

Marie E. Vastola, BS[a], **Bryn E. Mumma, MD, MAS**[b], **Jeffrey R. Fine, MPH**[c], **Daniel J Tancredi, PhD**[d], **Joshua W. Elder, MD**[b], **Angela F. Jarman, MD, MPH**[b]

[a]School of Medicine, University of California Davis, 4610 X Street, Sacramento, CA 95817 USA

[b]Department of Emergency Medicine, School of Medicine, University of California Davis, 4150 V Street, PSSB #2100, Sacramento, CA 95817, USA

[c]Department of Public Health Sciences, School of Medicine, University of California Davis, Medical Sciences 1-C, One Shield's Ave, Davis, CA 95616 USA

[d]Department of Pediatrics, School of Medicine, University of California Davis, 2516 Stockton Blvd, Sacramento, CA 95817, USA

Abstract

Background: There is conflicting data about sex-based differences in the treatment of acute pain in the ED. Little is known about sex-based disparities in analgesia in pediatric ED patients.

Objectives: Our objective was to determine whether analgesic administration rates differ between female and male pediatric patients presenting to the ED with abdominal pain.

Methods: We conducted a retrospective cohort study of ED patients 5–21 years old with abdominal pain between 6/1/19 and 6/30/21. The primary outcome was receipt of any analgesia, and secondary outcomes were receipt of opioid analgesia and time to receipt of analgesia. Multivariable regression models were fitted for each outcome.

Results: We studied 1,087 patients; 681 (63%) were female with a median age of 17 years (IQR 13, 19) and 406 (37%) were male with a median age of 14 years (IQR 9, 18). 371 female patients (55%) and 180 male patients (44%) received any analgesia. 132 female patients (19%) and 83 male patients (20%) received opioid analgesia. In multivariate analyses, female patients were equally likely to receive any analgesia (OR 1.30, 95% CI 0.97 – 1.74, p = 0.07), but time to analgesia was 14% longer (GMR 1.14, 95% CI 1.00 – 1.29, p = 0.04). Non-White patients were 32% less likely to receive opioids (OR 0.68, 95% CI 0.47 – 0.97, p = 0.04).

Address for Correspondence: Marie Vastola, 4610 X Street, Sacramento, CA 95817, Fax: 916-734-7055, mevastola@ucdavis.edu.

Author Contributions:

MEV, JWE, BEM, & AFJ conceived the study idea. JWE and BEM supervised data acquisition. JWE, AFJ, DJT, and JRF conceived the statistical analysis plan and conducted analyses. MEV, AFJ, & BEM drafted the manuscript, and all authors critically reviewed the content and approved the final version. MEV and AFJ take responsibility for the paper as a whole. This research was approved by the Institutional Review Board.

Conflicts of Interest: The authors have no relevant conflicts of interest.

Conclusions: Female pediatric ED patients were equally likely to receive any analgesia as male patients, but their time to analgesia was longer. Non-White patients were less likely to receive opioid analgesia than White patients.

Keywords

disparity; analgesia; opioid; sex differences; race

INTRODUCTION:

Over half of pediatric emergency department (ED) visits are related to pain, with abdominal pain being one of the most common ED chief complaint in the United States (1). The ED approach to pain generally includes treating the pain while simultaneously evaluating its etiology. Abdominal pain is an important area for research on ED pain management because it is one of the most common presenting complaints in emergency departments, has a broad differential diagnosis, and is unlikely to have a protocolized approach to treatment (2–5).

While sex disparities in many areas of medicine are well-established (6,7), data on sex disparities in ED pain management are mixed. Several studies show female patients with abdominal pain are less likely to receive analgesia in the emergency department or have to wait longer to receive it (2,4,5), but others show no difference in analgesia administration by sex (8–10). Nuances exist in this research. For example, one study found no sex difference in analgesia administration overall, but among patients with severe pain, female patients were more likely to receive analgesia (8). Another study showed that while women with abdominal pain waited longer than men to receive analgesia, women with fracture pain did not (2).

The majority of the research on sex differences in analgesia administration has been conducted in adult patients. Studies that include pediatric patients often do not usually analyze the data by age, which is an important predictor of receipt of analgesia, as opioid administration increases with patient age (11,12). The few studies that have evaluated sex disparities in analgesia administration among children have also produced mixed results. One study of ED visits for pediatric patients using 2006–2015 National Hospital Ambulatory Medical Care Survey (NHAMCS) data found that sex did not affect opioid prescribing (11), whereas another study of 2010–2016 NHAMCS data showed that male patients 5–25 years of age presenting with sport-related injuries were more likely to be given or prescribed opioid analgesics than female patients (12). Given the well-known and long-standing history of sex disparities in many areas of adult medicine (6,7), it is important to understand if female pediatric patients with pain are treated differently than male patients.

The objective of this study was to determine if there was a sex-based disparity in analgesia administration in pediatric ED patients with abdominal pain, and if so, at what age that disparity appeared. We hypothesized that a difference in analgesic administration exists between female and male children, and that, if present, the disparity would appear around the age of puberty.

MATERIALS AND METHODS:

Study Setting and Design:

We conducted a retrospective cohort study of pediatric patients presenting to a single academic tertiary care hospital ED between June 1, 2019, and June 30, 2021. The study site sees both adult and pediatric patients, with an annual volume of approximately 17,000 pediatric ED patients during the years of the study. Patients <21 years old are seen in the pediatric ED. This study was approved by the local Institutional Review Board and conducted in accordance with institutional standards on human research.

Patient Population

The cohort consisted of all non-pregnant patients with a normal mental status (defined as Glasgow Coma Scale 15) aged 5–21 years presenting to the ED with a chief complaint of abdominal pain (see Supplemental Table 1 for all included chief complaints). Abdominal pain was selected because it is a common reason for ED presentations with a broad differential diagnosis, and our ED does not have a protocol to guide the evaluation and treatment of pediatric patients with abdominal pain. Patients who were febrile at presentation (≥ 38.0°C) were excluded because triage nurses have protocols to administer antipyretic medications that are also analgesics to these patients prior to ED provider evaluation. Analgesic administration requires a provider evaluation and order in this ED. For patients with multiple qualifying encounters during the study period, only the index visit was included. Supplemental Figure 1 shows a flow diagram of included patients.

Data Collection:

Demographic and clinical data were directly exported from the electronic health record (EHR) by an experienced data analyst. These included age, sex, race/ethnicity (self-reported), primary language, initial pain score, opioid and non-opioid analgesic medications administered during the ED stay, and time to analgesic administration. The data set was iteratively validated by study personnel to ensure accuracy prior to the final export by the analyst. No data were manually abstracted.

Definition of Variables

Opioid analgesia was defined as any medication that contained an opioid alone or in combination. Non-opioid analgesia was defined as any medication with an approved indication for pain without an opioid component. Please see Supplemental Table 2 for a full list of analgesic medications included in the study. For both opioid and non-opioid analgesia, all routes of administration were included. Sex was defined as the legal sex assigned at birth, in accordance with the Sex and Gender Equity in Research (SAGER) guidelines (13). Primary language was categorized as English or non-English given the small numbers in each non-English language category. Self-reported race and ethnicity were collected categorically and then collapsed into a binary variable (non-Hispanic/Latino White, referred to as “White,” compared to all other race/ethnicities) due to the small numbers in each non-White category. In univariate analysis, the direction of an effect was similar across categories, thus supporting the decision to collapse categories. A similar strategy has been

employed in other studies (11). Time to receipt of analgesia was defined as time from ED arrival to medication administration. Pain score was reported by the patient to the triaging nurse upon arrival. Treating ED providers are not involved in this pain score entry. If the patient is unable to report a pain score, no score is recorded. Pain was scored by the patient on a numerical scale of 0–10 or a visual scale for younger patients (Wong-Baker FACES scale (14)), depending on the nurse's assessment of the patient's ability to use numerical versus visual scales.

Outcomes

The primary study outcome was the administration of any analgesia, opioid or non-opioid, during the ED visit. Secondary outcomes included the administration of opioid analgesia, time to any analgesia, and time to opioid analgesia.

Statistical Analysis:

All statistical analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, NC). Univariate analyses for sex differences among demographic characteristics were conducted using a Wilcoxon Rank Sum test for continuous variables and a chi-square test for categorical variables for a comparison of proportions. A multivariable logistic regression was performed to estimate the odds of administration of any analgesia, our primary outcome. The following predictors were included in the model: patient sex, age, initial pain score, race/ethnicity, and primary language. These independent variables were selected *a priori* based on published literature (14). This model was repeated to evaluate predictors of opioid analgesia administration. Two log-transformed multivariable linear regression models were performed for patients who received any analgesia as well as those who received opioid analgesia to evaluate factors associated with time to receipt of these medications. The log-transformation was motivated by examining histograms of these event times, which were approximately lognormally distributed. In the regression models, we performed a complete case analysis and patients with missing data were excluded. Linear regression coefficients were back-transformed by applying the inverse logarithm function and are thus interpretable as geometric mean ratios (GMR) or adjusted GMR (aGMR) that describe how much the typical event time was increased or decreased for a unit-change in the independent variable. In each initial regression model, an interaction term between patient age and sex was included, but found to not be statistically significant, and thus was not included in the final models. Age was treated as a continuous variable in the regression analysis but was dichotomized for a subanalysis of children less than or greater than 12 years, which was used as a marker of reproductive maturity. To evaluate if the need for pregnancy tests had an impact on time to analgesia, we also looked at the time to analgesia for patients above and below age 12. All hypothesis tests were two-sided and evaluated at a significance level of 0.05.

RESULTS:

We studied 1,087 eligible patient visits. The cohort was composed of 681 (63%) female patients and 406 (37%) male patients. In univariate analysis, female patients had a higher median age (17.0 yrs, IQR [13.0, 19.0]) than male patients (14.0 yrs, IQR [9.0, 18.0]) (see

Table 1), and a higher median pain score (7.0, IQR [5.0, 9.0] vs. 6.0, IQR [4.0, 8.0]). A higher proportion of female patients received any analgesia (371/681 [54.5%]) than male patients (180/406 [44.3%], p = 0.001), but there was no difference seen in the proportion of females and males who received opioid analgesia (132/681 [19.4%] vs 83/406 [20.4%], respectively; p = 0.67). Median time to first analgesic administration was longer for female patients compared to male patients (123 minutes vs 106.5 minutes, p = 0.04), but the difference in median time to opioid administration was not significantly different for female and male patients (133 minutes vs 91 minutes, p = 0.08). There were no baseline differences seen between females and males based on primary language.

In multivariable logistic regression analysis for any analgesia administration (n = 914), there was a trend toward increased odds of receiving analgesia for female patients, but this was not statistically significant (OR 1.30, 95% CI 0.97 – 1.74, p = 0.08; see Table 2). The primary predictor of analgesic receipt was initial pain score. The odds of receiving analgesia were 22% higher for every one-point increase in pain score after adjusting for sex, age, race/ethnicity, and language (OR 1.22, 95% CI 1.16–1.29, p < 0.01). Patients for whom English was not their primary language had a non-significant trend toward receiving less analgesia than English-speaking patients (OR 0.64, 95% CI 0.40 – 1.01, p = 0.06). In the linear regression model (n = 518, Table 2), time to analgesia was 14% longer for female patients (GMR 1.14, 95% CI 1.00 – 1.29, p = 0.04) than male patients. Among female patients, the time to analgesia was 27% longer for those who were less than 12 years old than those 12 or older (GMR 1.27, 95% CI 1.03 – 1.58, p = 0.03).

In the multivariable logistic regression analysis for opioid administration (n = 914), there was a non-significant trend towards decreased odd of receiving opioid analgesia for female patients, which is the opposite of the trend seen for any analgesia (OR 0.74, 95% CI 0.53 – 1.05, p = 0.09). Initial pain score continued to have the strongest association. The odds of receiving opioids were 31% higher for every one-point increase in first pain score (OR 1.31, 95% CI 1.21 – 1.41, p<0.01) after adjusting for sex, age, race/ethnicity, and language. Patients of other races and ethnicities were 32% less likely to receive opioids than Non-Hispanic White patients (OR 0.68, 95% CI 0.47 – 0.97, p = 0.04). Additionally, there was a non-significant trend towards older patients being more likely to receive opioid analgesia (OR 1.04, 95% CI 0.99 – 1.09, p = 0.09). After adjusting for sex, age, race/ethnicity, and language, there were no differences in time to receive opioid analgesia by patient sex (n=205, aGMR 1.17, 95% CI 0.94 – 1.45, p = 0.16).

DISCUSSION:

We evaluated analgesia administration in male and female pediatric patients presenting to the ED with abdominal pain. Our cohort was predominantly female, with the proportion of female patients increasing with age and switching from a male to female predominance in adolescence. These demographics are consistent with other similar pediatric studies, based in both the ED (8,14) and ambulatory setting (15). In the NHAMCS, the number of male and female patients presenting with complaints related to stomach and abdominal pain is more similar under the age of 15 (3.1% of visits made by females, 2.4% by males), however, between 15 and 65 years, female patients make far more visits for this reason

(7.1% vs 3.3%, respectively)(16). Among adult patients, female patients consistently are the predominant population with abdominal pain (3,4).

Female patients received analgesics more often, but that difference was not significant in adjusted analyses. There are many potential confounding factors, including psychosocial explanations (17). Amongst patients in our study, females were more likely to report higher pain scores, which is a trend also seen in other research analyzing pain scores in the ED (18,19). The causes for this discrepancy in self-reported pain are multi-factorial and not easily elucidated despite extensive research (20,21). Multiple articles have shown that adult female patients are more likely to report increased pain in controlled experiments (21), which may be related to gendered expectations by which it is more acceptable for women and girls to report pain. Cultural norms and gender stereotypes have a profound impact on the reporting of pain and utilization of healthcare services (22). Furthermore, numerous studies have sought to understand the clinical significance of differences in pain scores. Female patients in our study had a median pain score 1 point higher than males, but there is evidence to suggest the minimal clinically significant difference in pain is 1.38 to 2 points (23–25). These studies focused on change in pain scores for individual patients, whereas our study utilized the initial pain score and cannot compare pain scores between individuals. In our study, the primary driver of analgesia receipt was pain score, which is clinically appropriate.

Our analysis showed that the time to any analgesia was longer for female patients; this effect was not persistent for opioid analgesia. Previous studies have suggested that the need for pregnancy tests or pelvic examinations may delay analgesia delivery in female patients (4). However, we found an increased time to analgesia for female patients *less than* 12 years of age, suggesting pregnancy tests were not responsible for the delay in analgesia administration. Further, these tests and examinations are only pertinent to a subset of adolescent patients and do not warrant withholding of analgesia, as many can be given to pregnant patients safely.

Another concerning finding was seen in the opioid analysis, in which non-White patients were less likely to be administered opioid medication. Unfortunately, this finding is consistent with prior literature, both in pediatric and adult patient populations (3). In one study of ED patients aged 11–21, non-Hispanic Black patients and Hispanic patients were less likely to be prescribed opioid analgesia than non-Hispanic White patients (3). This disparity was most pronounced in non-Hispanic Black females (26). Another study found that although they were more likely to receive any analgesia, Black and Hispanic pediatric patients were less likely to receive opioid analgesia when presenting to the ED (27). Although it is worth noting that administration of opioid analgesia is not always indicative of better care, disparities based on race and ethnicity suggest a different approach to care of patients depending on race and ethnicity with different races, which may be inappropriate or harmful.

The non-statistically significant trend that non-English speaking patients are less likely to receive pain medication is concerning, especially as this study was conducted in a hospital with a diverse patient population and robust translation services. Increased time

to analgesia may be understandable considering the need to locate the translator and time spent translating. However, this should not affect whether patients will eventually receive analgesia. Studies have shown that patients with limited English proficiency are at increased risk of longer hospital stays, lower rates of curative treatment, and more adverse events (28–31). Thus, this is a vulnerable population of children deserving of particular attention.

Any disparity in medical treatment, whether based on age, sex, race, or socioeconomic status, necessitates further investigation, with the goal of raising awareness and developing interventions that successfully mitigate bias and associated health disparities. Although our study did not show a significant disparity in analgesia receipt between female and male pediatric ED patients, it uncovered several concerning and hypothesis-generating trends worthy of further investigation. The overall inconsistencies in published data on sex-based disparities and the dearth of data on pediatric patients demonstrate a need for further study.

LIMITATIONS:

Our study's primary limitations are those inherent to its retrospective design and the inability to control for unmeasured confounders retrospectively. However, we took multiple steps to mitigate potential confounding variables in the analysis. This study was conducted at a single academic center, limiting its generalizability. Our center also defines pediatric patients as those under 21 years of age which, although consistent with literature and guidelines, may differ from other centers. The primary outcome of this study looked at the binary outcome of analgesia receipt, but did not evaluate whether appropriate dosing was utilized for that analgesia. Although our ED uses a visual scale when deemed appropriate by nursing staff (Wong-Baker FACES), younger patients may not be as reliable in their reporting. Very young patients almost never reported pain scores to our ED staff and thus were excluded from the study; as such our results are only generalizable to children over the age of five. This study excluded 3990 patients for which GCS was less than 15 or not populated, which could lead to a selection bias. However, the sample includes all eligible patients presenting 24 hours a day, so we expect any bias to be evenly distributed across all groups. Our definition of time to analgesia does not control for waiting time or ED crowding. It also does not account for any medications that may have been given by EMS or at home prior to presentation, which could affect the timing of medications administered in the ED. Part of this study was done during the COVID-19 pandemic, which may have influenced ED volumes and practice patterns.

Conclusion:

Among pediatric patients presenting to the ED for a chief complaint of abdominal pain, female patients were equally likely to receive analgesia as male patients in multivariable analyses, but their time to analgesia was significantly longer. Initial pain score was the most important predictor of receiving any analgesia and opioid. Additionally, non-White patients were less likely to receive opioid analgesia than White patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ARTICLE SUMMARY:

Why is this topic important?

Sex-based disparities are common in clinical medicine, including in analgesia where there is some evidence that female and male patients with pain may be treated differently. Most research on this topic focuses on adult populations and little is known about whether sex-based disparities exist in pediatric populations.

What does this study attempt to show?

We attempt to elucidate whether there are differences in the treatment of pain among male and female pediatric patients with abdominal pain in a tertiary care pediatric emergency department; this includes an evaluation of type of analgesia and time to analgesia for these patients.

What are the key findings?

After adjusting for age, initial pain score, race/ethnicity, and language, we found that male and female patients were equally likely to receive any analgesia, however, female patients experienced a longer time to analgesia. Additionally, non-White patients were found to be less likely to receive opioid analgesia than White patients.

How is patient care impacted?

Our study demonstrates that some of the disparities in analgesia seen in adults may extend to pediatric populations. Providers should be aware of this possibility and work to mitigate any disparities in their clinical environments, particularly for patients from vulnerable populations.

Table 1:

Baseline Characteristics

Characteristic	Female (n = 681)	Male (n = 406)	
	N (%) or Median (25th, 75th)	N (%) or Median (25th, 75th)	p-value
Age (years)	17 (13, 19)	14 (9, 18)	0.0003
Non-White Race/Ethnicity	504 (74.0%)	272 (67.0%)	0.01
Non-English Language	71 (10.4%)	41 (10.1%)	0.86
First Pain Score (1–10) *	7 (5, 9)	6 (4, 8)	<0.0001
Received Any Analgesic	371 (54.5%)	180 (44.3%)	0.001
Time to First Analgesic (mins)	123 (77, 201)	107 (73, 170)	0.036
Received Opioid Analgesic	132 (19.4%)	83 (20.4%)	0.67
Time to First Opioid (mins)	133 (69, 212)	91 (64, 171)	0.082

* n=601 females and n=313 males

Continuous variables are reported as median (25^{th}, 75^{th}) and categorical and binary variables are reported as N (%).

Table 2:

Adjusted Predictors of Analgesia Receipt and Time to Medication Administration

	Receipt of Any Analgesia (n=914*)		Time to Any Analgesia (n=518)		Receipt of Opioid Analgesia (n=914)		Time to Opioid Analgesia (n=205)	
	OR (95% CI)	p-value	GMR (95% CI)	p-value	OR (95% CI)	p-value	GMR (95% CI)	p-value
First Pain Score	1.22 (1.16, 1.29)	<0.01	0.98 (0.96, 1.01)	0.15	1.31 (1.21, 1.41)	<0.01	0.97 (0.92, 1.02)	0.17
Female Sex	1.30 (0.97, 1.74)	0.08	1.14 (1.00, 1.29)	0.04	0.74 (0.53, 1.05)	0.09	1.17 (0.94, 1.45)	0.16
Non-White Race/Ethnicity	0.98 (0.72, 1.33)	0.88	0.91 (0.80, 1.04)	0.15	0.68 (0.47, 0.97)	0.04	1.00 (0.81, 1.24)	0.99
Non-English Language	0.64 (0.40, 1.01)	0.06	1.18 (0.96, 1.46)	0.11	0.93 (0.52, 1.67)	0.81	1.04 (0.72, 1.49)	0.84
Age	1.01 (0.97, 1.04)	0.79	0.99 (0.97, 1.01)	0.20	1.04 (0.99, 1.09)	0.09	0.99 (0.97, 1.03)	0.84

OR = Odds Ratio; GMR = Geometric Mean Ratio

*Patients with missing data were excluded from the regression analysis