Patient Preference and Adherence

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ORIGINAL RESEARCH

# Adherence to Opioids for Cancer-Related Pain Among Patients with Cancer in a Resource-Restricted Hospital in Palestine

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**Purpose:** Cancer-related pain is a critical symptom that significantly impacts patients' quality of life. This study aimed to assess adherence and identify factors influencing adherence to opioid analgesics for cancer-related pain among cancer patients at a hospital setting in Gaza, Palestine.

**Patients and Methods:** A cross-sectional study was conducted from December 2021 to March 2022, involving cancer patients receiving opioid for cancer-related pain. Participants completed a set of questionnaires on socioeconomic data, pain intensity and interference using the Brief Pain Inventory (BPI), adherence to opioids using the General Medication Adherence Scale (GMAS), and beliefs about pain and opioids using the Pain and Opioid Analgesic Beliefs-Cancer (POASB-CA) scale. Patients' clinical data were collected from the patients' medical records. Simple and multiple linear regression analyses were utilized to elucidate factors associated with adherence towards opioids for cancer-related pain.

**Results:** A total of 270 patients were recruited. Most patients (88.5%) were at least partially adherent to the opioid analgesic. The average pain intensity score was 5.796 (SD = 1.98), and pain interference scored 7.093 (SD = 3.63). Simple linear regression identified the following parameters to be significantly associated with adherence: education level, presence of comorbidity, average percentage of pain relief experienced over the past 24 hours, negative effect beliefs and pain endurance beliefs. Based on multiple linear regression analysis, education level, percentage of pain relief and presence of side effects were positive predictors of higher adherence score (B=1.082, CI 0.139 to 2.025, p=0.025; B=0.076, CI 0.046 to 0.105, p<0.001 and B=1.578, CI 0.116 to 3.041, p=0.034, respectively).

**Conclusion:** Adherence to opioids for cancer-related pain was generally good. Influencing factors included education level, average pain relief in the past 24 hours, and opioid side effects. These results highlight the complex nature of adherence in managing cancer pain and suggest areas for targeted interventions.

**Keywords:** analgesics, compliance, pain management, oncology patients

## Introduction

Pain significantly affects the quality of life for cancer patients.[1] Pain is reported by 50% of patients undergoing active treatment and by as many as 90% of those with advanced cancer.[2] It can heighten psychological distress, restrict social activities, and even reduce survival rates in some cancer patients,[3] especially those with advanced cancers.[4]

Despite advancements in pain management protocols, addressing cancer-related pain remains a major challenge for both patients and clinicians.[5] Managing cancer-related pain is particularly challenging in resource-limited settings due to inadequate availability and access to opioid analgesics, which are essential for effective pain management. This challenge is compounded by the fact that many patients in such settings are first diagnosed at advanced stages of cancer.[6] The Turkish Palestinian Friendship Hospital (TPFH) in Gaza, Palestine is classified as a resource-limited setting, where this present study was conducted.



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Opioid analgesics are the cornerstone of pharmacological pain management in cancer care, used either alone or in combination with other analgesics for moderate to severe pain after thorough assessment.[1] In 1986, the WHO introduced a three-step ladder approach to pain management, recommending non-opioid analgesics (eg paracetamol) for mild pain, weak opioids (eg tramadol, codeine) for moderate pain and strong opioids (eg, morphine, fentanyl, oxycodone) for severe pain. This framework has since been widely adopted.[7] However, evidence suggests that cancer pain control remains suboptimal, with ongoing negative impacts on patients' psychological well-being, physical functioning, and overall quality of life.[8–10] Guidance tailored to the realities of low- and middle-income countries (LMICs) is critical, particularly for opioid analgesic use, where accessibility, availability and prescribing knowledge remain limited.[11]

Adherence to prescribed medications is crucial for achieving positive patient outcomes and reliably evaluating treatment efficacy.[12] Improving medication adherence is among the most practical and effective strategies to enhance both cost-effectiveness and overall health outcomes.[13] This issue is further compounded in resource-restricted settings where alternatives are limited. Therefore, understanding not only adherence patterns but also the underlying personal and system-level barriers is crucial.[6]

Patient beliefs about pain and opioid use also play a significant role in adherence and treatment success. Misconceptions, such as fear of addiction, beliefs about pain endurance, or stigma can lead to intentional or unintentional nonadherence. However, these cognitive and cultural aspects are often underexplored in clinical research despite their importance for treatment outcomes.[14]

This study aimed to assess adherence to opioid analgesics and identify its associated factors, including pain beliefs, among patients with cancer in a resource-restricted hospital in Gaza, Palestine.

# Materials and Methods

## Study Design and Participants

This cross-sectional study was conducted at the Turkish Palestinian Friendship Hospital (TPFH) in Gaza between April 2022 to December 2022, focusing on oncology patients experiencing cancer-related pain. The study utilized validated questionnaires to collect data and was carried out with ethical approval and informed consent from all participants. Patients were enrolled in this study if they met the following inclusion criteria: 1) aged ≥ 18 years old diagnosed with cancer, 2) diagnosed with cancer related pain by an oncologist, 3) prescribed with opioid analgesics for cancer pain for at least three months, 3) conscious and able to sign the informed consent form. Patients who refused to participate or provided incomplete responses to the questionnaire were excluded.

This study was approved by the Research Ethics Committee of Universiti Kebangsaan Malaysia (Approval Reference: JEP-2022-237) and the Research Ethics Committee (Helsinki) in the Palestinian Ministry of Health (Approval Reference: PHRC/HC/1014/21). All procedures were conducted in compliance with the ethical standards established in the 1964 Declaration of Helsinki and its subsequent amendments. Patients were identified by the researcher through screening of patients' medical records and were selected using convenience sampling. Patient information sheet was used to explain the study to potential participants. Those who agreed to participate signed the informed consent prior to study commencement.

## Measures

The data collection tool used was a structured questionnaire, available in both English and Arabic versions, obtained with permission from the original authors. The questionnaire was divided into three sections. The first section collected demographic and socioeconomic information, including age, sex, level of education and household monthly income. This section also included clinical details such as cancer type, which was coded based on the ICD-10 classification system;[15] cancer stage, presence of comorbidity (presence of any chronic diseases such as diabetes, hypertension etc) and types of opioids used. The second section evaluated pain intensity and its effect on daily activities using the Brief Pain Inventory (BPI) in Arabic language, comprising nine items.[16] This section included questions on pain intensity (rated from 0 to 10), medications used for pain, pain interference (rated from 0 to 10) assessing the impact of pain on daily activities as well as the percentage of pain relief experienced in the past 24 hours (0–100%).[16]

The third section evaluated medication adherence using the General Medication Adherence Scale (GMAS).[17] This section included 11 questions assessing adherence behaviors, with responses ranging from "Always" to "Never." The GMAS score ranges from 0 to 33. Based on the original validation study by Naqvi et al (2018), adherence was categorized according to the total score as follows: low adherence (scores 3–15), partial adherence (scores 16–25), and high adherence (scores 26–33).[17] The Pain and Opioid Analgesic Beliefs - Cancer (POASB-CA) scale was included in the fourth section, which explored beliefs about opioid use and pain tolerance. Since an Arabic version was not available in the literature, the scale was translated into Arabic, validated by experts, and back-translated into English to ensure accuracy and reliability. This 10-item questionnaire uses a 5-point Likert scale, ranging from 0 ("Strongly Disagree") to 4 ("Strongly Agree"), to measure beliefs related to pain and opioid analgesics. It includes two subscales: negative effect beliefs, which focus on concerns about opioids, and pain endurance beliefs, which reflect attitudes toward enduring pain. Subscale scores were calculated as the average of the corresponding items, with higher scores indicating stronger negative beliefs about cancer pain and opioid use.[18] A data collection form was used to record information from patients' medical records on disease information such as cancer diagnosis, treatment status, staging, presence of metastasis (if any).

## Procedures

Data collection was conducted by trained research pharmacists who assisted participants in completing the questionnaires. Clinical data and prescribed opioid regimens were retrieved from electronic patient records. A pilot study was conducted with 10 patients to ensure clarity and comprehension of the questionnaire. Participants from the pilot study were excluded from the final sample.

## Statistical Analysis

Data were analyzed using IBM® SPSS Desktop version 24. Descriptive statistics were applied, with categorical data presented as frequencies and percentages. Continuous data were tested for normality using the Shapiro–Wilk test. For normally distributed data, such as age, results were reported as mean and standard deviation (SD), while non-normally distributed data, such as disease duration (in months) and pain interference, were reported as the median. Twenty-two separate simple linear regressions were performed, each assessing the relationship between a variable and the adherence score. The variables analyzed include socioeconomic factors (age, sex, level of education, and monthly income) and clinical data (pain intensity, pain interference, negative beliefs about opioids and pain endurance beliefs, cancer stage, cancer duration, cancer type, percentage of pain relief from opioids, other medications, comorbidities, and the presence of side effects). All 22 variables also underwent multiple linear regression analysis. Only variables with a p-value less than 0.05 were included in the final model using the stepwise method. Checks for interaction effects, multicollinearity, and model fit including the normality of residuals, linearity, homoscedasticity (equal variance), the linear relationship between residuals and selected independent variables, and the presence of potential outliers were conducted. The final model, which met all required assumptions and was free from influential outliers, was then used to interpret the relationship between adherence to opioids for cancer-related pain and each independent variable. A 95% confidence interval was utilized, and statistical significance was denoted by a p-value of $<0.05$.

# Results

A total of 270 individuals from the Turkish Palestinian Friendship Hospital participated in this study. The participants had a mean age of 53.1 years and a median disease duration of 36 months. In terms of educational attainment, 50.4% had completed primary education. The majority of the participants were married (80.4%, 217 patients) and had a monthly household income of less than 200 USD (68.1%, 184 patients). Breast cancer was the most common prevalent diagnosis (27.7%), followed by hematological malignancies (14%) and gastrointestinal cancers (12%). Details of the sociodemographic and clinical data of the participants are shown in Table 1.

The mean pain intensity score, assessed using the Brief Pain Inventory (BPI), was 5.7 (SD = 1.98), indicating moderate pain on the Numerical Rating Scale (NRS). The mean pain interference score, which measures the impact of pain on daily activities, was 7.3 (SD = 3.63). Additionally, the average percentage of pain relief experienced over the past

**Table 1** Sociodemographic and Clinical Data of the Participants (n=270)

| Characteristics | N (%) |
|---|---|
| Sex | |
| Male | 118 (43.7) |
| Female | 152 (65.3) |
| Marital status | |
| Single | 24 (8.8) |
| Married | 217 (80.3) |
| Divorced | 29 (10.8) |
| Educational level | |
| Primary Education (Grades 1–4; Age 6–10 years) | 136 (50.4) |
| Secondary Education (Grades 5–9; Age 11–17 years) | 76 (28.1) |
| Tertiary Education (Diploma/ Bachelor's degree; Age ≥ 18 years) | 47 (17.4) |
| Employment status | |
| Employed | 37 (14) |
| Unemployed | 233 (86) |
| Household income per month | |
| < 1000 SHEKEL (USD < 200) | 188 (69) |
| 1000–2999 SHEKEL (USD 200–799) | 39 (34) |
| 3000–4999 SHEKEL (USD 800–1299) | 24 (12.5) |
| ≥ 5000 SHEKEL (USD ≥ 1300) | 19 (7) |
| Cancer type | |
| Brain (C71, C71.8, C71.9) | 10 (3.7) |
| Breast (C50) | 64 (23.7) |
| Lung (C43) | 20 (7.4) |
| Osteosarcoma (C49) | 9 (3.3) |
| Thyroid (C73) | 11 (4.1) |
| Hematology (C90) | 38 (14.1) |
| Gastrointestinal (C16, C18, C18.9, C20) | 34 (12.6) |
| Others | 84 (31.1) |
| Stage | |
| 1 | 73 (27) |
| 2 | 30 (11.1) |
| 3 | 5 (1.9) |
| 4 | 162 (60) |

(*Continued*)

**Table 1** (Continued).

| Characteristics | N (%) |
|---|---|
| Presence of comorbidity | |
| Yes | 201 (74.4) |
| No | 69 (25.6) |
| Opioids used | |
| Morphine continuous release (MCR) | 64 (24) |
| Morphine immediate release (MIR) | 17 (6.3) |
| Oxycodone 5mg + paracetamol 500mg | 8 (3) |
| Tramadol | 163 (60) |

24 hours was 70.5% (SD = 24.20%). The mean score for negative effect beliefs and pain endurance beliefs based on the Pain and Opioid Analgesic Beliefs - Cancer (POASB-CA) scale was 20.7 (SD = 4.85) and 9.1 (SD = 3.76), respectively. Adherence to opioid therapy, as measured by the General Medication Adherence Scale (GMAS), revealed the following results: 73 patients (27%) were highly adherent (scores 26–33), 161 patients (61.5%) were partially adherent (scores 16–25), and 31 patients (11%) were non-adherent (scores 3–15).

Both simple and multiple linear regression analyses of the results revealed that the education level was a positive predictor of higher adherence score (B=1.02, CI 0.047 to 1.992, p=0.040 and B=1.082, CI 0.139 to 2.025, p=0.025, respectively). The average percentage of pain relief experienced over the past 24 hours based on the BPI questionnaire was also a positive predictor of higher adherence score based on both simple and multiple linear regression analyses (B=0.07, CI 0.041 to 0.100, p<0.001 and B=0.076, CI 0.046 to 0.105, p<0.001, respectively). Negative effect beliefs and pain endurance beliefs based on the POASB-CA scale were both significant in simple but not in multiple linear regression. This was similarly seen for presence of comorbidity. The presence of side effects was a significant predictor in multiple linear regression; however, it was not significant in simple linear regression analysis. Other variables did not show any significant relationship with adherence scores (Tables 2 and 3).

## Discussion

Managing cancer-related pain is particularly challenging in resource-limited settings due to limited access to opioid analgesics, insufficient clinical infrastructure, and delays in diagnosis.[6] The Turkish Palestinian Friendship Hospital (TPFH), where this study was conducted, exemplifies such a setting. In Gaza, shortages of chemotherapy, hormonal therapy, radiation, and immune-targeted therapies may have led to a higher proportion of late-stage cancer diagnoses, with 60% of patients in this study presenting at stage IV. All patients in the study were on opioids, which included tramadol, morphine continuous release (MCR) 30 mg, morphine immediate release (MIR) 15 mg, and oxycodone 5 mg with paracetamol 325 mg.

The mean pain intensity score was 5.7 (moderate pain) on the Brief Pain Inventory (BPI) scale, which is higher than the 4.6 mean score reported by Yeager et al[19] among black patients at a tertiary care cancer center in the United States. Pain interference scores in this study averaged 7.3, higher than that reported by other studies,[14,20] further reflecting the inadequacy of pain control among cancer patients in TPFH. More than 80% of our patients were at least partially adherent to the opioids. A similar high adherence to opioids for cancer-related pain utilizing other self-reported adherence questionnaires has also been reported in the literature.[14]

In the present study, education level, presence of comorbidity, average percentage of pain relief experienced over the past 24 hours based on the BPI questionnaire as well as negative effect beliefs and pain endurance beliefs based on the

**Table 2** Simple Linear Regression on Factors Influencing Adherence to Opioid Analgesic

| Variables | Beta Coefficient | Std. Error | T | Sig. | 95% Confidence Interval for B | |
|---|---|---|---|---|---|---|
| Socioeconomic variables | | | | | | |
| Education level | 1.02 | 0.494 | 2.064 | **0.040** | 0.047 | 1.992 |
| Age | −0.02 | 0.025 | −0.635 | 0.526 | −0.066 | 0.034 |
| Monthly income | 0.67 | 0.396 | 1.687 | 0.093 | −0.112 | 1.449 |
| Sex | −0.85 | 0.746 | −1.136 | 0.257 | −2.315 | 0.621 |
| Clinical Data | | | | | | |
| Cancer stage | −0.08 | 0.277 | −0.274 | 0.785 | −0.621 | 0.47 |
| Use of other medication | −0.84 | 0.848 | −0.985 | 0.325 | −2.506 | 0.834 |
| Presence of comorbidity | −1.59 | 0.746 | −2.127 | **0.034** | −3.056 | −0.118 |
| Presence of side effects | 1.03 | 0.746 | 1.374 | 0.171 | −0.444 | 2.495 |
| Cancer duration | 0.01 | 0.007 | 1.222 | 0.223 | −0.005 | 0.023 |
| Type of cancer | | | | | | |
| Breast | 2.12 | 1.959 | 1.084 | 0.279 | −1.733 | 5.979 |
| Brain | −0.17 | 0.872 | −0.192 | 0.848 | −1.883 | 1.549 |
| Lung | 2.37 | 1.408 | 1.683 | 0.094 | −0.402 | 5.142 |
| Osteosarcoma | −0.76 | 2.065 | −0.367 | 0.714 | −4.823 | 3.306 |
| Thyroid | 1.92 | 1.959 | 0.978 | 0.329 | −1.942 | 5.773 |
| Hematology | 0.62 | 1.054 | 0.590 | 0.556 | −1.453 | 2.696 |
| Gastrointestinal | −1.18 | 1.041 | −1.134 | 0.258 | −3.230 | 0.869 |
| Other | −0.88 | 0.816 | −1.072 | 0.285 | −2.482 | 0.732 |
| POABS-CA | | | | | | |
| Negative opioid beliefs | −0.23 | 0.075 | −2.984 | **0.003** | −0.373 | −0.077 |
| Endurance beliefs | −0.21 | 0.098 | −2.094 | **0.037** | −0.398 | −0.012 |
| BPI | | | | | | |
| Pain intensity | −0.02 | 0.187 | −0.109 | 0.914 | −0.389 | 0.348 |
| Pain interference | −0.04 | 0.142 | −0.283 | 0.777 | −0.319 | 0.239 |
| Percentage of relief | 0.07 | 0.015 | 4.704 | **<0.001** | 0.041 | 0.100 |

**Note:** Bold values indicate significance at P<0.05.
**Abbreviations**: POABS-CA, pain and opioid analgesic beliefs scale cancer; BPI, brief pain inventory.

POASB-CA scale were significantly associated with adherence based on simple linear regression. In our study, patients who reported higher relief from opioids (as assessed by the BPI) had significantly better adherence scores, which revealed similar trends with the findings reported by Yeager et al[19] utilizing the Barriers Questionnaire-13 (BQ-13) to measure beliefs and adherence. Although these were not found to be significant in the final regression model in the present study, they may still exert indirect influence via perceived pain relief or educational background. Other studies using the POABS-CA also reported that negative beliefs about opioids and a tendency to endure pain were associated

**Table 3** Multiple Linear Regression on Factors Influencing Adherence to Opioid Analgesics

| Variables | Beta Coefficient | Std. Error | T | Sig. | 95% Confidence Interval for B | |
|---|---|---|---|---|---|---|
| Education level | 1.082 | 0.479 | 2.259 | 0.025 | 0.139 | 2.025 |
| Percentage of relief | 0.076 | 0.015 | 4.969 | <0.001 | 0.046 | 0.105 |
| Presence of side effects | 1.578 | 0.742 | 2.126 | 0.034 | 0.116 | 3.041 |

**Notes**: All 22 variables were included in the variable selection process and the stepwise elimination was applied. The multicollinearity assumption for the variables was met. Interaction terms were checked. There was no interaction between variables. The overall fit of the model was checked and reported and considered fit according to the following: Residual of the model was normally distributed. Scatter dot plot shows linearity and equal variance between residual and predicted values. Scatter plot between residual and every independent variable show linear relationship.

with lower adherence.[14,21,22] Nonetheless, education level and average percentage of pain relief remained significant in multiple linear regression in the present study. The presence of side effects was the only other variable found to be significant in multiple linear regression; however, it was not significant based on simple linear regression. Other variables such as age, sex, monthly income, cancer type, cancer duration, cancer stage and use of other medications were not found to be significantly associated with adherence.

Few studies investigated factors that are associated with adherence. However, different methods of adherence assessment and variables investigated as possible factors between these studies make direct comparison difficult. Kan et al investigated the relationship between adherence to opioid analgesics and pain beliefs among patients with cancer pain at tertiary care hospitals in Malaysia and found that negative effect beliefs, pain endurance beliefs, pain interference composite score, aqueous morphine, SR morphine and strong opioids were significant factors towards opioid adherence based on simple linear regression analysis. However, in multiple linear regression, only negative effect beliefs, pain endurance beliefs, pain interference composite score and use of aqueous morphine remained significant. Other factors such as age, sex, education level and duration of treatment were not significant.[14]

Seangrung et al investigated the influence of socioeconomic factors, clinical data, patient understanding of pain and opioid use, and the number of medications on adherence. The study was conducted among cancer patients on strong opioids from a pain clinic in Thailand. They reported that age, sex, monthly income, education level, marital status, and employment status were not significantly associated with adherence.[21] However, a key difference is that our study identified educational level as a significant predictor of adherence, whereas Seangrung et al did not. Seangrung et al also observed that the use of multiple medications, patients' understanding of their pain and opioid use significantly influenced adherence.[21]

Graziottin et al reviewed factors hindering adherence to opioids and identified fear of side effects as a key barrier.[23] Similarly, Trafton et al identified the presence of side effects as a significant predictor of opioid use patterns.[24] Interestingly, contrary to these studies, the presence of side effects was found to improve adherence instead in our study. This could possibly be because those who are taking an opioid regularly are more prone to experiencing its side compared to non-adherent patients.

The variations in factors associated with adherence to opioids for cancer pain highlight how different studies may yield varying results depending on the sample population, study design, and focus areas. While some findings aligned, such as the insignificance of many socioeconomic factors, differences in the predictors identified underscore the importance of contextual and population-specific factors in adherence research. Identification of factors that influence adherence according to each population and setting is crucial to enable appropriate interventions to be implemented in overcoming non-adherence. Educational interventions targeting beliefs about pain and opioids, as demonstrated by Capewell et al[25] and Liu et al[10] have been shown to improve adherence significantly, which can be implemented in response to the present study findings.

This study has several limitations. First, adherence was assessed through self-report, which may be subject to recall or social desirability bias. Second, the study was conducted in a single, resource-limited setting, which may affect the generalizability of the findings to other populations or healthcare contexts. Third, although multiple factors influencing

adherence were examined, other unmeasured variables such as prior opioid use experience and psychological status (eg depression, anxiety), cultural beliefs, and systemic healthcare barriers may also play a role and should be considered in future investigations.

## Conclusion

Adherence to opioids for cancer-related pain was relatively good among patients in the present study. Factors associated with adherence in the final model include education level, the average percentage of pain relief experienced over the past 24 hours and presence of opioid side effects. The findings emphasize the multifactorial nature of adherence in cancer pain management, highlighting areas where interventions to improve adherence can be focused on.

## Abbreviations

BPI, brief pain inventory; GMAS, general medication adherence scale; MCR, morphine continuous release; MIR, morphine immediate release; POABS-CA, pain and opioid analgesic beliefs scale cancer; TPFH, The Turkish Palestinian Friendship Hospital; WHO, world health organization.

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## Disclosure

The authors report no conflicts of interest in this work.

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