ORIGINAL ARTICLE

Prevalence of Severe Pain and Inadequate Pain Treatment, Satisfaction, Quality of Life and Factors Associated with Severe Pain among Cancer Patients Receiving Palliative Care in Penang

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ABSTRACT

Introduction: Pain is prevalent and debilitating in cancer patients, particularly at advanced stages. However, data on pain control in this population is limited in Malaysia. Objective: This cross-sectional study aimed to determine the prevalence of severe pain and inadequate pain treatment, satisfaction with pain treatment, quality of life (QoL), and factors associated with severe pain among cancer patients receiving palliative care in Penang. Material and **Methods:** Eligible patients were recruited using convenience sampling from June 2019 to March 2020. Data was collected using validated interviewer-administered questionnaires. Pain severity, inadequate pain treatment, satisfaction with pain treatment and QoL were assessed using Numeric Pain Rating Scale, Pain Management Index (PMI), Treatment Satisfaction Questionnaire for Medication version 1.4 (TSQM 1.4) and European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 15 Palliative Care(EORTC QLQ-C15-PAL), respectively. **Results:** Of 162 patients, 35.8% experienced severe pain and 17.3% had negative PMI. The mean (SD) score of global satisfaction with pain treatment was 61.8±16.33. Patients showed diminished QoL, negatively affecting both physical and emotional functioning with the mean (SD) QoL score of 54.4±24.63. Negative PMI ($p<0.001$), lower global satisfaction score ($p=0.005$), higher insomnia score ($p<0.047$), and the interaction between adjuvant analgesics use and global satisfaction score ($p<0.002$) were significantly associated with severe pain. **Conclusion:** There is a need to improve pain management for the cancer patients under palliative care in Penang. Identifying patient subgroups experiencing severe pain and inadequate pain treatment is crucial for timely intervention.

Keywords: Cancer pain; Palliative care; Pain management; Patient satisfaction; Quality of life

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INTRODUCTION

The global burden of cancer grows rapidly. According to the International Agency for Research on Cancer (IARC), there were about 19.3 million new cases and 9.96 million deaths due to cancer worldwide in 2020 (1). The number of new cancer cases is estimated to increase by more than 50% to 30.2 million by 2040, while cancer deaths are projected to reach 16.3 million (1). The increasing trends of cancer cases and mortality pose significant challenges in managing this population especially those in the terminal stage. Literature has shown that advanced cancer patients typically have a high symptom burden, with pain being one of the most common and devastating symptoms (2).

A systematic review of studies published between 2014 and 2021 found that 54.6% of patients with advanced, metastatic or terminal cancer experienced pain, with 40.7% reporting moderate to severe pain (3). Severe or poorly controlled pain is often associated with a negative impact on quality of life (QoL) (4), compromised ability to cope with illness (5), disruption of cancer therapy (5), high complexity of pain treatment (6), increased desire for hastened death (7), frequent hospitalizations (8), and poorer survival (9).

Factors related to pain severity, such as socio-demographic factors, clinical factors, and treatment-related factors, have been studied. However, some of the findings were inconsistent across the studies (10-13). The divergent results were likely influenced by differences in study settings, methodologies, target populations, clinical characteristics, and various other factors. Therefore, it is essential to identify the influential factors in our local context and to recognize patient subgroups experiencing high-intensity pain that need prompt attention.

In Malaysia, research on the management of pain in cancer patients receiving palliative care receives little attention, and the available data are limited. Existing studies primarily focus on pain prevalence, severity of

pain and adequacy of pain management (14). Findings from the studies conducted in developed nations may not be directly applicable in the context of Malaysia, due to several factors such as the level of integration of palliative care into cancer care, healthcare resources, accessibility to palliative care services, and the diverse perceptions towards pain treatment in population with different socio-cultural backgrounds.

In this study, we investigated broader aspects of pain management, including the prevalence of severe pain and inadequate pain treatment, patient satisfaction with pain treatment, quality of life and factors associated with severe pain.

MATERIALS AND METHODS

Study design and study setting

This cross-sectional study was conducted at three palliative care units in Penang state from June 2019 to March 2020. The Penang General Hospital Palliative Care Specialist Clinic operates twice a week, where patients are reviewed by a team of Medical Officers led by a resident Palliative Care Consultant and/or Specialists. The Bukit Mertajam Hospital Palliative Care Clinic runs on a biweekly basis, with the presence of visiting Consultants or Specialists. At the Perak Road Palliative Care Unit, a subsidiary of Penang General Hospital Palliative Care, doctors occasionally review outpatients with scheduled appointments or walk-in cases.

Subject recruitment and data collection

In this study, the convenience sampling method was used to recruit subjects. Subjects were selected from a pool of patients based on their availability and accessibility on clinic days. The patients who met the eligibility criteria were approached but it relied on the interest or willingness of the individuals to participate. The inclusion criteria included being 18 years or older, being diagnosed with cancer, receiving out-patient palliative care, being prescribed analgesics or having untreated pain, and able to understand and answer questionnaires in English, Malay or Mandarin. Patients with cognitive, mental, or verbal impairment, and those who were too ill or frail, were excluded from the study. Informed consent was obtained from the patients and data was collected using interviewer-administered questionnaires. The sole interviewer in this study is a qualified and proficient healthcare professional who has been trained by experienced university researchers to conduct research and collect data. The data collection process was supervised by a Palliative Consultant/ Specialist.

Sample size

The sample size was estimated using the population proportion formula (15) based on the prevalence of severe cancer pain in a nationwide cross-sectional study conducted by Yamagishi et al. (16) in Japan. The rationale for choosing this study in the sample size calculation was its representation of an Asian population and the similarity of the study setting to the present study, focusing on outpatient palliative patients. This aspect is absent in both the Malaysian study, (14) which is limited to an inpatient setting, and the systematic review, (3) which encompasses mixed settings. A sample size of 190 was calculated with a confidence level of 95%, a precision level of 5% and an allowance of 10% for missing data.

Ethical approval

This study was approved by the Medical Research and Ethics Committee (MREC) and the research ID is NMRR-19-927-46270 (IIR).

Instruments

Case Report Form (CRF)

The Case Report Form was designed to gather patients' socio-demographic data, medical information and medication history from the medical records and interviews. Its validity was evaluated by three experts in palliative care and research.

Eastern Cooperative Oncology Group (ECOG)

The functional status of the patients was assessed by the attending doctors using ECOG Performance Status Scale (17).

Numeric Pain Rating Scale (NPRS)

Pain characteristics such as intensity, type, nature, timing and the incidence of breakthrough pain were also recorded. Pain intensity of "worst", "least", "average" and "now" in the past 24 hours were assessed using an 11-point Numeric Pain Rating Scale (18), with "0" indicating "no pain" and "10" denoting "worst pain imaginable". Pain scores were categorized as mild, moderate and severe at 1-4, 5-6 and 7-10 respectively (19).

Pain Management Index (PMI)

PMI was calculated by subtracting the patient-rated worst pain category score from the most potent analgesic category score (20). A positive value of PMI indicates acceptable pain management, whereas a negative PMI suggests potentially inadequate pain treatment.

Morphine Equivalent Daily Dose (MEDD)

For the patients who were prescribed weak or strong opioids, MEDD was calculated based on the conversion factors (21).

European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 15 Palliative Care (EORTC QLQ-C15-PAL)

The quality of life of the patients was assessed using the EORTC QLQ-C15-PAL (22, 23) in three language

versions: English, Malaysian Malay and Malaysian Chinese. It is abbreviated from the well-established EORTC QLQ-C30 (24), comprising 15 items identified as important and relevant in palliative care (22, 23). The scoring for each domain ranges from 0 to 100. Higher scores on the functioning scale indicate increased levels of functioning, and similarly higher scores on the global QoL scale correspond to better QoL. Conversely, on symptom scales, higher scores represent greater symptom burden. Despite its brevity, QLQ-C15-PAL shows similar coverage and predictive ability to those of QLQ-C30 (25). It has demonstrated good internal consistency (Cronbach's alpha ≥0.7), scalability (Spearman correlation coefficients ≥0.4), and convergent and discriminant validity for most items (26). The parent instrument has been psychometrically validated in Malaysian cancer patients across various settings and cancer types, showing good internal consistencies (Cronbach's alpha ≥0.70), test-retest reliability (Intraclass Correlation Coefficients ≥0.50), and meeting the criteria for convergent and discriminant validity for most items (27-29). Permission to use the original and translated versions was obtained from the copyright owners.

Treatment Satisfaction Questionnaire for Medication Version 1.4 (TSQM 1.4)

The TSQM 1.4 (30) was used to evaluate patient satisfaction with pain treatment, including the English version, and the translations in Malaysian Malay and Malaysian Chinese. Permission to use these three versions was granted by the copyright holder. The translations were performed by Oxford Outcomes Ltd, an organization specializing in the translation and linguistic validation of patient-reported outcome measures. The Malaysian Malay version underwent rigorous methodology, including forward-backward translation, pilot testing, and proofreading by native speakers, whereas the Malaysian Chinese version underwent a review process that did not involve pilot testing. Each domain is assigned a score between 0 and 100, with higher scores indicating increased levels of satisfaction. TSQM 1.4 has demonstrated good psychometric properties across patients with diverse medical conditions, including cancer, and taking a wide range of medications, with Cronbach's alpha values of 0.85, 0.87, 0.87, and 0.85 for the domains of effectiveness, side effects, convenience, and global satisfaction, respectively (30). Despite the lack of psychometric validation in the Malaysian cancer population, TSQM 1.4 underwent a comprehensive evaluation by three experts in palliative care and research to ensure the clarity, relevance, and appropriateness of language before its application in this study.

Statistical analysis

IBM SPSS version 26.0 was used for data entry and analysis. The demographics, clinical data, prevalence of severe cancer pain and inadequate pain treatment, satisfaction ratings, and quality of life scores were summarized using descriptive statistics, such as mean (± standard deviation, SD), median (± interquartile range, IQR), and frequency (%). Simple logistic regression analysis was performed to examine the clinical and socio-demographic variables associated with severe pain. Variables with *p*-value less than 0.25 (31) were selected and further analyzed using multiple logistic regression with Forward LR, Backward LR and Enter method, to determine the definite factors associated with severe pain. All *p*-values were two-tailed, and a value of less than 0.05 was considered statistically significant.

RESULTS

Socio-demographic data and clinical characteristics

Out of 516 patients screened, 162 were enrolled for the study. The flowchart of patient recruitment is depicted in Fig. 1. The mean (SD) age of the patients was 61.4±1.09 years (range 18 - 89 years) and the proportion of females was slightly higher than males. The majority of the patients were Chinese (59.3%, n=96), followed by Malays (23.5%, n=38), Indian (16.7%, n=27) and others (0.6%, n=1). Most patients (75.3%, n=122) had better performance status (ECOG 0-2). The three most common types of cancer were breast cancer (19.8%, n=32), colorectal cancer (17.3%, n=28) and lung cancer (9.3%, n=15). Most patients (67.9%, n=110) had stage 4 cancer and 16% (n=26) had recurrent cancer. Over 70% of the patients (n=118) were diagnosed with metastatic cancer and among them, 55.9% (n=66) had bone metastasis. More than half of the patients had prior or on-going cancer treatment such as surgery, chemotherapy and radiotherapy. The demographics and clinical characteristics of the study population are summarized in Table I.

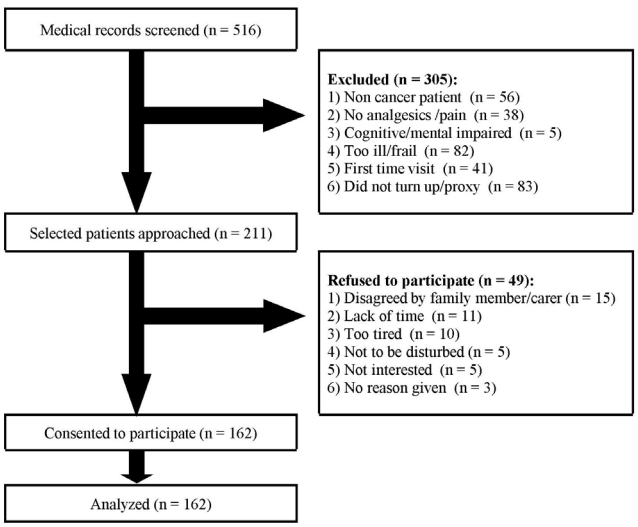

Fig. 1 : Patient recruitment.

Table I : Socio-demographic and clinical characteristics of study population

Variables	Number of patients	
	n	(%)
Age, mean (SD)	61.4	(1.09)
< 30	3	(1.9)
30 - 39	8	(5.0)
40 - 49	17	(10.5)
50 - 59	39	(24.1)
60 - 69	50	(30.8)
70 - 79	32	(19.7)
80 & above	13	(8.0)
Gender		
Male	78	(48.1)
Female	84	(51.9)
Race		
Malay	38	(23.5)
Chinese	96	(59.3)
Indian	27	(16.7)
Others	1	(0.6)
ECOG performance status		
ECOG 0 - 2	122	(75.3)
ECOG 3 - 4	40	(24.7)
Cancer type		
Head & neck	18	(11.1)
Nasopharyngeal	4	(2.5)
Oropharyngeal	1	(0.6)
Laryngeal	1	(0.6)
Lip and oral cavity	3	(1.9)
Salivary gland	3	(1.9)
Paranasal sinus and nasal cavity	2	(1.2)
Thyroid	2	(1.2)
Glioma	1	(0.6)
Angiosarcoma	1	(0.6)
Breast	32	(19.8)
Lung	15	(9.3)
Gastrointestinal	51	(31.5)
Colorectal	28	(17.3)
Liver	11	(6.8)
Pancreas	5	(3.1)
Oesophagus	4	(2.5)
Bile duct	2	(1.2)
GIST	1	(0.6)
Gynaecological	11	(6.8)
Cervical	4	(2.5)
Ovarian	3	(1.9)
Uterine	2	(1.2)
Vaginal	2	(1.2)
Genitourinary	22	(13.6)
Prostate	10	(6.2)
Renal	7	(4.3)
Bladder	4	(2.5)
Testes	1	(0.6)
Haematological	2	(1.2)
Others	5	(3.1)
> 1 primary cancer	4	(2.5)
Unknown origin	2	(1.2)
Cancer stage		
Stage 1-2	4	(2.5)
Stage 3	9	(5.6)
Stage 4	110	(67.9)
Unknown	13	(8.0)
Recurrent	26	(16.0)
Presence of metastasis		
Yes	118	(72.8)
No	28	(17.3)
Unknown	16	(9.9)
Prior surgery		
Yes	87	(53.7)
> 1 month ago	86	(53.1)
Within 1 month	1	(0.6)
No	75	(46.3)
Prior chemotherapy		
Yes	83	(51.2)
Completed > 1 month ago	66	(40.7)
Completed within 1 month/ on-going	17	(10.5)
No	79	(48.8)
Prior radiotherapy		
Yes	86	(53.1)
Completed > 1 month ago	76	(46.9)
Completed within 1 month/ on-going	10	(6.2)
No	76	(46.9)

SD: Standard deviation; ECOG: Eastern Cooperative Oncology Group; GIST: Gastrointestinal Stromal Tumour

Pain characteristics and pharmacological treatment for pain

As shown in Table II, the mean (SD) of the worst pain scores is 5.4 ± 0.19, indicating a moderate level within the range of 5-6. Nevertheless, 35.8% (n=58) of the patients reported their worst pain as severe (pain score range 7-10). More than half (54.9%, n=89) of the patients experienced mixed pain, which is a combination of nociceptive and neuropathic pain. Over 40% of the patients (n=70) complained of sharp pain and 38.9% (n=63) had dull pain. A significant proportion of the patients (>50%) had pain related to movement or spontaneous occurrence. Out of 78 patients who claimed taking pain medications according to the around-the-clock or combined treatment schedule (around-the-clock and on-demand), 66 (41.3%) experienced breakthrough pain.

The average number of prescribed pain medications was 2.4, ranging from 0 to 6. Out of 162 patients, only two (1.2%) were not given any medication for pain treatment. Among those with prescribed pain medications, over half had analgesics only, nearly half were given a combination of analgesics and adjuvant analgesics, and only one received adjuvant analgesics alone. Out of 160 patients, the proportions receiving strong opioids and weak opioids were 57.5% (n=92) and 38.8% (n=62) respectively, with MEDD reported at a median (IQR) of 20.0±35.00. Based on the calculation of the worst pain score and analgesic score, 17.3% of the patients (n=28) had negative PMI. Nearly half of the patients (n=71) received adjuvant analgesics, with antiepileptic drugs being the most frequently prescribed class. Notably, 70.5% of the patients with mixed pain (n=62) received adjuvant analgesics. A significant association was found between the use of adjuvant analgesics and mixed pain (p<0.001) (Supplementary Table I). Most patients (61.9%, n=99)were prescribed with a combination of regularly scheduled and as-needed pain medications. Only 13.6% of the patients (n=22) claimed concurrent use of alternative treatments, including but not limited to, traditional medicine, massage, aromatherapy, and acupuncture. As outlined in Table II, the observations of prescriber interventions revealed that treatment regimes were altered for over half of the patients (51.3%), including the initiation or escalation of treatment (29%), de-escalation of treatment (8.6%), and medication switching (7.4%). Notably, 3.7% of the patients (n=6) declined stronger analgesics despite the prescribers' intention to escalate the treatment. On the contrary, 45% of the patients experienced no changes in pain treatment; nevertheless, approximately one-third of them received re-counseling on medication taking.

Satisfaction with pain treatment

Satisfaction with pain treatment among the study population was reported based on the responses from

Table II : Pain characteristics and treatment

Variables	Number of patients	
	n	(%)
Pain score in the past 24 hours		
Worst pain, mean (SD)	5.4	(0.19)
No	2	(1.2)
Mild (1 - 4)	60	(37.0)
Moderate (5 - 6)	42	(25.9)
Severe (7 - 10)	58	(35.8)
Least pain, median (IQR)	1.0	(2.00)
No	63	(38.9)
Mild (1 - 4)	91	(56.2)
Moderate (5 - 6)	6	(3.7)
Severe (7 - 10)	2	(1.2)
Average pain [a], mean (SD)	3.3	(1.96)
No	8	(4.9)
Mild (1 - 4)	103	(63.6)
Moderate (5 - 6)	38	(23.5)
Severe (7 - 10)	8	(4.9)
Unable to score	5	(3.1)
Pain now, mean (SD)	2.7	(2.25)
No	34	(21.0)
Mild (1 - 4)	94	(58.0)
Moderate (5 - 6)	25	(15.4)
Severe (7 - 10)	9	(5.6)
Type of pain		
Nociceptive	73	(45.1)
Mixed (nociceptive & neuropathic)	89	(54.9)
Nature of pain		
Sharp	70	(43.2)
Dull	63	(38.9)
Tingling / numbness	53	(32.7)
Pricking	42	(25.9)
Pulling	42	(25.9)
Burning	40	(24.7)
Cramping	22	(13.6)
Throbbing	17	(10.5)
Stabbing	9	(5.6)
Colicky	9	(5.6)
Shooting	8	(4.9)
Stinging	8	(4.9)
Pressing	7	(4.3)
Cracking	4	(2.5)
Electric-like	3	(1.9)
Hyperalgesia	3	(1.9)

Table II : (*continued*)

Variables	Number of patients	
	n	(%)
Others	15	(9.3)
Unexplained	9	(5.6)
Location of pain		
Localized	128	(79.0)
Radiating	34	(21.0)
Temporal pattern of pain		
Persistent	53	(32.7)
Periodic	18	(11.1)
Spontaneous	82	(50.6)
Movement	90	(55.6)
Incidence of breakthrough pain [b]		
Yes	66	(41.3)
No	12	(7.5)
Not applicable	82	(51.3)
Number of pain medications, Mean (SD)	2.4	(0.10)
Regime of pain medications		
No	2	(1.2)
Yes		
Analgesic(s) only	89	(54.9)
Adjuvant analgesic(s) only	1	(0.6)
Both analgesic(s) and adjuvant analgesic(s)	70	(43.2)
Type of analgesics [c]		
Non-opioid only	15	(9.4)
Weak opioid only	33	(20.8)
Strong opioid only	59	(37.1)
Combination	52	(32.7)
MEDD [d]**, Median (IQR)**	20.0	(35.00)
Use of adjuvant analgesics		
No	91	(56.2)
Yes	71	(43.8)
Pain Management Index		
Zero / positive	134	(82.7)
Negative	28	(17.3)
Schedule of pain treatment [b]		
Around-the-clock	20	(12.5)
On demand	41	(25.6)
Combination (around the clock & on demand)	99	(61.9)
Use of alternative treatment		
No	140	(86.4)
Yes	22	(13.6)

Table II: (*continued*)

Variables	Number of patients	
	n	(%)
Intervention by prescriber		
No changes	49	(30.2)
No changes with re-counselling	24	(14.8)
Initiate/escalate the treatment	47	(29.0)
De-escalate treatment	14	(8.6)
Opioid /class/dosage form switching	12	(7.4)
Other changes	10	(6.2)
Patient refused stronger analgesics	6	(3.7)

SD: Standard deviation; IQR: Interquartile range; MEDD: Morphine Equivalent Daily Dose
[a] n = 157; [b] n = 160; [c] n = 159; [d] n = 144

155 out of the 162 patients, as 7 patients did not respond to the questionnaire, including 2 patients with no prescribed pain treatment and 5 patients who did not take the medications. As summarized in Table III, the mean (SD) score of global satisfaction was 61.8±16.33, with a wide range from 21.4 to 100. Considering all aspects of the prescribed pain treatment (i.e., global satisfaction domains), 87.8% of the patients (n=136) felt satisfied (at least "somewhat satisfied"), 9% (n=14) were dissatisfied and 3.2% (n=5) were very dissatisfied. In the effectiveness domain, more than 60% of the patients reported their satisfaction level as "somewhat satisfied" or "satisfied" for all three items. The mean (SD) satisfaction score for effectiveness was lower (60.1±16.77) compared to the domains of side effects (64.9±16.29) and convenience (69.4±12.32). Of the 155 patients who took the pain medications, 72.9% (n=113) experienced side effects. Approximately 80% of these patients (n=90) found the side effects were "somewhat bothersome" or "a little bothersome" to them, with higher interference on physical health than mental functions. Most patients reported that taking pain medications in the dispensed dosage form (66.4%, n=103), following the timing (78.7%, n=122), and adhering to the instructions (74.2%, n=115) were either "easy/convenient" or "very easy/convenient".

Quality of life

All the scores of EORTC QLQ-C15-PAL are summarized in Table IV. The mean (SD) global quality of life score was 54.4±24.63, ranging from 0 to 100. For the domains of physical and emotional functioning, the mean (SD) scores were 50.4±31.19 and 69.7±26.17, respectively. Apart from pain, other frequently reported symptoms included fatigue (87%), insomnia (66.7%), appetite loss (70.4%) and constipation (49.4%).

Factors associated with severe pain

In the simple logistic regression analysis of variables

Table III : Summary of the responses on TSQM 1.4 Questionnaire (n=155)

Domain	Score	Item	Response	Number of patients	
	Mean (SD)			n	(%)
Effectiveness	60.1 (16.77)	1. How satisfied or dissatisfied are you with the ability of the medication to prevent or treat your condition?	Extremely Dissatisfied	0	(0.0)
			Very Dissatisfied	3	(1.9)
			Dissatisfied	18	(11.6)
			Somewhat Satisfied	49	(31.6)
			Satisfied	49	(31.6)
			Very Satisfied	28	(18.1)
			Extremely Satisfied	8	(5.2)
		2. How satisfied or dissatisfied are you with the way the medication relieves your symptoms?	Extremely Dissatisfied	0	(0.0)
			Very Dissatisfied	3	(1.9)
			Dissatisfied	18	(11.6)
			Somewhat Satisfied	47	(30.3)
			Satisfied	51	(32.9)
			Very Satisfied	28	(18.1)
			Extremely Satisfied	8	(5.2)
		3. How satisfied or dissatisfied are you with the amount of time it takes the medication to start working?	Extremely Dissatisfied	0	(0.0)
			Very Dissatisfied	2	(1.3)
			Dissatisfied	25	(16.1)
			Somewhat Satisfied	50	(32.3)
			Satisfied	56	(36.1)
			Very Satisfied	20	(12.9)
			Extremely Satisfied	2	(1.3)
Side Effects[e]	64.9 (16.29)	4. As a result of taking this medication, do you experience any side effects at all?	Yes	113	(72.9)
			No	42	(27.1)
		5. How bothersome are the side effects of the medication you take to treat your condition? [e]	Extremely Bothersome	0	(0.0)
			Very Bothersome	16	(14.2)
			Somewhat Bothersome	40	(35.4)
			A Little Bothersome	50	(44.2)
			Not at All Bothersome	7	(6.2)
		6. To what extent do the side effects interfere with your physical health and ability to function (i.e., strength, energy levels, etc.)? [e]	A Great Deal	0	(0.0)
			Quite a Bit	19	(16.8)
			Somewhat	42	(37.2)
			Minimally	32	(28.3)
			Not at All	20	(17.7)
		7. To what extent do the side effects interfere with your mental function (i.e., ability to think clearly, stay awake, etc.)? [e]	A Great Deal	0	(0.0)
			Quite a Bit	5	(4.4)
			Somewhat	17	(15.0)
			Minimally	64	(56.6)
			Not at All	27	(23.9)
		8. To what degree have medication side effects affected your overall satisfaction with the medication? [e]	A Great Deal	0	(0.0)
			Quite a Bit	12	(10.6)

Table III : (*continued*)

Domain	Score	Item	Response	Number of patients	
	Mean (SD)			n	(%)
Side Effects[e] *(continued)*		8. To what degree have medication side effects affected your overall satisfaction with the medication? [e] *(continued)*	Somewhat	43	(38.1)
			Minimally	49	(43.4)
			Not at All	9	(8.0)
Convenience	69.4 (12.32)	9. How easy or difficult is it to use the medication in its current form?	Extremely Difficult	0	(0.0)
			Very Difficult	1	(0.6)
			Difficult	13	(8.4)
			Somewhat Easy	28	(18.1)
			Easy	47	(30.3)
			Very Easy	56	(36.1)
			Extremely Easy	10	(6.5)
		10. How easy or difficult is it to plan when you will use the medication each time?	Extremely Difficult	0	(0.0)
			Very Difficult	0	(0.0)
			Difficult	5	(3.2)
			Somewhat Easy	25	(16.1)
			Easy	51	(32.9)
			Very Easy	71	(45.8)
			Extremely Easy	3	(1.9)
		11. How convenient or inconvenient is it to take the medication as instructed?	Extremely Inconvenient	0	(0.0)
			Very Inconvenient	0	(0.0)
			Inconvenient	7	(4.5)
			Somewhat Convenient	31	(20.0)
			Convenient	58	(37.4)
			Very Convenient	57	(36.8)
			Extremely Convenient	2	(1.3)
Global Satisfactions	61.8 (16.33)	12. Overall, how confident are you that taking this medication is a good thing for you?	Not at All Confident	0	(0.0)
			A Little Confident	18	(11.6)
			Somewhat Confident	47	(30.3)
			Very Confident	86	(55.5)
			Extremely Confident	4	(2.6)
		13. How certain are you that the good things about your medication outweigh the bad things?	Not at All Certain	0	(0.0)
			A Little Certain	13	(8.4)
			Somewhat Certain	51	(32.9)
			Very Certain	87	(56.1)
			Extremely Certain	4	(2.6)
		14. Taking all things into account, how satisfied or dissatisfied are you with this medication?	Extremely Dissatisfied	0	(0.0)
			Very Dissatisfied	5	(3.2)
			Dissatisfied	14	(9.0)
			Somewhat Satisfied	58	(37.4)
			Satisfied	41	(26.5)
			Very Satisfied	29	(18.7)
			Extremely Satisfied	8	(5.2)

SD: Standard deviation; [e]n = 113

Table IV: Summary of scores on EORTC QLQ-C15-PAL

Domain	Score	
	Mean / Median*	(SD) / (IQR)*
Physical functioning	50.4	(31.19)
Emotional functioning	69.7	(26.17)
Symptoms		
a) Fatigue	46.0	(25.59)
b) Pain	54.1	(23.43)
c) Dyspnea	0.0 *	(33.30) *
d) Nausea & vomiting	0.0 *	(16.70) *
e) Insomnia	40.5	(35.39)
f) Appetite loss	38.3	(30.91)
g) Constipation	24.9	(29.33)
Global quality of life	54.4	(24.63)

Table V : Factors associated with severe pain in cancer patients using multiple logistic regression analysis

Variable	No/mild-moderate pain				Severe pain				Adjusted OR [f]	(95% CI)	*p*-value
	Mean	(SD)	n	(%)	Mean	(SD)	n	(%)			
PMI group											<0.001
Zero / positive			98	(73.1)			36	(26.9)	1.00	(Ref)	
Negative			6	(21.4)			22	(78.6)	26.53	(6.79, 103.71)	
Global satisfactions score	65.4	(15.30)			55.9	(16.39)			0.96	(0.93, 0.99)	0.005
Insomnia score	34.6	(31.82)			51.1	(39.10)			1.01	(1.00, 1.02)	0.047
Use of adjuvant analgesic(s) *Global satisfactions score [g]									1.02	(1.01, 1.04)	0.002

SD: Standard deviation; OR: Odds Ratio; 95% CI: 95% Confidence Interval; PMI: Pain Management Index

[f] The "Enter" method of multiple logistic regression was used in the analysis

Multicollinearity and interaction term were checked.

[g] Interaction term (use of adjuvant*global satisfactions score) was significant (p = 0.017)

Hosmer-Lemeshow test (p=0.197), classification table (overall correctly classified percentage = 78.1%) and area under the ROC curve (79.4%) were applied to check the model fit.

associated with severe pain (Supplementary Table II), certain variables such as race, living situation, cancer type, cancer stage, prior surgery and regime of pain medications did not meet the assumption of the analysis and were not further analyzed. Several variables were identified to be significantly associated with the presence of severe pain, including type of pain, persistent pain, use of adjuvant analgesics, schedule of pain treatment, PMI group, global satisfaction score, emotional functioning score, fatigue score, insomnia score, and appetite loss score. However, further analysis using multiple logistic regression showed that only four factors were significantly associated with severe pain in cancer patients, i.e., negative PMI, lower global satisfaction score, higher insomnia score, and interaction between use of adjuvant analgesics and global satisfaction score, after adjusting for confounding factor of age, as presented in Table V.

DISCUSSION

This study provides an overview of pain management in cancer patients receiving palliative care in Penang, though its representation of the entire population may be limited by the selection and sampling procedures.

The age distribution of the study population is primarily in the range of 50 to 79 years old. The mixed ethnicity within the study population highlights the diversity in religious and cultural backgrounds across various ethnic groups, which could potentially influence perceptions and attitudes towards cancer pain and its treatment (32). A diverse range of cancer types is observed, with breast, colorectal, and lung cancers being predominant. Cancer type has been shown to influence pain experiences (13, 33). In this study, mixed pain with neuropathic component was more prevalent than nociceptive pain. However, the prevalence of pain types according to pathophysiology varied greatly across the studies in the literature. In a systematic review, the prevalence of mixed pain (nociceptive and neuropathic pain) in cancer patients ranged widely from 18% to 52% (34). The presence of neuropathic pain is associated with higher pain intensity (12, 35), as it is typically more complex and tends to be less responsive to conventional analgesics, such as nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids (36). In this study, adjuvant analgesics such as antiepileptics and antidepressants were commonly used for the treatment of neuropathic pain. As anticipated, the use of anxiolytics as adjuvant analgesics was also observed in this study, as cancer-related pain is often associated with psychological distress (12, 37).

The prevalence of severe cancer pain was considerably high, with over one-third of the patients reporting their worst pain score as severe. A recent systematic review reported that 2-47.7% of advanced, metastatic or terminal cancer patients had severe pain, including those undergoing palliative treatment or not receiving active anti-cancer treatment (3). In comparison to the findings of the systematic review with mixed settings, several studies have reported a lower prevalence of severe pain in the outpatient palliative care setting. A nationwide survey of Japanese cancer patients revealed that approximately 12.8% of those experiencing pain rated their worst pain as severe (16). In our context, the higher prevalence of severe pain is likely attributed to the less well-developed state of palliative care services (e.g., shortages of trained staff, lack of integration of palliative care into routine oncology care, and limited accessibility to palliative care services), which potentially resulting in delayed referrals and treatment. In Malaysia, data on the prevalence of severe pain among palliative cancer patients is primarily limited to the in-patient setting (14). It should be noted, however, that a direct comparison between the findings of the present study and those of the literature is difficult due to differences in study settings, target populations, healthcare settings, definitions of cut-off points for severe pain, and types of pain ratings (worst, average or current) across the studies.

In this study, 17.3% of the patients had negative PMI, indicating possible undertreatment. A Malaysian study revealed that, upon ward admission, 30.1% of palliative cancer patients were identified as at risk of receiving inadequate pain treatment (14). The higher prevalence observed at admission, compared to our outpatient context, was likely linked to uncontrolled pain and acute conditions that complicate pain symptoms. In a systematic review, Roberto et al. reported that the percentage of negative PMI ranged from 9% to 42%, within the subgroup primarily comprising cancer patients with metastasis (38). Nevertheless, differences in cut-off points of pain severity categories between the systematic review and our study may lead to variations in negative PMI percentages, which should be considered when interpreting the results. Additionally, it is important to acknowledge that PMI has limitations, as it doesn't include certain pharmacological and patient-related factors, such as dosage, schedule, administration route, titration, patient compliance, and the use of adjuvant analgesics (10).

Despite the average global satisfaction score was relatively low, a high proportion of patients rated their satisfaction as at least "somewhat satisfied," and only a small number expressed dissatisfaction. Notably, patients were less satisfied with the effectiveness of the treatment compared to side effects and convenience of the treatment, possibly due to several reasons: effectiveness being prioritized over other aspects, the manageability of side effects with prophylactic medications routinely prescribed, potential benefits of certain side effects (e.g., drowsiness for sleep difficulties), and the decreased relevance of convenience aspect for advanced cancer patients who are primarily cared for by caregivers and have less direct involvement in medication preparation.

Based on the findings from our study and literature (39), we observed that some patients experienced significant pain but still perceived their pain treatment as satisfactory. This paradox is not clearly understood, but it is suggested the observed satisfaction might be influenced by the overall patient care experience (40), patients' misconceptions about the inevitability of cancer pain (39, 40), the perception of pain management practices (41), and patterns of pain relief (40).

In this study, a substantial pool of patients reported a marked decline in quality of life, with about half scoring below 50 out of 100 on the global QoL scale. The impact is not only on physical but also emotional functioning, consistent with the multidimensional concept of QoL, which acknowledges the various aspects influencing individuals' overall well-being (42). The relationship between pain and QoL in cancer patients has been well documented. In a study of

terminal cancer patients, 92.4% experienced moderate to severe pain and 92.7% reported impaired quality of life, encompassing physical, psychological, and social functioning (4).

Four factors significantly associated with severe pain in cancer patients were identified, i.e., negative PMI, lower satisfaction score, insomnia, and the interaction between the use of adjuvant analgesics and global satisfaction score.

It is justifiable that negative PMI emerges as an important factor contributing to severe pain, considering that a patient's worst pain score is one of the determinants for the Pain Management Index (PMI) (20). Several studies have shown that negative PMI is linked to higher pain intensity. In a pooled analysis of three randomized trials with advanced lung cancer patients, the rates of negative PMI increased with escalating pain severity, i.e., 79%, 84% and 88% for patients with mild, moderate and severe pain, respectively (43). In this study, despite the significant association between negative PMI and severe pain, a wide 95% confidence interval was observed, possibly due to the small sample size and wide variability of data.

Our analysis demonstrated an inverse association between satisfaction with pain treatment (global satisfaction score) and the presence of severe pain. Specifically, a 1-unit increase in global satisfaction scores corresponds to a 4% reduction in the likelihood of experiencing severe pain (p=0.005). This supports the findings of Lim et al. (44), who reported that satisfied patients had lower mean pain scores compared to those unsatisfied (3.36 vs. 4.59, p<0.0001).

Insomnia is consistently associated with severe pain in the literature (12), aligning with the concept of symptom clusters that suggest pain often co-occurs with other symptoms, including sleep disorders, in cancer patients (45). However, the observed effect size in this study is relatively weak; a 1-unit increase in the insomnia score is associated with a marginal 1% higher likelihood of experiencing severe pain. Several studies have highlighted that sleep disorders in cancer patients are frequently accompanied by impaired emotional functioning, including depression, anxiety, and other psychological disorders (46). Interestingly, impaired emotional functioning itself has consistently been associated with increased pain intensity (12, 35), supporting the concept of 'total pain,' which depicts cancer pain as multifaceted, with the psychological aspect being one of its important domains (47). Hence, it is essential to recognize the impact of compromised emotional well-being in understanding the connection between insomnia and severe pain.

Our findings suggest that the use of adjuvant analgesics was significantly associated with severe pain, in the context of its interaction with global satisfaction score. This aligns with the findings of Pina et al. (48), reporting that the use of adjuvant analgesics was a significant predictor of higher pain intensity (p=0.02). In this study, a wide range of adjuvant analgesics was prescribed to the patients, with over 90% indicated for the treatment of neuropathic pain. Although mixed pain with neuropathic component did not emerge as a predictive factor in the multivariate analysis, it was significantly associated with the use of adjuvant analgesics (p<0.001), and exhibited an approximately two-fold increase in the odds of having severe pain in the simple logistic regression analysis (p<0.045). The literature suggests that neuropathic pain often requires aggressive treatments, including high doses of opioids and the addition of adjuvant analgesics (6). Arthur et al. (35) found a significant association between neuropathic pain and higher pain scores in cancer patients (p=0.007). Similarly, Knudsen et al. (12) observed that cancer patients with mixed or neuropathic pain had relatively higher pain scores compared to those with visceral and somatic pain. Hence, we speculate that both the presence of neuropathic pain and the use of adjuvant analgesics were interrelated and contributed to the occurrence of severe pain.

Strengths and limitations

This is the first Malaysian study to examine the factors associated with severe pain in palliative cancer patients, providing useful baseline information for future research. This study used interviewer-administered questionnaires to minimize the risk of missing data and to increase the response rate. A single-interviewer approach was also employed for data collection to improve uniformity. However, several limitations in this study need to be acknowledged. Firstly, the use of convenience sampling may limit generalizability. Secondly, the target sample size was not achieved as the recruitment of subjects was halted during the COVID-19 pandemic to safeguard the vulnerable population. The decrease in sample size lowers statistical power. Thirdly, the potential sampling bias among patients recruited during the start of COVID-19 outbreak in Malaysia (i.e., early 2020), which may under-represent severely ill patients who might have been cautious about hospital visits due to their increased vulnerability. Fourthly, the cross-sectional design captures data only at a single time point as opposed to longitudinal trends. While longitudinal studies could provide better insights into temporal changes, the higher chance of dropout in this life-limiting population is a cause for concern. Overall, despite these limitations, this study brings to attention the unmet needs and areas for improvement in pain management among cancer patients.

CONCLUSION

This study highlights the need to improve pain management in cancer patients receiving palliative care in Penang, as indicated by the substantial occurrences of severe pain and inadequate treatment. Despite most patients experiencing diminished quality of life, their satisfaction with pain treatment was considerably acceptable. It is imperative to identify the subgroups of patients with severe pain and inadequate pain treatment and to provide timely intervention. Several approaches such as early integration of palliative care into cancer care, multidisciplinary palliative care teams and focus group discussions are advocated to improve the quality of palliative care in pain management.

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