RESEARCH ARTICLE

Cancer-Related Pain: Prevalence, Severity and Management in a Tertiary Care Center in the Middle East

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Abstract

Background: Despite pain awareness and the development of treatment guidelines, cancer-related pain assessment and management remain suboptimal. Our objectives were to estimate the prevalence and severity of pain and its interference with daily activities, and evaluate adequacy of treatment in cancer patients in Lebanon. **Methods:** A total of 400 cancer patients aged 18 and above were interviewed at the American University of Beirut Medical Center surgical and medical oncology floors, outpatient clinics and chemotherapy units from March 2016-February 2017. The subjects covered were socio-demographics, clinical data, and presence of pain in the past month with use of the Brief Pain Inventory questionnaire. Descriptive statistics were conducted using t-test, chi-square and Fischer's exact tests. Pearson's correlation coefficients were used to examine relationships between pain severity and pain interference. Logistic regression was employed to determine risk factors for pain. **Results:** The majority of participants were Lebanese (76.0%), females (62.7%), married (80.2%), of Muslim faith (64.2%), of urban residence (85.8%), and with insurance plans (81.3%). Most had breast cancer (38.8%), were stage 4 (52.7%) and underwent a combination of surgery and systemic therapy (55.1%). The prevalence of pain in the past month was 29.8%. Among patients with pain, the highest proportion had moderate pain (37.8%) and around 46% received inadequate treatment. **Conclusion:** More awareness about cancer-related pain is needed to improve pain management and encourage referral to palliative care and pain specialists early-on in diagnosis of disease.

Keywords: Pain- cancer- prevalence- severity- Lebanon

Introduction

Cancer-related pain is a serious health problem throughout the world. In fact, cancer is a prevalent disease and the majority of cancer patients experience pain throughout their illness (Foley, 2000). A meta-analysis of more than fifty studies conducted in the United States showed that more than 50% of oncology patients suffer from cancer-related pain, with similar data arising from Europe and Eastern Asia (Larue et al., 1995; Bruera and Kim, 2003; Hyun et al., 2003; Breivik et al., 2009; Alexopoulos et al., 2011; Kim et al., 2013). Cancer pain can result from the primary and metastatic sites or from treatment-related sequelae. It negatively affects patients and their caregivers' quality of life. Several guidelines have been developed for proper pain management with the use of safe and inexpensive drugs (Cleeland et al., 1994; WHO, 1996; Scottish Intercollegiate Guidelines Network (SIGN), 2000; Bruera and Kim, 2003; Gordon et al., 2005; National Comprehensive Cancer Network (NCCN) and American Cancer Society (ACS), 2005). The World Health Organization (WHO) developed a pain management algorithm for cancer pain relief with the 3-step analgesic ladder (WHO, 1996). When the WHO guideline is used appropriately, pain can be adequately treated in the majority of patients (Cleeland et al., 1994). However, despite two decades of guidelines development and pain awareness, pain assessment and treatment remain suboptimal (Gordon et al., 2005). In a study conducted by the Eastern Cooperative Oncology Group, 42% of patients were found to have inadequate analgesic prescription (Cleeland et al., 1994). Moreover, breakthrough pain was shown to be common with only a minority of patients prescribed an appropriate dose of rescue medication (Breivik et al., 2009).

As per the National Institutes of Health State-of-the-Science Panel, rigorous research is needed on the prevalence and management of pain (Patrick et al., 2004). Most research assessing pain prevalence, interference, treatment and barriers has been conducted in the United

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States, Europe and Eastern Asia. Few researchers have explored the cancer pain experience in the Arab world (Al Qadire, 2012; Al Qadire et al., 2013). In a study assessing the physical symptom profile of adult cancer patients presenting to the American University of Beirut Medical Center (AUBMC) in Lebanon, pain was found to be prevalent in 62% of patients and was the second most distressing symptom (Halawi et al., 2012). Similarly, Huijer et al. showed that cancer pain is common and inadequately treated among adult cancer patients presenting to the American University of Beirut Medical Center (AUBMC) (Abu-Saad Huijer et al., 2012). Since pain is a multimodal construct influenced by cultures, beliefs and socioeconomic factors, data could not simply be extrapolated to the Arab region (Bruera and Kim, 2003). Hence, there is a need for a preliminary comprehensive descriptive study of cancer-related pain in the Arab World, particularly in Lebanon.

Therefore, our objectives were to estimate the prevalence of pain, assess severity of pain and its interference with daily activities, and evaluate the adequacy of treatment in adult cancer patients presenting to AUBMC, a tertiary care center in Lebanon. The results of the study will help raise awareness about cancer pain to improve pain management and encourage referral to palliative care specialists and pain specialists early-on in the disease. Hence, it will have positive implications on pain assessment and management on the medical and the regulatory levels.

Materials and Methods

Setting and Subject Recruitment

After receiving the approval from the Institutional Review Board of the American University of Beirut, we conducted a cross-sectional study on 400 cancer patients, aged ≥18 years, who had adequate cognitive function, and presented to AUBMC surgical and medical oncology floors as well as outpatient clinics and chemotherapy units from March 2016- February 2017. After obtaining informed consent, the participants completed the questionnaire in a face-to-face interview. Afterwards, clinical data was collected from the patients' medical records.

Questionnaire
Demographics

Information on age, gender, marital status, religion, educational level, type of insurance, country and place of residence were collected (Appendix A).

Brief Pain Inventory Questionnaire (BPI)

The BPI is a self-reported 11-item questionnaire that allows patients to rate the severity of their pain and the degree to which their pain interferes with common dimensions of feeling and function. The Arabic validated version was adapted from the article entitled "Psychometric evaluation of the Arabic brief pain inventory on a sample of Lebanese cancer patients" (Ballout et al., 2011). Each item is rated from 0 to 10 with 0 being no pain or no interference and 10 being the worst pain one can have or complete interference (Appendix B).

Pain Management Index (PMI)

The PMI was based on the World Health Organization's (WHO) guidelines for the management of pain in cancer (WHO, 1996). It considers pain management appropriate when a patient's reported worst pain level is congruent with the prescribed analgesics according to the WHO analgesic ladder (last section in Appendix B). To construct the index:

• Analgesics were rated in four levels: 0 is no analgesic; 1 is non-opioid; 2 is weak opioid and 3 is strong opioid.

• Pain was scored in four groups: 0 is no pain, 1 is mild pain; 2 is moderate pain; and 3 is severe pain.

The PMI was computed by subtracting the pain level from the analgesic level. It ranged from -3 to +3. Negative PMI scores were considered an indication of inadequate analgesic prescription while a score of zero or greater indicated adequate treatment. In our study, it was considered as a dichotomous variable: <0 is inadequate and ≥0 is adequate treatment.

Clinical Data Sheet

Information included cancer-related clinical data such as date of diagnosis, cancer site, cancer stage, treatment received (surgery, systemic therapy and a combination of surgery and systemic therapy) and pain medication (Appendix C).

Statistical analysis

Analysis was performed using the statistical package IBM SPSS version 20.0 (SPSS Inc., Chicago, IL, USA). Descriptive analyses were computed to describe the demographic and clinical characteristics such as independent t-tests for comparing the mean age among patients with pain versus patients with no pain. In addition, Chi-square and Fisher's exact tests were used to compare the categorical variables such as gender, marital status, education, place and type of residency, religion, and clinical characteristics in these two populations.

Pearson's r correlations were used to examine the relationship of pain severity (least, average, worst and total) and pain interference. Logistic regression was used to assess the relationship of pain with age, gender, educational level, type of residency, cancer site, cancer stage and type of treatment. Only variables with a statistical significance of a p-value ≤0.05 were included in the multivariate analysis. All P values ≤0.05 were considered statistically significant.

Results

The majority of participants were Lebanese (76.0%), females (62.7%), married (80.2%), of Muslim faith (64.2%), of urban residence (85.8%), and with insurance plans (81.3%). Most had breast cancer (38.8%), were stage 4 (52.7%) and underwent surgery and systemic therapy (55.1%) (Table 1). Cancer site was statistically different in patients with pain versus patients with no pain (P=0.01). Female sex (P =0.001), non-urban place of residency (P =0.03) and non-Lebanese nationality (P =0.04) were statistically significant in patients with pain compared to those with no pain.

Table 1. Demographic and Clinical Characteristics of 400 Cancer Patients at AUBMC

	Total N=400	Patients with pain N=119	Patients without pain N=281	P
Demographic characteristics				
Mean (SD) age, years	54.7 (14.4)	53.3 (14.2)	55.3 (14.5)	0.23 □
Female, %	62.7	74.8	57.7	0.001*§
Married, %	80.2	77.1	81.5	0.39 §
Education (university level/below university level), %	48.5/51.5	48.6/51.4	48.4/51.6	1.00 §
Living in urban areas, %	85.8	79.8	88.3	0.03* §
Insured, %	81.3	75.2	83.8	0.06 §
Nationality (Lebanese/ Iraqi/other), %	76.0/12.3/3.8	70.6/18.5/2.5	78.3/9.6/4.3	0.04* ¶
Religion (Christian/Muslim/unknown), %	19.8/64.2/16.0	15.1/62.2/22.7	21.7/65.1/13.2	0.30 §
Clinical characteristics				
Cancer site, %				
Breast	38.8	48.7	34.5	0.01*§
Lung	4.5	3.4	5	
Colon	12.3	5	15.3	
Non-colon gastrointestinal	11.5	14.3	10.3	
Hematologic	17.3	14.3	18.5	
Other	15.6	14.3	16.4	
Cancer stage, %				
Stage I	4	5.9	3.2	0.13¶
Stage II	16	18.5	14.9	
Stage III	15.3	18.5	14	
Stage IV	52.7	44.5	56.2	
Not applicable (e.g. hematologic)	12	12.6	11.7	
Type of treatment, %				
Surgery	1.4	2.8	0.8	0.22 ¶
Systemic therapy	43.5	45.9	42.5	
Surgery and systemic therapy	55.1	51.4	56.7	

*, pvalue≤0.05; ¶, Fisher's exact test; §, Chi-square test; □, Independent t-test

The prevalence of pain in the past month was 29.8% where 119 patients had pain out of the whole population. Among patients with pain, the mean duration of pain was 2.9 ±1.3 weeks and its median was 4.0 weeks (Table 2). The highest proportion had moderate pain (37.8%) and only 4.2% had severe pain in the past 24 hours. Extremities were the most cited pain location (40.3%).

Approximately 78% of participants adhered to the prescribed pain medications of which 61.8% were non-opioid. Pain moderately improved in 48.0%. Around 46% of the patients had inadequate treatment that was assessed according to the patients' reported pain as well as their usage of analgesics.

Total pain severity was only positively and mildly correlated with total pain interference (r=0.16, p=0.01) (Table 3). Least pain was positively and mildly correlated with general activity (r=0.42, p<0.001), mood (r=0.33, p<0.001), normal work (r=0.28, p=0.002), relation with other people (r=0.35, p<0.001), sleep (r=0.45, p<0.001) and enjoyment of life (r=0.50, p<0.001). Average pain was positively and mildly correlated with total pain interference (r=0.19, p=0.05), relation with others (r=0.23, p=0.01) and enjoyment of life (r=0.31, p=0.001). Worst

pain was positively correlated with pain interference in all its forms. In other terms, worst pain was positively and moderately correlated with general activity (r=0.58, p<0.001), mood (r=0.60, p<0.001), normal work (r=0.51, p<0.001), sleep (r=0.58, p<0.001) and enjoyment of life (r=0.62, p<0.001). It was also positively and mildly correlated with total pain interference (r=0.28, p=0.003), walking activity (r=0.45, p<0.001) and relation with other people (r=0.46, p<0.001).

After analyzing the association of demographics and clinical characteristics in relation to pain, only gender, type of residency and cancer site were statistically associated with pain (Table 4). Participants who were female (OR=2.18, 95%CI=1.35-3.51, P=0.001), and those living in rural areas (OR=1.90, 95%CI=1.07-3.38, P =0.03) were at a higher risk of having pain than their counterparts. Patients with colon cancer were at a lower risk of developing pain compared to those with breast cancer (OR=0.23, 95%CI=0.09-0.58, P =0.002). At a multivariate analysis, these variables remained statistically significant.

Table 2. Characteristics of 119 Cancer Patients with History of Pain at AUBMC

	N=119
Mean (SD) duration of pain, weeks	2.9 (1.3)
Duration of pain, Median	4
Adherence to prescribed pain medications, %	
Yes	78.2
No	1.7
No need for medications	20.1
Pain improvement	
Yes	67.9
Mildly	13.3
Moderately	48
Completely	38.7
No	32.1
Pain severity in the past 24 hours, %	
No pain	26.1
Mild pain	31.9
Moderate pain	37.8
Severe pain	4.2
Analgesics used, %	
Non-opioid	61.8
Weak opioid	32.9
Strong opioid	5.3
Pain Management Index, %	
Adequate treatment	44.5
Inadequate treatment	55.5
Location of pain*, %	
Head	16.8
Back	23.5
Extremities	40.3
Trunk	30.3
Other	5

*Percentages do not add to a hundred since every participant chose more than one pain site

Discussion

Our study is among the first few studies to assess the pain experience in cancer patients in the Arab World and in Lebanon. We found that the prevalence of pain in the past month was around 30% which is consistent with previous studies where it ranged from 28 to 36% (Menzies et al., 2000; Beck and Falkson, 2001; Garcia de Paredes et al., 2011). This finding is inconsistent with other studies done in Jordan, France, Korea and Shanghai where the prevalence ranged from 50 to 73% (Larue et al., 1995; Yun et al., 2003; Forgeron et al., 2006; Wang, 2008; Breivik et al., 2009; Al Qadire et al., 2013).

In cancer patients with pain, 37.8% of patients had moderate pain and 4.2% had severe pain. This finding is inconsistent with previous studies done in Europe and Greece where in Greece, 28% of 134 patients perceived the pain as low to moderate and 70% as high (Alexopoulos et al., 2011) and in 11 European countries, 56% of 5084 adult cancer patients perceived it as moderate to severe pain (Breivik et al., 2009). The extremities were the most frequently cited pain location (40.3%) which is higher compared to the Greek study (11%). However, our results were lower than theirs for the back site (24.5% versus 30 %) (Alexopoulos et al., 2011).

Around 78% of participants adhered to the prescribed pain medications of which 61.8% were non-opioid and 5% were strong opioids. The usage of strong opioids was lower compared to the Jordanian study (Al Qadire et al., 2013) and the usage of non-opioids and adherence to pain medication were lower than those in the Greek study (Alexopoulos et al., 2011).

In our study, around 46% of the patients had inadequate treatment. This finding is comparable to that of studies in France, Italy, Germany, Netherland, United Kingdom, India, Korea, China, United States and South Africa (Deandrea et al., 2008). However, it is lower compared to that in Jordan (65%), Taiwan (69%) and Greece (100%) (Ger et al., 1998; Alexopoulos et al., 2011; Al Qadire et al., 2013) and higher than that in Canada (25%) (Mitera et al., 2010).

Similar to previous studies, our study shows that pain had an impact on patients' physical and psychological functioning, including symptoms such as fatigue, generalized weakness, mood and sleep disorders (Valeberg et al., 2008a; Caltagirone et al., 2010).

The present study shows that female cancer patients were at higher risk of having cancer-related pain than male patients. Similarly, a study conducted at a large cancer center in Norway by Valeberg et al. showed that females were at higher risk of experiencing both cancer-related and non-cancer related pain compared to males with pain being more severe in females (Valeberg et al., 2008b; Valeberg et al., 2008c). Also, a study by Reyes-Gibby et al. including adult cancer patients aged 50 and older in the United States showed that females were more likely to report the symptoms of pain, fatigue and

Table 3. Pearson's Correlation Coefficients of Pain Interference and Pain Severity

Variables	Pain interference							
	Total	General activity	Mood	Walking activity	Normal work	Relation with other people	Sleep	Enjoyment of life
Total pain severity	0.16*	0.15	-0.01	0.13	0.15	0.08	0.15	0.11
Least pain	0.16	0.42*	0.33*	0.28*	0.29*	0.35*	0.45*	0.50*
Average pain	0.19*	0.14	0.16	0.11	0.17	0.23*	0.13	0.31*
Worst pain	0.28*	0.58*	0.60*	0.45*	0.51*	0.46*	0.58*	0.62*

* pvalue≤0.05

Table 4. Risk Factors for Pain in Cancer Patients at AUBMC

	Unadjusted OR (95%CI)	P	Adjusted OR (95% CI)	P
Age	0.99 (0.98-1.01)	0.23	0.99 (0.98-1.01)	0.56
Gender				
Male	1.00	0.001*	1.00	0.03*
Female	2.18 (1.35-3.51)		1.97 (1.07-3.62)	
Type of residency				
Urban	1.00	0.03*	1.00	0.04*
Rural	1.90 (1.07-3.38)		1.89 (1.04-3.44)	
Cancer site				
Breast	1.00	0.02*	1.00	0.10
Lungs	0.48 (0.15-1.52)	0.21	0.78 (0.23-2.71)	0.7
Colon	0.23 (0.09-0.58)	0.002*	0.36 (0.14-0.94)	0.04*
Non-colon gastrointestinal	0.55 (0.29-1.03)	0.06	0.77 (0.38-1.57)	0.47
Hematology	0.98 (0.50-1.94)	0.96	1.71 (0.76-3.84)	0.2
Other	0.62 (0.32-1.18)	0.14	0.89 (0.43-1.83)	0.75
Education				
Below university level	1.00	0.94		
University level	0.98 (0.62-1.55)			
Cancer stage				
Stage I	1.00	0.14		
Stage II	0.67 (0.22-2.05)	0.49		
Stage III	0.73 (0.24-2.22)	0.57		
Stage IV	0.43 (0.15-1.22)	0.11		
Type of treatment				
Surgery	1.00	0.28		
Systemic therapy	0.30 (0.05-1.85)	0.20		
Surgery + systemic therapy	0.25 (0.04-1.55)	0.14		

* pvalue≤0.05

depression compared to males (Reyes-Gibby et al., 2006). This could be partly due to the elevated inflammatory response in females brought about by the high estrogen levels compared to males as discussed by Straub et al. (Straub, 2007).

Our study also shows that patients living in rural areas had more cancer-related pain than those living in urban areas. This data is consistent with a pilot study conducted by Passik et al. which concluded that cancer patients in rural areas have limited access to pain control (Passik et al., 2002).

Furthermore, we found that patients with colon cancer were at lower risk of developing pain compared to those with breast cancer probably because of the nature of the pain elicited by each type and its mode of spread. Advanced stage breast cancer metastasizes to the bones leading to fractures and even spinal cord compression in turn leading to severe pain (Mantyh, 2013). Another common site of breast cancer spread is the lungs in which the metastatic deposits in addition to pain, cause cough and dyspnea (Leppert et al., 2016). As for colon cancer, tumors may enlarge locally for a long time before causing any pain. As the tumor grows locally it causes visceral pain from obstruction (Mercadante et al., 2000).

The discrepancy between our findings and the international and regional studies' findings could be due to the lack/absence of pain specialists and palliative care referral documentations by the oncologists and healthcare providers or absence of the referral by itself. Hence, referral to palliative care and pain specialists is needed at early cancer stages to reduce the healthcare costs and utilization as well as to avoid psychological distress from untreated pain since pain is associated with uncontrolled hospital admissions (Fortner et al., 2002), anxiety and depression (Green et al., 2009). In addition, the fact of having 46% of inadequacy of treatment and a higher proportion of moderate levels of pain shows that pain is perceived based on the cultural beliefs. In other terms, it might be related to fear of addiction to drugs which was mostly reported by the physicians in certain Asian countries such as China, Taiwan, Japan and Korea (Koshy et al., 1998; Yau et al., 2004). The inadequate treatment could result from certain barriers related to physicians, patients and health care factors. They might include lack of knowledge in pain assessment and management, fear of the adverse effects of opioids, poor communication between physicians and patients, inadequate appreciation of the intensity of pain by the physician, under-reporting of pain, non-adherence to treatment and regulatory barriers to opioid prescription and dispensing (Von Roenn et al., 1993; Pargeon and Hailey, 1999; Breivik et al., 2009; Hakonsen et al., 2009).

Our study has multiple strengths including the adequacy of sample size which empowered the study. It is among the first studies to comprehensively address cancer pain in Lebanon and the Arab world. In addition, it includes all types of cancer-related pain, all cancer stages and types and all age groups aged above 18.

However, it has limited generalizability since the setting is a tertiary cancer center in Beirut that welcomes patients of medium to high socio-economic status. But, the choice of the institution was purposeful because the pain assessment can be properly assessed due to the availability of data. Another important limitation is that patients complaining of severe pain were more likely to refuse participation than those without pain or those in mild to moderate pain. This can result in an underestimation of the severity of cancer-related pain and its interference with functioning, while overestimating the adequacy of treatment in our sample. In addition, the majority of participants were recruited from an outpatient setting, which constitutes another potential source of selection bias. Patients who are hospitalized in inpatient units are expected to experience more symptoms including pain.

In conclusion, our study is among the first few studies to assess the pain experience in cancer patients in Lebanon and the Arab World. The prevalence of pain in the past month was 29.8%. Among patients with pain, the highest proportion had moderate pain (37.8%) and around 46% received inadequate treatment. Hence, raising awareness about cancer pain such as educational programs and awareness campaigns for physicians, patients and their caregivers are needed to improve the pain management.

Statement on conflict of interest

The authors declare that they have no competing interests.

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