



Pain management in cancer patients in the main hospitals in Mozambique

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Background: Pain is the most feared and distressing symptom in palliative care. In advanced stages of cancer, its incidence is 70–80%. In Mozambique there is little published information concerning to the prevalence, intensity, and pain's management in cancer patients.

Methods: A cross-sectional observational study was conducted between August 2018 and January 2019, in Mozambique's main hospitals, and in the only hospital with an isolated provision of palliative care service. The analyzed data included demographic data, pain intensity and its treatment. The Pain Management Index was used to calculate the adequacy of the analgesia.

Results: A total of 294 patients were included. The mean patients' age was 46.1 years old. Concerning to pain, 83.7% of the patients had pain, most of them moderate to severe pain. The prevalence of pain was frequent in women mainly in cervical cancer (84.3%) and in men with Kaposi sarcoma (80%). The main analgesic used for severe pain was paracetamol, and it was used alone in 40.9% of the patients. Morphine was used in 8.1% and adjuvants less than 10%. Pain Management Index was negative for 68.7% of the sample, meaning an inadequate analgesia. Significant differences were found in Pain Management Index levels between hospitals.

Conclusions: The prevalence of pain in the main health institutions in Mozambique is high. Paracetamol was the analgesic most used in severe pain. Further studies are needed to understand the main reasons of patients' suffering.

Keywords: Cancer pain; opioids; pain management index; palliative care

Submitted Oct 12, 2020. Accepted for publication Dec 31, 2020.

doi: 10.21037/apm-20-2009

View this article at: <http://dx.doi.org/10.21037/apm-20-2009>

Introduction

Mozambique is a low-income country with a gross domestic product per capita of 460 USD per year, and about 46% of the population below the poverty line (1). Financial resources, according to the Mozambique Health Sector Strategic Plan 2013-17, were very limited, only about 7% of the national budget was spent on health. Expenditure per capita on health

in Mozambique was only about 21 USD per year, and it was much less than the World Health Organization (WHO) recommendation of a minimum of 44 USD (2).

Adequate pain relief is considered as a human right by different organizations of health professionals (3,4). According to the International Council on Narcotic Control (INCB), opioids are indispensable in the management of

moderate to strong pain, and about 80% of the world's population, most in developing countries lack of access to strong analgesia. The legal and policy restrictions negatively affect the opioids' availability in some African countries mainly in Mozambique, Zimbabwe and Swaziland (5).

In most of the low-income countries the majority of cancer patients are diagnosed with advanced-stage disease, and the only realistic treatment option is pain relief and palliative care (6). When the disease cannot be treated even with the best available treatment alternatives, what remains important is symptom management and providing comfort care to these patients. In developing countries, the incidence of cancer pain in advanced stages is 70–80% (7).

We aim to describe the prevalence, intensity, and pain management in Mozambican oncologic patients in the 3 main hospitals and in the only provincial hospital with an isolated provision of palliative care service. We present the following article/case in accordance with the STROBE reporting checklist (available at <http://dx.doi.org/10.21037/apm-20-2009>).

Methods

A cross-sectional observational study was conducted between August 2018 and January 2019, in Mozambique's main hospitals namely, Maputo Central Hospital (MCH), Nampula Central Hospital (NCH), Beira Central Hospital (BCH), and Xai-Xai Provincial Hospital (XXPH). The latter is the main hospital in the only province of the country that provides a standalone palliative care service. This is the reason why it was included in the study, even not being a big hospital as the others, but to see if there is any difference in pain management. Nevertheless, palliative care has been provided in the reference hospital in the country.

Sample size was calculated for the estimate of proportions based on the combined inpatient capacity of each hospital using a confidence interval of 95% and a margin of error of 5%, generating an estimated minimum sample size of 344 from a population of 3,264 patients in the 4 hospitals. A consecutive sample of cancer patients were recruited: 158 participants from MCH, 101 from BCH, 56 from NCH and 29 from XXPH, until the sample size was reached, (in Xai-Xai Provincial Hospital it was not reached because in this hospital there were not enough cancer patients during the period study). The services included in the study due to having the majority of oncologic patients were: Oncology, Gynecology, Gastrology, Surgery, Urology, Pain Unit, Dermatology, Otorhinolaryngology,

Maxillofacial and Ophthalmology.

Patients ≥ 14 years old (limited age to Mozambique pediatric services), and < 18 years with caregiver or legal representative or ≥ 18 years able to understand the questionnaire, who agreed to participate in the study were included. Thirty-five eligible patients were excluded due to incomplete surveys (16 from MCH, 9 from BCH, 10 from NCH). Additionally, 11 patients in agony were excluded (1 from NCH, 3 from BCH and 7 from MCH).

In this study, was excluded any treatment for pain relief to the patients by the research team—if a participant was identified in need of medical attention, the patient's medical team was informed.

The analyzed data comprised demographic data, pain intensity and its management.

Pain intensity was rated using a five-point verbal rating scale from none to maximum pain. The pain was classified as: 0, no pain; 1, mild pain; 2, moderate pain; and 3, severe pain. The Pain Management Index (PMI) was used to calculate the adequacy of the analgesia (8).

According to the PMI, the analgesics were classified as: 0, no analgesics; 1, non-opioids for mild pain (e.g., nonsteroidal anti-inflammatory or acetaminophen); 2, weak opioids for mild to moderate pain (e.g., codeine and tramadol); and 3, strong opioids for moderate to severe pain (e.g., morphine). Then, the PMI was computed by subtracting the pain level from the analgesic level. The PMI ranges from -3 (a patient receiving no analgesics with severe pain) to $+3$ (a patient receiving opioids for moderate to severe pain with no pain, that is, completely controlled pain). Negative scores were considered inadequate analgesia, and scores of 0 or positive indicate acceptable to good analgesia. In this study, for computing the PMI, severe and maximum pain were classified together as severe.

Statistical analysis

Statistical analysis was performed using SPSS statistical software, version 25 (IBM Corp, Armonk, NY, USA). Regarding descriptive statistics, absolute and relative frequencies were used for categorical variables, means with 95% confidence intervals (95% CI) for normally distributed continuous variables and medians with interquartile interval [Q1, Q3] otherwise. Inferential statistics were employed according to the level of measurement: χ^2 for independence of categorical variables (or Fisher exact test if more than 20% of expected counts were less than 5), Mann-Whitney and Kruskal Wallis for ordinal variables distributions comparison

Table 1 Demographics data for the 294 patients

Sample characteristics	n (%)
Gender	
Female	177 (60.2)
Male	117 (39.8)
Average age [95% CI]	46.1 [44.4, 47.8]
Age group (years old)	
18–34	62 (21.0)
35–54	144 (49.5)
Above 55	86 (29.6)
Participants by Hospital	
MCH	143 (48.6)
NCH	45 (15.3)
BCH	92 (31.3)
XXPH	14 (4.8)

MCH, Maputo Central Hospital; NCH, Nampula Central Hospital; BCH, Beira Central Hospital; XXPH, Xai-Xai Provincial Hospital.

between 2 or more groups, respectively. In all tests, P values were considered significant if less or equal to 0.05.

Ethics and consent to participate

All purposes objectives were explained to all participants, and informed consent in paper were given. Signed written consent was requested to all participants. Patients under 18 years old, consent was requested from the caregiver or legal representative.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Committee of Bioethics for Health of the Faculty of Medicine & Maputo Central Hospital with number CIBS FM&HCM/08/2018 and by the Bioethics Committee of the Faculty of Medicine of the University of Porto, and informed consent was taken from all the patients.

Results

A total of 294 patients were included, corresponding to a margin of error of 5.45%. The study had an 85% response rate (294/344 forms fully completed): 143 respondents (90.5%) from MCH, 92 (91.1%) from BCH, 45 (80.3%)

Table 2 Most common cancers distribution n (%), by gender (N=294)

Type of cancer	Female (n=177)	Male (n=117)	Total
Cervix cancer	83 (46.9)	–	83 (28.2)
Kaposi sarcoma	12 (6.8)	35 (29.9)	47 (16.0)
Breast cancer	25 (14.1)	1 (0.9)	26 (8.8)
Prostate cancer	–	18 (15.4)	18 (6.1)
Rectal cancer	7 (4.0)	4 (3.4)	11 (3.7)
Bladder cancer	6 (3.4)	4 (3.4)	10 (3.4)
Mandibular cancer	2 (1.1)	8 (6.8)	10 (3.4)
Esophageal cancer	4 (2.3)	6 (5.1)	10 (3.4)
Others	38 (21.5)	41 (35.0)	79 (26.9)

from NCH and XXPH with 14 (48.3%). Patient's average age [95% CI] was 46.1 [44.4, 47.8] years old and 60.2% were female (see *Table 1*). The most prevalent cancers were: cervical cancer 83 (46.9%), breast cancer 25 (14.1%) and Kaposi sarcoma 12 (6.8%) in women, and Kaposi sarcoma 35 (29.9%), prostate cancer 18 (15.4%) and mandibular cancer 8 (6.8%) in men (see *Table 2*).

Pain was frequent mainly in cervical cancer (84.3%) in women, and Kaposi sarcoma (80%) in men (see *Figure 1* and *Figure 2*). All patients with head and neck's cancer, lung, abdominal, epidermoid cancers and osteosarcoma, reported intensive pain.

Of the total of 177 women, 84.2% had pain, most of them moderate (38.4%) to severe (27.7%) pain, mainly in cervix, breast cancer and Kaposi sarcoma. In the 117 men of our sample, 82.9% reported pain, mostly moderate (31.6%) and severe pain (33.3%), and the most frequent cancer related pain resulted from prostate, Kaposi sarcoma and jaw cancer.

Regarding Kaposi sarcoma, the most prevalent cancer present in both genders, there were no significant differences in pain (dichotomous variable) reported by gender (P=0.435) nor in the distribution of pain intensity by gender (U=171.5; P=0.355).

For pain relief, the non-opioid analgesic most used was paracetamol (35.7%). The weak opioids used by patients who reported pain were tramadol (6.5%) and codeine (4.1%); morphine (8.1%) was the only strong opioid used (see *Figure 3*). Paracetamol was used alone in 40.9% of the patients with severe pain. Morphine was mainly prescribed to severe pain (75%) and tramadol to moderate and severe

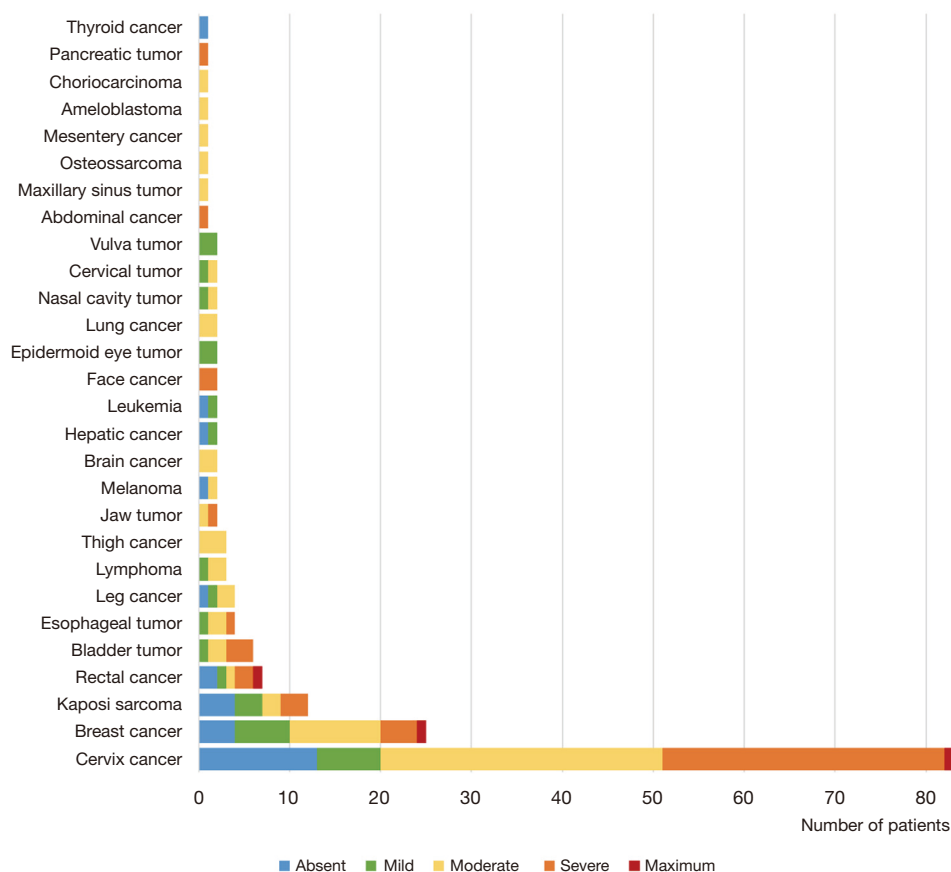


Figure 1 Pain intensity by cancer diagnosis in women.

pain in 43.8% each. XXPH was the hospital where most of the patients were doing morphine for moderate to severe pain relieve (see *Figure 4*). The adjuvants were little used (9.5%): corticosteroids (prednisolone and dexamethasone) in 4.4% and antidepressant (amitriptyline) in 5.1% of the patients (see *Table 3*). No invasive techniques were used to control pain.

PMI was negative for 68.7% of the sample, meaning an inadequate analgesia, and 31.3% were 0—positive meaning acceptable to good analgesia (see *Figure 5*). Significant differences were found in PMI levels between hospitals [$\chi^2_{KH}(3)=12.909$, $P=0.005$, $n=294$]. After multiple comparisons, it was found that Xai-Xai hospital had a different PMI distribution [median = 0 and IQI = (-0.5, 1)] than MCH [$P=0.002$, median = -1 and IQI = (-2, 0)], NCH [$P=0.015$, median = -1 and IQI = (-2, 0)] and BCH [$P=0.019$, median = -1 and IQI = (-2, 0)].

There was also a significant difference [$\chi^2(3)=16.231$; $P=0.001$] between the proportions of adequate/inadequate analgesia in the 4 hospitals. The most inadequate analgesia

was found at the reference hospital of the country, Maputo Central Hospital (86.8%), Nampula Central Hospital (100%) and Beira Central Hospital (78.5%). Overall, only 17.9% of the patients had adequate analgesia (see *Table 4* and *Figure 6*).

The main co-morbidity was Human Immunodeficiency Virus-Acquired Immunodeficiency Syndrome (HIV-SIDA) in 41.8% and 74% of them were doing antiretroviral treatment.

All Kaposi sarcoma's patients in both sexes, with or without pain were HIV positives.

Of the 98 patients with moderate pain, 44.9% were HIV positive and of the 86 patients with severe pain, 33.7% were HIV positive. There were no significant differences in the proportion of HIV patients between the group of moderate and severe pain [$\chi^2(1)=2.391$; $P=0.122$]. Moderate-severe pain was present in 61.8% of HIV patients.

Of the 63 women with moderate pain, 41.3% were HIV positive, and of the 48 women with severe pain, 41.7% were HIV positive. There was no significant difference in

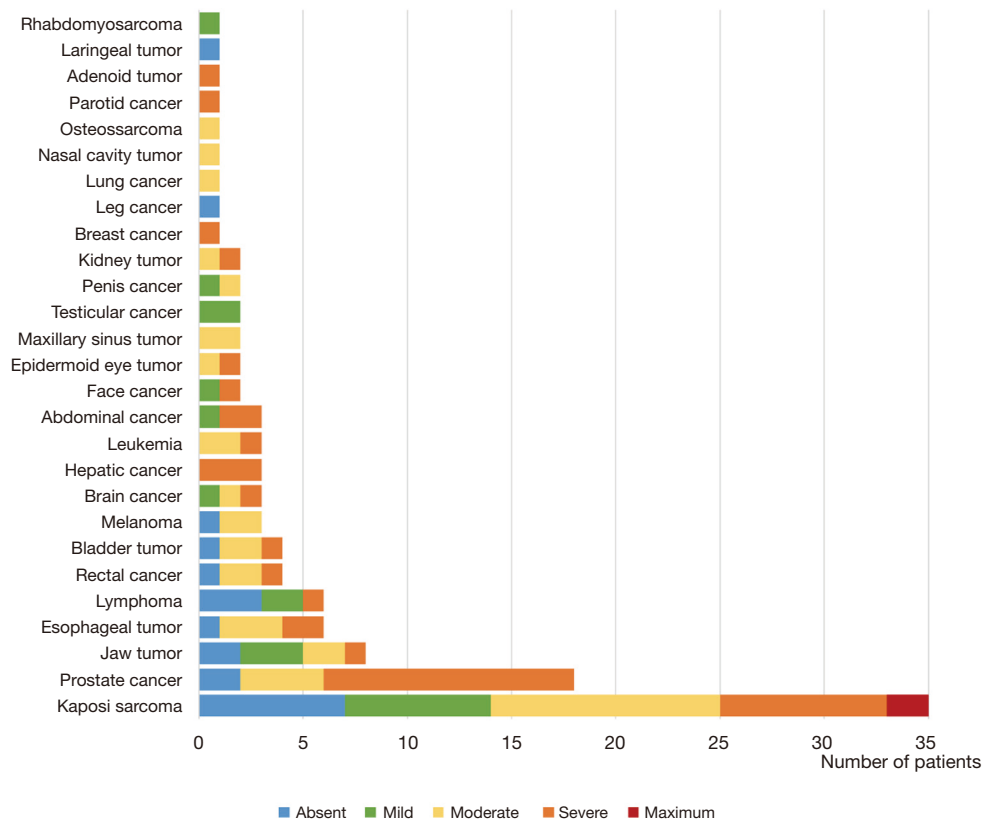


Figure 2 Pain intensity by cancer diagnosis in men.

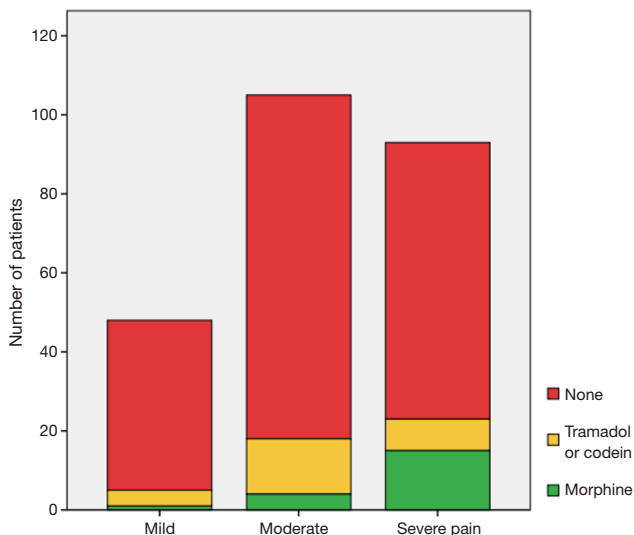


Figure 3 Number of patients receiving tramadol or codeine and morphine by pain's intensity in all hospital.

the proportion of women with HIV positive between the moderate pain group and the severe pain group [$\chi^2(1)=0.002$; $P=0.966$].

Of the 35 men with moderate pain, 51.4% were HIV positive and of the 38 men with severe pain 23.7% were HIV positive. There were significant differences in the proportion of men with HIV positive between the moderate pain group and the severe pain group [$\chi^2(1)=6.017$; $P=0.014$].

Discussion

To our knowledge, this was the first study to assess the prevalence, intensity and pain management in cancer patients in Mozambique. The analysis comprised a total of 294 patients, from the 3 main hospitals in the north, center and south of the country, and in Xai-Xai Provincial Hospital

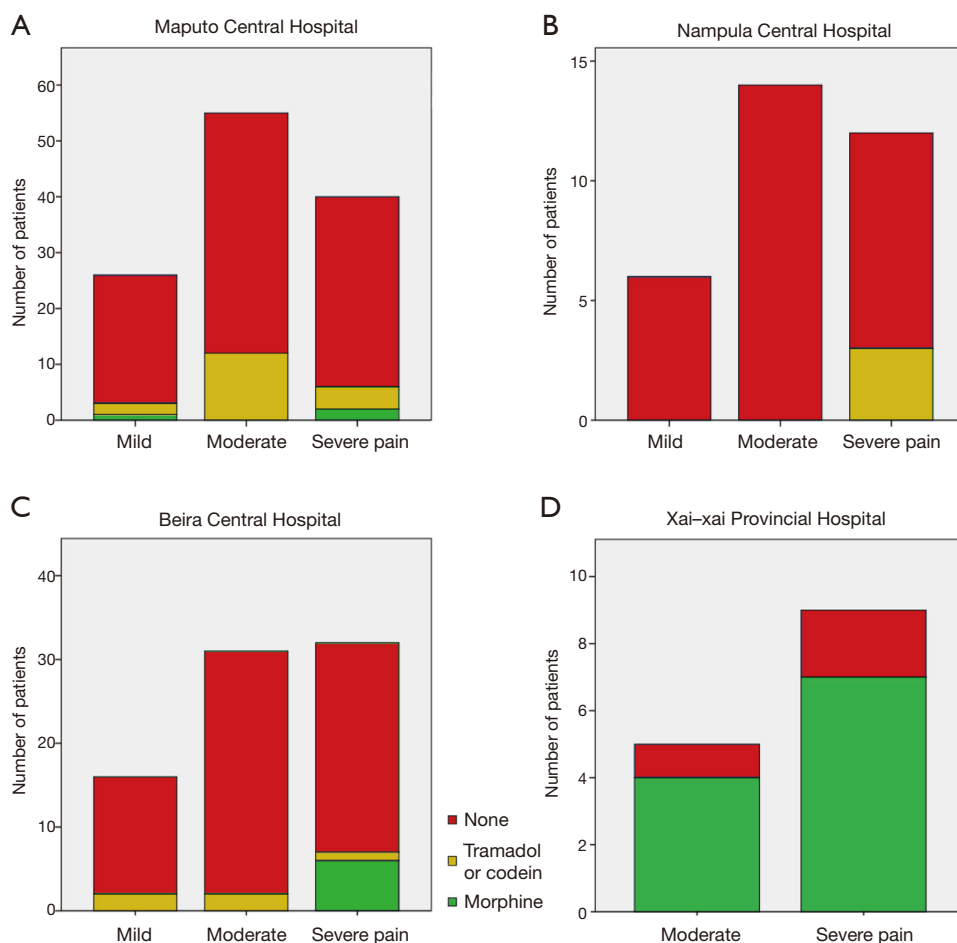


Figure 4 Number of patients receiving tramadol or codeine and morphine by pain's intensity in each hospital: Maputo Central Hospital (A), Nampula Central Hospital (B), Beira Central Hospital (C) and Xai-Xai Provincial Hospital (D).

Table 3 Frequencies, n (%), of analgesic's class and adjuvants administered to patients in pain, by hospital (n=246)

Analgesics and adjuvants	MCH (n=121)	NCH (n=32)	BCH (n=79)	XXPH (n=14)	Total (n=246)
NSAID	0 (0)	2 (6.3)	12 (15.2)	0 (0)	14 (5.7)
Paracetamol	45 (37.2)	9 (28.1)	38 (48.1)	13 (92.9)	105 (42.7)
Codeina	6 (5)	0 (0)	4 (5.1)	0 (0)	10 (4.1)
Tramadol	12 (9.9)	3 (9.4)	1 (1.3)	0 (0)	16 (6.5)
Morphine	3 (2.5)	0 (0)	6 (7.6)	11 (78.6)	20 (8.1)
Dexamethasona	4 (3.3)	0 (0)	1 (1.3)	0 (0)	5 (2)
Prednisolone	1 (0.8)	0 (0)	6 (7.6)	0 (0)	7 (2.8)
Amitriptylyne	2 (1.7)	0 (0)	2 (2.5)	10 (71.4)	14 (5.7)

NSAID, Non-Steroidal Anti-Inflammatory Drugs; MCH, Maputo Central Hospital; NCH, Nampula Central Hospital; BCH, Beira Central Hospital; XXPH, Xai-Xai Provincial Hospital.

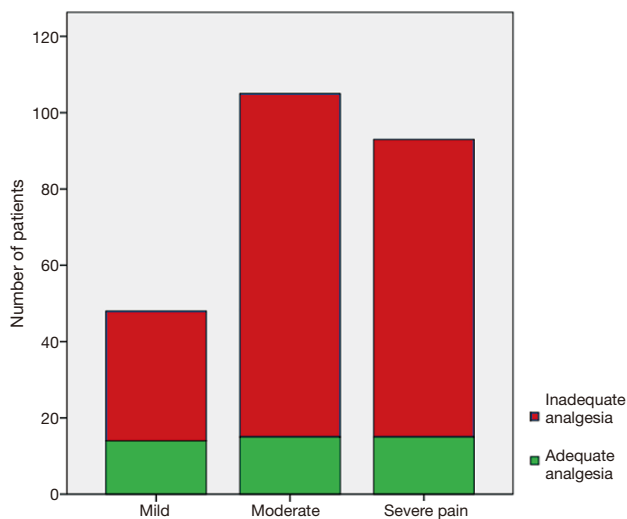


Figure 5 Number of patients with adequate and inadequate analgesia by pain's intensity.

(the only province of the country with isolated provision of palliative care services).

The prevalence of cancer pain was 83.6% mainly in cervix and breast cancer in women and Kaposi sarcoma and prostate cancer in men. Most of the patients had moderate to severe pain, and there were no significant differences in pain reported by gender in Kaposi sarcoma, in any assessment of the pain involved in the study. Paracetamol was the main analgesic used for severe pain. Morphine and adjuvants was used most in Xai-Xai Provincial Hospital. Most of the patients had an inadequate analgesia and significant differences were found in PMI levels between hospitals. Inadequate analgesia was found in the reference hospital of the country—MCH. Moderate-severe pain was present in 61.8% of HIV patients.

According to WHO's projections for 2030, the 2 main cancer diagnoses in women (cervical and breast cancer), and the 2nd and 3rd in men (prostate and liver cancer), in Maputo-Mozambique will be the main causes of cancer mortality in Sub-Saharan Africa (9-11). Cervical cancer among females were the leading cause of cancer deaths in Mozambique with 42/100,000 people (12,13).

The type of cancer, treatments performed or ongoing and characteristics of the patient determine the intensity of the pain and its effects. The prevalence and severity of pain depends on the progression of the disease (3).

According to the WHO guidelines for cancer pain's management, it is considered adequate management when there is a congruence between the patient's reported level of

pain and the potency of prescribed analgesic drug (based on the analgesic ladder). The pain-management index compares the most potent analgesic prescribed for a patient with that patient's reported levels of pain (14), and it measures the health care provider's response to a patient's pain.

The global context of opioids consumption shows that Australia, Canada, New Zealand, the United States, and several European countries account for more than 90% of the global consumption of opioid analgesics. Furthermore, the consumption of opioids in most Asian countries continues to increase at a slower rate than global averages (15). Opioid consumption is an indicator of palliative care services in a country, and morphine is a WHO essential medicine, however it is drastically limited, or absent, in many developing countries where its consumption is only 6% of global opioid consumption (3,16). In India, less than 1% of the population has access to pain relief and palliative care (17). According to the International Narcotics Control Council (INCB), about 80% of the world population, the majority in developing countries, do not have access to strong analgesia (5,18).

Adequate pain relief can be achieved in more than 75% of patients using simple WHO analgesic ladder such as techniques, opioids, non-opioid analgesics, and adjuvant medications (19).

Many health professionals in developing countries are focused on treating diseases that cause pain, rather than to relieve the pain itself, and this contributes greatly to inadequate pain relief (20).

The main barriers that interfere with adequate pain management in Africa are problems related to health-care system, health professionals and patients (21). One of the main gaps between pain management needs and what was provided was the health-care system; many governments remain passive while people is suffering. Part of this passivity contributes to the chain: absence of policies or guidelines for pain's treatment or palliative care's guidelines for health professionals and insufficient efforts to ensure morphine access and availability for those who need it (6).

In Mozambique, the legal and policy restrictions negatively affect the opioids' availability (5). Comparing to Uganda's consumption (100 kg/42 million population), Mozambique's consumption was only 4.7 kg out of the expected 322 kg per year for 26 million inhabitants in 2015.

The obstacles to the use of opioids in Mozambique also include: inadequate knowledge, lack of information and negative attitudes towards controlled substances (22).

In Mozambique compared to other countries, did not have another alternatives such as oxycodone, hydromorphone and

Table 4 Frequencies n (%), of analgesia adequacy by hospital and gender (N=246)

Hospital	Female (n=149)		Male (n=97)		Total	
	Inadequate Analgesia	Adequate Analgesia	Inadequate Analgesia	Adequate Analgesia	Inadequate Analgesia	Adequate Analgesia
MCH	70 (84.3)	13 (15.7)	35 (92.1)	3 (7.9)	105 (86.8)	16 (13.2)
NCH	14 (100.0)	0 (0.0)	18 (100.0)	0 (0.0)	32 (100.0)	0 (0.0)
BCH	33 (80.5)	8 (19.5)	29 (76.3)	9 (23.7.0)	62 (78.5)	17 (21.5)
XXPH	0 (0)	11 (100.0)	3 (100.0)	0 (0.0)	3 (21.4)	11 (78.6)
Total	117 (78.5)	32 (21.5)	85 (87.6)	12 (12.4)	202 (82.1)	44 (17.9)

MCH, Maputo Central Hospital; NCH, Nampula Central Hospital; BCH, Beira Central Hospital; XXPH, Xai-Xai Provincial Hospital.

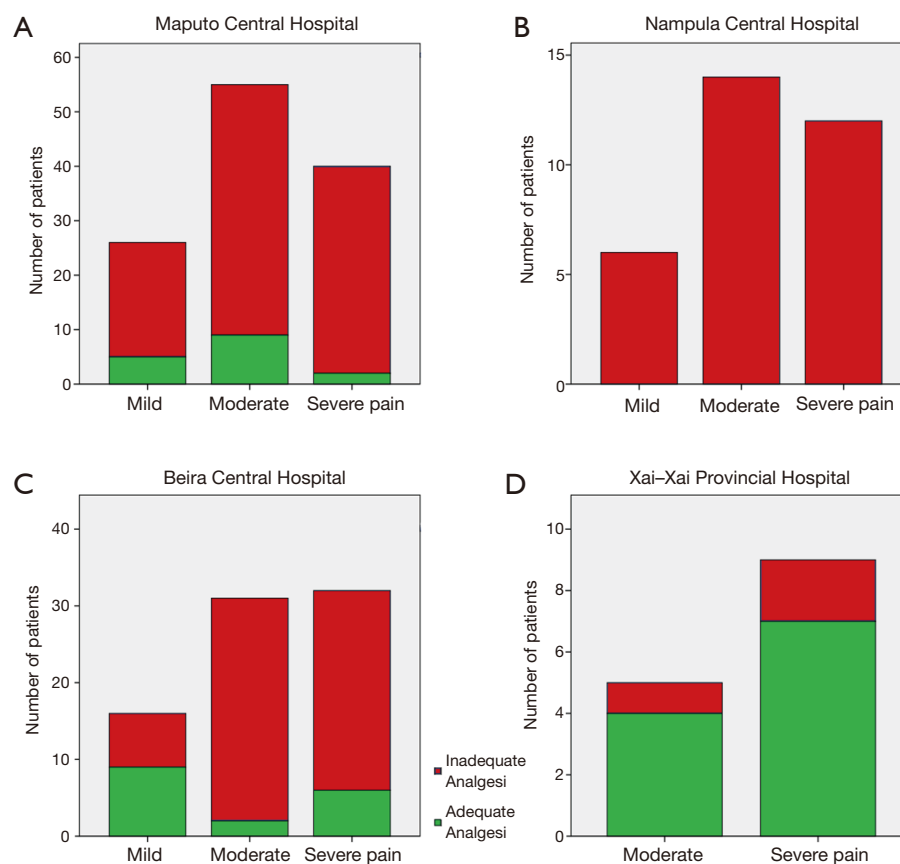


Figure 6 Number of patients with adequate and inadequate analgesia by pain's intensity (mild, moderate and severe) in each hospital: Maputo Central Hospital (A), Nampula Central Hospital (B), Beira Central Hospital (C) and Xai-Xai Provincial Hospital (D).

transdermal opioids presentations as an essential medicines. It could be found in some private pharmacies and hospitals, however they were very expensive for the most of the population.

Access to health care in Mozambique was limited by

distances to the nearest health service provider and the few health professionals, as well as frequent stock outs of medicines in general and opioids in particular. The estimation method for Mozambique's national annual opioid requirements was consumption-based and it

considered only the past year's consumption and existing stocks. Studies carried out in Mozambique already pointed to a low consumption of morphine, and this limited access and availability of opioids, increases patients' suffering and deeply impacts their quality of life.

This study revealed a slightly higher pain's prevalence compared to world statistics that point to 70–80% for moderate-severe pain in cancer patients, and most of them in developing countries (7).

The Xai-Xai Provincial Hospital although being small and with simple size, demonstrated better pain's control than other hospitals. The training actions on pain management and palliative care developed in this hospital contributed significantly to better symptomatic pain control in oncologic patients. Unrelieved pain negatively affects the patient's quality of life and family economy; it also influences a patient's ability to withstand treatment changes and overloads the healthcare system (23).

In 2012, in MCH-Pain Unit, paracetamol was also the most commonly used drug (33.9%) and morphine was used in 10.2% of cancer patients (24,25). The OMS guidelines address first-line treatment with strong opioids for patients who have been assessed as requiring pain relief at the third level of the WHO pain ladder (26).

Along with opioids, adjuvant drugs such as antidepressants and anticonvulsants, play an important role in pain management. In these hospitals, amitriptyline and corticosteroids were less used for pain control.

Significant differences were found in PMI levels between hospitals in our study. It was at the Xai-Xai Provincial Hospital that the highest PMI levels were observed, with adequate levels for 78.6% of its sample patients while the remaining hospitals had adequate PMI levels in less than 21.5% of sample patients. In Portugal, the PMI results were acceptable to good (25).

Pain can also be relieved by the modification of the disease process, when appropriate, with surgery, chemotherapy, and radiotherapy (27). Although Mozambique has all these techniques, they are inaccessible to many patients, because most of them usually get to the hospital at an advanced stage of illness, and others live in rural areas where these services are non-existent.

Pain is a common symptom in people living with HIV/AIDS. Several studies claim that 60–80% of HIV/AIDS patients report pain in an advanced stage of the disease. They may experience pain as (I) a direct result of the viral replication mechanisms on the peripheral or central nervous systems; (II) pain may be due to immune suppression and

resultant opportunistic infections; or (III) pain may arise because of the side effects of the continuous anti-retroviral treatment (3,28). Close to half of the oncologic patients in this study had HIV-AIDS as the main co-morbidity, and most of them (74%) were taking antiretroviral treatment. Most of these patients were moderate-severe pain's intensity related. In these patients, they may experience pain not only due to the cancer disease itself, but also concomitant infection and/or HIV treatment.

The excessive strict drug control regulations that unnecessarily prevent access to morphine or establish excessive penalties for misuse; lack of adequate supply of opioids and other drugs for pain relief, strong bureaucracy involved in terms of procurement and dispensing of opioids; the lack of training of health professionals on pain management and palliative care as part of their training that negatively influences attitudes towards controlled substance (3,6,15,24,29).

Limitations

The main limitations were:

- (I) Related to the sample in Xai-Xai Provincial Hospital, we did not complete the sample because of limited time.
- (II) Disparity of resources between the different hospitals in the country, which does not allow to staging for all tumors.
- (III) Only 4 hospitals were surveyed, so this data may not be generalizable to the whole country.

Conclusions

The overall prevalence of pain is slightly higher than reported by other studies. Most of the oncologic patients in Maputo, Beira and Nampula Central hospitals in Mozambique, were suffering because of inadequate analgesia. Less than 10% of oncologic pain's patients in these hospitals had access to strong analgesia as morphine. Xai-Xai Provincial Hospital, (the only Provincial hospital in the country with a standalone palliative care Service) was the only hospital with adequate analgesia were all the patients with moderate to severe pain was taking morphine. We also concluded that the presence of health professionals trained and qualified in the management of pain and palliative care significantly improves the symptomatic control of patients. Further studies are needed to understand if the suffering reported by the patients is due to the lack of medicines or lack of professional's knowledge in

pain management or both.

Acknowledgments

We would like to thank Gulbenkian Foundation grant number N°.144879, and Ministry of Health of Mozambique for individual PhD grants' contributions.

Funding: None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <http://dx.doi.org/10.21037/apm-20-2009>

Data Sharing Statement: Available at <http://dx.doi.org/10.21037/apm-20-2009>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/apm-20-2009>). The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Committee of Bioethics for Health of the Faculty of Medicine & Maputo Central Hospital with number CIBS FM&HCM/08/2018 and by the Bioethics Committee of the Faculty of Medicine of the University of Porto, and informed consent was taken from all the patients.

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Cite this article as: Pinto E, Gonçalves F, Sacarlal J, Castro L, Rego G. Pain management in cancer patients in the main hospitals in Mozambique. *Ann Palliat Med* 2021;10(4):4069-4079. doi: 10.21037/apm-20-2009