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# OUTCOMES IN PALLIATIVE CARE FOR ADVANCED PROSTATE CANCER IN THE RADIOTHERAPY AND ONCOLOGY DEPARTMENT OF THE AHMADU BELLO UNIVERSITY TEACHING HOSPITAL, ZARIA.

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## ABSTRACT

**BACKGROUND:** Adoption of palliative care approach in the management of advanced prostate cancer is important because of the advanced nature of the disease, long course of disease and the fact that prostate cancer predominantly affects the elderly people who are at greater risk of having other comorbidities. Most patients with prostate cancer present at an advanced stage in Radiotherapy and Oncology Department (ABUTH) requiring the use of palliative radiotherapy, chemotherapy, hormonal manipulations, bisphosphonates, analgesics, psychosocial, spiritual and financial support.

**AIM:** The aim was to evaluate the effect of palliative care in the management of advanced prostate cancer. The objectives were to determine the effect of palliative external beam radiotherapy, chemotherapy, bisphosphonates and analgesics in symptom control.

This study is a 9 years retrospective study of patients with advanced prostate cancer from January 2006 to December 2014. Information was obtained from the treatment cards as well as case files.

**RESULTS:** Results showed that 139 patients received palliative External Beam Radiotherapy (EBRT). Commonest indication was pain of bone metastases seen in 84(60%) patients. Others included obstructive uropathy in 41(30%) patients, spinal cord compression in 8(6%) patients and bleeding in 6 (4%) patients. One hundred and eight (77.7%) patients received analgesics and 123 (88.5%) patients received haematinics. Bisphosphonates were administered to 34(24%) patients, while 26(17%) patients received chemotherapy. These various forms of treatment resulted in good symptom control and improved quality of life.

**CONCLUSION:** Palliative care plays a pivotal role in the management of advanced prostate cancer, and the earlier it is commenced, the better the outcome for the patients.

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## INTRODUCTION

Traditionally, advanced prostate cancer was considered as disease that had metastasized beyond the prostate, to the surrounding tissue, pelvic lymph nodes and considered incurable.<sup>1-2</sup> Current evidence indicates that patients with significant risk of progressive disease, and patients with cancer outside the capsule with disease stage as low as T3 N0 M0 have advanced disease.<sup>3</sup>

Worldwide, prostate cancer is the second commonest malignancy in men.<sup>4</sup> Studies in Nigeria revealed a rising incidence of prostate cancer.<sup>5-6</sup> This can be attributed to increased awareness and improved screening methods.

Most patients (90%) present at an advanced stage due to ignorance, poverty, inadequate diagnostic facility and absent screening. Prostate specific antigen (PSA) blood test and yearly digital rectal examination (DRE), beginning at age 50 should be offered to men who are at average risk of prostate cancer. Some also present with other co morbidities, necessitating the adoption of palliative care as an important management approach.<sup>7</sup> This requires the use of palliative radiotherapy, palliative surgery, hormonal manipulations, chemotherapy, bisphosphonates and analgesics, aimed at improving quality of life.<sup>8</sup>

We review our experience in palliative care of advanced prostate cancer over a 9 year period to highlight the effect of palliative EBRT, chemotherapy bisphosphonates and analgesics in symptom control.

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## PATIENTS AND METHODS

This was a nine year retrospective study of advanced prostate cancer patients from January 2006 to December 2014. Information was obtained from patient's treatment card and folders. Data was analyzed using SPSS version 20.

## RESULTS

Hundred patients were studied from 2006 to 2014. The highest number of patients was seen in 2010 (Table 1). The age ranged from 50 years to 90 years with median age of 60 years (Figure 1). Commonest histological type was adenocarcinoma seen in 137(98%) patients. Leiomyosarcoma occurred in a (0.7%) 55 year old patient and a (0.7%) case of urothelial carcinoma was recorded (Table 2). Eighty-four (60.4%) patients had Gleason score between 8 and 10, 38(27.4%) patients had Gleason score between 4 and 6, while 15(10.8%) patients had Gleason score of 7 (Table 3). Prostate specific antigen (PSA) value between 0-10ng/ml were seen in 42(30.2%) patients, 47(33.8%) patients had PSA value between 11ng/ml - 20ng/ml, 25(18%) patients had between 21ng/ml-100ng/ml while another 25(18%) patients had PSA value greater than 100ng/ml. (Figure 2).

Pain of bone metastasis was seen in 84 (60%) patients followed by urinary obstruction in 41 (30%) patients, spinal cord compression in 8 (6%) patients, bleeding in 6 (4%) patients were the commonest symptoms seen in our department (Figure 3).

Duration of symptoms ranged from 6 months to 3 years. Pelvic bone was the commonest site of metastasis seen in 54(39%) patients, followed by the lumbar bone in 32 (23%) patients (Table 4). Other sites of bony metastases were thoracic 17 (12%) patients, cervical 11(8%) patients sacral 11(8%), humerus 8 (6) patients and femur 6 (4%) patients. Thirty four (24%) patients received bisphosphonates. Goserelin (Zoladex) was

administered to 17(12%) patients. Twenty four (17%) patients received chemotherapy using intravenous docetaxel 75mg/m<sup>2</sup> and prednisolone once every 3 weeks which was repeated for up to 6 to 10 cycles as tolerated. The case of urothelial carcinoma received intravenous Cisplatin 75mg/m<sup>2</sup> and 5 fluorouracil 500mg/m<sup>2</sup> combination chemotherapy while the case of leiomyosarcoma received Vincristine 2mg/m<sup>2</sup>, Adriamycin 50mg/m<sup>2</sup> and Cyclophosphamide 500mg/m<sup>2</sup> (Table 5). Oral morphine (10mg tds) was administered to 38(27%) patients and 70(50.4%) patients received non steroidal anti-inflammatory drugs. Record of analgesic prescription was not found in 32(23%) patients. All the patients received palliative external beam radiotherapy (EBRT). The commonest site of metastasis requiring palliative external beam radiotherapy was the pelvic region. 15 Gray (Gy) in 5 fractions (#) over 1 week was the commonest prescribed dose which was followed by 8Gy in single fraction (table 6).

Sixty patients (43%) received financial support from their families and careers. 54(39%) patients supported themselves financially. State governments assisted 6(4.3%) patients while ministry of health assisted only 1(0.7%) patient. Public institutions rendered financial aid to only 4(2.9%) patients while religious bodies supported 14 (10.1%) patients financially (Fig 4). There was no health insurance cover for cancer patients during the period. Twenty eight (20.1%) patients benefited from spiritual support given mainly as part of end of life care. At six months follow up 28(20.1%) patients were referred back to their primary referral centers, 21(15.1%) patients were lost to follow up and 14 (10.1%) patients died. Fifty six 56(40.3%) patients had immediate relief of symptoms after completion of treatment, while 20(14.4%) patients experienced symptom relief within 6 months of treatment (Table 7).

YEAR	NO. OF PATIENTS	Percentage %
2006	10	7.2
2007	10	7.2
2008	22	15.8
2009	14	10.1
2010	24	17.3
2011	20	14.4
2012	18	12.9
2013	6	4.3
2014	15	10.8
<b>TOTAL</b>	<b>139</b>	<b>100</b>

Fig. 1: Bar Chart showing the age distribution.

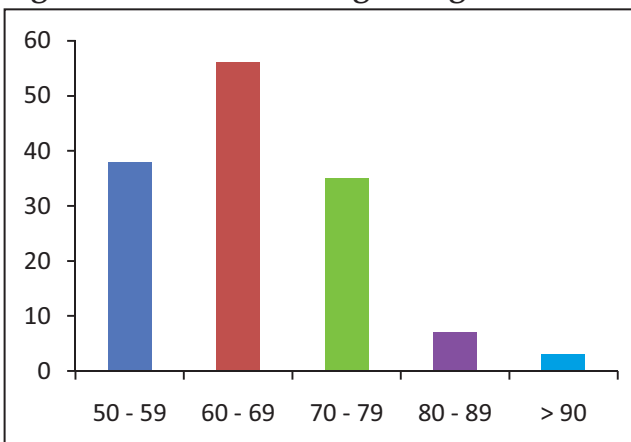


Table 2: Table showing the tumor histological types

Histological Types	Frequency	Percentage %
Adenocarcinoma	137	98.6
Leiomyosarcoma	1	0.7
Urothelialcarcinoma	1	0.7
<b>TOTAL</b>	<b>139</b>	<b>100</b>

Table 3: Gleason score

Gleason Score	Frequency	Percentage %
No Gleason score	2	1.4
6	38	27.4
7	15	10.8
8 - 10	84	60.4
<b>TOTAL</b>	<b>139</b>	<b>100</b>

Fig. 2: Bar chart representing PSA distribution

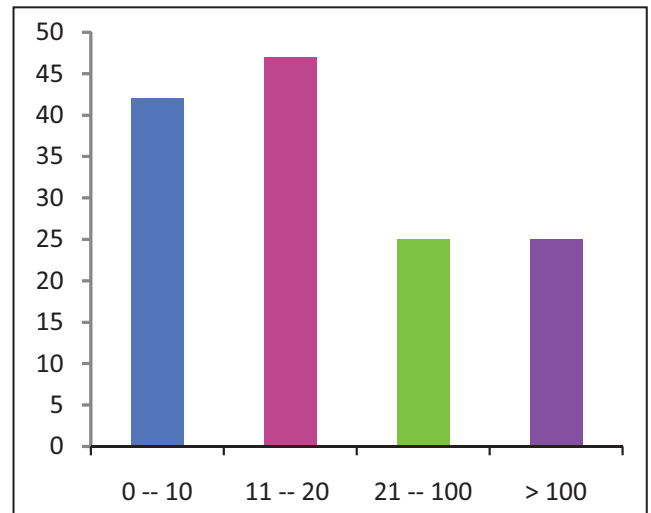


Fig. 3: Pie chart showing indication for Palliative EBRT

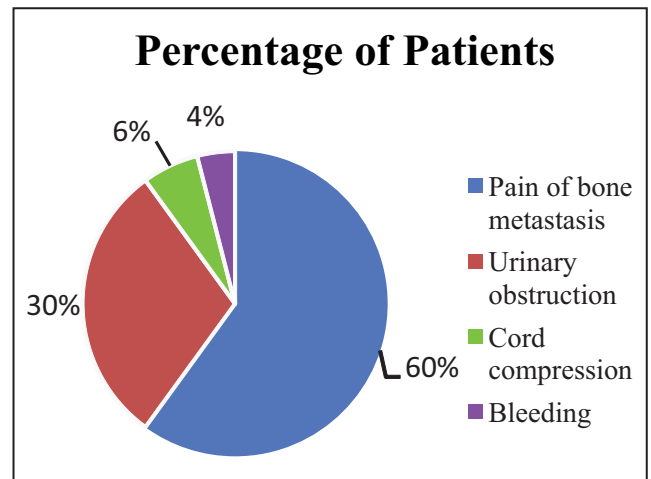


Table 4: Table showing Patients metastatic site

Metastatic Site	Frequency	Percentage %
Pelvis	54	39
Lumbar	32	23
Thoracic	17	12
Cervical	11	8
Sacral	11	8
Humerus	8	6
Femur	6	4
<b>TOTAL</b>	<b>139</b>	<b>100</b>

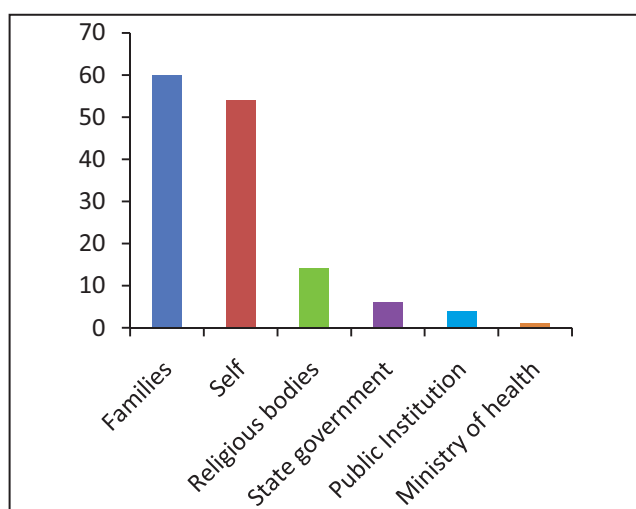
**Table 5: Table showing Chemotherapy agents received by patients**

Chemotherapy Agents	Frequency	Percentage
Docetaxel + Prednisolone	24	92.4
VAC	1	3.8
Cisplastin + 5FU	1	3.8
<b>TOTAL</b>	<b>26</b>	<b>100</b>

**Table 6: Table showing EBRT Schedule of Patients**

EBRT Schedule	Frequency	Percentage
15Gy in 5 fractions(#)	43	31.0
8Gy in 1#	42	30.2
20Gy in 5#	21	15.1
30Gy in 10#	19	13.6
50Gy in 25#	14	10.1
<b>Total</b>	<b>139</b>	<b>100</b>

**Fig. 4: Bar chart representing financial support received by patients**



**Table 7: Table showing EBRT treatment outcome of patients at 6 months**

Treatment Outcome	Frequency	Percentage
Immediate pain relief	56	40.3
Pain relief after 6 months	20	14.4
Referred back	28	20.1
Loss to follow up	21	15.1
Passed on	14	10.1
<b>Total</b>	<b>139</b>	<b>100</b>

## DISCUSSIONS

Utilization of palliative care approach in the management of advanced prostate cancer impacts positively on the quality of life of these patients. Significant pain reduction as well as improvement in physical, emotional and social functions can be achieved.

In this study, the median age of the patients was 60 years. Although this is earlier than that reported in Ibadan and Port Harcourt which were 71.6 years and 71.4 years respectively but it still confirms that prostate cancer is a disease that occurs with old age.<sup>6-7</sup> These patients may be prone to other co morbidities as a result of advancing age.

Levels of prostate specific antigen in the blood are significantly elevated in prostate cancer. There is no clear “cut-off” level for normality, though >4ng/ml in the blood is associated with a 20% risk of cancer of the prostate. The rate of fall in the treatment is a good prognostic indicator of response.

The pelvic region was the commonest metastatic site followed by the lumbar spine. This does not correspond with what was found in advanced countries where the lumbar vertebrae was the commonest, followed by sternum, pelvic, ribs and femur.<sup>9</sup> However some studies also reported the pelvis as the commonest metastatic site.<sup>10</sup>

Fifteen Gray (15Gy) in 5# over one week was the most frequently prescribed dose as reported in this study. However, studies showed that 8Gy in single fraction a form of short course treatment is also effective, reduces cost and stress on the patient and care givers. However, studies found that re-treatment is commoner with 8Gy in single fraction.<sup>11</sup> Commonest indication for palliative radiotherapy in our setting was pain from bony metastasis (60%). This is in agreement with similar studies which recorded pain from bony metastasis highest in their list.<sup>12</sup>

Other indications included obstructive symptoms 30%, cord compression 6% and bleeding 4%.

Chemotherapy agent that was used in this study was docetaxel which was given intravenously to 24 patients. A case of leiomyosarcoma in a 55 year old man received VAC regimen and the only case of urothelial carcinoma received Cisplatin and 5FU combination chemotherapy.

The use of intravenous docetaxel with prednisolone is the practice globally supported by the landmark clinical trial (TAX 327 study).<sup>13</sup>

The quality of life improved, and pain was reduced, decreasing the need for analgesics which was among the outcome that was seen in the TAX 327 study. The use of analgesics as symptom relief was also documented in a study by Adenipekun et al in Ibadan.<sup>14</sup> However this comes with an increased cost.

24 patients benefited from the administration of bisphosphonates. Intravenous Zoledronic acid 4mg every 3 weeks was the only type prescribed according to this study. The aim was to reduce skeletal related events and improve quality of life which is supported by different studies.<sup>15</sup>

Pain relief was also achieved using the World Health Organization (WHO) step ladder principle. Most patients in this study had moderate to severe pain for which weak opioids such as tramal and also non-steroidal anti-inflammatory drugs (diclofenac) were given. Thirty eight (27.3%) patients received strong opioids (Morphine) which was able to reduce their pain significantly.<sup>16-17</sup>

Other forms of palliative care services including spiritual care were rendered by the palliative care team in Radiotherapy and Oncology Department of ABUTH. Seventy (50.4%) patients benefitted as well as their family members. Patients who benefitted from palliative care were more stable psychologically and their family members were more satisfied. Studies have supported palliative care as a means of improving the quality of life of the patients and their care givers.<sup>18</sup>

Immediate pain relief was recorded in 56 patients (40.3%) after receiving palliative EBRT treatment. Other symptoms such as bleeding, urinary obstruction, spinal cord compression were significantly reduced. However, the degree of pain, symptomatic relief, duration of relief of pain and other symptoms which a prospective study considering patients reported outcome will discover is ongoing in our center.

## CONCLUSION

The approach to treatment is influenced by age, histological grade, co-morbidities and PSA level.

Palliative care approach is effective in the symptomatic control of patients with advanced prostate cancer. A multi-disciplinary team approach to treatment and other modalities such as EBRT chemotherapy will reduce the level of dependency on analgesics use among others.<sup>12</sup> The side effects of different forms of treatment are to be considered in determining appropriate management.

There is need for awareness and more research efforts which will ultimately result in improving the quality of life of these patients and their care givers. The advanced prostate cancer is not usually curable, and a substantial fraction of the patient will eventually die of their cancer. Median survival is usually 1 to 3 years. Men with advanced prostate carcinoma should be encouraged to participate in clinical trials and referred early to a clinical oncologist for a better outcome.

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