

# Role of Ethnicity and Tumour Factors in Pain Perception and Radiation Analgesia among Breast Cancer Patients with Metastatic Bone Pain

Usman Bello<sup>1\*</sup>, Hassan Ibrahim<sup>2</sup>

<sup>1</sup>Department of Morbid Anatomy and Forensic Medicine / Histopathology College of Health Sciences, Usmanu Danfodiyo University/ Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria

<sup>2</sup>Department of Radiotherapy, Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria

DOI: [10.36348/sjm.2022.v07i11.002](https://doi.org/10.36348/sjm.2022.v07i11.002)

| Received: 24.07.2022 | Accepted: 31.08.2022 | Published: 04.11.2022

\*Corresponding Author: Usman Bello

Department of Morbid Anatomy and Forensic Medicine / Histopathology College of Health Sciences, Usmanu Danfodiyo University/ Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria

## Abstract

**Background:** Palliative external beam radiotherapy (PRT) had been reported as an indispensable tool for an effective pain relief in cancer patients with metastatic bone pain. Although many scholars reported a link between pain perception and ethnic background of an individual, but its role in cancer patients with interplay of other tumour factors needs to be evaluated to ascertain the actual impact it may have on pain perception and responses to radiation analgesia. **Methods:** We retrospectively reviewed patient's data of breast cancer with metastatic bone pain between 2015 and 2018. Patient's demographic factors like age, sex, ethnic group, tumour histology, RBS grade and sites of metastasis were extracted and grouped accordingly. Other Radiotherapy doses used for palliation of pain were extracted. Visual analogue pain assessment scale (0-10) was used by doctors (majority from Hausa-Fulani ethnic origin) to assess pain at presentation and four weeks post-irradiation. SPSS version 23 was used for data analyses; univariate and multivariate analyses were conducted to test for any significant associations between predictive factors and dependent variables. Results were presented in pie-charts, bar-charts and tables. **Results:** A total of 161 patients reviewed during the study period, 159 (99%) were females and 2(1%) were males with mean age of 45.2 years, the age groups of 20-29 yrs presented with highest pain score. Among the three major ethnic groups, Yoruba constituted 31.7% with mean pain score of  $7.5 \pm 1.4$ , followed by Igbo (26.1%) with mean pain score of  $7.1 \pm 1.4$ . The commonest histology were invasive ductal (IDC) and invasive lobular (ILC) carcinoma with each having 7 as the highest mean pain score. Patients with grade 2 and 3 were the commonest and presented with mean pain score of  $6.9 \pm 1.4$  and  $6.7 \pm 1.6$  respectively. Patients with spinal cord compression (5.6%) presented with highest mean pain score of  $7.3 \pm 1.3$ , followed by metastasis to long bones with pain score of  $7.0 \pm 1.5$ . Pain alone was the highest presenting symptom (92.5%) from bone metastasis and Conventional X-ray was the common imaging modality used in confirmation of metastatic sites (68.3%). Common palliative radiation doses used were 11-20Gy in 4-6# (60%). Overall mean pain score at presentation was  $6.8 \pm 1.5$  and  $0.6 \pm 0.7$  four weeks after irradiation. In univariate analysis (binary comparison) only ethnicity was highly significant ( $p < 0.001$ ) in pain perception pre-radiotherapy and the significance exist after controlling other influential factors using multivariate analysis ( $p < 0.001$ ). In post-irradiation using univariate analysis, ethnicity and metastatic sites shows significant association with pain relief, after multivariate analysis when influential factors were controlled, it appeared only metastatic sites with p-value of 0.008. **Conclusion:** Ethnicity of three major tribes in Nigeria played a role in pain perception from bone metastasis at presentation, with Yoruba higher pain perception compared to Hausa-Fulani and Igbo. But ethnicity appeared insignificant in response to radiation analgesia. Similarly, tumour factors appeared in significant in pain perception and response to radiation analgesia. However, metastatic sites influence response to radiation analgesia, with good pain relief in patients with metastasis to ribs and long bones.

**Keywords:** Ethnicity, breast cancer, bone metastasis, pain and palliative external beam radiotherapy.

**Copyright © 2022 The Author(s):** This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

## INTRODUCTION

The most frequent consequence of bone metastases is pain [1]. It was estimated that fifty percent of all cancer pain is due to bone metastases [2]. Bone

pain most frequently affects the spine and the chest, although pain in the hip, girdle and shoulder are also common [2]. The periosteum, a thick membrane covering all bones, contains many receptors and is

highly sensitive to mechanical or chemical stimulation. Increasing pressure from an expanding tumor, cytokine release, the formation of micro fractures, and pathological fracture may all stimulate the periosteum, and produce the sensation of pain [1]. Bone pain is generally a dull aching pain that may be interspersed with a stabbing discomfort. Pain is often worsened by movement, and this debilitation is associated with a reduction in quality of life [1]. Although currently available therapies have the potential to be effective in most cases, under treatment is common, and about 30 percent of cancer patients even in developed nation never achieve adequate relief [3].

Perception to pain and the ways it's being managed by many societies had been linked with socio-cultural factors and ethnic background [4]. Although no study dwell on impact of pain perception on cancer patients in Nigeria, however, several studies were conducted among Nigerian population (non-cancer) that show substantial evidence of the role of ethnicity in pain perception [5]. Several factors were considered to affect pain perception on cancer and non-cancer patients, but lack of adequate knowledge on those factors between patients and health care providers serve as barriers to adequate cancer pain management [6]. Variety of management modalities were involved in relieving pains from metastatic deposits, these include the use of analgesics, palliative radiotherapy, chemotherapy, hormone therapy, bisphosphonates, and surgery. In many cases, the management of bone metastases involves a combination of treatments; however, one treatment modality (palliative external radiotherapy) stand very effective in pain relief from bone metastasis especially when opioid failed [7]. The exact mechanism of radiation-induced pain relief remain a mystery, some authorities speculate that the analgesic effect of radiation is achieved by reducing tumour burden via amplification of ossification process and depression of osteoclasts activity as well as decreasing concentration of chemical pain mediators in the radiation field [8]. No doubt about the fact that numerous studies have reported a link between patient's ethnic background and their degree of pain perception [9], however, what remain unclear is whether ethnicity and other tumour factors influence responses of cancer patients to radiation analgesia.

## **MATERIALS AND METHODS**

### **Patients**

We retrospectively reviewed patient's data of breast cancer with bone metastasis between 2015 and 2018. Only patients with histological diagnoses of breast cancer and radiological (X-rays, MRI, CT- scan and bone scan) confirmation of bony metastasis were considered eligible. Patient's bio-data like age, sex, tumour histology and tumour grade were extracted and grouped accordingly. Patients were also grouped according to three major ethnic groups in Nigerian (Hausa-Fulani, Yoruba and Igbo). Records of pain

assessment by doctors (Hausa-Fulani ethnic origin) using Visual analogue pain scale at presentation and four weeks post-irradiation were extracted. The form is graded from 0 to 10 with 0 score as no pain and 10 as the worst pain ever experienced in life by the patient. Sites of bony metastasis were also extracted according to bone affected or number of metastases. Presenting complaint were also recorded and grouped as pain alone, pain and sensory deficits, pain- sensory and motor deficits.

### **Treatment**

Palliative radiotherapy was delivered using Elekta precise linear accelerator machine. Doses ranging between 5-35Gy at 2.5-8Gy per fraction were used to treat patients between 1-10 working days. The target volume consist of the primary lesion with margins of 1-3cm or one vertebra above and below the affected vertebral disc in the case of vertebral metastasis or spinal cord compression, direct single field for vertebral region and two opposing fields were used for long bones.

### **Statistical Methods**

Age of patients were grouped, their mean age together with standard deviation were calculated. Percentage figures of presenting symptoms, sites of metastatic and ethnic groups were calculated. Pain scores were assessed at presentation and four weeks after the radiotherapy for all the patients under their demographic factors. A univariate analysis was conducted using Binary comparison to assess for any significant association between mean pain score pre and post irradiation with the patient's demographic factors. Similarly, multivariate analysis was conducted using regression analysis to control for other influential factors that may alter the results. Results were represented in tables, bar-charts and pie-charts.

## **RESULTS**

One hundred and sixty one patients were eligible during the study period with only two male patients (fig1). Table 1 shows the demographic factors of patients with painful bone metastasis from breast cancer and their mean pain score at presentation, with mean age was 45.2 years with standard deviation of 11.2. Age group between 20-29 yrs accounted for 5% of patients with highest mean pain score of 7.6 at presentation, 30-39 (25.5%) with 6.9, 40-49 (38.5%) with 6.6, 50-59 (16.8%) with 7.1, 60-69 (12.4%) with 7.0 and  $\geq 70$  years with 7.0. Patients were grouped in to three major ethnic groups, Hausa-Fulani (42.2%) with mean pain score of 6.2 pre-irradiation, Yoruba (31.7%) with 7.5 and Igbo (26.1%) with 7.1. The invasive ductal carcinoma (IDC) accounted for 58% of the histology with mean pain score of 7, 28% for invasive lobular carcinoma (ILC) with mean pain score of 7 and other histology types of 14% with mean pain score of 6.7. Patients with grade 1 tumour (11.8%) presented with mean pain score of 6.7, grade 2 (39.7%) have 6.9, grade

3 (33%) have mean pain score of 6.7 and those patients whose tumour grades were not known have mean pain score of 6.6. Multiple bone metastasis accounts for 65.2% with mean pain score at presentation of 6.8, followed by metastasis to the ribs (11.8%) with 6.9, long bones (9.9%) with 7.0, then 5.6% for Spinal cord compression with mean pain score of 7.3. Figure 2 shows pain as the commonest presenting symptom (92.5%) followed by pain-sensory and motor deficits (4.3%) then pain and sensory deficit (3.1%). Table 2 shows conventional X-ray as the commonest imaging modality (72.4%) used in our centre for confirmation of bone metastasis followed by CT-scan (9.9%), occasional use of M.R.I (1.9%) and in rare cases the use of bone scan (7.9%) or combination of X-ray plus other modalities (4.6%). The dose fractionation schemes used for pain palliation were 11-20GGy in 4-6# (60.2%), 21-30Gy in >6# (36.6%) and 1- 10Gy in 1-2# which account for 3.1% (Figure 3).

Overall mean pain score at presentation was  $6.8 \pm 1.5$  and  $0.6 \pm 0.7$  four weeks after irradiation. In univariate analysis (binary comparison) only ethnicity was highly significant ( $p=0.001$ ) in pain perception pre-radiotherapy (table 3), and the significance exist even after controlling other influential factors in multivariate

analysis (table 4) with  $p < 0.001$ . In post-irradiation, using univariate analysis (table 3), ethnicity and sites of metastatic shows significant association in response to radiation analgesia, after multivariate analysis (table 5) when factors that may influence the outcome were controlled, sites metastasis still appeared to be the a significant factor with  $p$ -value of 0.008.

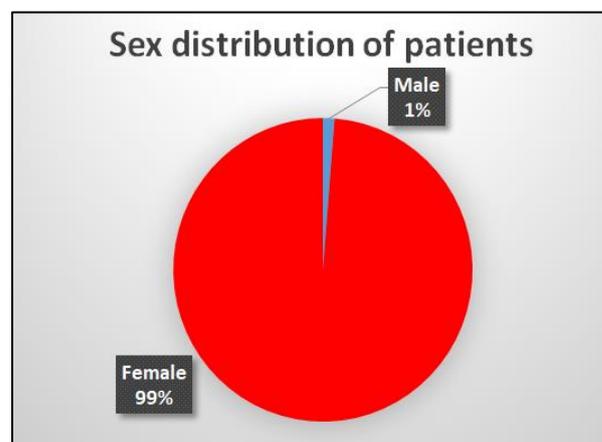


Fig 1: Sex distribution of patients referred for palliative radiotherapy

Table 1: Pain score at presentation under patient’s demographic factors

Characteristics of patients	N (%)	Mean pain score pre-irradiation
<b>Age</b>		
20-29	8 (5)	7.6 ±0.9
30-39	41 (25.5)	6.9 ±1.5
40-49	62 (38.5)	6.6 ±1.5
50-59	27 (16.8)	7.1 ±1.1
60-69	20 (12.4)	7.0 ±1.6
≥70yrs	3 (1.9)	7.0 ±0.9
<b>Ethnic groups</b>		
Hausa-Fulani	68 (42.2%)	6.2 ±1.3
Yoruba	51 (31.7%)	7.5 ±1.4
Igbo	42 (26.1%)	7.1 ±1.4
<b>Histology types</b>		
IDC	93 (58%)	7.0 ±1.5
ILC	45 (28%)	7.0 ±1.4
Others	23 (14%)	6.7 ±1.7
<b>Tumour grade</b>		
Grade 1	19 (11.8%)	6.7 ±1.5
Grade 2	64 (39.7%)	6.9 ±1.4
Grade 3	53 (33%)	6.7 ±1.6
Unknown	25 (15.5%)	6.6 ± 1.3
<b>Metastatic Sites</b>		
Multiple metastases	105 (65.2)	6.8 ±1.5
Ribs	19 (11.8)	6.9 ±1.7
Long bones	16 (9.9)	7.0 ±1.5
Spinal cord compression	9 (5.6)	7.3 ±1.3
Others	8 (5)	6.7 ±1.4
Impending fracture	4 (2.5)	6.4 ±1.7

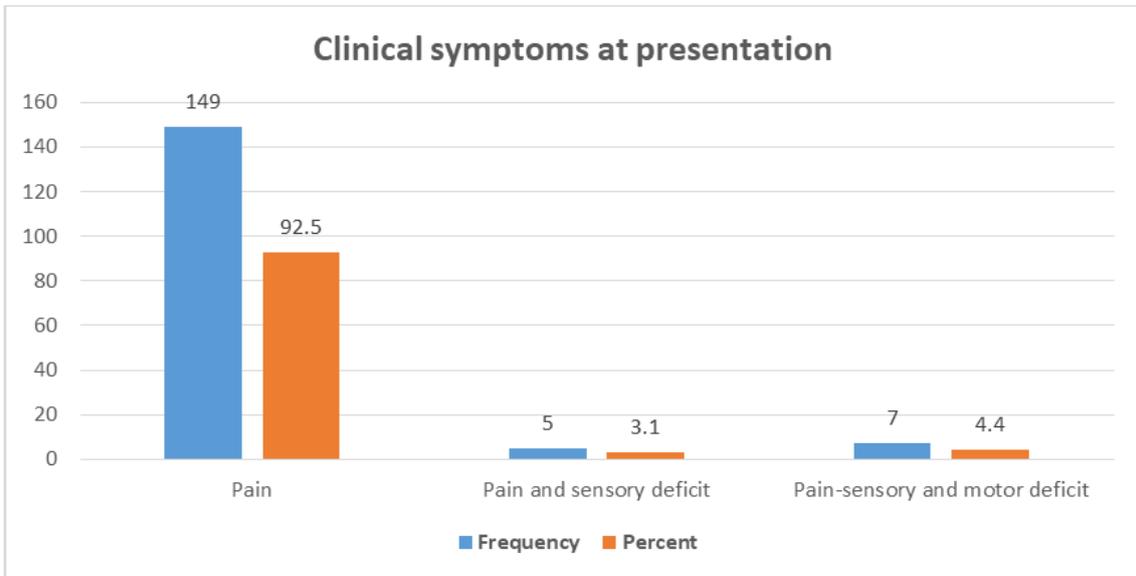


Figure 2: Presenting symptoms

Table 2: Imaging modalities used for confirmation of bone metastasis

Types of imaging modalities	Number of patients (%)
Conventional X-rays	110 (68.3%)
CT Scan	23 (14.3%)
MRI	7 (4.3%)
Bone scan	12 (7.5%)
Combined	9 (5.6%)

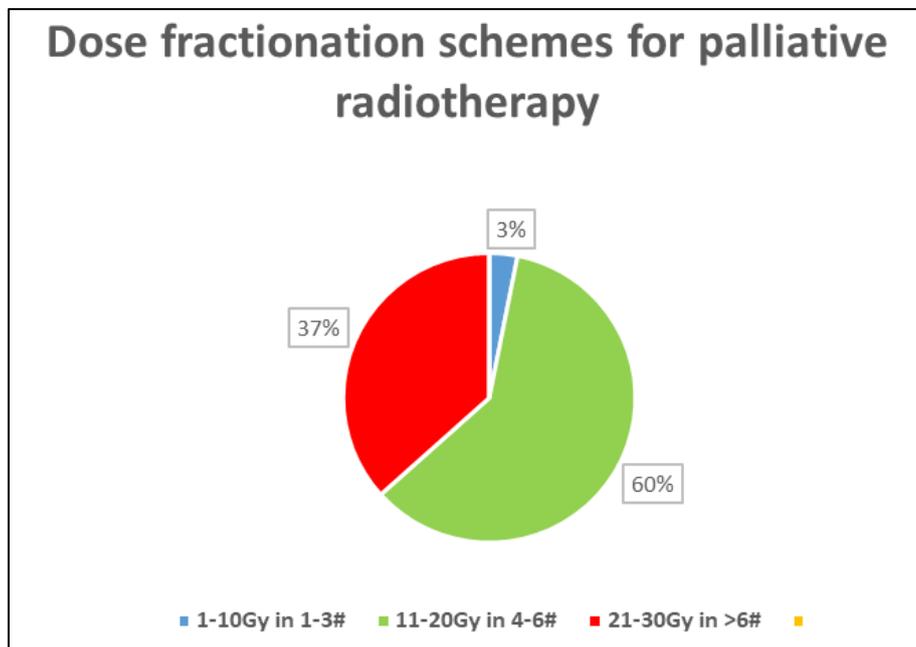


Figure 3: Dose fractionation schemes used for palliative radiotherapy

Table 3: Univariate analysis of Pain score pre and post radiotherapy using patient’s demographic factors

Characteristics Factors	N	Mean pain score			
		pre-irradiation	P value	post radiation	p value
<b>Age</b>					
20-29	8	7.6 ±0.9	0.381	0.6 ±0.8	0.173
30-39	41	6.9 ±1.5	-	0.5 ±0.8	-
40-49	62	6.6 ±1.5	-	0.5 ±0.7	-

50-59	27	7.1 ±1.1	-	0.9 ±0.9	-
60-69	20	7.0 ±1.6	-	0.4 ±0.8	-
≥70yrs	3	7.0 ±0.9	-	0.1 ±0.2	-
<b>Ethnic groups</b>					
Hausa-Fulani	68	6.2 ±1.3	0.001	0.7 ±0.9	0.05
Yoruba	51	7.5 ±1.4	-	0.6 ±0.8	-
Igbo	42	7.1 ±1.4	-	0.3 ±0.4	-
<b>Histology types</b>					
IDC	93	7.0 ±1.5	0.378	0.6 ±0.8	0.610
ILC	45	7.0 ±1.4	-	0.5 ±0.7	-
Others	23	6.7 ±1.7	-	0.6 ±0.9	-
<b>Tumour grade</b>					
Grade 1	19	6.7 ±1.5	0.713	0.5 ±0.6	0.438
Grade 2	64	6.9 ±1.4	-	0.6 ±0.8	-
Grade 3	53	6.7 ±1.6	-	0.7 ±0.9	-
Unknown	25	6.6 ± 1.3	-	0.6 ±0.7	-
<b>Metastatic Sites</b>					
Multiple metastases	105	6.8 ±1.5	0.886	0.5 ±0.7	0.039
Ribs	19	6.9 ±1.7	-	0.4 ±0.8	-
Long bones	16	7.0 ±1.5	-	0.4 ±0.5	-
Spinal cord compr.	9	7.3 ±1.3	-	0.8 ±0.9	-
Others	8	6.7 ±1.4	-	0.9 ±0.8	-
Impending fracture	4	6.4 ±1.7	-	1.1 ±1.2	-

**Table 4: Multivariate analysis of patient’s demographic factors and Pain score pre-radiotherapy**

Characteristics		Mean pain score		95% CI	
Factors	N	pre-irradiation	P value	Lower Bound	Upper Bound
<b>Age</b>					
20-29	8	7.6 ±0.9	0.865	-0.209	0.249
30-39	41	6.9 ±1.5			
40-49	62	6.6 ±1.5			
50-59	27	7.1 ±1.1			
60-69	20	7.0 ±1.6			
≥70yrs	3	7.0 ±0.9			
<b>Ethnic groups</b>					
Hausa-Fulani	68	6.2 ±1.3	<0.001	0.322	0.915
Yoruba	51	7.5 ±1.4			
Igbo	42	7.1 ±1.4			
<b>Histology types</b>					
IDC	93	7.0 ±1.5	0.248	-0.156	0.599
ILC	45	7.0 ±1.4			
Others	23	6.7 ±1.7			
<b>Tumour grade</b>					
Grade 1	19	6.7 ±1.5	0.977	-0.31	0.319
Grade 2	64	6.9 ±1.4			
Grade 3	53	6.7 ±1.6			
Unknown	25	6.6 ± 1.3			
<b>Metastatic Sites</b>					
Multiple metastases	105	6.8 ±1.5	0.904	-0.183	0.207
Ribs	19	6.9 ±1.7			
Long bones	16	7.0 ±1.5			
Spinal cord compr.	9	7.3 ±1.3			
Others	8	6.7 ±1.4			
Impending fracture	4	6.4 ±1.7			

**Table 5: Multivariate analysis of Pain score post-radiotherapy using patients demographic factors**

Characteristics Factors	N	mean pain score		95% CI	
		post-irradiation	P value	Lower Bound	Upper Bound
<b>Age</b>					
20-29	8	0.6 ±0.8	0.795	-0.148	0.113
30-39	41	0.5 ±0.8			
40-49	62	0.5 ±0.7			
50-59	27	0.9 ±0.9			
60-69	20	0.4 ±0.8			
≥70yrs	3	0.1 ±0.2			
<b>Ethnic groups</b>					
Hausa-Fulani	68	0.7 ±0.9	0.622	-0.209	0.126
Yoruba	51	0.6 ±0.8			
Igbo	42	0.3 ±0.4			
<b>Histology types</b>					
IDC	93	0.6 ±0.8	0.911	-0.217	0.194
ILC	45	0.5 ±0.7			
Others	23	0.6 ±0.9			
<b>Tumour grade</b>					
Grade 1	19	0.5 ±0.6	0.782	-0.152	0.201
Grade 2	64	0.6 ±0.8			
Grade 3	53	0.7 ±0.9			
Unknown	25	0.6 ±0.7			
<b>Metastatic Sites</b>					
Multiple metastases	105	0.5 ±0.7	0.008	0.039	0.254
Ribs	19	0.4 ±0.8			
Long bones	16	0.4 ±0.5			
Spinal cord compr.	9	0.8 ±0.9			
Others	8	0.9 ±0.8			
Impending fracture	4	1.1 ±1.2			

## DISCUSSION

Bone metastases are a common complication of end stage cancers. The incidence of bone metastases is difficult to determine with any certainty. However, in Nigeria, Ketiku *et al.*, reported that 26% of 38 patients with stage III breast cancer have detectable bony metastasis at presentation [10]. Patanaphan *et al.*, found the commonest site of distant metastasis to be in the bone by 51% [11], and in most cases the bone metastases are multiple [12], and the commonly involved sites are the spine, pelvis, femur, ribs, humerus, and skull [13], These findings are consistent with our study where we recorded 65.2% as multiple metastases affecting long bones (femour and humerus), spine, ribs and others (skull and clavicle). The most frequent consequence of bone metastases is pain [13]. The estimated cancer pain due to bone metastases was reported to be as higher as 50% [14], this is consistent with our finding, 92.5% of patients presented with pain alone as presenting symptom.

The way in which individuals perceived pain and its link to cultural and ethnic background generate a lot of debate concerning their influence on the outcome of pain treatment [15]. Greenwald studying the role of ethnicity on pain perception reported insignificant finding [16]. However, Weisenberg reported a contrary

view which showed that inter- ethnic differences exist in pain perception among individuals [17]. B.V. Owoyele also reported ethnicity as a factor in pain perception among ethnic groups in Nigeria [5]. In both univariate and multi-variate analyses this study shows a highly significant association between pain perception pre-irradiation and ethnic origin of our cancer patients which is consistent with Weisenberg result. Similarly, the study also confirmed disparities in pain perception among the studied cancer patients in pre and post-irradiation. In univariate analyses, Hausa-Fulani and Igbo shows a statistically significant low pain perception (pre-irradiation) than Yoruba with  $p < 0.05$ . Adesola A. Oniyide also confirmed the role of ethnicity in pain perception and existence of disparities among Nigerian ethnic groups. However, he reported a contrary finding of Igbo having the lowest pain perception as against Hausa-Fulani [18], he further reported that no differences exist in pain perception between Hausa and Yoruba ethnic groups [18], In this study ethnicity still expressed significant association in multivariate analysis when other influential factors like age, sex, tumour histology and grade were controlled, with Hausa-Fulani and Igbo expressing low pain perception compared to Yoruba ethnic groups ( $P < 5\%$ ). Despite the complexity associated with pain perception from ethnic perspective, many scholars were of the opinion that ethnicity is a factor responsible for the

disparities in pain perception [19, 20]. In fact, it had been shown that even ethnicity of the caregiver played a role in patient's pain assessment and appropriate respond to it; caregiver may underestimate or overestimate the pain perceived by the patient if they are from different races or ethnic groups. Although no studies in the literature concerning ethnicity and response to radiation analgesia were reported, but from what we recorded in this study, site of metastasis appeared to be the only factor that showed a highly significant association to radiation analgesia in both univariate and multivariate analysis post-irradiation. Therefore, this study is very important to cancer caregivers in Nigeria to understand these disparities and strategize in appropriate treatment of patients.

There are some limitations to this study. First, we couldn't consider the rate of analgesic intake by patients during radiotherapy so as to ascertain the real impact of radiation analgesia. Secondly, some patients were lost to follow up after the PRT, although their number is insignificant but it may affect the outcome of the study. We have not come across any paper investigating the influence of ethnicity on pain experience by cancer patients in Nigeria, this really add strength to this paper. Further research should focus more on factors that may influence response to radiation analgesia, because it will guide radiation oncologist on individualizing radiation doses to patients.

## CONCLUSIONS

This study confirmed that ethnicity brings disparities in pain perception among breast cancer patients with bone metastasis. At presentation, Yoruba and Igbo shows higher pain perception compared to Hausa-Fulani. However, their response to radiotherapy analgesia is independent of their ethnic origin and other tumour factors, but site of metastasis influence response to radiation analgesia. Therefore, the radiation oncologist should be aware of how individuals from different ethnic origin conceptualize pain from site of metastasis so as to guide him in decision making for an appropriate treatment.

## REFERENCES

1. Rubens, R. D. (1998). Bone metastases—the clinical problem. *Eur J Cancer*, 34(2), 210-213.
2. Kanis, J. A. (1995). Bone and cancer: pathophysiology and treatment of metastases. *Bone*, 17(2), S101-S105.
3. Cleeland, C. S., Janjan, N. A., Scott, C. B., Seiferheld, W. F., & Curran, W. J. (2000). Cancer pain management by radiotherapists: a survey of radiation therapy oncology group physicians. *International Journal of Radiation Oncology\* Biology\* Physics*, 47(1), 203-208.
4. Im, E. O., Ko, Y., & Chee, W. (2013). Symptom clusters among multiethnic groups of cancer patients with pain. *Palliative & supportive care*, 11(4), 295-305.
5. Owoyele, B. V., Akintoye, O. O., Oniyide, A. O., & Yusuf, F. A. (2019). Pain variability in nigeria: effect of ethnicity, occupation and some chronic diseases. *IBRO Reports*, 7, 45-46.
6. Im, E. O., & Chee, W. (2001). A feminist critique of research on cancer pain. *Western Journal of Nursing Research*, 23(7), 726-752.
7. Wu, J. S. Y., Wong, R. K., Lloyd, N. S., Johnston, M., Bezjak, A., & Whelan, T. (2004). Radiotherapy fractionation for the palliation of uncomplicated painful bone metastases—an evidence-based practice guideline. *BMC cancer*, 4(1), 1-7.
8. Goblirsch, M., Mathews, W., Lynch, C., Alaei, P., Gerbi, B. J., Mantyh, P. W., & Clohisey, D. R. (2004). Radiation treatment decreases bone cancer pain, osteolysis and tumor size. *Radiation research*, 161(2), 228-234.
9. Reyes-Gibby, C. C., Anderson, K. O., Shete, S., Bruera, E., & Yennurajalingam, S. (2012). Early referral to supportive care specialists for symptom burden in lung cancer patients: a comparison of non-Hispanic whites, Hispanics, and non-Hispanic blacks. *Cancer*, 118(3), 856-863.
10. Ketiku, K. K., & Azodo, M. V. (1996). Detection of skeletal metastases in Nigerian breast cancer patients: evaluation of radioisotope bone scan and radiography. *West African journal of medicine*, 15(2), 81-84.
11. Patanaphan, V., Salazar, O. M., & Risco, R. (1988). Breast cancer: metastatic patterns and their prognosis. *Southern medical journal*, 81(9), 1109-1112.
12. Hoegler, D. (1997). Radiotherapy for palliation of symptoms in incurable cancer. *Current problems in cancer*, 21(3), 129-183.
13. Rubens, R. D. (1998). Bone metastases—the clinical problem. *European Journal of Cancer*, 34(2), 210-213.
14. Kanis, J. A. (1995). Bone and cancer: pathophysiology and treatment of metastases. *Bone*, 17(2), S101-S105.
15. Künzler, E. (2005). Ethnopsychanalytische Untersuchung bei schmerz-und chronisch kranken Arbeitsmigrantinnen und-migranten sowie Flüchtlingen aus dem Kosovo. *Universität Zürich, Studentendruckerei Zürich, Zürich (Dissertation)*.
16. Greenwald, H. P. (1991). Interethnic differences in pain perception. *Pain*, 44(2), 157-163.
17. Weisenberg, M., & Caspi, Z. (1989). Cultural and educational influences on pain of childbirth. *Journal of Pain and Symptom Management*, 4(1), 13-19.
18. Oniyide, A. A., Olaniyi, K. S., Olasehinde, O. F., Yusuf, F. A., & Owoyele, B. V. (2018). Effect of ethnicity on pain perception among healthy Nigerians. *Pacific Journal of Medical Sciences*, 27.
19. Ramer, L., Richardson, J. L., Cohen, M. Z., Bedney, C., Danley, K. L., & Judge, E. A. (1999).

Multimeasure pain assessment in an ethnically diverse group of patients with cancer. *Journal of Transcultural Nursing*, 10(2), 94-101.

20. Lubeck, D. P., Kim, H., Grossfeld, G., Ray, P., Penson, D. F., Flanders, S. C., & Carroll, P. R.

(2001). Health related quality of life differences between black and white men with prostate cancer: data from the cancer of the prostate strategic urologic research endeavor. *The Journal of urology*, 166(6), 2281-2285.