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Original Research

Prevalence of Osteoporosis and Osteopenia among Cancer Patients and Its Risk Factors: A Retrospective Analysis at Najran Cancer Center, Saudi Arabia

Ahmed Badheeb	Department Oncology, King Khalid Hospital, Najran, Saudi Arabia. Department of Medicine, Faculty of Medicine, Hadhramaut University, Hadhramaut, Yemen.
Mohamed Al Sulieman	Department of Internal Medicine, King Khalid Hospital, Najran, Saudi Arabia.
Faisal Ahmed	Urology Research Center, Al-Thora General Hospital, Department of Urology, School of Medicine, Ibb University of Medical Sciences, Ibb, Yemen.
Ahmed Asiri	Department of Internal Medicine, King Khalid Hospital, Najran, Saudi Arabia.
Mohamed Badheeb	Department of Medicine, Faculty of Medicine, Hadhramaut University, Hadhramaut, Yemen. Internal Medicine, Yale New Haven Health, Bridgeport Hospital, Bridgeport, USA.

Objective: The assessment of bone mineral density (BMD) in patients with a higher risk for significant bone loss, such as cancer patients, was recommended by recent clinical guidelines. Herein, we aim to report the prevalence of osteoporosis and osteopenia and their associated factors in cancer patients.
Methods: This retrospective cross-sectional study was conducted from February 2021 to March 2022, and it included 39 adult cancer patients who were being treated at the King Khalid Hospital Cancer Center in Najran, Saudi Arabia. The participants were interviewed, and their BMD was assessed using Dual-energy X-ray absorptiometry (DXA) scans of the lumbar spine and femur neck. Univariate analysis was carried out to examine the association between osteoporosis and osteopenia and other variables.
Results: The study involved 39 adult cancer patients in Najran, Saudi Arabia with a mean age of 60.15 ± 12.26 years, the majority of patients (53.8%) were aged between (60-69) years old, and most of them (64.1%) were female. The primary diagnosis was mostly breast cancer (35.9%) followed by prostate cancer (25.6%). 66.7% received chemotherapy and 64.1% received hormone therapy. Results showed osteopenia, osteoporosis, and normal BMD in 7 (17.9%), 28 (71.8%), and 4 (10.3%) patients respectively. 43.6% had low serum vitamin D levels. There was no significant relationship between osteopenia/osteoporosis and various factors, but it was more frequent in older patients, those undergoing chemotherapy, and those with low vitamin D levels (p=0.04, 0.05, 0.005).
Conclusion: Higher prevalence of osteoporosis and osteopenia were observed in cancer patients undergoing chemotherapy, older patients, and those with low vitamin D levels. Further research is necessary to determine the most effective strategies for minimizing bone loss in this population.

Introduction

Decreased bone density (BMD) is attributed to reducing bone mass index with architectural distortion, resulting in fractures [1]. Following adjuvant chemotherapy, cancer patients are more likely to develop osteopenia and osteoporosis, which affects two-thirds of males, more than half of

premenopausal women, and approximately one-fifth of postmenopausal women [2,3].

Cancer therapy–induced bone loss is a leading cause of secondary osteoporosis, which results in bone fragility, increased fracture risk, decreased quality of life, and increased mortality. With the recent introduction of newer chemotherapy agents, improved survival and life expectancy of many cancer patients, and increased imaging use, the incidence, and prevalence of secondary osteoporosis have risen significantly, which has been associated with an impairment in activities of daily living and worsened the quality of life. Some observational studies reported a tenfold increased bone following cancer chemotherapy than the healthy population [4-6].

Recent clinical guidelines recommend evaluating bone mineral density (BMD) in high-risk patients. Lifestyle modifications, vitamin D, calcium supplementations, and anti-resorptive agents for cancer patients with established osteoporosis or increased fracture risk are strongly recommended. Newer agents, like denosumab, are currently replacing the bisphosphonates in most cancer centers due to the easy administration [7, 8].

In Saudi Arabia, published data are scarce on the impact of chemotherapy on bone loss among cancer survivors in the literature [6]. This study aims to evaluate osteoporosis and osteopenia and their associated factors in cancer patients treated at Najran Cancer Center.

Materials and Methods

Study design

In this retrospective cross-sectional study, we included 39 adult cancer patients treated at the cancer center in King Khalid Hospital in Najran, Saudi Arabia, from February 2021 until March 2022, who were interviewed. This study's approval was obtained from our center's Institutional Review Board. Informed consent was obtained from all participants to include in our study which was carried out in accordance with the Helsinki Declaration.

Inclusion criteria

All adult cancer patients treated at the cancer center during the study period were included in our study.

Exclusion criteria

Patients with incomplete records, those aged less than 18 years, those outside the study period, or those treated at other centers were excluded.

Data collection

Data collection included demographic characteristics, history of bone pain, awareness regarding jaw necrosis, the serum concentration level of 25-hydroxycholecalciferol (25-vitamin D), and bone mineral density (BMD). Tumors were characterized by the type, the date of diagnosis, the stage, and treatment with chemotherapy and/or hormonal therapy. Then, bone health status (osteopenia, osteoporosis, and normal bone health) was compared with other variables.

Definition of terms

Bone densitometry (dual-energy X-Ray absorptiometry (DEXA; Hologic Inc) of the hip, femur, and column (from L1 to L4), was used to evaluate the BMD and investigate the presence of osteopenia or osteoporosis during treatment. Normality was considered when the. Patients' T-scores were compared to the reference population standard deviation (SD) to assess the BMD. The normal finding was defined with a T-score of ≥ −1 (SD), and a T-score of −1.1 to −2.4 SD, and ≤ −2.5 were considered as osteopenia and osteoporosis, respectively [9]. Vitamin D ranges can be categorized based on serum 25 (OH) D levels. Typically levels lower than 20 ng/mL indicate a deficiency, while levels of 20–29 ng/mL indicate insufficiency, and a sufficient level is considered with levels of 30 ng/mL or greater [10].

Study outcome

To evaluate osteoporosis and osteopenia and their associated factors in cancer patients.

Statistical Analysis

Quantitative variables included the mean and the standard deviation, and frequency and percentage were used to analyze the qualitative variables. Additionally, the one-way analysis of variance (ANOVA) test analyzed qualitative variables with more than two categories. A p-value of 0.05 or less was deemed statistically significant. SPSS software (IBM SPSS, version 20, Armonk, New York: IBM Corp) was used for data analysis.

Results

Table 1 summarizes the study participants'demographic and clinical features. The mean age of patients was 60.15±12.26 years (range 29-83 years).

Variables (N=39)	Subgroup	N (%) & Mean (SD)
Age (year)		60.15 ± 12.26
Gender	Male	14 (35.9)
	Female	25 (64.1)
Age group (year)	≤ 49	6 (15.4)
	50-59	6 (15.4)
	(60-69)	21 (53.8)
	(70-79)	4 (10.3)
	≥ 80	2 (5.1)
Primary diagnosis	Breast cancer	14 (35.9)
	Prostate cancer	10 (25.6)
	Lung cancer	4 (10.3)
	Colorectal cancer	3 (7.7)
	Ovarian cancer	3 (7.7)
	Giant cell tumor	3 (7.7)
	Multiple myeloma	2 (5.1)
History of bone pain	Yes	18 (46.2)
	No	21 (53.8)
Chemotherapy use	Yes	26 (66.7)
	No	13 (33.3)
Duration of chemotherapy	≥ 5years	9 (23.1)
	4-2 years	6 (15.4)
	≤ 1 year	11 (28.2)

	Not used	13 (33.3)
Hormone therapy use	Yes	25 (64.1)
	No	14 (35.9)
Duration of hormone therapy	≥ 5years	4 (10.3)
	4-2 years	12 (30.8)
	≤ 1 year	9 (23.1)
	Not used	14 (35.9)
Bone scan	No bone metastasis	24 (61.5)
	Bone metastasis	15 (38.5)
DEXA scan	Osteopenia	7 (17.9)
	Osteoporosis	28 (71.8)
	Normal range	4 (10.3)
Serum vit D level	<20 (ng/ml)	17 (43.6)
	20-30 (ng/ml)	10 (25.6)
	≥ 30 (ng/ml)	12 (30.8)
Aware of jaw necrosis	Yes	10 (25.6)
	No	29 (74.4)

Table 1. Demographic and Clinical Characteristics of Patients.

The majority of patients, 21 (53.8%) aged between (60-69). In addition, 25 (64.1%) were female, and 14 (35.9%) were male. The primary diagnosis was breast cancer in 14 (35.9%) patients, followed by prostate cancer in 10 (25.6%) patients. Additionally, 22 (56.4%) patients were in the metastatic stages, and 26 (66.7%) patients received chemotherapy.

The duration of chemotherapy was more than five years in 9 (23.1%) of patients. 25 (64.1%) patients received hormone therapy, half of them for a duration of 2-4 years. The primary hormonal therapy was Tamoxifen in 34%, followed by letrozole in 23%, and steroids in 15.4%. Bone scans showed bone metastasis in 24 (61.5%) patients. Osteopenia, osteoporosis, and normal BMD were found in 7 (17.9), 28 (71.8), and 4 (10.3%) patients, respectively. 25-hydroxycholecalciferol (25-vitamin D) was lower than 20 (ng/ml) in 17 (43.6%) patients, 20-30 (ng/ml) was seen in 10 (25.6%) patients, and more than 30 (ng/ml) was seen in 12 (30.8%) patients. Just 10 (25.6%) of patients were aware of jaw necrosis.

Factors associated with osteopenia and osteoporosis: The incidence of osteoporosis and osteopenia was found to be higher among patients older than 60 years of age, with 22 patients out of the total sample, compared to those younger than 60 years, with 6 patients (p=0.044). However, no significant difference was found between osteopenia or osteoporosis and gender, primary diagnosis, hormone therapy, metastatic stage, duration of chemotherapy or hormone therapy, history of bone pain, and awareness of jaw necrosis (p≥ 0.05). Patients undergoing chemotherapy and those with lower serum levels of 25-hydroxycholecalciferol (25-vitamin D) were found to have a significantly higher incidence of osteoporosis and osteopenia (p= 0.058 and 0.005, respectively). Table 2 shows the relationship between osteopenia and osteoporosis with various factors.

Variables	Subgroup		Osteopenia	Osteoporosis	Normal	P-value*
		Total	N (%) & Mean(SD)	N (%) & Mean(SD)	N (%) & Mean(SD)	
		N (%)	7 (17.9)	28 (71.8)	4 (10.3)	
Age (year)	-	60.15 ± 12.26	55.71 ± 4.11	62.29 ± 12.73	53.00 ± 16.00	0.213
Age group (year)	<60	12 (30.8)	5 (41.7)	6 (50.0)	1 (8.3)	0.044
	≥60	27 (69.2)	2 (7.4)	22 (81.5)	3 (11.1)	
Gender	Male	14 (35.9)	1 (7.1)	10 (71.4)	3 (21.4)	0.139
	Female	25 (64.1)	6 (24.0)	18 (72.0)	1 (4.0)	
Primary	Breast cancer	14 (35.9)	2 (14.3)	11 (78.6)	1 (7.1)	0.218

diagnosis						
	Prostate cancer	10 (25.6)	1 (10.0)	6 (60.0)	3 (30.0)	
	Other	15 (38.5)	4 (26.7)	11 (73.3)	0 (0.0)	
History of bone pain	Yes	18 (46.2)	2 (11.1)	14 (77.8)	2 (11.1)	0.597
	No	21 (53.8)	5 (23.8)	14 (66.7)	2 (9.5)	
Chemotherapy use	Yes	26 (66.7)	4 (15.4)	21 (80.8)	1 (3.8)	0.05
	No	13 (33.3)	3 (23.1)	7 (53.8)	3 (23.1)	
Duration of chemotherapy	≥ 5years	9 (23.1)	2 (22.2)	6 (66.7)	1 (11.1)	0.522
	4-2 years	6 (15.4)	1 (16.7)	5 (83.3)	0 (0.0)	
	≤ 1 year	11 (28.2)	1 (9.1)	10 (90.9)	0 (0.0)	
Hormone therapy use	Yes	25 (64.1)	4 (16.0)	17 (68.0)	4 (16.0)	0.372
	No	14 (35.9)	3 (21.4)	11 (78.6)	0 (0.0)	
Duration of hormone therapy	≥ 5years	4 (10.3)	1 (25.0)	2 (50.0)	1 (25.0)	0.268
	4-2 years	12 (30.8)	2 (16.7)	7 (58.3)	3 (25.0)	
	≤ 1 year	9 (23.1)	1 (11.1)	8 (88.9)	0 (0.0)	
Serum Vit D level	<20 (ng/ml)	17 (43.6)	1 (5.9)	16 (94.1)	0 (0.0)	0.005
	20-30 (ng/ml)	10 (25.6)	4 (40.0)	6 (60.0)	0 (0.0)	
	≥ 30 (ng/ml)	12 (30.8)	2 (16.7)	6 (50.0)	4 (33.3)	
Bone scan	No bonemetastasis	24 (61.5)	4 (16.7)	17 (70.8)	3 (12.5)	1
	Bone metastasis	15 (38.5)	3 (20.0)	11 (73.3)	1 (6.7)	
Aware of jaw necrosis	Yes	10 (25.6)	3 (30.0)	7 (70.0)	0 (0.0)	0.292
	No	29 (74.4)	4 (13.8)	21 (72.4)	4 (13.8)	

Table 2. Comparison between Osteopenia, Osteoporosis, and Normal Bone Health Status with Other Factors.

*P-values < 0.05 were considered significant.

Discussion

In Saudi Arabia, 27,885 new cancer cases were reported in 2020, with 13,069 cancer-related deaths. The Age-standardized incidence rate of all forms of cancer is 96.4 per 1,00,000 individuals whereas the age-standardized mortality rate is 51.3 per 1,00,000 individuals (total population = 34,813,867) [11]. Additionally, breast, colorectal, prostate, brain, lymphoma, kidney, and thyroid cancers represent in Saudi Arabia [12]. Secondary osteoporosis, in cancer survival or chemotherapy recipients, represents a debilitating and disabling condition that results in lifestyle impairment and dysfunction in cancer patients. Furthermore, loss of bone density following cancer chemotherapy should be avoided, as restoring the prior density may not be feasible. The prevalence of bone loss after chemotherapy ranges between 1% and 5% per year [6]. Abnormal BMD, including osteopenia or osteoporosis, was observed in 80% of breast cancer patients [13]. These abnormalities persisted even after discontinuation of treatment, as reported by Al Amri et al. that 59.67% of cancer survivors have had an abnormal BMD, either osteopenia or osteoporosis [6]. Similarly, in our study, 89.7% of patients suffered from abnormal BMD, indicating osteopenia in 17.9% and osteoporosis in 71.8%.

In our study, the mean age of patients was 60.15± 12.26 years (range 29-83 years), and a higher

prevalence of osteopenia and osteoporosis was seen in patients aged ≥ 60 years compared to ≤ 60 years and the difference was statistically significant. Other studies found a higher prevalence of osteoporosis among older cancer survivors [14,15]. In contrast, AlAmri et al. reported a higher trend of osteopenia and osteoporosis in patients aged 50 years old or younger (65.6% vs. 56.4%, P = 0.001) [6]. We believe further studies to investigate the presence of cofounders or effect modifiers may be necessary to elaborate on such differences.

Several factors that may BMD in cancer patients have been reported in various studies. For instance, Reuss-Borst's study found that factors such as age, body weight, menopausal status, and hormonal replacement therapy in women and body weight in men were significantly associated with the prevalence of osteoporosis [16]. A study by Choi et al. evaluated the prevalence and osteoporosis-associated factors among 556 Korean cancer survivors and compared them to 17,623 non-cancer participants. The results showed that older age, female gender, and lower monthly income in cancer survivors were associated with a higher prevalence of osteoporosis while being underweight and inadequate calcium consumption in male cancer survivors were also linked to the condition [14]. Go et al. conducted a study to examine the relationship between breast cancer and osteoporosis in 74 breast cancer patients compared to 296 non-cancer controls. The authors found no statistically significant differences in fracture incidence or BMD between the two groups. Additionally, they observed that chemotherapy and endocrine therapy were not associated with low BMD in breast cancer survivors, although recipients of these treatments did have a higher risk of osteopenia and this difference was not statistically significant. The study also found no significant difference in BMD related to physical activity, vitamin D supplementation, or calcium supplementation [17]. In our analysis, we found that only chemotherapy use and low levels of vitamin D were significantly associated with the prevalence of osteoporosis and osteopenia. However, other risk factors, including hormone therapy, duration of chemotherapy, age, and metastatic status, were not statistically significant. We attribute this to the small sample size and short follow-up period of our study, which limited our ability to perform a robust statistical analysis. Thus, a multicentric study is recommended to further investigate these findings. In this study, the relationship between hormone therapy and bone loss was not statistically significant and it may attribute to heterogenicity, small sample size, and short follow-up period. Positive associations with bone health (higher BMD) were observed by Yip et al. in premenopausal Chinese patients after adjuvant chemotherapy for early breast cancer, including larger family size, higher height, and higher BMI. In contrast, negatively associated factors included longer intervals since the last adjuvant treatment, peri and postmenopausal status, and having received adjuvant Tamoxifen [18].

Pharmacological interventions to address bone loss are recommended for patients with a high risk of osteoporosis and insufficient dietary intake. These interventions include daily supplementation of Vitamin D (1000-2000 IU) and calcium (1000 mg). Patients with a baseline T score of -2.0 or those with two or more clinical risk factors for fracture should also be prescribed antiresorptive therapy to manage their bone loss [19]. In randomized clinical trials involving more than 5000 patients, the administration of bisphosphonates or denosumab, in a similar manner to postmenopausal osteoporosis patients, has limited the progression or even increased the BMD in breast cancer patients [20,21]. In our patients, Vit D, calcium, and denosumab were administrated for all patients with osteoporosis.

The current study has several limitations that should be noted. Firstly, its retrospective nature, single-center design, and small sample size limit the robustness of the statistical analysis. Secondly, the incidence of osteopenia and osteoporosis was determined using DEXA scans and may be subject to misclassification. Thirdly, factors such as physical activity, economic status, comorbid conditions (e.g., diabetes, obesity, hypertension), and diet, which may impact osteopenia and osteoporosis status, were not included in the study. Fourthly, increased surveillance for bone health in breast cancer survivors and longer cancer-free duration may result in overdiagnosis of osteopenia and osteoporosis. Finally, no comparison was made with the general population.

In conclusion, treatment-related bone loss is a significant potential side effect in cancer patients.

Effective screening procedures should be used to identify those at risk of bone loss, and therapy should be offered if risk factors are detected. The results of our study showed that osteoporosis and osteopenia were more prevalent in older patients, those undergoing chemotherapy, and those with low levels of serum Vitamin D. Further research is needed to determine the most effective methods to minimize bone loss in this population.

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none.

Study approval

The study was reviewed and approved by the King Khalid Hospital research ethics committee.

Availability of data

Data is available from the authors upon written request.

Conflict of Interest

The authors declare that they have no competing interests.

Authors’ contributions

MS, AA, and MB conducted data collection and interpretation, and drafting of the manuscript. FA was responsible for data analysis and interpretation, and revision of the manuscript. AB did conception of work, data interpretation, and critical revision of the manuscript. All authors have read and approved the final manuscript.

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