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Patterns of Bone Metastases in Cancer Patients Referred for Bone Scintigraphy in the Hail Region: A Retrospective Cross-Sectional Study

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Abstract **Background:** Bone metastases are a common complication of advanced malignancies. Data on their patterns in northern Saudi Arabia are scarce. **Objective:** To characterize the prevalence, anatomical distribution and scintigraphic image of bone metastases of cancer patients undergoing SPECT/CT bone scan in the Hail region. **Methods:** Retrospective evaluation of patients with solid tumors (adults) who received Tc-99m MDP whole-body SPECT/CT bone scintigraphy at King Khalid General Hospital between January 2020 and December 2024 (n = 222). Demographic, clinical and imaging data were analyzed using descriptive statistics and the chi-square test, while multivariate logistic regression was performed to identify independent associations with bone metastasis. **Results:** Breast cancer was the highest primary tumor (71.6%) followed by prostate (9.9%). Definite bone metastases were detected in 23.4% of the patients and 63.5% had no involvement of the skeleton. Among the patients with abnormal scans, multiple lesions (2-10) were the predominant pattern (24.8% of all patients), with the lumbar spine (70.0%), ribs (64.3%), thoracic spine (57.1%) and pelvis (57.1%) being the predominant sites of involvement. Suspected as benign uptake was recorded in 65.3% of patients mainly caused by degenerative changes. In multivariate analysis, age, gender and type of primary tumor and pathological fracture were not independent risk factors for bone metastasis. **Conclusion:** In this regional cohort population there was a predominance of metastatic bone tumors to the axial skeletal system with breast cancer and prostate cancer being the predominant tumor in group observed. Bone scintigraphy with SPECT/CT is a useful screening tool for potential whole-body diseases, however, the high rate of uptake classified as most likely benign makes it critical to provide careful clinical correlation and more specific use of other imaging modalities.

Key Words Bone Metastases, Bone Scintigraphy, Technetium-99m, Cancer Epidemiology, Skeletal Imaging, Saudi Arabia, Hail Region

INTRODUCTION

Bone metastasis is a prevalent and significant complication in cancer and it is often associated with significant morbidity and a decreased quality of life. It is a common site of distant metastasis in a variety of different malignancies, with breast and prostate cancers being the most common types of primary sources of skeletal involvement [1-2]. The pathophysiology of adequate metastasis to bone involves complex interactions between tumor cells and the bone microenvironment. Tumor cells release factors that suppress osteoblast activity and enhance osteoclast activity, resulting in a destructive cycle that leads to weakening of the bone structure with the release of growth factors that further promote tumor growth [3]. As a result, the skeleton becomes a common site of secondary cancer, with patients suffering debilitating complications including bone pain, hypercalcemia and pathological fractures, which have a devastating effect on their quality of life [4]. Bone metastases affect mainly the axial skeleton, the vertebrae being the most common site for metastasis in patients with solitary lesions, followed by the pelvis, sternum and femur [5-6].

The clinical management of bone metastases is based on a timely and accurate detection, which is favored by a multimodal approach to diagnosis. Traditional imaging modalities, e.g., X-ray

radiography, Computed Tomography (CT) and bone scintigraphy, are often used for the evaluation of bone metastasis [7]. Among these, Magnetic Resonance Imaging (MRI) is said to be the most sensitive for detecting bone marrow involvement [8]. However, bone scintigraphy or bone scans still have significant importance from a clinical point of view because of their potential to allow screening of the entire body, the low cost of the tests and the adequate sensitivity to detect osteoblastic activity; thus, they are very frequently used procedures around the world [9-10]. Despite its widespread usage, bone scintigraphy has its limitations, in particular, the reduction in specificity, leading to cases of false positives. This is particularly true in the vertebral column and ribs, because bony reactive processes due to degenerative changes are easily mistaken for metastatic lesions [11-12].

Moreover, a significant part of the interpretation of bone scintigraphy is to recognize the "flare phenomenon," which is characterized by apparent worsening of lesions in size or number or intensifying of radiotracer uptake following the start of treatment [13]. This phenomenon, seen most commonly with breast and prostate cancer patients going through hormonal therapy or chemotherapy, can be mistaken as a disease progression, when in fact it is a response to treatment - in the case of bone, a regrowth of bone and inflammatory changes as the tumor tissue dies off [14]. Such misinterpretations may encourage the premature stopping of effective therapies, indicating the importance of correlation with the clinical setting and the follow-up imaging in changing the interpretation of the bone scintigraphy scan and permitting effective treatment decisions.

Despite extensive research on bone metastasis across populations, there is limited information on the pattern of bone metastases in northern Saudi Arabia. The Hail region, owing to its unique geographic and demographic characteristics, may exhibit cancer behaviors and metastatic patterns distinct from those in other areas. The understanding of such patterns is essential to the clinical physician, ensuring appropriate diagnostic strategies and treatment protocols for this population. Furthermore, our study provides useful data on regional variations that can affect clinical decision-making and resource allocation within the healthcare system.

METHODS

Study Design, Setting and Ethical Considerations

This was a retrospective study using routinely gathered clinical and imaging records in a period of one year, from January 2020 to December 2024. There was no contact with patients or extra procedures. The research ethics committee of the University of Hail approved retrospective use of free from information data and waived the need for individual informed consent (Approval Number: H-2025-794).

Study Population and Sampling

Patients were identified under well-defined inclusion and exclusion criteria. We included adult patients (>18 years) with histologically proven primary solid malignancies who underwent Tc-99m MDP bone scintigraphy at King Khalid General Hospital, Hail. Exclusion criteria were hematologic malignancies, bone trauma and orthopedic conditions and poor-quality scintigraphic studies. This is a descriptive study that employed descriptive statistics in the case of demographic and chi-square tests in the case of categorical variables. Multivariate logistic regression analysis was used to find possible predictors of bone metastasis as factors such as age, gender, tumor type and presence of pathological fractures. The regression model was controlled for confounding factors, which ensured that the associations of predictors with bone metastasis were robust. After using these criteria, 222 consecutive eligible patients were included in the final analysis.

Data Collection and Variables

Data was extracted through a standardized data extraction form according to previous literature. The different and extracted variables were the demographic information sharing age (Y), presented in form of Mean + SD, Min - Max and categorized as age groups 18-39, 40-59, > = 60, gender (Male, Female) and nation (Saudi, Non-Saudi). Clinical variables included primary tumor type, presence or absence of bone metastases, number of metastatic lesions and site of anatomically involved lesions. Imaging Findings were Bone scan patterns (Normal, solitary lesions, multiple lesions, diffuse/superscan) and skeletal distribution (axial, appendicular, both, diffuse). Clinical complications included pathologic fractures and fracture locations. Technical assessments covered the topic of suspected false-poses, the cause of the pseudo-poses and established follow-up imagining approaches.

Imaging Protocol

All the bone scintigraphy examinations were done under the standard departmental protocol for Tc-99m methylene diphosphonate (Tc-99m MDP) bone imaging. Patients were given an intravenous injection Tc-99m MDP and whole-body planar images of anterior and posterior projections were obtained about 3-4 hours after the tracer was administered. Imaging was performed with a dual-head gamma camera with low energy high-resolution collimators and continuous table movement from the skull to feet to obtain a complete skeletal image. When suggested by suspicious or equivocal results from planar scans, additional targeted views were obtained and tomographic acquisition with combined SPECT/CT was performed over the relevant areas so as to better characterize the respective lesions, to correct for attenuation and to better localize them anatomically. Fused SPECT/CT images were generated using standard clinical software and processed in comparison with planar images, using a specialized work station. All studies were interpreted by an experienced nuclear medicine physician and potential cases of uncertainty were resolved by consensus review.

Data Analysis

Continuous variables were summed up as mean (± Standard Deviation/SD) or median (interquartile range) and categorical variables as frequencies and percentages. Age

was classified as 18-39, 40-59 and > = 60 years. Associations between categorical variables and presence of definite bone metastases were evaluated with the use of the chi-square test or Fisher's exact test, as appropriate. Variables with $p<0.10$ in univariate analysis were included in a multivariate logistic regression modelling to investigate independent predictors of bone metastasis. A $p<0.05$ on a two-sided basis was considered to be statistically significant.

RESULTS

Demographic Characteristics

Table 1 describes a study population of 222 participants with a mean age of 55.59 years (SD 14.61) with a wide age range from 19 to 92 years, indicating that both young adults and very old individuals will be included in the study but with a clear skew toward later adulthood. The age-group distribution reveals that only 12.61% are in the younger age group of 18-39 years and half of the sample 50.9% is in the age group range of 40-59 years and the third group of 36.9% are in the age of 60 years or above so the findings will be mostly for middle-aged and older age groups rather than younger age group. Gender distribution is very unbalanced with a female rate of 77.03% (n = 171) and a male rate of 22.97% (n = 51), the predominance of the female sex suggests that the studied underlying condition or service is more common among women or that recruitment pathways were more or less accessible to women, which may limit the applicability of the results to men. Nationality data reveal that the fraction of Saudi (77.48%, n = 172) and non-Saudi (22.52%, n = 50) is 77.48% and 22.52%, respectively; this means that although the sample is highly local, there is a good proportion of non-Saudi and hence some degree of cultural and possibly socioeconomic heterogeneity. Overall, the data presented in Table 1 suggest an older, predominately Saudi and primarily female cohort with a non-trivial non-Saudi dimension, suggesting that interpretation and generalisation of the results in this study must be ground in this demographic profile rather than assumed to be the same for a younger, male or non-local group.

Figure 1 below displays counts and percentages of individuals categorized by age group, gender and nationality.

Clinical and Tumor Characteristics

The predominance of primary cancer was breast cancer 71.62% (n = 159) and prostate cancer 9.91% (n = 22) out of the cohort. Colorectal and lung cancer made up 4.50% of each case (n = 10). Bladder and kidney cancers accounted for 2.70 (n = 6) and 1.35 (n = 3), cancers respectively; rarer cancers (less than or equal to 1%) included cancers of the esophagus, hematologic, jejunum, liver, nasopharynx, oral, pancreas and thyroid. With regard to bone metastasis 63.51% (n = 141) had no bone metastasis, 23.42% (n = 52) had confirmed bone metastasis and 13.06% (n = 29) had unconfirmed metastatic status.

Bone Scintigraphy Findings

The Table 2 gives an overview of the finding in bone scintigraphy 'bone scan' among 222 subjects with additional information about distribution, sites of metastasis and pathological fractures. Bone scintigraphy is a diagnostic tool for locating abnormalities in the skeleton frequently in the context of metastatic disease of the bone.

Of the 222 patients, 141 (63.5%) had normal bone scans where abnormal uptake of radiotracer was not observed. Abnormal scintigraphic findings in 81 patients (36.5%) were found. Among the patients with abnormal results, multiple suspicious lesions (2-10 lesions) were most common and were detected in 55 patients (24.8% of the whole cohort), followed by solitary suspicious lesions in 19 patients (8.6%) and diffuse skeletal involvement (more than 10 lesions/superscan pattern) in 7 patients (3.2%).

Table 1: Demographic Characteristics of Study Population (n = 222)

Variable	Number	Percentage
Age Mean ± SD (years)	55.59±14.61	12.61
Age Range (years)	19-92	
Age Group 18-39	28	
Age Group 40-59	112	50.9
Age Group ≥60	82	36.9
Gender (Male)	51	22.97
Gender (Female)	171	77.03
Nationality (Saudi)	172	77.48
Nationality (Non-Saudi)	50	22.52

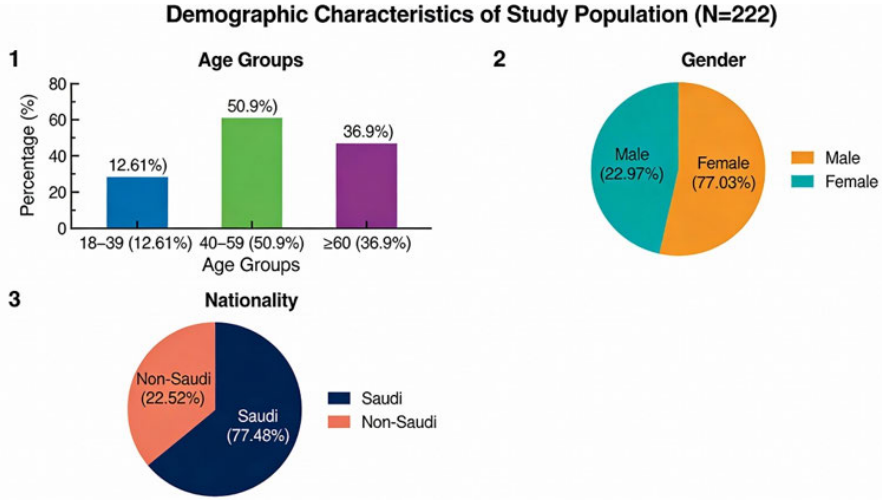

Figure 1: Participants Demographics

Table 2: Bone Scintigraphy among the Study Participants

Variable		Number	Percentage
Bone Scan Findings (n = 222)	Normal/No abnormal uptake	141	63.514
	Solitary suspicious lesion	19	8.559
	Multiple suspicious lesions (2-10)	55	24.775
	Diffuse skeletal involvement (superscan) >10	7	3.153
Distribution (n = 81)	Both Axial and Appendicular skeleton	39	48.1
	Axial skeleton	31	38.2
	Appendicular skeleton	4	4.9
	Diffuse/Superscan Pattern	7	8.6
Sites of Metastasis in the Axial Skeleton (n = 70)	Skull	23	32.9
	Cervical spine	16	22.9
	Thoracic spine	40	57.1
	Lumbar spine	49	70.0
	Ribs	45	64.3
	Sternum	24	34.3
	Clavicles	8	11.4
	Scapulae	9	12.9
	Humerus	6	8.6
	Pelvis	40	57.1
	Femur	17	24.3
	Tibia	3	4.3
Pathological Fracture Present (n = 222)	yes	4	1.802
	no	218	98.198
Site of Pathological Fracture (n = 4)	Spine	3	75
	humorous	1	25

Table 3: Evaluation of False-Positive Uptake Findings and Planned Confirmatory Imaging

Variable		Number	Percentage
False Positive Suspected (n = 222)	yes	145	65.315
	no	77	34.685
Suspected Cause of Uptake (n = 145)	Degenerative changes	118	81.3
	Benign bone disease	1	0.6
	Fracture	3	2
	Inflammation	1	0.6
	Inflammation and degenerative changes	4	2.7
	Other	7	4.8
	Trauma	2	1.3
	Trauma and degenerative changes	9	6.2
Planned Confirmatory Modality (n = 145)	None	116	80
	CT/ MRI	5	3.4
	CT scan	11	7.5
	MRI	13	8.9

Skeletal distribution analysis was performed in the 81 patients who had abnormal scan results and showed that 39 patients (48.1%) showed involvement of both axial and appendicular skeleton, 31 patients (38.2%) had involvement of axial skeleton alone, 4 patients (4.9%) were found to have involvement of appendicular skeleton only and 7 patients (8.6%) had diffused or superscan patterns.

Among 70 patients with axial skeletal involvement, the most common sites of involvement were the lumbar spine (49 patients, 70.0%), ribs (45 patients, 64.3%), thoracic spine (40 patients, 57.1%) and pelvis (40 patients, 57.1%). Other frequently affected sites were sternum (24, 34.3%), skull (23, 32.9%), femur (17, 24.3%), cervical spine (16, 22.9%), scapulae (9, 12.9%), clavicles (8, 11.4%), humerus (6, 8.6%) and tibia (3, 4.3%). Moreover, pathological fractures were not frequent, with only 4 cases, i.e., 1.8% of the total cohort. Of these cases of fractures, three affected the spine (75%) and one affected the humerus (25%).

The Figure 2 summarizes findings of bone scan (A) showing different gradation of abnormal uptake, distribution of skeletal involvement (B) with majority affecting both axial and appendicular skeleton, sites of metastasis in the axial skeleton (C) showing predominant involvement in the lumbar spine and thoracic spine and pathological fracture (D).

False-Positive Findings and Diagnostic Considerations

The Table 3 shows the analysis of false-positive findings of uptake in bone scintigraphy from participants of the study and planned confirmatory imaging modalities in suggested cases where false positive result of bone scintigraphy is suspected.

Suspected false-positive uptake was detected in 145 (65.3%) patients and 77 (34.7%) patients did not show suspected false-positivity. Among the 145 patients who had suspected false-positive findings, degenerative changes were the most common cause in 118 of the patients (81.3%). Other identified causes included trauma with degenerative change (9 patients, 6.2%), other unspecified causes (7 patients, 4.8%), inflammation associated with degenerative change (4 patients, 2.7%), fractures (3 patients, 2.0%), trauma alone (2 patients, 1.3%), benign bone disease (1 patient, 0.6%) and isolated inflammation (1 patient, 0.6%).

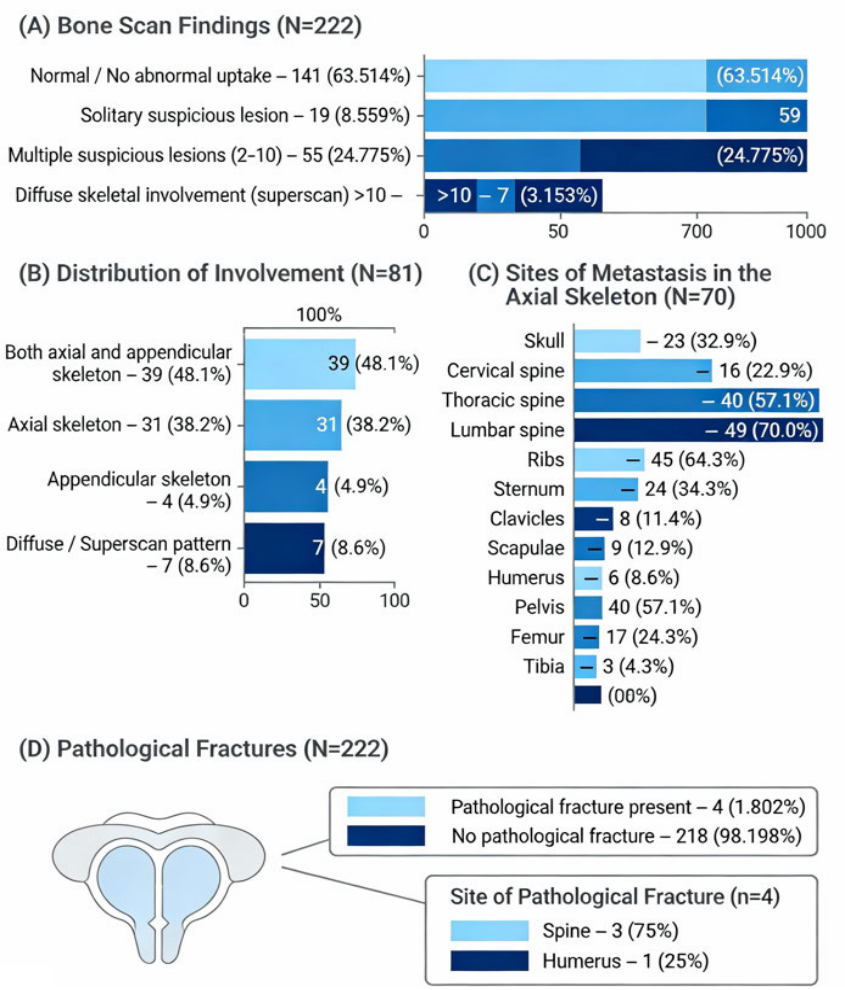

Figure 2: Distribution of Bone Scan Findings, Skeletal Involvement, Sites of Metastasis in the Axial Skeleton and Pathological Fractures in Patients (n = 222)

Table 3: Evaluation of False-Positive Uptake Findings and Planned Confirmatory Imaging

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Suspected Cause of Uptake (n=145)	Degenerative changes	118	81.3
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	Other	7	4.8
	Trauma	2	1.3
	Trauma and degenerative changes	9	6.2
Planned Confirmatory Modality (n=145)	None	116	80
	CT/ MRI	5	3.4
	CT scan	11	7.5
	MRI	13	8.9

With respect to planned confirmatory imaging for the 145 patients with suspected false-positive results, most (116 patients, 80%) children had no additional imaging studies planned. In patients who had known to have confirmatory studies, 13 patients (8.9%) were planned for MRI, 11 patients (7.5%) were planned for CT imaging alone and 5 patients (3.4%) were planned for combined CT/MRI evaluation.

The figure shows the data on suspected false positives (65.3% yes), causes of uptake (predominant degenerative changes), planned confirmatory modalities (80% no further confirmatory imaging was planned).

The following Figure 3 shows the data on suspected false positives (65.3% yes), causes of uptake (predominant degenerative changes), planned confirmatory modalities (80% no further confirmatory imaging was planned).

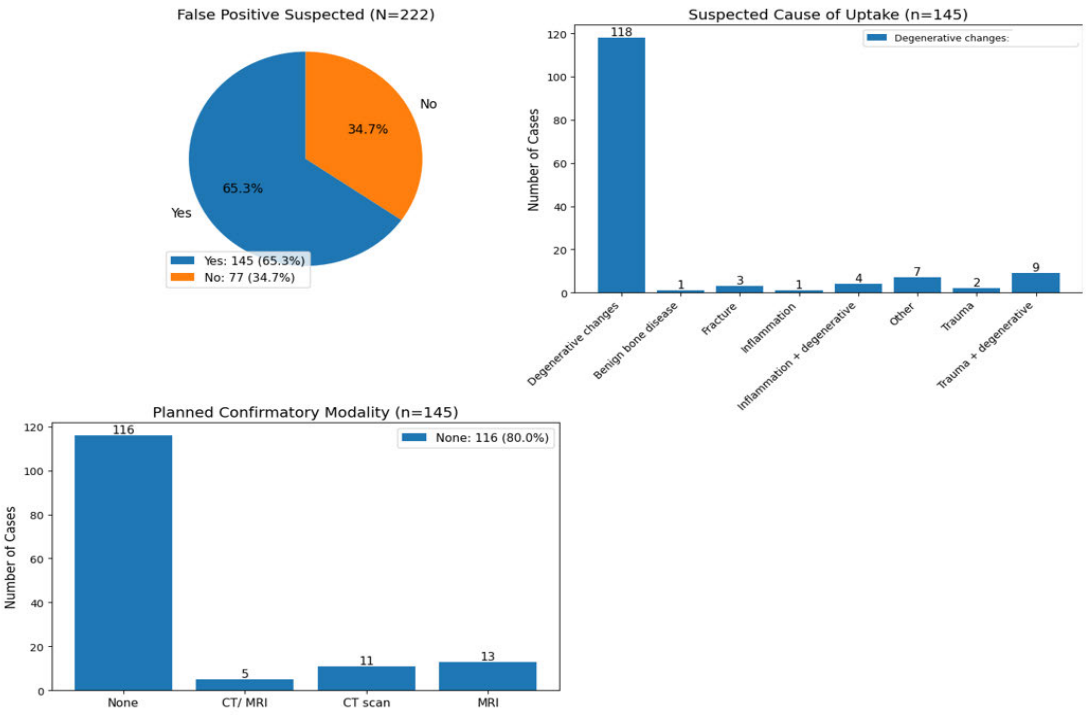

Figure 3: Distribution of Suspected False Positive Uptake, Underlying Causes and Planned Confirmatory Imaging Modalities

Association between Demographics and Bone Metastasis

This part delves into the correlation between demographic factors and the rate of bone metastasis between age groups and genders and primary types of cancer. Statistical analysis showed there are significant associations, namely that bone metastasis is more common in older people and is more common in males with triple negative breast cancer and it also varies by cancer type. The results highlight the different metastatic buckle on the basis of these demographic variables.

Age-Related Associations

Statistical analysis chaired that there was a significant association between the age group and the occurrence of bone metastasis ($p = 0.003$). The youngest age group (18-39 years) showed the least incidence of confirmed bone metastasis with just 4 cases. The intermediate burden was in the middle-aged cohort (40-59 years) which reported 19 confirmed cases of metastasis. The oldest age group (> = 60 years) showed the greatest metastatic burden of 29 confirmed cases. This trend shows that bone metastasis likelihood becomes much higher as people get older.

Gender-Related Associations

It was found that there was statistically significant difference in the patterning of bone metastasis among genders ($p = 0.002$). Although females had the greater sample ($n = 171$), there was a greater incidence of confirmed bone metastasis found in males (19/51 males = 37.3%) within soluble triple-negative breast cancer than females found in the study (33/171 females = 19.3%). On the contrary, females showed a greater percentage of cases without bone metastasis.

Primary Tumor Type Associations

Significant association was established between primary cancer type and the occurrence of bone metastasis ($p = 0.010$). Breast cancer, being the most common primary malignancy, accounted for the largest number of certain cases of metastasis (32 patients). Prostate cancer showed large amounts of metastatic burden with 8 confirmed lesions. Bladder cancer (3 cases) and colorectal cancer (4 cases) also contained metastatic involvement, but in lower absolute quantity (relative to their lesser prevalence). Rare types of cancers such as esophageal, jejunal, pancreatic and thyroid cancers showed no confirmed evidence of metastasis in this group.

Tumor Type and Metastatic Site Distribution

Analysis of the associations between primary tumor type and distribution of metastatic sites was carried out ($p = 0.584$, not statistically significant). Breast cancer patients had the most diverse patterns of metastasis, with 25 patients exhibiting both axial and appendicular metastasis, 17 patients with axial involvement only, 3 patients with exclusively appendicular involvement and 4 patients with diffuse superscan patterns of metastasis. Prostate cancer patients presented 5 cases with both axial and appendicular involvement, 3 with axial only pattern, 1 with appendicular involvement and 2 with diffuse superscan. Other malignancies showed fewer cases of metastasis as a result of a low baseline prevalence.

Bone Scan Findings by Tumor Type

Among the 81 patients who had abnormal bone scans, significant variation in the findings of bone scans between types of primary tumors was noted ($p = 0.198$, not statistically significant). Breast cancer patients presented the greatest metastatic burden (12 solitary, 33 multiple and 4 diffuse superscan patterns).

Table 4: Multivariate Logistic Regression for Predictors of Bone Metastasis

Variable	B	SE	Wald	df	p-value	Adjusted OR (Exp(B))	95% CI for OR
Age ≥60 (Vs <60)	0.112	0.503	0.050	1	0.824	1.119	0.417-3.001
Male gender (Vs female)	-1.414	1.314	1.159	1	0.282	0.243	0.019-3.192
Primary Cancer Type (breast cancer: Other types)	-1.364	1.275	1.145	1	0.285	0.256	0.021-3.109
Pathological fracture (yes Vs no)	-1.824	1.187	2.362	1	0.124	0.161	0.016-1.652

Prostate cancer had 1 solitary lesion, 8 multiple lesions and 2 diffuse superscan cases. Colorectal cancer had 1 singular and 4 multiple lesions. Lung cancer showed 1 (solitary) and 4 (multiple) lesions. Several rare types of cancer (esophageal, jejunal, pancreatic, thyroid) showed no skeletal involvement in this group.

Pathological Fractures and Tumor Type

A borderline statistically significant link between the type of primary cancer and the occurrence of a pathological fracture was identified ($p = 0.050$). Although, pathological fractures overall were rare (4 cases), they occurred in breast cancer (2 cases), hematologic malignancy (1 case) and kidney cancer (1 case). No fractures were recorded for prostate cancer, bladder cancer, colorectal cancer, lung cancer and other types of cancer.

Multivariate Logistic Regression Analysis

The result of a multivariate logistic regression analysis investigating predictors of bone metastasis is reported in Table 4. The table contains estimates denominated with B for the regression coefficient, Standard Error (SE) and Wald statistic, the number of degrees of freedom (df), the p-value, the adjusted Odds Ratio (OR) and the 95% Confidence Interval (CI) for the OR for each of the variables. The variables considered are age, gender, type of cancer that caused the tumor and pathologic fracture.

Moreover, the age variable (> = 60 Vs <60) also shows a positive but non-significant association with bone metastasis ($B = 0.112$, $p = 0.824$), suggesting that age is not a good predictor. The Odds Ratio (OR) for this comparison is 1.119, (95% CI: 0.417 to 3.001) (weak evidence of association). Similarly, male gender (Vs female) is not significantly associated with bone metastasis as well ($B = -1.414$, $p = 0.282$), with an OR of 0.243 (95% CI: 0.019 - 3.192), suggesting that there is a low probability for bone metastasis in males than in females. There is also no significant association with primary cancer type (breast cancer vs. other cancers) and bone metastasis ($B = -1.364$, $p = 0.285$), OR: 0.256, 95% CI: 0.021-3.109. Finally, the presence of pathological fracture (yes Vs no), is also not statistically significant ($B = -1.824$, $p = 0.124$), with an (OR) of 0.161 (95% CI: 0.016-1.652). Overall, the results suggest that none of the studied variables have a statistically significant effect on the probability of bone metastasis.

DISCUSSION

The study presents the first comprehensive characterization of the bone metastasis patterns among cancer patients of the Hail region, Saudi Arabia, which provides valuable baseline data for protocols of diagnosis and patient management for this region. It finds breast cancer the most prevalent malignancy in this cohort consistent with worldwide trends though prostate cancer was curiously high in male patients. The overall rate of bone metastasis (23.4% confirmed, 13.1% unconfirmed) is in line with the international estimates. A large proportion of patients (63.5%) had no confirmed metastasis - this may have reflected the inclusion of early-stage cancers among the patient population and the heterogeneity of this patient population. The results emphasize the importance both of the incidence of breast cancer and of the referral patterns resulting in nuclear medicine consultation for staging of metastasis.

The present study also discusses the patterns of anatomical distribution of bone metastasis. Consistent with previous studies, the most frequent sites of skeletal involvement were the lumbar spine (70%), ribs (64.3%) and pelvis (57.1%) with the lumbar spine being the most frequent because of its rich vascular supply and high bone marrow content. The association of the ribs and pelvis indicates the predilection of metastatic disease for areas of the axial skeleton with active bone marrow. The relatively lower frequency of involvement of the appendicular skeleton, especially the femur and tibia, may reflect referral bias because patients with symptomatic involvement of the femur may have undergone orthopedic intervention before bone scintigraphy. These results are consistent with those of earlier studies that emphasize axial skeleton predominance in metastasis of bone.

A significant age and gender-related associations with metastatic burden are revealed by the demographic analysis. Older patients showed greater prevalence of positive bone metastasis, strengthening the correlation of advanced cancer with older age. In addition, the study shows a gender-related difference with males having a disproportionate higher metastatic burden than females. This may reflect biological factors (higher aggressiveness of skeletal dissemination is common in prostate cancer) or a source of bias in diagnosis and referral factors (poorly differentiated males with cancer underwent bone scintigraphy at more progressed stages). The gender disparity needs further investigation, especially with regard to prostate cancer metastatic behavior.

One of the main limitations highlighted by the study is the high rate of false positives (65.3%) mostly by degenerative changes. This means there is a high diagnosis difficulty in distinguishing cancerous and benign tumors in the bone, especially in the presence of degenerative diseases such as arthritis. Despite this, the clinical practice of failing to follow up with further imaging in a significant proportion of suspected false positives (i.e., 20% of suspected false positives underwent CT or MRI) suggests that radiologists relied on clinical judgement in the interpretation of the scintigraphic results. Additionally, the present study reports a low incidence

of pathological fractures (1.8%), which may reflect good oncological and supportive care and the primacy of the focus of bone scintigraphy in the detection of metastases and not of fractures. The strengths of the study are the regional interest, solid statistical analysis and exhaustivity of the data obtained, providing new relevant information on the patterns of bone metastasis in the Arabian Peninsula.

Comparative Analysis

The demographic and tumor-related results of the cohort in Hail region are different and similar to international studies. In the same cohort, the percentage of breast cancer was 71.6%, which is certainly more than that of Yousef *et al.* [18], who evaluated the Jeddah cohort and where the incidence of prostate cancer was higher (15%). This disparity may be a result of geographic differences, institutional referral patterns, or a difference in cancer epidemiology from region to region. In addition, the rate of bone metastases among the Hail population (23.4%) is consistent with other international estimates. However, a study by Bruckmann *et al.* [20] found a higher prevalence of 38.3% in the newly diagnosed breast cancer patients with sensitive PET/MRI imaging. The lower detection rate in the Hail study is likely to be attributable to inclusion of patients with both early and advanced disease whereas the Bruckmann study was focused on patients with newly diagnosed cancer undergoing comprehensive staging examination.

The anatomical distribution patterns of the bone metastasis of the Hail cohort, predominantly in the lumbar spine (70%), ribs (64.3%) and pelvis (57.1%), are very similar to those reported in other studies. For example, Yousef *et al.* [18] reported similar distribution among their cohort of metastatic bone disease patients with 93% involving the spine, 68% the ribs and 66.5% the pelvis. This consistency of different geographical regions implies a role of bone vascular anatomy and of tumor microenvironment in determining metastatic localization. These patterns are important in order to understand disease progression in metastasis and may determine treatment approaches in different areas [18-20].

When imaging modalities are compared, there are studies showing that the sensitivity for detecting bone metastases with advanced imaging techniques, such as PET/CT and PET/MRI, are better than with traditional bone scintigraphy. Cristo Santos *et al.* [19] found that PET/CT had a sensitivity of 93.83%, in contrast with 81.48% sensitivity of bone scintigraphy in detecting bone metastases in breast cancer patients. Additionally, Bruckmann *et al.* [20] proved that PET/MRI and MRI are significantly superior to CT and bone scintigraphy in terms of sensitivity. Despite the limitations, the use of bone scintigraphy is considered clinically useful because it is available, cost-effective and has adequate specificity for clinical decision-making. The addition of CT to bone scintigraphy (SPECT/CT) further improves specificity and accuracy in localization enabling its use for routine clinical assessments. Regional factors unique to the Hail region including genetic, environmental and lifestyle influences contribute to the unique epidemiology of cancer in the Hail region. The high rate of breast cancer in this cohort is consistent with the global patterns, especially GLOBOCAN [12] estimates for breast cancer being the most common malignancy among Saudi women.

Clinical Implications and Recommendations

Based on our findings, we recommend that tailored approach should be used for the diagnostic and management strategy in bone metastasis for the Hail region. For breast cancer patients, bone scintigraphy should be the first line imaging modality, however, advanced imaging modalities such as PET/CT or MRI should be considered in high-risk patients, particularly those who have elevated serum tumor markers or advanced stage disease. For prostate cancer, the result of bone scintigraphy is generally adequate, but patients with high PSA levels or high Gleason scores should be considered to get further imaging. A high number of false positives in our cohort indicates the importance of careful follow-up imaging especially if degenerative changes of the bone are noted. The role of MRI or CT is considered within 4-8 weeks within a time to consider by clinicians in equivocal diagnosis while scintigraphy results are always correlated with clinical history and patient symptoms.

Moreover, gender and age-specific thoughts are crucial in-patient management. The study shows that the metastatic burden in males appears to be greater and bone scintigraphy should be ordered in these specimens at lower clinical levels than in females. Additionally, patients aged > = 60 years have significantly higher confirmed metastasis, indicating imaging of older patients. Advanced imaging modes such as PET/CT scanners for high-risk malignancies and MRI for evaluation of soft tissues and marrow selectively should be included for nonprofit purposes of improved diagnostic Selatan. The use of SPECT/CT also is recommended to improve the diagnostic performance to ensure continuous investment in this advanced imaging technology.

Strengths of this Study

This study incurs a few major strengths that begin with first-ever regional characterization of bone metastasis pattern in the Hail region that will serve as a baseline for future research. The inclusion of 222 patients has provided one statistically powerful with over 80% power to find moderate effect size associations across various factors of demographic and clinical. The study uses modern SPECT/CT imaging (co-registered CT), which provides a more accurate diagnosis than the technique of old bone scintigraphy studies. Comprehensive data gathering which varies from demographic, clinical to imaging and outcome variables form the basis of detailed analysis under the control of potential confounders. The population is representative of consecutive patients referred for bone scintigraphy and therefore there is less selection bias and represents typical clinical practice. To achieve consistency, clear and objective definitions of outcomes such as presence of bone metastasis, anatomical site distribution and pathological fractures were used. Conducted at a single centre, the study has the

advantage of standardized protocols, interpretation and documentation of imaging. Ethical oversight was provided for by formal committee approval, informed consent procedures and patient confidentiality protections and so the integrity of the research process was preserved.

Limitations of the Study

This study has several limitations that need to be taken into account while interpreting the study result. The retrospective nature of the design leaves room for selection bias because patients who were scanned with a bone scintigraphy may not be representative of the overall population of patients with cancer. Additionally, the sample presented was mainly females (77.03%), so this might affect the applicability of these findings for male patients. The single-center design of the study may also restrict the generalizability of the findings to other parts of the world that have different demographic and healthcare profiles. Furthermore, in a significant proportion of suspected false-positive cases (80%), confirmatory imaging was not performed, which poses a problem in the determination of the true diagnostic accuracy of bone scintigraphy in this study group.

Areas of Future Research

Future studies should address several important areas in order to increase the understanding of metastatic bone disease. Prospective validation studies using standardized referral criteria and confirmatory imaging could help minimize bias and increase the quantitative validity of the study. Comparative studies between bone scintigraphy, PET/CT and MRI in the same number of patients would aid in evaluating their performance for diagnosis. Longitudinal studies are needed to examine researches on the correlation between scintigraphic patterns and clinical outcomes such as survival and progression-free survival. Investigating the flare phenomenon in patients receiving systemic therapy could elucidate its prevalence and clinical implications of the phenomenon. Additionally, assessment of the cost-effectiveness of combining advanced imaging (including PET/CT) with bone scintigraphy would help in guiding the allocation of resources. Genetic and molecular studies that link tumor profiling with images of skeletal metastases could help to identify predictors of the risk of skeletal metastases. Applying artificial intelligence to bone scintigraphy might help improve diagnosing. Finally, multicenter studies in Saudi Arabia would provide valuable national data and establish variations in cancer patterns in the region.

CONCLUSION

This study provides the first comprehensive analysis of patterns of bone metastasis found in cancer patients referred for BSG in the Hail region of Saudi Arabia. Among 222 patients, the largest numbers were breast cancer patients (71.6%), followed by prostate cancer (9.9%) A total of 23.4% of patients demonstrated definitive bone metastasis whereas 63.5% of patients did not have any skeletal involvement. The most common sites of metastasis were the lumbar spine, ribs, thoracic spine and the pelvis, which was consistent with the site patterns worldwide. Pathological fractures were quite uncommon (1.8%). Significant associations were observed between bone metastasis and patient age ($p = 0.003$), gender ($p = 0.002$) and primary tumor type ($p = 0.010$). However, in multivariate analysis there were no independent predictors for metastasis. A high prevalence of potentially false positive findings (due mostly to degenerative changes, 65,3%), emphasizing the need of clinical correlation as well as confirmatory imaging in insufficient results. Despite these problems, however, bone scintigraphy is a valuable cost-effective tool for screening skeletal metastasis throughout the body. This regional information provides a baseline for formulating diagnostic strategies and patient management strategies at the regional level. Future prospective studies, with the incorporation of sophisticated imaging techniques, would be useful in improving the precision of the diagnosis and in providing prognostic information. Implementing the clinical recommendations of the study could lead to improvement in bone metastasis detection and patient outcomes in Hail, which can also serve as a basis for further studies in the region and the country.

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