Therapeutic Regimens of Osteoporosis in Bahrain: A Drug Audit

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ABSTRACT

Objective: We examined the protocol for drug selection and bone mineral density follow up for a sample of osteoporosis patients in Bahrain.

Methods: This was a retrospective study. Data was collected from three hospitals in Bahrain over the period 2016-2018. We collected subject`s demographic data, osteoporosis drug therapy, and the schedule of dual-energy X-ray absorptiometry (DXA) scan before and after therapy.

Results: The number of subjects who were included in this study was 4572 (mean age 59.36 years: 92.5% females, 7.5% males). We found that 41.8% of the patients used osteoporosis medications, whereas the rest were not on any pharmacotherapy (58.2%). The following drugs were used: Vitamin D (82.4%), Calcium (76.6%), Denosumab (14.9%), Bisphosphonate (4.5%) and Tamoxifen (4.3%). Almost all subjects were offered BMD scan before therapy (96.5%), but minority received a follow up after starting medications (17.2%). The follow up scan was performed 2-3 years following therapy in 46.9% of subjects, whereas for the rest, it was requested 1-2 years (31.1%) or 3 years (17.1%) later. Pharmacotherapy was associated with age ($p<0.001$), female gender ($p<0.05$) and being postmenopausal ($p<0.001$). Follow up BMD was positively associated with age ($p<0.001$), postmenopausal status ($p<0.001$) and medication use ($p<0.001$).

Conclusions: Osteoporosis patients were undertreated with anti-resorptive drugs and most of them were not offered a follow up DXA scan to assess response to therapy. Protocol for pharmacotherapy and follow up of osteoporosis in Bahrain needs review.

Keywords: Osteoporosis, DXA, Regimen, Anti-resorptive drugs

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INTRODUCTION

Osteoporosis is a common metabolic bone disorder that results from progressive loss of bone mineral density (BMD), but it is typically asymptomatic, until devastating fractures of the spine and femur happen[1]. Indeed, global data reported that around 30 percent of women and 20 percent of men suffer from fracture related to low BMD during their lifetime[2]. In the Eastern Mediterranean region, where Bahrain is located, osteoporosis is a major health problem[3]. In a recent study, we reported that osteopenia and osteoporosis are common in Bahrain. We revealed that the overall prevalence of abnormal BMD was 62.3% (46.4% osteopenia and 15.9% osteoporosis) (unpublished data). Clinically, the diagnosis of osteoporosis is made if BMD is at least 2.5 standard deviations below the mean values of young healthy adult women reference population (T-score≤ -2.5) and relative to healthy young men, or Z-scores ($Z < -2.5$) for men or young subjects[4].

Osteoporosis is associated with several risk factors, including female gender, white race, ageing, long-term immobility, cigarette smoking and the chronic use of certain drugs such as corticosteroids[5]. Postmenopausal women are particularly at risk of developing brittle bones largely because of the natural decline of female sex hormones, which is normally observed during this period of life[6]. The progressive loss of bone mineralization could eventually result in serious complications, particularly catastrophic hip and spine fractures. Those fractures cause huge impact on patient's quality of life because they result in lengthy hospitalization, need for long-term care, and disability[7].

Osteoporosis is currently considered a preventable and treatable disease, thanks to the introduction of effective medications, which has transformed the prognosis of this condition. The ultimate goal of prescribing anti-resorptive drugs is to preserve bone mass, and eventually lower risk of catastrophic fractures. Bisphosphonates are the drugs of first choice for osteoporosis, but because they have to be administered daily, non-compliance remains a major problem[8]. This adherence issue has been eliminated with the advent of Denosumab, which is a newer monoclonal anti-body. This medication is administered subcutaneously once every six months, and thus requires little adherence[9]. Adequate supplementation of vitamin D and Calcium is considered integral to the standard treatment of osteoporosis for slowing the decline in bone mass. Indeed, adequate intake of those two supplements is strongly recommended for all postmenopausal women, irrespective of their BMD[10]. Despite the availability of effective anti-resorptive drugs, the main question is whether or not those medications are underutilized. A study conducted in Ireland showed that only 21% of patients, diagnosed with osteoporosis, were prescribed medications[11]. The gold standard diagnostic test for BMD is dual-energy X-ray absorptiometry (DXA) scan. This test should be performed for naïve patients to measure baseline BMD, and following pharmacotherapy to assess response to medications[12].

In this study, we sought to audit the drug selection and follow up protocol for osteoporosis patients in Bahrain. Indeed, we aimed to describe the appropriateness of drug selection and whether or not follow up is scheduled at appropriate interval, based on the latest recommendations.

METHODS

Ethical Approval: Ethical approval for the current study was obtained from the Research and Ethics Committee at the Arabian Gulf University (ethical approval number: E003-PI-10/18). Moreover, this investigation was granted approval from the Secondary Health Care Research Sub Committee at Salmaniya Medical Complex, and King Hamad University Hospital (approval number 273/2019).

Settings

Participants and Study Design: The current study was conducted using a retrospective and universal technique. That is, all patients who were investigated for abnormal BMD in the target hospitals over the study period were included. Data was retrieved from the electronic medical records of three hospitals in Bahrain: Salmaniya Medical Complex (SMC), King Hamad University Hospital (KHUH), and King Abdallah Medical City (KAMC). Data was collected over three years: January 2016 to December 2018. Female patients were labeled menopausal if their age was beyond 56 years.

Bone Mineral Density (BMD) Measurement: Data on bone densitometry was based on the results of the DXA scan, which were retrieved from the patient's record. The machine, which was employed for performing the DXA scan, was manufactured by General Electric Lunar, Chicago, Illinois, USA, whereas the software used was the GE NHANES III. BMD was expressed as the ratio between the total bone mineral content (g) over surface area (cm^2). BMD was measured by expert technicians for two bones: left femur neck and lumbar spine. BMD data were interpreted according to the World Health Organization criteria, which diagnose osteoporosis when the T score is -2.5 or below (≤ -2.5), while the diagnosis of osteopenia was made if the T score was between -1.0 and -2.5[13]. When inconsistency was detected between the BMD measurement of lumbar and femur, the lowest score was recorded.

Statistical Analysis: Descriptive statistics, including means, standard deviations and percentages were used to represent quantitative and qualitative variables. Chi-square test was used to measure associations between the categorical variables. A p-value less than 0.05 was considered statistically significant. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS- version 29) and GraphPad Prism 9 software.

RESULTS

The number of subjects, who were included in this study, was 4752 (92.5% females, 7.5% males) (Table 1). The mean age of participants was 59.36 years (SD = 11.19). Majority of them belonged to the age category 44-75 (82.6%), whereas the percentage of those who were aged more than 75 was 8.7%. The number of postmenopausal females in our sample was 2965 (62.4%). According to the hospital, where information was retrieved, most of our data was extracted from SMC (72.5%), while the rest were from KHUH (21.0%) and KAMC (6.6%).

Table 1: Demographic data of the participants (n = 4752)

Characteristic	Subgroup	n	%
Age category	< 44	414	8.7
	44 - < 60	2000	42.1
	60 - < 75	1920	40.5
	≥75	411	8.7
Year of testing	2016	1163	33.8
	2017	959	27.8
	2018	1322	38.4
Gender	Male	357	7.5
	Female	4388	92.5
Hospital	SMC	3444	72.5
	KHUH	996	21.0
	KAMC	312	6.6

SMC=Salmaniya Medical Complex; KHUH=King Hamad University; KAMC=King Abdullah Medical Center.

The participants were stratified based on whether or not they received drug therapy, and according to the prescribed medications (Table 2). Our data revealed that the percentage of patients who were not on any anti-osteoporosis drug therapy was 58.2%, whereas the rest were using drugs (41.8%). Chronologically, the rate of using drug treatment was 25.4%, 31.5% and 43.1% in 2016, 2017, and 2018, respectively ($p<0.001$). Our data revealed that the most commonly used drug was vitamin D (82.4%), followed by Calcium (76.6%). Anti-resorptive drugs were used in minority of subjects (23.7%). Indeed, Denosumab was used in 14.9%, Bisphosphonates were prescribed for 4.5% and Tamoxifen was utilized in 4.3%. The Bisphosphonate which was used in all patients was Zoledronic acid.

Table 2: Anti-resorptive drug therapy of the participants

Drug therapy (n = 4752)	n	%
No	2768	58.2
Yes	1984	41.8
Drug used (n = 1984)		
Vitamin D	1634	82.4
Calcium	1519	76.6
Denosumab	296	14.9
Zoledronic acid (Bisphosphonate)	90	4.5
Tamoxifen	85	4.3

Data on the schedule of the initial and follow up BMD scan were also retrieved in this study (Table 3). Our records showed that almost all patients had a baseline BMD scan (96.5%), but only a small percentage of them were offered a follow up scan following initiating therapy (17.2%). For subjects who had first and second BMD scans, we found that the follow up scan was performed following the initial one as follows: less than 1 year (4.7%), 1 to less than 2 years (31.1%), 2 to less than 3 years (46.9%) and after 3 years (17.1%).

Table 3: Baseline and follow up BMD[a] data of the participants

	n	%
Initial BMD among all participants (n = 4752)		
No	168	3.5
Yes	4584	96.5
Follow up BMD in those who had baseline BMD (n = 4584)		
No	3797	82.8
Yes	787	17.2
	n	%
Time gap between baseline and follow up BMD (n = 787)		
< 1 year	32	4.7
1 - < 2 years	241	31.3
2 - < 3 years	320	46.9
≥ 3 years	117	17.1

[a]BMD=bone mineral density

Medication use was associated with age ($p<0.001$), female gender ($p<0.05$) and being a postmenopausal woman ($p<0.001$). However, the rate of follow up BMD was positively associated with age ($p<0.001$), postmenopausal status ($p<0.001$) and medication use ($p<0.001$).

DISCUSSION

Osteoporosis is a silent bone disease, which does not usually cause manifestations until serious complications ensue[14]. Indeed, catastrophic fractures associated with this metabolic bone disease affect the spine and hip, and result in severe morbidity and mortality[15]. A recent study conducted by our team has reported a relatively high prevalence of osteopenia and osteoporosis in Bahrain (unpublished data). In the current study, we examined the anti-osteoporosis drug regimens in the country as well as the follow up protocol for patients before and after initiating therapy. To fulfil our objectives, we retrospectively targeted a cohort of 4752 patients in three hospitals over a period of three years. Our data revealed that minority of subjects received potent anti-osteoporosis drugs. Additionally, a small proportion of them were offered a follow up BMD after the baseline scan, albeit less than one third of those who were offered the follow up, received it after 1-2 years of therapy as recommended by the latest guidelines. Those data indicate the need for reviewing the protocols for the pharmacotherapy and follow up of osteoporosis in Bahrain.

Our data revealed that most of the subjects were not on any drug therapy, including vitamin D and Calcium. Despite the fact that the rate of drug therapy progressively increased over the three years of study, the overall findings revealed that patients were undertreated and were thus at high risk for developing complications. Underutilization of anti-osteoporosis medications is not uncommon. A recent study in the United States has shown that only 26% of patient, who had survived a hip fracture, were prescribed anti-osteoporosis drugs, for secondary prevention[16]. In another study in Ireland, similar data were observed, in which the authors reported that only 21% of elderly diagnosed with low BMD received drug therapy[17].

In our study, we showed that most of those who were maintained on drug therapy were prescribed vitamin D and Calcium. Latest evidence showed that adequate intake of Calcium and vitamin D is considered first-line therapy for preventing further bone loss in osteoporosis[18]. In fact, a recent meta-analysis concluded that Calcium carbonate combined with vitamin D3 and consumption of diet rich in those essential nutrients improved BMD[19]. On the other hand, only a small proportion of patients, who were maintained on drug therapy, were offered potent anti-resorptive drugs. Indeed, only 4.5% of subjects were prescribed Bisphosphonates, while 14.9% were maintained on Denosumab. Those two anti-resorptive drugs are currently considered anti-osteoporosis drugs of first choice[20,21]. In addition to their benefits as the most effective therapeutic options for osteoporosis, they have excellent efficacy for preventing catastrophic spinal fractures[22]. The latest update on the drug therapy of osteoporosis made by the American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE) was published in 2020. This update recommended the use of Bisphosphonates and Denosumab, because of their broad-spectrum anti-fracture efficacy[22]. Our data reported alarming underutilization of anti-resorptive drugs for osteoporosis patients in Bahrain, an observation that leaves those patients at high risk of developing serious complications.

Another observation of this study was related to scheduling follow up BMD scan to assess response to therapy. Our data reported that only 17.2% of patients who were diagnosed with low BMD were offered a follow up scan. Moreover, less than half of those who were offered a second scan received it at the optimum timing which is 1-2 years following therapy. DXA scan is considered the gold standard for the diagnosis of osteoporosis and for evaluating response to therapy. The latest guidelines of the AACE and ACE for the diagnosis and treatment of postmenopausal osteoporosis recommend a follow up DXA scan every 1-2 years following initiation of drug therapy to check response[23]. Postmenopausal women, who comprised the majority of our sample, were shown to have higher rates of medication use and follow up BMD compared to the overall sample. However, the rate of drug use in this age group was still less than 50%. Postmenopausal women are not only at higher risk of developing osteoporosis compared to males or

other female age groups, but they are at higher risk of experiencing devastating osteoporotic fractures also. That is why, during this period of their life, postmenopausal women need prompt preventive management for osteoporotic fractures including screening and prophylactic drug therapy[24].

Our study has several strengths. We believe that our sample adequately represented the population of Bahrain (1,748,296 as of 2021). Moreover, data was collected from different hospitals in the kingdom, which are located in different regions of the country. On the other hand, our study had certain limitations. Firstly, due to the study design, which was retrospective, no history was collected from the subjects regarding their drug therapy and follow up. Indeed, we could not identify the reasons for not receiving anti-resorptive drugs albeit receiving calcium and vitamin D. Similarly, no data was collected for failure to receive follow up DXA scan.

In conclusion, patients with osteoporosis, including postmenopausal women, were undertreated with anti-resorptive drugs. In addition, most of them were not offered a follow up DXA scan to assess response to therapy. Our data call for review the current drug therapy and follow up protocols of osteoporosis in Bahrain.

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Competing Interest: None

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