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ARTICLE

Prevalence and clinical risk factors for morphometric vertebral fractures in older subjects in KwaZulu-Natal†

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Objectives: There are limited data on vertebral fractures (VFs) in South Africa (SA). Therefore a study was undertaken to compare the demographic profile, clinical risk factors and bone mineral density (BMD) in subjects aged 60 years and over with and without morphometric VFs.
Patients and methods: In a descriptive case-controlled study, demographic data, clinical risk factors (CRF) and BMD were collected. Morphometric VFs were identified using the semi-quantitative Genant method. Descriptive analysis was undertaken using Student's t-test, the Mann–Whitney U-test and the chi-square test.
Results: In the 197 subjects enrolled, the median age was 72.0 years (IQR 67.0–78.5 years) and morphometric VFs were identified in 41 subjects (20.8%). The prevalence of VFs increased with age, and while more common in women compared with men (23.8% vs. 13.0%), this was not significant (p 0.095). There was no difference in the prevalence of VFs between African and Indian subjects (23.4% vs. 17.4%; p 0.240), nor CRFs between subjects with and without VFs. Subjects with a VF had a significantly lower BMD at the spine ($p = 0.020$), but not at the neck of femur and total hip.
Conclusion: This study highlights the need for adequate screening and management protocols for osteoporosis in all ethnic groups in SA.

Keywords: bone mineral density, morphometric vertebral fractures, osteoporosis, prevalence, South Africa

Introduction

Vertebral fractures (VFs) are the most common complication of osteoporosis.[1] In a multinational study in postmenopausal women newly diagnosed with osteoporosis, 68% of the subjects had an undiagnosed VF.[2] The majority of VFs usually occur during normal activities and are asymptomatic with only 40% occurring after a fall.[3] These fractures often develop insidiously over time, and at presentation patients may have multiple prevalent fractures, with progressive loss of stature and disability.[4] Due to their silent nature, most fractures are undiagnosed and not referred for appropriate treatment.[3]

Whilst the prevalence and clinical risk factors for VFs are established in developed countries, there are limited studies from developing countries. The prevalence of VFs in women aged 50 years and over in India and Latin America (between 15% and 18%) is similar to the Western population.[5,6] A similar prevalence (16.2%) has also been reported in Tunisian postmenopausal women, while a higher prevalence (25.6%) was reported in Moroccan women.[7,8] In contrast, a lower prevalence of morphometric VFs was seen in postmenopausal black women in a multi-centre study from Central Africa (11%)[9] and in Gambian women (6%).[10] These differences may be due to methodological or ethnic differences.

South Africa has a unique multi-ethnic population, in whom risk factors and disease profile may vary significantly. Several studies have reported a lower BMD at the lumbar spine in African women compared with white women.[11,12] In a recent study, George *et al*. also reported a lower BMD in Indian South African women compared with black women.[13]

An early study by Dent reported a lower prevalence of morphometric abnormalities of the lumbar spine in black women compared with white women.[14] In this study, VFs were identified on visual assessment of the lumbar spine on lateral X-rays; the participants were not age matched and not screened for secondary causes of osteoporosis. In addition, there was a marked difference in diet across the different groups. Recent studies question the notion that VFs are rare in black women. In a multi-ethnic study, 38% of black South African women aged 60 years and over had sustained new vertebral deformities over a five-year period[15] and a similar prevalence of morphometric VFs has been reported in pre- and postmenopausal white and black South African women (8.3% and 11.5% respectively).[16] There is no information, however, on Indian women in SA nor are there any data on men.

This study was undertaken to further define the prevalence and risk factors for VFs in women and men in SA.

Methods

The Biomedical Research Ethics Committee of the University of KwaZulu-Natal (UKZN) granted ethical approval for the primary study (BF043/09) and for this study (BE612/16). Approval was also obtained from the participating hospitals and KZN

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Provincial Department of Health. The study was conducted according to the ethical guidelines and principles of the International Declaration of Helsinki and Guidelines for Good Clinical Practice in the Conduct of Clinical Trials with Human Participants in SA.

A descriptive study using historical data collected in an age- and gender-matched control cohort, in a primary longitudinal study on osteoporotic hip fracture in persons aged 60 years and over, was undertaken. The initial study was conducted in five public-sector regional hospitals in the eThekwini area, KZN, which provide an orthopaedic service, namely King Edward VIII, Addington, RK Khan, Mahatma Gandhi Memorial and Prince Mshiyeni Memorial Hospital. Volunteer subjects who were able to give informed consent were enrolled from the outpatient departments of these hospitals, old-age community groups and by word of mouth between August 2010 and July 2013. Exclusion criteria included prior history of osteoporosis or hip fractures.

A structured questionnaire was used to collect demographic details, education level, clinical risk factors for osteoporosis and gynaecological history. The Danish Health and Morbidity Survey was used to assess alcohol use[17] and the World Health Organization (WHO) Monitoring Trends and Determinants in Cardiovascular disease scale (MONICA scale) was used to determine smoking exposure.[18] The International Osteoporosis Foundation (IOF) calcium intake diary was used to quantify calcium intake.[19] Functional level was assessed using the validated Physical Self-Maintenance Scale (PSMS) and the Lawton Instrumental Activities of Daily Living scale (IADL) scales, which have good inter-rater reliability at 0.87 and 0.91, in multiple studies respectively.[20,21] Weight and height were recorded, and body mass index (BMI) calculated.

Radiological assessment

Antero-posterior (AP) and lateral radiographic views of the thoracic and lumbar spine were acquired using a standardised protocol in 197 control subjects on the day of enrolment. All radiographs were reported by a single blinded experienced specialist radiologist. Thoracic and lumbar vertebrae were deemed abnormal (morphometric fracture), using the semi-quantitative Genant method, i.e. a reduction in height of $\geq$ 20% in its anterior, middle or posterior section compared with its own or nearest intact posterior vertebra.[22] The percentage loss was calculated using the differences in height. Fractures were graded as mild (20–25%), moderate (25.1–39.9%) or severe (> 40%) according to the degree of deformity.[22]

Bone mineral density (BMD) measurements at the hip and spine were obtained using the Hologic Discovery A densitometer (Hologic Inc, Marlborough, MA, USA) by trained radiographers. In order to ensure reliability a spine phantom was scanned weekly to determine the coefficient of variation, which was < 1.5%. Bone mineral density *T*-scores were categorised according to the World Health Organization (WHO) diagnostic criteria as normal (< −1), osteopenia (> −1 to −2.5) and osteoporosis (< −2.5). The National Health and Nutrition Examination Survey III (NHANES III) data were used for the reference population.[23]

Descriptive data are presented as means and standard deviations or median and interquartile range, depending on the distribution of the data. Demographic characteristics are expressed as frequencies and percentages. To compare variables inferential statistics were applied including Student's t-test or the Mann–Whitney U-test for numerical variables, chi-square test for categorical variables and Fisher's exact test where frequencies were small.

Results

Of the 200 control subjects enrolled in the primary study, 197 subjects who had vertebral radiographs were enrolled in this study. Their median age was 72.0 years (IQR 67.0–78.5 years), and the majority of subjects were women 72.6% (Table 1).

Morphometric VFs were identified in 41 (20.8%) subjects, and the majority 25 (61%) had a single VF and 12 (29.3%) had more than three fractures. The most common sites for VF were the eleventh and twelfth thoracic (T11 and T12) and the first lumbar vertebrae (Table 2). Subjects with VFs were significantly older compared with those without VFs (76.0 years [IQR 69.0–82.0 years] vs. 72.0 years [IQR 66.0–77.0 years]; $p = 0.009$). There was a significant increase in the prevalence of fractures with age, with 14.7% in the 60–69 years age group increasing to 35.7% in subjects aged 80 years and above, $p = 0.023$ (Table 1).

Although a higher proportion of women had a VF of 34 (23.8%) compared with men 7 (13%), this did not reach statistical significance ($p = 0.095$). Similarly, there was no difference in ethnicity or educational level in the prevalence of VFs (Table 1).

Clinical risk factures of vertebral fractures

No differences were observed in mean height, weight or BMI between subjects who had a VF compared with those who did not (Table 1). Although smoking and alcohol use were more common in VF subjects compared with the subjects who did not have a VF, this was not statistically significant. Similarly, no difference was observed in calcium intake, sunlight exposure or paternal history of osteoporotic fracture. Although not significant, subjects with VF were more likely to have a prior fragility fracture (Table 1).

There were no significant differences observed in age of menarche, parity and use of hormonal replacement therapy in women with or without VF. Counterintuitively, a later age at menopause was noted in women with VF than those without (49.6 ± 5.7 years vs. 46.6 ± 7.0 years; $p = 0.037$) (Table 3).

Comparison of bone mineral density

Subjects with a VF had a significantly lower median BMD at spine compared with subjects without a VF (0.745 g/cm^2 [IQR 0.639–0.958 g/cm^2] vs. 0.870 g/cm^2 [0.722–0.988 g/cm^2], $p = 0.020$). There was no statistically significant difference in BMD at the neck of femur or total hip (Table 4). Subjects with VF were more inclined to have osteopenia than subjects without VF, but there was a similar prevalence of osteoporosis.

Discussion

This is a first study to our knowledge to assess the prevalence of morphometric VFs in a predominantly Indian and African cohort and in both men and women in SA.

Several factors influence the prevalence of osteoporotic fractures, individually and/or in combination. These include age, sex, ethnicity, menopausal status, BMD and clinical risk factors for osteoporosis, with the highest fracture rates recorded in older, white postmenopausal women.[3]

Table 1: Comparison of baseline demographic features and clinical risk factors in 197 subjects with and without vertebral fractures

Factor	VF subjects, *n* (%)	No VF, *n* (%)	Total subjects, *n* (%)	*p*-value	HR	95% CI
No. of subjects	41 (20.8)	156 (79.1)	197 (100)			
Age (years)*	76.0 (69.0–82.0)	72.0 (66.0–77.0)	72.0 (67.0–78.5)	0.009[a]	1.061	1.02–1.11
Age categories:						
60–69	11 (14.7)	64 (85.3)	75 (100)			
70–79	15 (18.7)	65 (81.3)	80 (100)	0.023	0.309	0.13–0.76
≥ 80	15 (35.7)	27 (64.3)	42 (100)		0.415	0.18–0.97
Gender:						
Male	7 (13.0)	47 (87)	54 (100)	0.095[b]	2.094	0.87–5.06
Female	34 (23.8)	109 (76.2)	143 (100)			
Ethnicity:						
African	15 (23.4)	49 (76.6)	64 (100)	0.240[b]	0.997	0.72–1.38
Indian	19 (17.4)	90 (82.6)	109 (100)			
Education level:						
No schooling	2 (4.9)	19 (12.2)	21 (10.7)	0.428		
Primary	14 (34.1)	45 (28.8)	59 (29.9)	0.130	0.281	0.05–1.46
Secondary	16 (39.0)	68 (43.6)	84 (42.6)	0.707	0.830	0.31–2.20
Higher education	9 (22.0)	24 (15.4)	33 (16.8)	0.331	0.627	0.25–1.61
Anthropometry:						
Height (cm)**	156.9 ± 8.6	157.2 ± 9.3	157.1 ± 9.2	0.856	0.996	0.96–1.04
Weight (kg)**	70.2 ± 15.8	73.4 ± 16.5	72.7 ± 16.3	0.267	0.988	0.97–1.01
BMI (kg/m^2)**	28.7 ± 6.6	29.6 ± 6.1	29.4 ± 6.2	0.403	0.976	0.92–1.03
Smoking history	6 (14.6)	14 (8.9)	20 (10.2)	0.286[b]	0.575	0.21–1.60
Alcohol intake	2 (4.9)	6 (3.8)	8 (4.1)	0.766[b]	0.780	0.12–4.02
Sun exposure (minutes per day)**	19.2 ± 33.0	31.7 ± 59.9	28.2 ± 55.5	0.528	0.994	0.99–1.00
Dietary calcium intake (grams/day)**	501.5 ± 302.4	466.8 ± 261.8	474.1–270.3	0.504	1.000	0.99–1.00
Paternal history of hip fracture	4 (9.7)	19 (12.1)	23 (11.7)	0.667[b]	1.283	0.44–4.00
Prior fragility fracture	7 (7.1)	10 (6.4)	17 (8.6)	0.054[b]	0.333	0.12–0.94
PSMS**	13.6 ± 1.9	13.9 ± 0.4	13.8 ± 0.9	0.587	0.732	0.51–1.05
IALD**	25.2 ± 4.2	25.5 ± 3.1	25.5 ± 3.3	0.545	0.976	0.89–1.08

*Median and interquartile range or **mean ± standard deviation.
[a]Mann–Whitney U-test.
[b]Pearson's chi-square test.
VF: vertebral fracture, BMI: body mass index; PSMS: Physical Self-Maintenance Scale.
IADL: Lawton Instrumental Activities of Daily Living scale.

Table 2: Sites of vertebral fractures in 41 subjects

Site of fracture: vertebral level *n* (%)	
T1	1 (0.5)
T2	1 (0.5)
T4	1 (0.5)
T5	3 (1.5)
T6	6 (3.0)
T7	7 (3.6)
T8	7 (3.6)
T9	7 (3.6)
T10	6 (3.0)
T11	12 (6.1)
T12	13 (6.6)
L1	12 (6.1)
L2	6 (3.0)
L3	8 (4.1)
L4	7 (3.6)
L5	1(0.5)

L: lumbar, T: thoracic.

The 20.8% prevalence of morphometric VF in subjects aged 60 years and over in this study is consistent with the internationally published prevalence rates of between 20% and 23%[5,6,24,25] in developed countries and that in Morocco (25.6%),[8] and Lebanon (19.9%).[26] However, the prevalence is higher than that seen in the Democratic Republic of Congo (DRC), Cape Town and in The Gambia.[9–11] This may be explained by the inclusion of younger and/or premenopausal women in The Gambia and Cape Town or the lower mean age of the postmenopausal female subjects in the DRC, which was 15 years lower than that in the current study.

The higher, albeit non-significant, prevalence of VFs in women compared with men (23% vs. 13%) is similar to that found in the multicentre European Vertebral Osteoporosis Study (EVOS), in which the prevalence of VFs in women was 20.2% and 12.2% in men aged 50 years and over recruited from 18 European countries.[24] In contrast, a lower prevalence of VFs was reported in men and women in The Gambia, 3% and 6%, respectively, which reflected the overall lower prevalence of fractures in that country.[11]

Table 3: Comparison of gynaecological history in women with or without vertebral fractures

Women	Subjects with VF $n = 34$	Subjects without VF $n = 109$	p value	HR	95% CI
Age of menarche (years)	14.3 ± 1.9	14.0 ± 1.8	0.446*	1.090	0.88–1.36
Age of menopause (years)	49.6 ± 5.7	46.6 ± 7.0	0.037*	1.075	1.00–1.15
Parity	3.2 ± 2.1	3.9 ± 2.4	0.185*	0.882	0.73–1.06
History of HRT	1 (2.9)	12 (11.0)	0.179**	2.656	0.58–12.15

Results presented as mean ± SD.
Statistical analysis with *Student's t-test and **chi-square test with Fisher's exact test.
HRT: hormone replacement therapy.
VF: vertebral fracture.

Table 4: Comparison of bone mineral density in subjects with or without vertebral fractures

Factor	Subjects with VF, $n = 41$	Subjects without VF, $n = 156$	p = value	OR/HR	95% CI
BMD spine (g/cm^2)*	0.75 (0.64–0.96)	0.87 (0.72–0.99)	0.020***	0.137	0.02–0.95
BMD neck of femur (g/cm^2)**	0.69 ± 0.14	0.72 ± 0.13	0.433	0.232	0.01–8.80
BMD total hip (g/cm^2)**	0.88 ± 0.17	0.88 ± 0.16	0.977	0.969	0.11–8.31
WHO BMD classification *T* score at hip:					
Normal > −1	15 (36.6)	62 (39.7)	0.934		
Osteopenia −1.1 to −2.4	19 (46.3)	69 (44.2)	0.777	0.864	0.32–2.37
Osteoporosis > −2.5	7 (17.1)	25 (16.0)	0.973	0.983	0.37–2.62
T score at spine:					
Normal > −1	10 (24.4)	58 (43.6)	0.084		
Osteopenia −1.1 to −2.4	18 (43.9)	56 (35.9)	0.038	0.368	0.14–0.94
Osteoporosis > −2.5	12 (29.3)	30 (19.2)	0.616	n/a	

Results expressed as *median and interquartile range or **mean ± standard deviation. ***Statistical analysis with Mann–Whitney U-test.
BMD: bone mineral density.
VF: vertebral fracture.

The lower prevalence in men is consistent with international studies,[5,6,24,25] and can be explained by the higher peak bone mass in men and the absence of the abrupt and accelerated bone loss that occurs in women at the menopause. However, a slightly higher prevalence of morphometric VFs has been reported in men (18.8%) compared with women (17.1%) in India,[6] and a recent study reported a prevalence of 29.5% in Indian men.[27] In the latter study, the use of lateral vertebral assessment on DXA rather than lateral radiographs may have overestimated VF. Alternatively, Indian men may be at higher risk of VFs, which was not seen in our study.

Interestingly, in our study the prevalence of VFs was higher, although not statistically different, in African subjects compared with Indian subjects (23.4% and 17.4% respectively), which is contrary to the general belief that Africans have lower rates of VFs. There is no national study comparing the prevalence of VFs in the different ethnic groups in SA. However, ethnic differences have been noted in the United States where Hispanic women had the highest risk of fractures, followed by Native American, black and Asian American women, who had the lowest risk of fractures.[28]

Of the several risk factors for osteoporotic fractures, subjects with VFs were older and had a lower BMD at the spine than subjects without VFs. Both advancing age and low BMD are established risk factors for fragility fractures.[4,23] Bone mass is one of the most significant determinants of bone strength and has an inverse relationship with the risk of fragility fractures.[3] The risk of VFs increases 1.5–3 times for each one standard deviation decrease in BMD.[1] Interestingly, this relationship was not seen in The Gambia, where despite a lower BMD compared with British women, no fractures were seen in the Gambian cohort.[10]

A prior fragility fracture is associated with a five-fold higher risk of future fractures, and this risk increases further with the number of prior fractures.[29] Despite prior fragility fractures being more common in VF subjects, in this study it did not quite reach statistical significance, which may be explained by the small sample size. There was, also, no association with between low calcium intake, smoking and alcohol use, unlike other studies.[1,4] Earlier menopause is an established risk factor for osteoporosis and fractures, and it is surprising that in this study subjects who had a morphometric VF were older at age of menopause than those who did not have a VF. This is difficult to explain, but age of menopause was obtained from recall and may have been erroneous in older women.

In our study the prevalence of VFs was highest in the lower thoracic and lumbar vertebrae followed by the thoracic region (T7–T9). These findings are in line with previous studies.[30,31]

Limitations

This study was limited to the public sector and therefore did not adequately represent the different ethnic groups due to differences in socio-economic status and utilisation of health service providers. The sample size was small, with the majority being either Indian or African individuals. The subjects were volunteers and age groups were not equally represented in this study.

Conclusion

Morphometric VFs are common in African and Indian individuals in SA and this study highlights the need for increased

awareness and screening for osteoporosis in all South Africans, regardless of ethnicity. Although age and a low BMD at the spine were the only significant risk factors, this may be due to the small sample size. In view of the association with prior fractures, further studies are required to determine the population-based prevalence and clinical risk factors of VFs in SA to guide screening and management protocols.

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