**Vertebral fracture prevalence and risk factors for fracture in The Gambia, West Africa: The Gambian Bone and Muscle Ageing Study**

**Kate A. Ward, PhD,**  MRC Lifecourse Epidemiology Centre, Human Development and Health, Southampton, UK, MRC Unit The Gambia at London School of Hygiene and Tropical Medicine, The Gambia. ORCID: 0000-0001-7034-6750

**Landing Jarjou PhD,** MRC Unit The Gambia at London School of Hygiene and Tropical Medicine, The Gambia. ORCID: 0000-0001-6211-5119

**Camille Pearse, PhD,** MRC Lifecourse Epidemiology Centre, Human Development and Health, Southampton, UK. ORCID: 0000-0003-3486-8353

**Mícheál Ó Breasail** **, PhD,** Department of Medicine, School of Clinical Sciences at Monash Health, Monash University, Monash Medical Centre, Clayton, VIC, Australia. ORCID: 0000-0002-9695-6378

**Ramatoulie E. Janha, PhD,** MRC Unit The Gambia at London School of Hygiene and Tropical Medicine, The Gambia. ORCID: 0000-0003-1151-6400

**Ayse Zengin PhD,** Department of Medicine, School of Clinical Sciences at Monash Health, Monash University, Monash Medical Centre, Clayton, VIC, Australia ORCID: 0000-0001-6428-6165

**Ann Prentice, PhD, CBE,** MRC Unit The Gambia at London School of Hygiene and Tropical Medicine, The Gambia; MRC Nutrition and Bone Health Group, Cambridge, UK;5 MRC Epidemiology Unit, University of Cambridge, United Kingdom. ORCID: [0000-0003-0254-6659](https://orcid.org/0000-0003-0254-6659)

**Nicola J Crabtree PhD,** Birmingham Women’s and Children’s NHS Foundation Trust, Birmingham, UK**.** ORCID 0000-0001-6729-5841

**Corresponding author:** KA Ward, MRC Lifecourse Epidemiology Centre, Human Development and Health, University of Southampton, Southampton General Hospital, Tremona Road, Southampton, SO16 6YD, UK

Email: kw@mrc.soton.ac.uk

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**Abstract**

There are limited data describing the epidemiology of vertebral fractures (VF) from resource-limited settings, where the ageing population is growing most rapidly. We aimed to determine the prevalence, incidence, and risk factors for VF in The Gambia, West Africa. The Gambian Bone and Muscle Ageing Study is a prospective observational study in men and women aged 40 years and over. Rural participants had baseline measurements and plasma samples collected and were followed up 6-8 years later; urban participants had a single measurement. DXA scans were obtained to assess areal bone mineral density (aBMD), body composition and VF. Prevalence and incidence were calculated. Risk factors for prevalent and incident fracture were tested using logistic regression, in men and women separately, with and without adjustment for age and BMI. At baseline,581 individuals (298 women) had useable scans, 214 (127 women) at follow-up. Prevalence of VF was 14.8%. Those with VF were older (65.6(11.2) vs 61.7(12.3) years, p=0.01) and had lower aBMD Z-scores. For example, in women, a 1SD increase in femoral neck Z-score resulted in a lower risk of having a prevalent VF (OR [95% CI]) 0.51 [0.38, 0.73]. In men, lumbar spine Z-scores were predictive of prevalent fracture; (0.71 [0.53, 0.97]). The incidence of VF over follow-up was 12.1%. Low BMD and grip strength were associated with the odds of having an incident VF. Given the importance of prevalent VF in predicting future VF and other fragility fractures in other populations, our findings are a major cause for concern. VF prevalence in Gambian older adults is similar to elsewhere despite fractures not being a perceived issue. Risk factors were like those identified elsewhere including age, aBMD and bone resorption. Understanding the impact of these fractures is important in a region where health of the ageing population needs to be prioritized.

**Lay summary**

The ageing population is growing rapidly, and most in low- and middle-income countries leading to inevitable increases in occurrence of low trauma fractures. In Africa, we know little about fractures and how often they occur in older people. Fractures of the spine are the most common fragility fracture in older people and lead to further increased risk of fragility fracture. Women and men aged 40 years and above, living in The Gambia, West Africa, were invited to take part and followed for 6-8 years. Participants received spine images to determine prevalence of spinal fractures, and completed surveys, physical function and muscle measurements, and blood samples to identify risk factors for prevalent (pre-existing) and incident (new) fractures. Of the581 individuals with useable baseline scans, the prevalence of vertebral fractures was 15%. Areal BMD and age were the strongest factors associated with VF. Of the 214 participants with longitudinal scans, the incidence of spinal fracture was 12%. The number of spine fractures in Gambian older adults is similar to elsewhere in the world; this is despite fragility fractures not being considered an issue in African adults. Risk factors were like those identified elsewhere. Understanding the impact of these fractures is important in a region where the health of the ageing population needs to be prioritized.

**Introduction**

The prevalence and risk factors for vertebral fractures (VF) vary among populations and there are limited data from resource-poor settings, where the ageing population is growing most rapidly. In such populations, access to care for osteoporosis is limited, with many competing priorities for healthcare [1]. There are few clinicians and common treatments for prevention of fracture are not included on the essential medicines list [1]. In addition, access to imaging for vertebral fracture assessment (VFA) is limited and can be expensive, with radiographs being the most affordable technology. As with elsewhere on the globe, prevalence estimates vary, and methods of assessment and imaging often differ, as do the age-ranges of inclusion.

VF are a major public health burden and are the commonest fragility fracture causing significant pain and mortality [2]. Vertebral fractures can be clinically challenging to detect and estimates range between 65-75% being undetected [3]. This is due to the fractures often occurring asymptomatically, and symptoms not manifesting until multiple fractures are present. In the UK, the 12-month survival rate in women aged 65 years and over, was 86.5% compared to 93.6% expected, and a 5-year survival rate of 56.5% compared to 69.9% expected [4]. Importantly, VF are preventable and are risk factors for future vertebral fracture and other major osteoporotic fractures. A limiting factor in determining the epidemiology of VF prevalence has been that there are several methods of assessment with lack of agreement on the best methodology to assess the presence or absence of fractures. In addition, incidental reporting on standard radiology is not common practice. Together these make the comparison across populations difficult. In 2017, Ballane *et. al.* [5], reported global prevalence data in men and women, with estimates ranging from 7% to 25%. Of note at the time there was a lack of data from the Indian subcontinent, Middle East or Africa, or globally across ethnic groups indicative of disparities in healthcare and access to preventative treatment.

In South Africa, Conradie *et. al.* reported VF prevalence in Black and White African women aged 40 years and above, assessing lumbar spine and thoracic radiographs. Most fractures were classified as mild (60%), with a higher prevalence in Black (9.1%) versus White (5.0%) women [6]. More recently, in older Black African and Indian South African adults from KwaZuluNatal, prevalence was reported to be higher than in the Conradie study at, 20.8%, with no apparent difference between African and Indian participants [7]. In Black women from the Republic of Congo, Central Africa, prevalence from CT scans was reported to be 11.2% [8]. Currently, no data are available for incidence in Black African men and women, and few data to describe risk factors for fracture with none in West Africa.

The primary aim of this study was to determine VF prevalence, and risk factors for VF in men and women aged 40 years and over in rural and urban regions of The Gambia, West Africa. Secondary aims were to calculate fracture incidence and associated risk factors for incident fractures in rural participants (who had been followed longitudinally).

**Material and Methods**

**Participants**

The Gambian Bone and Muscle Ageing Study (GamBAS-rural) is a prospective observational study in Black African men and women aged ≥40 years (ISRCTN17900679). The study protocol has been published previously [9]. In brief, rural participants were identified using the Kiang West Demographic Surveillance System (KWDSS) [9]. The target study sample for rural participants was 240 women and 240 men, with participants recruited and stratified by gender and by 5-year age bands to ensure equal distribution. The oldest age band was 75+. Rural participants had baseline measurements in 2011-12 and were followed-up 6 – 8 years later (2017-19). A group of urban participants, aged 60-80 years, were recruited in 2019 using same inclusion criteria as GamBAS and had one assessment. Participants in GamBAS Urban were recruited through convenience sampling through community networks in Sukuta, West Coast Region, The Gambia. Ethnic group was self-reported. Assessments took place at the MRC Keneba and MRC Fajara bone imaging facilities. Ethics approval for all visits was granted by The Joint Gambia Government/MRC Unit The Gambia at London School of Hygiene and Tropical Medicine Ethics Committee (original reference SCC1222, new reference 28118).

**Vertebral Fracture Assessment & Bone Mineral Density Measurement**

A GE-Lunar Prodigy Advance (GE-Lunar, Waltham, MA, USA, software version 15.0) was used to acquire baseline scans, and GE-Lunar iDXA for longitudinal and urban scans (GE-Lunar, Waltham, MA, USA, software version 15.0). Scans of the lateral spine, proximal femur, lumbar spine and whole body were acquired for measurement of areal bone mineral density (aBMD); cross calibration was performed between scanners [10]. T- and Z-scores were calculated as per International Society of Clinical Densitometry (ISCD) guidelines, using National Health and Nutrition Examination survey (NHANES) III data for T-score calculations and manufacturer reference for Z-scores [11]. Body composition measurements were: total body fat mass (kg) and total body lean mass (kg). Vertebral fracture assessment (VFA) scans were obtained to determine the presence of any spinal degeneration, by assessing vertebral shape, fracture and osteoarthritic changes. Presence or absence of VF were determined at each vertebral level using the Genant semi-quantitative method defining mild, moderate and severe fracture based on reductions in vertebral anterior, middle or posterior height/s [12].

All scans were analyzed by a single expert reader (NJC) using version 18.0 of GE-iDXA software. Manufacturer standard procedures were followed for daily quality assurance and weekly quality control procedures. The same trained operators acquired scans across the two bone imaging facilities; co-efficient of variation of repeat measurements in 30 Gambian adults was 0.7% at the total hip.

**Assessment of predictors of vertebral fracture**

*Anthropometry:* Baseline height (cm) was measured to the nearest 1mm using a wall-mounted stadiometer (Seca GmbH, Hamburg, Germany) and weight (kg) measured to the nearest 0.1 kg using a digital scale (Seca GmbH, Hamburg, Germany) while the participants wore light clothing without footwear. Body mass index (BMI, kg/m2) was calculated by dividing weight by squared height. Similarly fat mass (FMI) and lean mass indices (LMI) were calculated by dividing total body fat mass or total body lean mass by height squared.

*Hand grip strength:* Grip force (kg) was measured using a dynamometer (Jamar Hand Dynamometer, IL, USA) [13]. The individual was seated in an upright position with the dominant arm supported on the armrest of the chair, with the wrist in a neutral position, and the thumb facing upwards. Participants were instructed to exert maximal force. The maximum measurement of three test measurements was used for analysis (kg).

### *Lower limb muscle power:* To assess lower limb muscle function, a Leonardo Ground Reaction Force Platform (Leonardo software version 4.2; Novotec Medical GmbH, Pforzheim, Germany) was used as described previously [14, 15],[16]. Participants were asked to perform a jump as high as possible; this was repeated three times, and the maximum was taken for analysis.

### *Calcium intake:* A prospective 2-day weighed dietary assessment was conducted in the participant’s home on days close to the measurement day by trained and experienced fieldworkers. This method was developed in, and has been validated and used in previous studies in Kiang West with Gambian Food Tables being used to assess intake [17, 18]. Briefly, fieldworkers visited participants’ homes and recorded and weighed all food and drink items the participants consumed (total prepared minus amount left) over 48 hours. Data were coded and analyzed using Diets-In, Nutrients-Out program with Gambian Food Tables [19, 20].

*Biochemical assays:* Blood samples were collected in lithium heparin (LH) and EDTA blood tubes from a forearm vein in the morning after an overnight fast. Plasma was separated by centrifugation at 1800 × g for 10 min at 4°C, stored at -80°C, and subsequently transported for analysis to the MRC Elsie Widdowson Laboratory, Cambridge, UK on dry ice and stored at -80°C. EDTA plasma was used for analysis of parathyroid hormone (PTH) and LH serum for bone turnover markers (procollagen type I N-terminal propeptide [P1NP], and serum collagen type 1 crosslinked β‐C‐telopeptide [β‐CTx]) and 25-hydroxyvitamin D [25(OH)D]. Commercially available assay kits and platforms were used as follows for plasma: intact PTH, β-CTX and P1NP were measured on the iSys platform (Immunodiagnostics Systems Ltd, Tyne and Wear, UK). For internal plasma drift control: NEQAS (Edinburgh, UK) was used for PTH and NEQAS IIA EQA (Sheffield, UK) for β-CTX and P1NP. 25(OH)D was analysed in LH plasma using DiaSorin chemiluminescent immunoassay (Liaison; DiaSorin Inc., Stillwater, MN, USA) on an automated analyser.  Assay performance was monitored using kit and in-house controls and by participation in the Vitamin D External Quality Assessment Scheme ([www.deqas.org](http://www.deqas.org)). All assays performed well and were within specification (details are provided in Supplementary information)

**Statistical analysis**

Data analyses were conducted in Stata 17 (StataCorp, College Station, TX, USA). Normality of distribution of continuous variables was assessed graphically through histograms and were summarised using means and standard deviations (SDs), unless otherwise stated. Differences in continuous variables between fracture and non-fracture groups were compared using t-tests and those in categorical variables using chi-squared tests. Risk factors considered were anthropometric measures, bone turnover markers, PTH, 25(OH)D, grip strength, lower limb muscle power, mean calcium intake and aBMD. Descriptive data are presented in all, and by gender separately. For prevalence estimates and determination of risk factors data for prevalent fracture data are analysed by men and women separately. Prevalence of VF at baseline was calculated based on the number of individuals with at least one VF divided by the study population [21].

In rural participants, we calculated the incidence of vertebral fractures as any new fracture identified at follow-up, irrespective of fracture status at baseline. Incidence was calculated overall and by sex. If sex-specific incidence was low, we combined and included sex as a potential risk factor.

Risk factors for prevalent and incident fracture were tested using univariable logistic regression, with and without adjustment for age and BMI. Data are presented as odds ratio (95% confidence intervals). No adjustments were made for multiple comparisons.

**Results**

Prevalence of vertebral fractures was determined in 581 participants (298 women) at baseline (488 rural, 93 urban) (see supplementary Figure 1**)**. Of the 488 original rural participants, 281 were followed up in 2017-19 (mean follow up time 7.2 SD years) 214 of 281 participants scanned had available scans due to a database issue and formed the group in which incidence was determined.

Table 1 shows descriptive statistics of anthropometry, body composition, muscle function and biochemistry for the whole group and by gender. All participants were Black African, being prominently of Mandinka ethnic group (>90%).

*Vertebral fracture prevalence*

Prevalence of VF was 14.8% (95% CI: 12.01% - 18.0%); no differences were found in women compared to men (16.4% (95% CI: 12.4% - 21.1%) vs 13.1% (95% CI: 9.4% - 17.6%), p=0.25). In participants aged 60 years and over, it was 22.2 %, in women (20.0%) and in men (16.3%). Supplemental Figure 2 shows the distribution of fractures by severity. Most fractures were mild (62.8%), with the rest being moderate (31.4%) or severe (4.7%).

Eighty-six participants (49 women) had at least one prevalent vertebral fracture; the total number of prevalent fractures was 138. Those with vertebral fracture at baseline were older (65.6 vs 61.7 years) than those without (p<0.01). They were slightly leaner (mean (SD) LMI 14.9 (2.1) kg vs. 15.3 (2.0) kg in the whole group, p=0.08) with no significant differences in body weight, BMI or adiposity. Β-CTX was higher in those with a prevalent vertebral fracture than in those without; this difference was more pronounced in women (p=0.02). Whilst overall, 25(OH)D was at sufficient levels by international standards, there was a trend for women with vertebral fractures to have lower plasma concentrations of 25(OH)D than those without fracture (63.2(17.9) versus 69.6 (18.5) nmol/l, p=0.05).

Table 2 presents the baseline dual energy X-ray absorptiometry (DXA) data. aBMD at the femoral neck, total hip and lumbar spine was lower in the fracture compared to no fracture group; in women and overall, this was statistically significant. In men, mean differences between groups were smaller, except for lumbar spine T-score (p-value=0.01). Figure 1 shows T-score distributions in women and men separately. Lower femoral neck and L1 – L4 T-score and Z-scores were also observed in those with VF compared to those without fracture, these differences were also observed in women but only L1 – L4 T-scores and Z-scores were significantly different in men (Table 2). In the whole population, osteoporosis prevalence was low; 5.7% women, 1.4% men, 27.5% had osteopenia (38.9% women; 15.6% men). In those aged >60-years, 90.5% had a femoral neck T-score < -2.5 and 83.5% at the lumbar spine. In the 235 with information on VF and <60 years, 0.9% had osteoporosis (1.7% women; 0% men) and 9.4% had osteopenia (16.2% women; 2.5% men). In the 345 with information on VF and ≥60 years, 5.5% had osteoporosis (8.3% women; 2.4% men) and 40.0% had osteopenia (53.9% women; 24.9% men). Degenerative changes were reported in 10.8% of individuals at baseline, 13.3% at follow-up.

*Associations between risk factors and baseline prevalent fracture in rural and urban participants (Table 3)*

For a 1 SD higher femoral neck Z-score, women were 48% less likely to have a prevalent vertebral fracture (OR [95% CI]: 0.51 [0.34, 0.78], p<0.001); similarly, for a 1SD higher total hip Z-score they were 47% (0.53 [0.37, 0.77], p<0.01) and 42% for a 1SD higher lumbar spine Z-score (0.58 [0.42, 0.80], p<0.01), less likely to have a prevalent vertebral fracture. In men only lumbar spine Z-scores were predictive of prevalent vertebral fracture; a 1SD higher Z-score associated with 34% decreased risk of fracture (0.66 [0.47, 0.93], p=0.03).

In women, a SD increase in β-CTX was associated with 40% higher likelihood of having a prevalent VF (1.43 [1.04,1.95]), which was attenuated after adjustment for age and BMI 1.25 [0.89, 1.75]). A 1SD increase in 25(OH)D was associated with 32% reduction in the likelihood of having a prevalent vertebral fracture in women (p=0.05) although this was attenuated after adjustment for age and BMI.

Area of residence, weight, height, BMI P1NP and PTH were not associated with prevalent VF in Gambian men and women.

*Vertebral fracture incidence in rural participants*

Of 214 individuals with follow-up data 6-8 years later, 180 had no prevalent vertebral fractures at baseline, there were and 16 incident fractures (11 women, 5 men), while among the 34 with a prevalent vertebral fracture at baseline, 7 women and 3 men had aan incident fracture at another vertebral location at follow-up (10 fractures). Overall this equates to an incidence of vertebral fractures in this population of 12.1%.

*Risk factors for incident fracture at follow-up (Table 4)*

Similar risk factors were observed for incident fracture in the smaller sample of those successfully followed up (N=26 incident fractures). For a 1SD higher Z-score and after adjusting for age and BMI, the odds (OR[95% CI]) of having an incident vertebral fracture reduced between 49-61% (femoral neck 0.51 [0.27, 0.98] p=0.04, total hip 0.47 [0.28, 0.80] p=0.01, lumbar spine 0.39 [0.21, 0.73], p <0.001). . A 1SD reduction in grip strength Z-score was associated with 47% reduction in the odds of having an incident fracture (0.53, (0.32,0.88); adjustment for age and BMI attenuate this slightly (0.59, (0.34, 1.00), p=0.05). Of the 34 people with prevalent fracture at baseline, 10 (29%) had a new fracture at follow-up in comparison, 9% of those without fracture at baseline had an incident fracture.

**Discussion**

Given the importance of prevalent vertebral fractures in predicting future vertebral fractures and other fragility fractures in other populations, our findings are a major cause for concern in a population where resources are poor and fracture liaison services and prevention measures do not yet exist [1, 22]. Bisphosphonates and hormone replacement therapy are not currently on the World Health Organisation Essential Medicines list for osteoporosis medication, limiting access to only private patients (in The Gambia this is less than 3% of the general population) [1, 22]. In this gender- and age-band stratified sample of men and women aged 40 years and above, one in six individuals had at least one prevalent fracture. Women had more prevalent fractures than men, although the differences were not as large as those reported elsewhere (16% versus 13%); in women aged over 60-years, 1 in 5 had at least one prevalent fracture. Vertebral fracture prevalence in The Gambia, one of the lowest income countries in the world (in 2022 gross domestic product per capita was 840 USD [23]), is therefore similar to higher-income countries.

Areal BMD and age were the strongest factors associated with VF. A 1 SD lower Z-score was associated with 40% to 50% greater chance of having at least one prevalent VF; in men the relationship was not as strong with approximately 30% greater risk of prevalent fracture. Only a small proportion of individuals with VF, would be diagnosed with osteoporosis using femoral neck T-score thresholds. In those under 60 years of age, only 1.7% women would be osteoporotic, and 0% men. In those aged over 60 years, the proportions are greater, but remain low, 8.3% women, 2.4% men. More than 60% of women in this rural population would be diagnosed with osteopenia and approximately 25% men. Caution is therefore needed in attributing the VF prevalence reported in this study to osteoporosis. Men with VF were younger than women with VF. The younger age of men may indicate trauma-related fractures rather than fragility fractures per se, though this cannot be determined in the current study. In general, these findings show the use of a -2.5SD T-score threshold, determined using NHANES III, cut-offs to distinguish fracture versus non-fracture cases is inappropriate. Furthermore, whilst the use of NHANES III is currently the only recommended and recognized way to diagnose osteoporosis and osteopenia in diverse populations, there is clearly a need to generate country-specific references for creation of appropriate reference data curves [1]. A further example of the limitation of using international references for diagnosis of osteoporosis was in a study of post-menopausal women in Zimbabwe, where racial and ethnic differences in body composition and body size were shown to impact diagnosis of osteoporosis [24].

Cross-country comparison of vertebral fracture prevalence is difficult given differences in imaging technology and population sampling. In South Africa, prevalence in Black and Indian African men and women, median age 72.0 years, was 20.8% in women, 13.0% in men [7]. Women were twice as likely to have a prevalent vertebral fracture than men. These more recent data from South Africa are more than twice the prevalence previously described in Black and White South African women aged 40 years and over, where they were reported to be 9.0% and 5.1% respectively. The data potentially indicate increasing VF prevalence though the differences in the age range and methodologies of the respective study populations should be noted [6]. In the Republic of the Congo in Central Africa, prevalence was reported to be 11.2% in women aged 40 years and above, though it should be noted, these assessments were using reformatted CT scans and the women were mostly in high socioeconomic classes of the country [8]. The recent South African study is the only other African study, to present aBMD in individuals with and without vertebral fractures. Lumbar spine aBMD was lower in those with fracture consistent with our findings in GamBAS though in contrast to GamBAS there were no differences in femoral neck or total hip aBMD. No other risk factors differed, though sample size was limited which may have impacted results.

Understanding the underlying causes and potential risk factors for VFs is important to address the need for prevention of future fragility fractures. In our study, age was higher and aBMD lower, and consequently Z-scores were lower, in those with fractures than those without. Women with vertebral fractures had lower 25(OH)D (63.2nmol/l) compared to those without (69.5nmol/l) with aa trend towards lower 25(OH)D in women being risk factors for fracture. Despite 25(OH)D being adequate, compared to international standards, there is a possibility that in a population with ubiquitous UVB sunshine, that the contribution of low dietary calcium intakes leads to skeletal sequalae at higher 25(OH)D concentrations and /or differing thresholds for sufficiency [25]. Although habitual calcium intake was very low relative to international standards [26], calcium intake was not associated with increased risk for fracture. In addition, there was no evidence that BMI, fat mass index and lean mass index were factors associated with prevalent VF. One potential explanation for the lack of association with BMI, lean or fat mass is that the study population was relatively homogenous, with few people with high BMI. Whilst incident VF numbers were low, bone turnover was also associated with increased risk of incident VF, P1NP associations were robust to adjustment for age, whereas CTX were not. There was a trend toward baseline grip strength being predictive of incident VF, albeit attenuated by adjustment for age, potentially reflecting the frailty status of the participants with fractures.

The implications of these findings are several-fold. In a cohort of older Gambia adults, prevalence of vertebral fractures was similar to that reported elsewhere in the world [5]. Secondly, findings demonstrate the importance of not assuming risk factors translate across contexts. As the number of older individuals living in low and middle income countries increases exponentially, strategies to identify, prevent and to treat such fractures becomes even more important [27]. In these resource-poor settings, access to anti-resorptive therapies, expertise in bone health, fracture liaison services and hormone replacement therapy is limited. Therefore, understanding better the risk factors for fracture, seeking implementable ways of identifying VF and predicting risk of future VF, with context specific primary and secondary prevention strategies is paramount. More broadly, facilitating community knowledge and care is also an extremely important aspect of addressing the challenge posed by rising numbers of the ageing population.

*Strengths and limitations*

The rural component of this work is one of the most detailed, prospective musculoskeletal phenotyping in ageing adults in Africa to date. This is strengthened by study design, which ensured, through use of the Kiang West Demographic Surveillance Survey [28], random stratified sampling in 5-year age bands and by gender, ensured rural participants were distributed appropriately across the region. All scans were read and analysed by a single expert reader. Cross-calibrations for aBMD and body composition measured on the different instruments were performed, making all rural and urban measurements directly comparable [10]. The addition of urban subjects, prominently of the same ethnic group as rural sample (Mandinka) allowed comparison of prevalence between urbanised and rural sites in The Gambia.

There are some limitations to this study. Findings may not be generalizable to the whole population, the focus here was on two regions (Sukuta is one of the most densely populated Urban conurbations of the Gambia). GamBAS was powered to detect change in total hip aBMD, not to ascertain VF prevalence or incidence, or the associated risk factors. The number of incident fractures was low, making the generalizability of findings uncertain, more adequately powered studies are required. Secondly, DXA equipment was upgraded mid-study. Urban recruitment was at a different time to rural recruitment. Methods to recruit differed ue to a lack of Demographic Surveillance System in Urban Gambia meaning convenience sampling was not used. Older adults were weighted towards older ages (60-80 years), making the mean age slightly older than in the rural region. In addition. some risk factor data were not available for the urban sample, limiting power to detect associations and to predict incident fracture. Self-report fracture data were incomplete meaning the association between pervious fracture and prevalent and vertebral fracture could not be tested. We did not adjust for multiple comparisons and cannot rule out findings may have been due to chance, though the analyses performed were based on a priori hypotheses formed by known associations between age, BMD, body composition, bone turnover on bone. Setting more conservative thresholds for significance may have increased the likelihood of missing true associations.

**Conclusions**

In conclusion, contrary to common perception, vertebral fracture prevalence in Gambian women and men is similar to that seen in higher income countries across the world. Given the rising ageing population in low- and middle-income countries, and the consequent rises in non-communicable diseases such as osteoporosis, this is concerning. There are currently no treatment options for vertebral fractures apart from pain relief. Finding scalable and achievable ways to inform communities and healthcare professionals of fractures and their consequences is of utmost important to prevent further challenges to already stretched healthcare resources and most importantly to individuals themselves.

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**Author contributions:**

**Kate A Ward:** Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; resources; supervision; writing – original draft; writing – review and editing. **Landing Jarjou:** Investigation; project administration; writing – review and editing; **Camille Pearse:** Data curation; formal analysis; methodology; visualization; writing – review and editing. **Mícheal Ó Breasail**: Data curation; formal analysis; investigation; methodology; writing – review and editing; **Ayse Zengin:** Data curation; investigation; methodology; writing – review and editing. **Ramatoulie E. Janha:** Investigation; project administration; writing – review and editing; ; **Ann Prentice:** Conceptualization; funding acquisition; investigation; methodology; resources; supervision; writing – review and editing. **Nicola J Crabtree** image analysis; methodology; data analysis; writing – review and editing.

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Table 1. Baseline characteristics of cohort

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **All** | |  | **Men** | |  | **Women** | |  |
|  | **No fracture**  **(n=495)** | **Vertebral Fracture**  **(n=86)** |  | **No fracture (n=246)** | **Vertebral Fracture (n=37)** |  | **No fracture (n=249)** | **Vertebral Fracture (n=49)** |  |
| Baseline age (years) | 61.7 (12.3) | 65.6 (11.2) | 0.006 | 62.1 (12.5) | 64.3 (11.4) | 0.313 | 61.4 (12.1) | 66.7 (11.0) | 0.005 |
| Area of residence a |  |  |  |  |  |  |  |  |  |
| Urban (n (%)) | 86 (17.4%) | 12 (14.1%) | 0.455 | 45(18.4%) | 4 (10.8%) | 0.258 | 41 (16.5%) | 8 (16.7%) | 0.973 |
| Rural (n (%)) | 408 (82.6%) | 73 (85.9%) | 200 (81.6%) | 33 (89.2%) | 208 (83.5%) | 40 (83.3%) |
| Weight (kg) | 59.5 (12.5) | 57.6 (13.4) | 0.211 | 61.9 (12.3) | 61.0 (13.2) | 0.687 | 57.1 (12.2) | 55.0 (13.2) | 0.285 |
| Height (cm) | 163.4 (8.8) | 162.9 (8.6) | 0.639 | 169.2 (7.3) | 169.6 (6.5) | 0.783 | 157.7 (5.9) | 157.8 (6.3) | 0.906 |
| Body mass index (kg/m2) | 22.3 (4.3) | 21.6 (4.4) | 0.204 | 21.6 (3.7) | 21.1 (4.1) | 0.520 | 23.0 (4.7) | 22.0 (4.6) | 0.194 |
| Grip strength (kg) | 25.0 (9.4) | 23.2 (8.5) | 0.101 | 30.4 (9.4) | 28.9 (8.5) | 0.347 | 19.8 (5.8) | 18.9 (5.6) | 0.351 |
| Fat mass index (kg/m2) | 6.1 (3.4) | 5.9 (3.5) | 0.712 | 4.3 (2.3) | 4.0 (2.7) | 0.599 | 7.9 (3.3) | 7.4 (3.4) | 0.360 |
| Lean mass index (kg/m2) | 15.3 (2.0) | 14.9 (2.1) | 0.084 | 16.4 (1.8) | 16.3 (1.9) | 0.610 | 14.2 (1.7) | 13.9 (1.5) | 0.151 |
| 2-leg jump power b (Watt/kg) | 23.8 (10.8) | 24.0 (11.7) | 0.916 | 28.5 (12.1) | 29.9 (12.7) | 0.587 | 18.7 (6.1) | 18.0 (6.9) | 0.610 |
| Calcium intake (mg/day) | 342.0 (188.2) | 333.2 (146.3) | 0.712 | 383.7 (185.5) | 358.3 (122.4) | 0.463 | 302.5 (182.6) | 312.6 (162.0) | 0.751 |
| PTH b (pg/mL) | 77.6 (33.1) | 76.7 (35.8) | 0.836 | 75.4 (32.8) | 69.8 (33.2) | 0.373 | 79.6 (33.4) | 82.2 (37.2) | 0.663 |
| Β-CTX b (ng/mL) | 0.69 (0.32) | 0.79 (0.36) | 0.013 | 0.70 (0.32) | 0.78 (0.35) | 0.237 | 0.68 (0.31) | 0.80 (0.36) | 0.022 |
| P1NP b (ng/mL) | 90.3 (38.9) | 96.6 (43.9) | 0.218 | 83.5 (31.3) | 90.7 (35.1) | 0.229 | 96.9 (44.0) | 101.4 (49.9) | 0.560 |
| 25(OH)D b (nmol/L) | 67.1 (18.5) | 65.2 (19.6) | 0.406 | 64.6 (18.2) | 67.6 (21.4) | 0.400 | 69.5 (18.5) | 63.2 (17.9) | 0.046 |

All continuous data are mean(SD) unless otherwise stated

a Area of residence had 2 missing values b Data are only available in rural participants

PTH, parathyroid hormone; β‐CTX: collagen type 1 crosslinked β-C-telopeptide; P1NP, Procollagen type 1 N-terminal propeptide; 25(OH)D 25-hydroxyvitamin D

Table 2. Areal bone mineral density in participants with and without vertebral fracture

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **All** | |  | **Men** | |  | **Women** | |  |
|  | **No fracture**  **(n=494)** | **Vertebral Fracture**  **(n=84)** |  | **No fracture (n=245)** | **Vertebral Fracture (n=36)** |  | **No fracture (n=249)** | **Vertebral Fracture (n=48)** |  |
|  |  |  |  |  |  |  |  |  |  |
| Lumbar spine aBMD (g/cm2) | 0.97 (0.19) | 0.85 (0.19) | <0.001 | 1.04 (0.17) | 0.96 (0.18) | 0.009 | 0.90 (0.19) | 0.77 (0.15) | <0.001 |
| Lumbar spine T-score | -0.88 (1.79) | -1.99 (1.80) | <0.001 | -0.24 (1.57) | -0.98 (1.71) | 0.009 | -1.50 (1.78) | -2.77 (1.46) | <0.001 |
| Lumbar spine Z-score | -1.21 (1.39) | -1.93 (1.33) | <0.001 | -1.15 (1.40) | -1.75 (1.53) | 0.030 | -1.26 (1.37) | -2.06 (1.18) | <0.001 |
| Femoral neck aBMD (g/cm2) | 0.87 (0.15) | 0.78 (0.15) | <0.001 | 0.91 (0.14) | 0.86 (0.15) | 0.088 | 0.83 (0.15) | 0.73 (0.12) | <0.001 |
| Femoral neck T-score | -0.1 6(1.33) | -0.88 (1.29) | <0.001 | 0.19 (1.22) | -0.19 (1.29) | 0.088 | -0.51 (1.34) | -1.40 (1.04) | <0.001 |
| Femoral neck Z-score | -0.29 (0.99) | -0.74 (0.89) | <0.001 | -0.32 (0.97) | -0.62 (0.98) | 0.090 | -0.26 (1.00) | -0.83 (0.80) | <0.001 |
| Total hip aBMD (g/cm2) | 0.91 (0.16) | 0.82 (0.17) | <0.001 | 0.98 (0.14) | 0.94 (0.15) | 0.090 | 0.84 (0.16) | 0.73 (0.13) | <0.001 |
| Total hip T-score | -0.52 (1.44) | -1.31 (1.50) | <0.001 | 0.08 (1.23) | -0.30 (1.36) | 0.090 | -1.12 (1.38) | -2.07 (1.10) | <0.001 |
| Total hip Z-score | -0.32 (1.05) | -0.86 (1.03) | <0.001 | -0.18 (1.01) | -0.51 (1.14) | 0.075 | -0.47 (1.07) | -1.13 (0.86) | <0.001 |

All continuous data are mean(SD) unless otherwise stated

T-scores were derived using NHANES III and Z-scores using manufacturers references as per International Society for Clinical Densitometry guidance.

Table 3. Baseline risk factors for prevalent vertebral fractures determined by logistic regression, unadjusted and adjusted for age and BMI. Data are presented as Odds ratio (OR) (95% confidence intervals 95% CI))

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Women** | | | | **Men** | | | |
| **Baseline determinants** |  | **Unadjusted** |  | **Adjusted for age and BMI** |  | **Unadjusted** |  | **Adjusted for age and BMI** |
| **N** | **OR (95% CI)** | **N** | **OR (95% CI)** | **N** | **OR (95% CI)** | **N** | **OR (95% CI)** |
| Urban (rural as reference) | 297 | 1.01 (0.44,2.33) | 296 | 1.03 (0.40,2.68) | 282 | 0.54 (0.18,1.60) | 282 | 0.45 (0.13,1.50) |
| Weight Z-scorea, | 296 | 0.83 (0.60,1.16) |  |  | 281 | 0.93 (0.64,1.33) | 281 |  |
| Height Z-scorea, | 296 | 1.03 (0.65,1.62) |  |  | 281 | 1.06 (0.70,1.61) | 281 |  |
| Max grip strength Z-score b | 296 | 0.79 (0.47,1.30) | 295 | 1.31 (0.69,2.49) | 281 | 0.84 (0.59,1.20) | 281 | 0.92 (0.58,1.46) |
| Lower limb muscle power Z-score b | 188 | 0.82 (0.39,1.75) | 188 | 1.50 (0.59,3.78) | 201 | 1.11 (0.76,1.61) | 201 | 1.56 (0.91,2.67) |
| Total hip BMD Z-score b | 297 | 0.41 (0.28,0.62) | 296 | 0.42 (0.25,0.69) | 281 | 0.70 (0.46,1.06) | 281 | 0.69 (0.43,1.13) |
| Femoral neck BMD Z-score b | 297 | 0.43 (0.29,0.65) | 296 | 0.43 (0.26,0.72) | 281 | 0.71 (0.48,1.05) | 281 | 0.70 (0.43,1.13) |
| Lumbar spine BMD Z-score b | 297 | 0.43 (0.29,0.63) | 296 | 0.40 (0.24,0.65) | 281 | 0.55 (0.35,0.87) | 281 | 0.52 (0.32,0.87) |
| Total hip Z-scorec | 297 | 0.53 (0.38,0.73) |  |  | 282 | 0.73 (0.51,1.03) |  |  |
| M-Femoral neck Z-scorec | 297 | 0.51 (0.35,0.73) |  |  | 282 | 0.72 (0.49,1.05) |  |  |
| M-Lumbar spine Z-scorec | 277 | 0.61 (0.47,0.80) |  |  | 241 | 0.71 (0.53,0.97) |  |  |
| M-Mean dietary calcium Z-score | 238 | 1.06 (0.75,1.48) | 238 | 1.06 (0.76,1.48) | 220 | 0.85 (0.56,1.30) | 220 | 0.87 (0.56,1.34) |
| PTH Z-score | 244 | 1.07 (0.78,1.48) | 244 | 0.97 (0.68,1.39) | 224 | 0.83 (0.54,1.26) | 224 | 0.76 (0.49,1.19) |
| Β-CTX Z-score | 247 | 1.43 (1.04,1.95) | 247 | 1.25 (0.89,1.75) | 230 | 1.23 (0.87,1.73) | 230 | 1.19 (0.84,1.69) |
| P1NP Z-score | 247 | 1.09 (0.82,1.45) | 247 | 1.01 (0.74,1.37) | 230 | 1.31 (0.84,2.05) | 230 | 1.33 (0.84,2.10) |
| 25(OH)D Z-score | 247 | 0.68 (0.46,0.99) | 247 | 0.68 (0.47,1.00) | 230 | 1.17 (0.81,1.67) | 230 | 1.18 (0.82,1.70) |

a Weight and height Z-scores were not adjusted for BMI as weight and height are component parts of BMI calculation. b Z-scores for exposures were calculated by individual value minus population mean, divided by population SD to allow comparison of effect size across exposures. c Manufacturer Z-scores are not adjusted for age as already expressed as a function of age. M – manufacturer Z-score PTH, parathyroid hormone; β‐CTX: collagen type 1 crosslinked β-C-telopeptide; P1NP, Procollagen type 1 N-terminal propeptide; 25(OH)D 25-hydroxyvitamin D

Table 4. Baseline risk factors for incident vertebral fracture in rural participants, mean follow-up time 7.2 years. Logistic regression unadjusted and adjusted for age and BMI. Data are presented as Odds ratio (OR) (95% confidence intervals (CI))

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Baseline Determinant** | **Unadjusted** | | **Adjusted for age** | | **Adjusted for age and BMI** | |
| **ORs (95% CI)** | **p-value** | **ORs (95% CI)** | **p-value** | **ORs (95% CI)** | **p-value** |
|  |  |  |  |  |  |  |
| Gender | 0.62 (0.25,1.50) | 0.29 | 0.66 (0.27,1.63) | 0.37 | 0.65 (0.26,1.60) | 0.34 |
| Weight Z-score a, b | 0.76 (0.45,1.29) | 0.31 | 0.88 (0.51,1.53) | 0.66 |  |  |
| Height Z-score a, b | 0.80 (0.51,1.28) | 0.36 | 0.87 (0.54,1.41) | 0.57 |  |  |
| Max grip strength Z-score b | 0.53 (0.32,0.88) | 0.01 | 0.59 (0.34,1.00) | 0.05 | 0.59 (0.34,1.00) | 0.05 |
| Lower limb muscle power Z-score b | 0.60 (0.35,1.03) | 0.06 | 0.71 (0.39,1.29) | 0.26 | 0.70 (0.38,1.29) | 0.25 |
| Total hip BMD Z-score b | 0.43 (0.26,0.72) | <0.001 | 0.44 (0.24,0.81) | 0.01 | 0.44 (0.24,0.82) | 0.01 |
| Femoral neck BMD Z-score b | 0.48 (0.28,0.81) | 0.01 | 0.52 (0.27,0.97) | 0.04 | 0.51 (0.27,0.98) | 0.04 |
| Lumbar spine BMD Z-score b | 0.39 (0.23,0.66) | <0.001 | 0.40 (0.22,0.74) | <0.001 | 0.39 (0.21,0.73) | <0.001 |
| M\_Total hip Z-score c | 0.45 (0.27,0.74) | <0.001 |  |  |  |  |
| M\_Femoral neck Z-score c | 0.55 (0.32,0.94) | 0.03 |  |  |  |  |
| M\_L1 -L4 z-score c | 0.44 (0.27,0.72) | <0.001 |  |  |  |  |
| Mean dietary calcium z-score b | 1.09 (0.69,1.71) | 0.72 | 1.03 (0.64,1.65) | 0.91 | 1.03 (0.64,1.65) | 0.92 |
| PTH z-score b | 1.11 (0.77,1.60) | 0.59 | 1.03 (0.70,1.51) | 0.89 | 1.04 (0.70,1.54) | 0.85 |
| Β-CTX z-score b | 1.38 (0.89,2.12) | 0.15 | 1.24 (0.78,1.96) | 0.36 | 1.23 (0.78,1.96) | 0.38 |
| P1NP z-score b | 1.39 (0.97,1.99) | 0.07 | 1.32 (0.91,1.91) | 0.14 | 1.32 (0.91,1.91) | 0.14 |
| 25(OH)D z-score b | 0.95 (0.61,1.47) | 0.81 | 0.91 (0.59,1.41) | 0.68 | 0.90 (0.58,1.40) | 0.64 |

a Weight and height Z-scores were not adjusted for BMI as weight and height are component parts of BMI calculation. b Z-scores for exposures were calculated by individual value minus population mean, divided by population SD to allow comparison of effect size across exposures. c Manufacturer Z-scores are not adjusted for age as already expressed as a function of age. M – manufacturer Z-score PTH, parathyroid hormone; β‐CTX: collagen type 1 crosslinked β-C-telopeptide; P1NP, Procollagen type 1 N-terminal propeptide; 25(OH)D 25-hydroxyvitamin D