

The normal reference of bone mineral density ranges for young women age 16 to 30 in central region, Uganda. A cross-sectional study.

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Abstract

Background

Osteoporosis is a prevalent skeletal disorder characterized by reduced bone mineral density (BMD) and increased fracture risk. This study establishes normal reference ranges of bone mineral density for young women aged 16 to 30 in the central region of Uganda.

Methods

This cross-sectional study used secondary data from the Bone Care Study, the Bone Mineral Density Study, and the Kampala Women's Bone Study. Descriptive statistics were used to summarize the data. The normal reference ranges were established, and they are presented as mean BMD values and standard deviation per age group, with the Shapiro-Wilk test assessing normality and non-parametric methods applied if needed. Comparisons with white women's NHANES (National Health and Nutrition Examination Survey) BMD standards were done using a one-sample t-test.

Results

The mean \pm SD age was 21.4 \pm 3.2 years, the mean body mass index (BMI) for all the study participants was 23.4 (3.9), 496 (64.9%) were from KWBS, 227 (29.7%) from the Bone care study, and 41 records (5.4%) from the BMD study. The average (SD) age was 21.4 (3.2) years. 50.3% of the participants were aged 16 to 20. Mean BMD at Lumbar spine (LS), Total hip (TH), Femoral Neck (FN), and whole body (WB) increased with age. BMD values range from 0.932 to 0.980 at LS, 0.953 to 0.989 at the TH, 0.868 to 0.889 at the FN, and 0.937 to 1.020 for the whole body.

Conclusion

The established BMD for Ugandan women was significantly lower than the current references. The use of inappropriate, non-representative reference values compromises the accuracy of osteoporosis screening.

Recommendation

The Ministry of Health, in collaboration with relevant professional bodies, should spearhead the development of context-specific clinical guidelines for the assessment, interpretation, and management of low BMD and osteoporosis in Uganda.

Keywords: Bone Mineral Density (BMD), Normal Reference Ranges, Young Women, Age 16–30 Years, Central Region, Uganda.

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Background

Osteoporosis is a silent, prevalent skeletal disorder defined by reduced bone density and increased susceptibility to fractures (Foundation, 2019). According to the NIH Consensus Development Panel on Osteoporosis,

osteoporosis is a skeletal disorder characterized by compromised bone strength that increases the risk of fracture (Akkawi and Zmerly, 2018; Lorentzon and Cummings, 2015). The World Health Organization (WHO) defines osteoporosis as a bone mineral density (BMD) that

lies 2.5 standard deviations (SD) or more below the average value for young healthy women (Cosman et al., 2014, WHO, 1998)

Globally, epidemiological data from the International Osteoporosis Foundation reveal that approximately 33.3% of women and 20% of men over the age of 50 will experience osteoporotic fractures at some point in their lives (Sözen et al., 2017). Additionally, osteoporosis leads to over 8.9 million fractures yearly, translating to one osteoporosis-related fracture every 3 seconds (Foundation, 2019; Hernlund et al., 2013). According to the WHO definition of osteoporosis, about 6.3% of men and 21.2% of women over 50 years have osteoporosis globally. In sub-Saharan Africa (SSA), data on osteoporosis are scarce. However, the limited studies conducted in the region indicate that osteoporosis and fractures are increasing across the continent. However, the incidence of osteoporosis varies significantly between different regions in Africa and ethnic groups: it ranges from 13.4% to 43.7% in men, 24.3% to 65.8% in post-menopausal women, and from 9% to 23.3% in healthy women (Paruk et al., 2021). In Uganda, epidemiological studies reporting the incidence of hip fractures or vertebral fractures are limited. The studies are usually limited as they are based on retrospective data and small study numbers, and often from a single study site.

While assessing bone health among young adults below 30 years might not seem a top priority, a closer look at important facts and epidemiological statistics reveals why it deserves our attention. Osteoporosis among this age group is often overlooked because it's uncommon. Unfortunately, there is a lack of united and consistent guidance to properly screen and diagnose young adults, which adds a barrier to optimal management of this condition, among young women below the age of 30 years (Ferrari et al., 2012; Shuhart et al., 2019). Also, there is no clear definition of osteoporosis nor intervention thresholds in younger individuals. Establishing reference ranges for this age group is crucial because it is during this time that individuals are expected to achieve peak bone mass. After this point, bone mineral density begins to decline due to accelerated bone mineral loss, consequently leading to increased risk of osteoporosis and fragility fractures (Sözen et al., 2017).

Furthermore, the progression from low bone mass to osteoporosis has no clinical manifestations until there is a fracture. The clinical symptoms like back pain, stooped posture or kyphosis, and loss in height by more than 2-3cm (attributed to a vertebral fracture), are usually fracture-related. Fragility fractures –following low-impact trauma or force, like lifting, bending, coughing, or even sneezing, is another manifestation. The commonest sites for fragility fractures are the hip, spine, and the distal forearm. Osteoporosis can be prevented with an early diagnosis

before fractures occur, assessing the bone mineral density, and early treatment (Sözen et al., 2017). Several treatments have been shown to reduce the risk of osteoporotic fractures by enhancing bone mass and minimizing the risk of falls or their consequences. Adults who have suffered vertebral, rib, hip, or distal forearm fractures should be evaluated for osteoporosis and receive appropriate treatment. This may include pharmacotherapy (bisphosphonates), increased exposure to the sun (vitamin D synthesis), ensuring adequate calcium and vitamin D intake, avoiding smoking and excessive alcohol consumption, engaging in weight-bearing (weight lifting, aerobics) and resistance-training exercises like jogging, fast walking for at least 90 minutes every week, and implementing fall prevention strategies. These measures form an effective approach to preventing fractures (LeBoff et al., 2022). Estrogen supplementation, especially at the time of menopause, may be considered, although there is a small increased risk of stroke (due to blood clots) and breast cancer. (NIH) Research has shown that predisposing factors are similar to those in developed countries, but awareness of osteoporosis is surely lacking in SSA. There is a lack of awareness among the population and health authorities, making it extremely difficult to quantify the disease burden (Njeze Ngozi et al., 2017). Therefore, this study aims to determine the normal reference BMD ranges for young women below the age of 30 in central Uganda and to compare the normal reference of BMD ranges for this age group with the current age-matched standard ranges of white women.

Methodology

Study design

This was a descriptive cross-sectional study that used secondary data from the Bone Care Study, Bone Mineral Density Study, and Kampala Women's Bone Study (KWBS) at the MUJHU site.

Study sites and settings

The study extracted data/records from the Bone care study, Bone mineral density study, and the Kampala women's bone study done at Kasangati by Infectious Disease Infection (IDI). All these studies had their BMD measured by a DXA unit at the MUJHU research site. Results/records from the DXA Machine at MUJHU Research collaboration were considered for each participant.

Study population

Target population

All records of women aged 16 – 30 years in central Uganda.

Accessible population

All records of women aged 16-30 years who participated in the Bone Care Study, Bone Mineral Density Study,

Kampala Women's Bone Study, and underwent a DXA scan at the MUJHU DXA unit.

Actual or study population

All records of women aged 16-30 years who participated in the Bone Care Study, Bone mineral density study, and Kampala women's bone Study and underwent a DXA scan at the MUJHU DXA unit, and fulfilled the eligibility criteria.

Eligibility criteria

Inclusion criteria

All baseline records of women aged 16–30 years with available DXA data at the MUJHU site.

All baseline records of participants in the control arms of the Bone Care and Bone Mineral Density studies within the age range of 16-30years were included.

All baseline DXA records of participants of the KWBS study within the age range of 16-30years were included.

Exclusion criteria

Participants who were pregnant or currently breastfeeding women.

Participants with chronic illness or conditions affecting bone health.

Participants on medication affecting bone health or metabolism.

Women 16-30 years old with missing or incomplete data.

Participants with other known risk factors had been excluded from the 3 studies at enrollment.

Sample size

We did not need to calculate the sample size; all records that met the inclusion criteria with complete data were utilized in this study for analysis.

A total of 764 participant records combined from the three studies were used.

Sampling procedure

The Kampala Women's Bone Study recruited sexually active, HIV-negative women aged 16 to 25 between May 2018 and March 2020. The study was a component of an observational cohort study that examined bone health in women who used condoms or daily oral FTC/TDF for HIV prevention and DMPA (depot medroxyprogesterone) in conjunction with condoms for pregnancy prevention. HIV-at-risk and contraceptive-seeking women were sourced from higher education institutions, youth-based centers, and family planning clinics. Those who were pregnant or breastfeeding, currently using an implant, intrauterine device, or oral contraceptives, had previously undergone a hysterectomy, oophorectomy, or tubal ligation, had used

DMPA for more than 90 days in the previous two years or for more than two years in total, had used PrEP continuously for the last three months, had Hepatitis B virus infection or abnormal kidney function, had a history of primary or secondary amenorrhea, or were taking medications known to interfere with bone metabolism were not eligible to participate in the Kampala women bone study (Heffron et al., 2022). All the baseline data of this study were considered and included because at baseline, all the women with the known risk factors had not been enrolled. The bone care study was a prospective cohort study that enrolled women between the ages of 18 and 35 from 11 general health and HIV care clinics in Kampala, Uganda. Based on their combination of HIV status, TDF use, and DMPA-IM use, the participants were divided into four groups: HIV-positive, DMPA-positive, and TDF-positive women living with HIV starting TDF-containing antiretroviral therapy (ART) with DMPA-IM; HIV-positive, DMPA-positive, and TDF-negative women living with HIV using DMPA-IM but not eligible for ART as per local guidelines at the time of study enrolment; HIV-positive, DMPA-positive, and TDF-negative women living with HIV starting TDF-containing ART without DMPA-IM (HIV positive, DMPA-negative, and TDF-positive); and HIV-negative controls using non-hormonal contraceptives (HIV negative, DMPA-negative, and TDF-negative) (Kiweewa Matovu et al., 2022). Only BMD data of participants who were HIV negative and not using hormonal family planning methods were included in the determination of the reference ranges. For this study, only the records of the participants in the control arm of the study were included. The control arm had HIV-negative women who were not using hormonal family planning. Women with other known risk factors for low BMD had not been enrolled into the study, except for the factors/conditions under study, such as those who were HIV positive and on ART, and those combining ART with hormonal family planning. For my study, only the records of the women in the control arm (HIV negative and not on hormonal family planning) were used.

The bone mineral density study was a cross-sectional study in which a sample of 152 women aged 18 to 45 years was studied at the Mulago National Specialized Hospital Family Planning Clinic in Uganda. Of these, 72 women were current depot medroxyprogesterone acetate (DMPA) users, and 80 were on non-hormonal contraception (condoms or intra-uterine contraceptive device). Current DMPA use was defined as documented consistent use of DMPA, and non-hormonal contraceptive users had no exposure to hormonal contraceptives in the two years before study participation. Women were excluded if pregnant or breastfeeding in the last two years. Hypovitaminosis D was defined as a serum 25-hydroxyvitamin D (25OHD) concentration ≤ 29 ng/ml. BMD assessments of the lumbar spine, total hip, and

femoral neck were performed according to international densitometry guidelines using Dual-energy X-Ray absorptiometry. (Kiweewa Matovu et al., 2022).

For my study, only the records of the women in the control arm (HIV negative and not on hormonal family planning were used.

Study procedure

This study consequently sampled out and included all participant records from the Kampala women's Bone study, Bone mineral density study, and the bone care study that had complete data on the essential variables: age and DXA results in our study, and who met our inclusion criteria.

From all the 3 studies, the information extracted for the participants who were eligible and met the inclusion criteria was the age, BMI, height, weight, and BMD (measured at 3 skeletal sites, the hip, the whole body, and the lumbar spine; L1-L4). BMD assessments of the whole body, lumbar spine (L1-L4), total hip, and femoral neck were performed according to international densitometry guidelines using Dual-energy X-Ray absorptiometry.

Data Management

Data extraction

Data extraction was conducted using a developed data abstraction tool. The variables of interest were extracted from an Access database to Excel spreadsheets as guided by the data abstraction form. This approach ensured that all required information for the study was thoroughly extracted from the Bone Care Study dataset, the Bone Mineral Density Study, and the Kampala Women's Bone Study, minimizing the risk of missing data. The tool below was used to extract the data.

Table 1 Data Abstraction Tool

Variable	Category	Measured
Age	1. 16-20 (years) 2. 21-25 (years) 3. 26-30 (years)	Proportion and mean/ median for continuous age
BMI	Continuous	Mean (SD) and/or Median (IQR)
Weight	Continuous	Mean (SD) and/or Median (IQR)
Height	Continuous	Mean (SD) and/or Median (IQR)
Lumbar Spine BMD	Continuous	Mean (SD) and/or Median (IQR)
Total Hip BMD	Continuous	Mean (SD) and/or Median (IQR)
Femoral Neck BMD	Continuous	Mean (SD) and/or Median (IQR)
Whole body BMD	Continuous	Mean (SD) and/or Median (IQR)

Table 1 shows the (dependent variable) BMD and the age and BMI (Independent variables).

Data Cleaning

Data was exported from Excel to STATA 17 for data cleaning and management before analysis. Records that were missing BMD data or incomplete were dropped from the analysis. Records of participants who were older than 30 years were also excluded from the analysis. Age was coded according to the different categories to facilitate reporting and comparison.

DXA imaging of their lumbar spine (L1-L4), femoral neck of the hip, total hip, and whole body using a QDR DISCOVERY Wi; S/N 84650 bone densitometer. (Hologic, Inc, Bedford, Massachusetts, USA), performed

All these 3 studies used the same DXA facility at MUJHU and had their DXA scans performed by the same trained research imaging technologists at the Makerere University Johns Hopkins University Research Collaboration (MUJHU) clinical trial site in Kampala. T- and Z-scores were derived by comparing participant total hip and lumbar spine measurements to the NHANES III reference database for U.S. white women as provided by the manufacturer. All these studies used the same DXA scanner: a QDR DISCOVERY Wi, S/N 84650 bone densitometer (Hologic, Inc, Bedford, Massachusetts, USA)

BMD values were calculated using Hologic Apex 4.5.4 Software and TBS iNSIGHT version 3.0.2.0 (to generate TBS values, although not used in this study).

Data Analysis

Descriptive statistics were used to summarize data. Continuous variables were summarized using mean (standard deviation (SD)) and/or median (interquartile range (IQR)). Categorical variables were summarized using frequencies and percentages. Bar charts and tables were used to present the data.

For Objective 1, the study aimed to determine the normal reference BMD ranges for young women between the ages of 16 and 30 in Central Uganda. This involved analyzing BMD values measured at key skeletal sites, including the total hip, lumbar spine, and femoral neck, using DXA.

Descriptive statistics (mean and SD) were used to summarize the data. Bar charts were used to check for normality of the BMD data before summarizing it. Mean

BMD values were reported by the different age categories: 16-20, 21-25, and 26-30 years.

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For Objective 2, the study aimed to compare the normal reference BMD ranges of young women in Central Uganda with the established standard ranges for white women. We also compared the local Ugandan reference ranges to those of NHANES non-Hispanic black (African-Americans in the USA). The assumption is that this non-Hispanic black population would have a BMD range closer to or similar to that of the Ugandan women since they are both of African descent.

These comparisons were performed using a one-sample t-test since the data were normally distributed. Further subgroup analysis was conducted by stratifying participants into age categories: 16-19 and 20-29 to facilitate comparison with the NHANES age groups. Statistical significance was set at 0.05. All analyses were performed using STATA statistical software (version 17.0).

Quality assurance

An Excel checklist was used to ensure that there was no missing data. We checked for missing data and assessed for missingness. The analysis followed complete case analysis since we had less than 1% missing data on BMD.

RESULTS

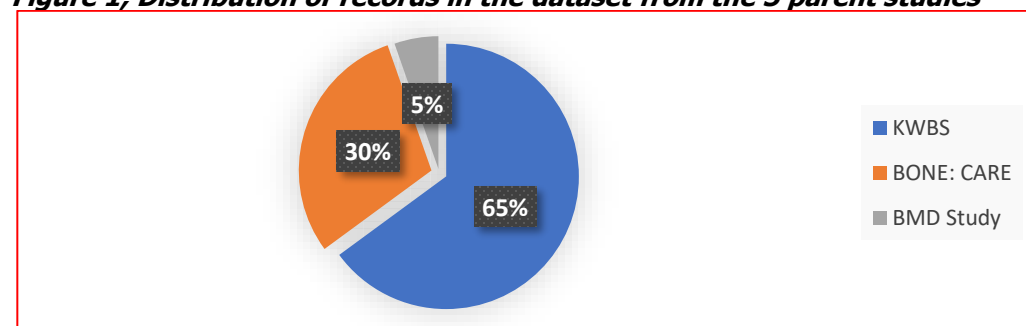
Anthropometric Characteristics

Records of 764 adolescents and young women were extracted from the three studies. The mean \pm SD age was 21.4 \pm 3.2 years. In terms of weight, the participants had a median weight of 57 kgs (IQR: 51 – 64) kgs. Those aged 26 to 30 years had a median weight of 66.5 years, and it was the highest amongst the three age categories. The mean body mass index (BMI) for all the study participants was 23.4 (3.9), and it was highest among the 26–30-year-olds.

Table 2, Anthropometric Characteristics

Characteristic	16-20	21-25	26-30	Total
	n=384 (50.3%)	n=274 (35.9%)	n=106 (13.9)	N=764
Age (Years)				
Mean (SD)	18.9 (0.9)	22.4 (1.4)	27.5 (1.3)	21.4 (3.2)
Median (IQR)	19.0 (18.0-20.0)	22.0 (21.0-23.0)	27.0 (27.0-28.0)	20.0 (19.0-23.0)
Weight				
Mean (SD)	56.5 (8.4)	59.1 (10.3)	66.0 (14.7)	58.8 (10.6)
Median (IQR)	55.0 (50.0-61.0)	58.0 (52.0-65.0)	66.5 (56.8-77.0)	57.0 (51.0-64.0)
Height				
Mean (SD)	157.9 (5.9)	159.2 (6.1)	159.2 (5.9)	158.5 (6.0)
Median (IQR)	158.0 (154.0-162.0)	159.7 (155.0-164.0)	159.8 (154.8-164.3)	158.0 (154.0-163.0)
Body Mass Index				
Mean (SD)	22.7 (3.2)	23.3 (3.6)	25.9 (5.3)	23.4 (3.9)
Median (IQR)	22.4 (20.4-24.4)	22.9 (20.8-25.2)	25.7 (21.8-28.6)	22.9 (20.7-25.3)

Figure 1, Distribution of records in the dataset from the 3 parent studies



In terms of study representation, the Kampala Women's Bone Study (KWBS) had the highest number of records (n=496), contributing to 64.9%. This was followed by the Bone care study, with 227 records contributing to 29.7%, and the BMD study had the least, with only 41 records contributing to 5.4%.

Age distribution

Figure 2, Age distribution across the used combined data from the three parent studies

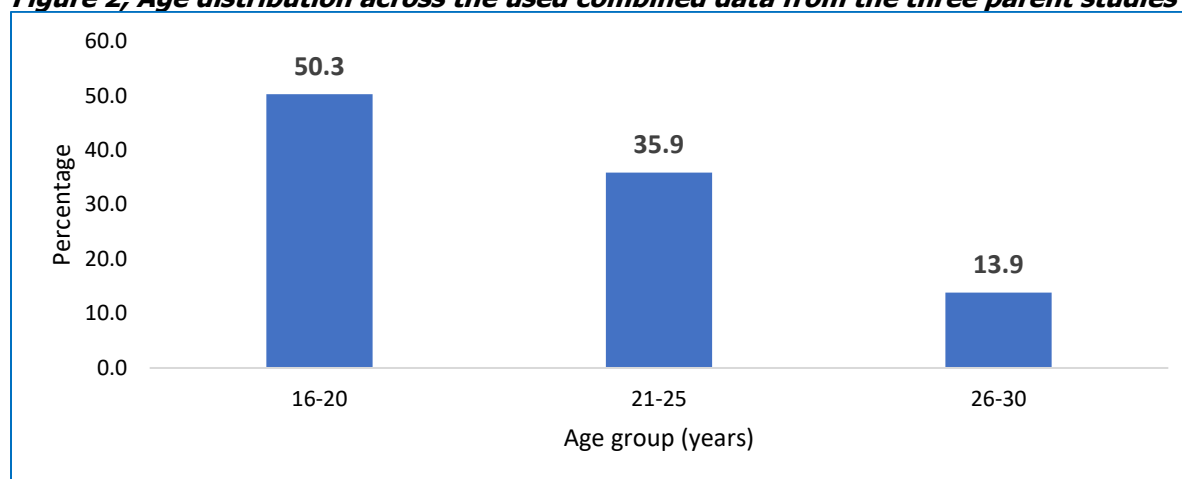


Figure 2 shows that age was categorized into three categories: 16-20, 21-25, and 26-30 years. Half (50.3%) of the participants were aged between 16 and 20 years inclusive. A smaller proportion (35.9%) of the participants were aged 21 to 25 years inclusive, and 13.9% were aged 26 to 30 years.

Mean BMD at the different skeletal sites.

Mean BMD at the Lumbar Spine (L1-L4), Total Hip, Femoral Neck and whole body.

Figure 3, Mean BMD at Lumbar spine, Total hip, Femoral Neck and Whole body.

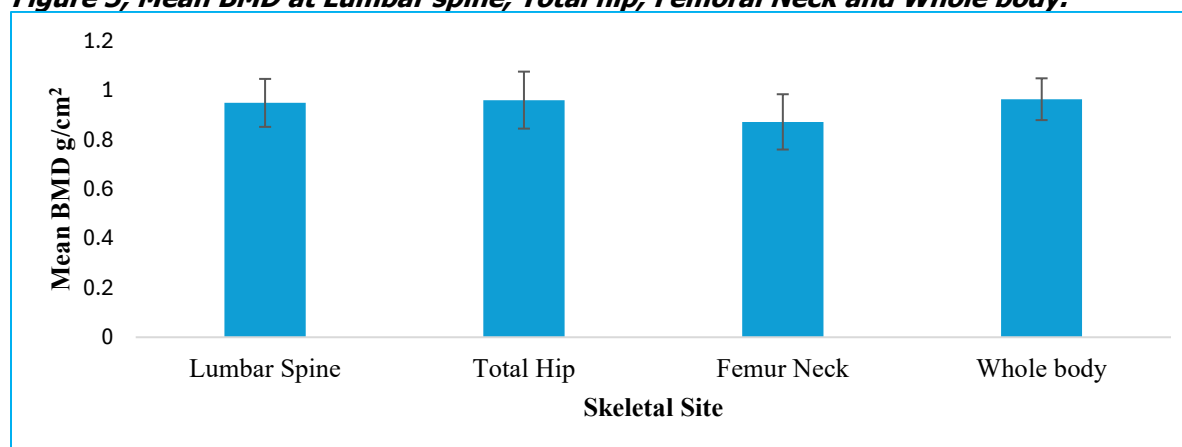


Figure 3 shows the mean BMD for all the study participants at the different body sites –Lumbar spine, Total hip, Femoral Neck, and whole body. From the graph, Lumbar spine, Total hip, and whole body mean BMDs were almost the same (~0.96). The mean femoral neck BMD was lower than that of the 3 body sites.

Mean BMD (g/cm²) for Ugandan Women at the Lumbar Spine (L1-L4), Total Hip, Femoral Neck and Whole body by age group.

Table 3, Mean BMD (g/cm²) for Ugandan Women at the Lumbar Spine (L1-L4), Total Hip, Femoral Neck and Whole body

Table 3 below shows the mean (SD) BMD and percentiles for the Ugandan adolescent girls and young women at the LS, TH, FN, and whole body, presented per different age groups. The sample size for each age category is also presented in the table. At the lumbar spine, the mean BMD among the 16–20-year-olds was 0.932 (SD=0.095), for

those 21-25, 0.964 (SD=0.098), while that of 26-30-year-olds was 0.980 (SD=0.091). Similar trends of mean BMD at the total Hip, FN, and whole body were observed, where the adolescents had a lower mean BMD than the young women, as shown in Table 3.

Body Site	Sample Size	Mean BMD	Standard deviation	Percentile								
				5th	10th	25th	50 th	75th	90th	95th	99th	
Lumbar Spine												
16-20	384	0.932	0.095	0.768	0.804	0.872	0.930	0.995	1.044	1.075	1.164	
21-25	274	0.964	0.098	0.802	0.842	0.891	0.965	1.030	1.100	1.128	1.178	
26-30	105	0.980	0.091	0.820	0.850	0.913	0.994	1.046	1.090	1.114	1.145	
Total	763	0.950	0.097	0.788	0.826	0.887	0.949	1.021	1.071	1.114	1.169	
Total Hip												
16-20	384	0.953	0.122	0.759	0.796	0.868	0.951	1.034	1.117	1.166	1.262	
21-25	274	0.962	0.108	0.801	0.837	0.878	0.954	1.040	1.109	1.139	1.217	
26-30	106	0.989	0.107	0.835	0.841	0.897	0.988	1.069	1.118	1.181	1.221	
Total	764	0.961	0.116	0.787	0.818	0.875	0.955	1.040	1.115	1.156	1.235	
Femoral Neck												
16-20	384	0.868	0.114	0.679	0.726	0.803	0.864	0.927	1.023	1.067	1.162	
21-25	274	0.874	0.106	0.714	0.746	0.798	0.863	0.946	1.023	1.055	1.122	
26-30	106	0.889	0.120	0.693	0.741	0.814	0.876	0.960	1.041	1.087	1.205	
Total	764	0.873	0.112	0.696	0.736	0.803	0.866	0.941	1.024	1.057	1.184	
Whole body												
16-20	314	0.937	0.068	0.827	0.856	0.895	0.932	0.975	1.028	1.044	1.097	
21-25	244	0.978	0.088	0.860	0.879	0.915	0.961	1.032	1.094	1.162	1.213	
26-30	106	1.020	0.089	0.872	0.905	0.940	1.023	1.081	1.125	1.157	1.227	
Total	664	0.965	0.085	0.845	0.873	0.907	0.952	1.018	1.081	1.118	1.208	

Summary of results:

Lumbar Spine (LS): Mean BMD ranges from **0.932 - 0.980** g/cm²

Total Hip (TH): Mean BMD ranges from **0.953 - 0.989** g/cm²

Femoral Neck (FN) Mean BMD ranges from **0.868 - 0.889** g/cm²

Whole Body (WB): Mean BMD ranges from **0.937 - 1.020** g/cm²

The table 4 below shows the percentage accrual of bone mass (BMD) with increasing age. Highest gain at the WB, followed by the LS TH and FN BMD increases the least, reflecting slower or earlier plateauing bone accrual.

Table 4, Percentage accrual of bone mass (BMD) with increasing age

Age Group Comparison	Lumbar Spine	Total Hip	Femoral Neck	Whole Body (% increment)
	(% increment)	(% increment)	(% increment)	
16–20 → 21–25	+2.79%	+1.57%	+1.38%	+4.70%
21–25 → 26–30	+2.30%	+2.17%	+1.02%	+3.98%
16–20 → 26–30	+5.15%	+3.78%	+2.42%	+8.86%

The table above shows % BMD increment with age and the total increment % (16-30y).

Comparison of Mean BMD (g/cm²) between Ugandan Women and US Women (NHANES 2005-2008) at the Lumbar Spine (L1-L4), Total Hip and Femoral Neck.

Table 5 shows a comparison of mean BMD (g/cm²) between Ugandan women and US women. There were no comparisons at the whole-body site between the Ugandan women and the NHANES white and black because the NHANES data were not available on BMD ranges for the whole body. From the table below, we found statistically significant differences between Ugandan women and NHANES non-Hispanic white at the lumbar spine and femoral neck since the p-values were less than 0.05. Among the 16-19-year-olds, the mean lumbar spine BMD among local Ugandan women was 0.934g/cm², compared to 1.004g/cm² in NHANES white women, representing a 7% lower value relative to the NHANES white women. Similarly, among the 20-29-year-olds, we observed a 10% lower BMD among local Ugandan women compared to NHANES white women. Similar trends were observed when we compared mean BMD between local Ugandan women and NHANES non-Hispanic Black women. However, the NHANES non-Hispanic black had higher BMD ranges than the NHANES white and the local Ugandan women's reference ranges. Additionally, significant statistical differences were seen between local Ugandan women and NHANES non-Hispanic black women at all three sites (LS, TH, and FN). There were minor differences at the femoral neck between Ugandan women and NHANES non-Hispanic white women (the current reference). The current Total hip references are applicable in our setting (Uganda) for the TH; there were no significant differences noted. The differences at the TH and LS were significant when compared with the African-American (non-Hispanic black). Ugandan women had 7.2% lower at TH and 9.3% lower at the FN. Comparison of Mean BMD (g/cm²) between Ugandan Women and US Women (NHANES 2005-2008) at the Lumbar Spine (L1-L4), Total Hip, and Femoral Neck is presented in Table 5 below.

Table 5, Comparison of Mean BMD (g/cm²) between Ugandan Women and US Women (NHANES 2005-2008) at the Lumbar Spine (L1-L4), Total Hip and Femoral Neck

Body Site	Local Ugandan			NHANES Non-Hispanic White					NHANES Non-Hispanic Black				
	N	Mean BMD	SD	n	Mean BMD	SD	Percent Diff	P-value	n	Mean BMD	SD	Percent Diff	P-value
Lumbar Spine													
16-19	257	0.934	0.095	172	1.004	0.107	-7.0	<0.001	202	1.077	0.115	-13.3	<0.001
20-29	496	0.957	0.097	236	1.064	0.106	-10.0	<0.001	127	1.118	0.131	-14.4	<0.001
Total Hip													
16-19	257	0.961	0.122	198	0.967	0.125	-0.6	0.429	206	1.035	0.128	-7.2	<0.001
20-29	497	0.962	0.113	262	0.971	0.114	-1.0	0.069	136	1.036	0.147	-7.2	<0.001
Femoral Neck													
16-19	257	0.875	0.111	198	0.896	0.122	-2.4	0.002	206	0.964	0.136	-9.3	<0.001
20-29	497	0.873	0.114	262	0.884	0.113	-1.3	0.025	136	0.962	0.151	-9.3	<0.001

SD – Standard deviation, BMD – Bone Mineral Density, Percent Diff – Percentage Difference in BMD, NHANES - National Health and Nutrition Examination Survey.

Table 6, calculated Z-scores and T-scores at the different skeletal sites by age group.

Skeletal site	Age Group (Ugandan women)	Z-score	T-score
		(age-matched) SD	(healthy US-White -Peak BMD) SD
Lumbar Spine	16–19	-0.65	-1.23
	21–29	-1.01	-1.01
Total Hip	16–19	-0.05	-0.09
	21–29	-0.08	-0.08
Femoral Neck	16–19	-0.17	-0.08
	21–29	-0.10	-0.10

Table 6 shows the calculated T- and Z- scores of the Ugandan women's BMD values. The calculations are made using the current standards (for US white women, NHANES database). According to WHO and IOF, clinically significant low bone mineral density is a Z-score <-2.0 or T-score < -2.5. Neither the Z- nor the T-scores

raise any clinical concerns for the age groups, but they highlight osteopenia (low BMD) – a preclinical stage of osteoporosis. Osteopenia is observed at the Lumbar spine; T-score of -1.01, a value within -1 to <-2.5. Every SD (-1) below normal doubles one's risk for a fragility fracture. (WHO, IOF)

DISCUSSION

The implications of Inaccurate BMD Reference Ranges Diagnostic Errors

Using a non-representative reference range (e.g., Caucasian data applied to African populations) introduces significant diagnostic inaccuracy; overdiagnosis in populations with naturally lower BMD but low fracture risk (e.g., Ugandans and Asians). Misclassification in different populations leads to inappropriate risk stratification and, in turn, either unnecessary treatment or missed intervention opportunities. Evidence-based practice dictates a customized approach for each population. These findings show that continued use of these references may negatively affect effective monitoring of bone health trends, neglect of necessary interventions in individuals truly at risk, and psychological distress from misclassification.

Misguided Treatment and Resource Allocation

The results show lower BMD for our local women, which had already been observed in prior studies. (Mirembe et al., 2016; Kiweewa et al., 2020; Heffron et al., 2022).

This means that Ugandan women are more likely to develop osteoporosis and have an increased risk of fragility fractures. We must prevent the occurrence of osteoporosis as much as we can through early screening, since Uganda is a resource-strained country with an already struggling health care system. Uganda is listed as a low-income country (World Bank data, 2023). Incorrect diagnoses based on inappropriate references can result in pharmacological overtreatment, which may carry unnecessary side effects and healthcare costs, or failure to prescribe preventive measures such as vitamin D and calcium supplementation or lifestyle modification in truly at-risk individuals. Public health resources should be directed to the prevention of osteoporosis so as not to overwhelm the health sector in the future.

Inhibited Policy and Guideline Development

In many low- and middle-income countries (LMICs) like Uganda, the absence of local reference ranges hinders the formulation of region-specific clinical guidelines, prevention strategies, policy interventions, and effective health education programs. The continued use of global standards can propagate health disparities by neglecting context-specific needs.

There is a need for Population-Specific Normative BMD Data.

The development of localized normative BMD databases is essential for validating diagnostic criteria for osteoporosis

in diverse populations and for creating tailored public health strategies for prevention and early detection, and lastly ensuring equity in clinical decision-making and access to care. Our research efforts should aim to stratify BMD reference values by age, sex, race/ethnicity, and geographical region, especially in younger populations (e.g., women <30 years) who are at or approaching peak bone mass, as noted in the summary of results table 4. Establishing these baselines is crucial for monitoring bone health over the life course and predicting the risk of future bone loss and fragility fractures. These individuals have higher cortical bone mass and thickness, resulting in enhanced bone strength (Bonjour et al., 2009). They also have a delayed onset of bone loss, with slower age-related declines in BMD compared to Caucasians. In addition, they exhibit a lower incidence of osteoporotic fractures, particularly in the hip and vertebrae, even when controlling for fall risk and body mass index (BMI) (Barrett-Connor et al., 2005).

The findings in this study reveal that while African-American individuals may have a higher BMD, Ugandan women actually have lower BMD, which suggests that there are other secondary factors beyond ethnicity/race that affect bone mineral density and peak bone mass. BMD is influenced by a complex interplay of genetic, environmental, nutritional, and hormonal factors, many of which are associated with racial and ethnic background. Data about osteoporosis in Uganda is scarce. There is an apparent discrepancy; while Ugandan women have low BMD in the findings, there is a low incidence of osteoporosis/fragility fractures in this population. The possible explanations are that Ugandan women may have better femoral bone geometry and bone quality. Individuals of African descent have thicker cortices and a favorable hip axis length, making them more resistant to fractures. (Bonjour, et al, 2007)

Another possible explanation could be the higher physical activity (weight-bearing daily routines like manual labor, farming, and walking, which improve muscle strength and stamina, hence reducing falls). Uganda has a younger age population profile and lower life expectancy (Uganda Bureau of Statistics, UBOS e0=64Y, 2024) – which means that Uganda has a low elderly population (>70-80), which masks the disease burden. Other possible explanations include: the alterations in bone metabolism, like slower bone turnover or slower bone loss, the lack of diagnostic capabilities coupled with underutilization or prohibitive costs, and the result is that there is no data collected, which could be due to a lack of clinical awareness. Medical pluralism is another possibility; Ugandans seek out traditional bone setters/healers, and the true burden is under-reported (lost statistics). Lastly, missed diagnostic opportunities and scanty data on osteoporosis may result

from fragility fractures being wrongly attributed to trauma and systematically recorded as such.

Bone-related differences among Asian and Caucasian populations

These typically present with lower BMD values, especially in the spine and femur. However, fracture risk may not correlate linearly with BMD due to differences in bone geometry and trabecular microarchitecture, suggesting that bone quality also plays a critical role (Nakamura et al., 2005). Caucasians serve as the reference standard for most global BMD thresholds and osteoporosis diagnostic criteria. The Caucasians are characterized by moderate BMD values and high fracture rates, particularly in post-menopausal women. These inter-population differences necessitate the development of localized reference standards, particularly for underrepresented groups such as young Ugandan women, whose bone health parameters remain poorly characterized in the global literature. In our study, our BMD values were statistically and clinically lower than those of the Caucasians (white US female). The findings of low BMD could be evidence of delayed or slow bone accrual, early plateauing as noted at the HIP, which could suggest predisposition to early osteoporosis. The findings also suggest evidence of geographic and ethnic disparities, not just race. The African-Americans have statistically significantly higher BMD at all skeletal sites. The comparison strongly demonstrates the need for population-specific references.

Conclusion

The established BMD ranges are 0.932 to 0.980 at LS, 0.953 to 0.989 at the TH, 0.868 to 0.889 at the FN, and 0.937 to 1.020 for the whole body. The mean BMD was lower than the standard references in use. At the LS, the mean BMD of Ugandan women was lower (up to 7-10% difference) when compared to the white women of the same age groups, and up to 13-14% difference lower than the established reference for the US black (African-American) population. The percentage differences are less pronounced at the FN and TH. At the FN, the mean BMD of Ugandan women was lower (up to 1.3 to 2.4% difference) when compared to the white women of the same age groups, and up to 9.3% difference lower than the established reference for the US black (African-American) population. Race and ethnicity are important considerations in BMD and Osteoporosis evaluation. These disparities in BMD have grave implications that affect the diagnosis and management of osteoporosis.

The BMD for our local Ugandan women was found to be within normal ranges according to WHO standards; however, they were significantly lower than the internationally used BMD references. Modern clinical practice prescribes evidence-based practice and a refined

approach –for each patient, a customized treatment plan. Population-specific BMD values would be more appropriate.

This study underscores the urgent need for the establishment of local, population-specific BMD reference ranges tailored to Ugandan young adult women. By generating normative data that accurately reflect this demographic, clinicians will be better equipped to interpret BMD results within the correct epidemiological and physiological context. This will not only improve the precision of osteoporosis diagnosis but also enhance preventive strategies, enable early intervention, and ultimately reduce the burden of fragility fractures and associated morbidity in later life.

Limitations of the study

It was a cross-sectional study; this study does not evaluate causal relationships between race/ethnicity and BMD.

The lack of assessment of PTH, 25-hydroxyvitamin D, bone-turnover biomarkers, or cytokine levels precluded us from drawing more detailed conclusions about the underlying mechanisms of the observed associations. The factors affecting bone metabolism can be explored further in future analyses. The study comprised only records of women from the central region of Uganda, which may limit the generalizability of our findings. The distribution of the sample size and the accessible population justifies a larger population-based study that should be designed to reduce bias.

Recommendations

The Ministry of Health, in collaboration with relevant professional bodies, should spearhead the development of context-specific clinical guidelines for the assessment, interpretation, and management of low BMD and osteoporosis in Uganda. These guidelines should clearly define age-appropriate screening protocols, including recommendations for early detection among young adults at risk of low bone mass. In a resource-strained setting like Uganda, a preventive approach would reduce the risk and occurrence of osteoporosis. The goal should be to avoid increasing the burden on a health care system with limited resources. Emphasis should be placed on lifestyle interventions, including dietary calcium intake, vitamin D supplementation, and physical activity earlier throughout childhood; during the peak bone mass accrual period (before age 30). These findings suggest that population-specific normative data should be adopted for clinical use. Local health institutions and academic bodies should collaborate to establish and disseminate updated BMD reference ranges that reflect ethnic, genetic, nutritional, and lifestyle factors unique to Ugandan populations. A large multi-center research study is recommended for older Ugandan women (post-menopausal or above age 55

generation) for comparison with the current NHANES standards in use to determine if natural factors like aging affect all populations the same way, and to determine a reference database for older Ugandan women, since they had low peak bone mass (low BMD) as demonstrated in these findings. Low peak BMD may not necessarily translate into increased incidence of osteoporosis due to other factors, like differences in rates of bone loss across the different populations. A study involving older Ugandan women may address this concern to determine vulnerability and prevalence.

Abbreviations

ART:	Antiretroviral Therapy
BMD:	Bone Mineral Density
CI:	Confidence Interval
DXA:	Dual-energy X-ray Absorptiometry
FN:	Femoral Neck
HIV:	Human Immunodeficiency Virus
IOF:	International Osteoporosis Foundation
IQR:	Inter-Quartile Range
LS:	Lumbar Spine
MUJHU:	Makerere University-John Hopkins University
NHANES:	National Health and Nutrition Examination Survey
NIH:	National Institute of Health
PLHIV:	People living with human immunodeficiency virus
SD:	Standard deviation
SSA:	Sub-Saharan Africa
TDF-FTC:	Tenofovir Disoproxil Fumarate Emtricitabine
TH:	Total Hip
WB:	Whole Body
WHO:	World Health Organization

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Conflict of interest

There is no conflict of interest.

Availability of data

Data used in this study is available upon request from the corresponding author

Author's contribution

AK designed the study, conducted data collection, MN and VN cleaned and analyzed data. AK drafted the manuscript and SB, VN & FMK supervised all stages of the study from conceptualization of the topic to manuscript writing and submission. Dr Flavia Matovu Kiweewa is a renowned researcher with special interest in bone health

Ethical approval

Ethical approval was sought from the Mengo Hospital Research and Ethics Committee (MHREC), with a waiver of informed consent requested from MUJHU due to the use of de-identified secondary data. All data was anonymized to ensure confidentiality and strict data protection measures were implemented to prevent unauthorized access. Identifiers such as the participant's name were not used in this analysis. The study adhered to ethical guidelines for research involving human subjects, ensuring compliance with data privacy regulations and maintaining participant confidentiality throughout the analysis.

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