A descriptive study of biochemical parameters and bone mineral density at Helen Joseph Hospital.

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Declaration

I Sulaymaan Kajee declare that this Research Report is my own, unaided work. It is being submitted for the Degree of Master of Internal Medicine at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

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(Signature of candidate)

19th day of July 2024 in Johannesburg

Presentations and Publications arising from this research project

There were no presentations or publications arising from this research project.

Abstract

Purpose:

This study aimed to analyze the correlation between biochemical parameters and bone mineral density (BMD), as diagnosed on a dual-energy X-ray absorptiometry (DXA) scan, within a South African setting.

Methods:

The study is a retrospective clinical audit of patients who underwent DXA scans and bone related biochemical testing between 1st January 2014 and 31st December 2021 at Helen Joseph Hospital, South Africa. Inclusion and exclusion criteria were established, and the entire population of patients meeting the inclusion criteria were analyzed. The data collected included demographics, parameters from DXA scans, and various biochemical investigations. Data was captured electronically and analyzed using basic descriptive statistics.

Results:

The results showed no significant relationship between 25 hydroxyvitamin D (25(0H)D) levels (p=0.83), serum calcium (p=0.275), serum magnesium (p=0.22), serum phosphate (p=0.816) and BMD. However, an elevated parathyroid hormone (PTH) level showed a negative correlation with BMD (p=0.044), consistent with previous findings. The study also showed a gender disparity in osteoporosis screening (95.6% female) and an age-related increase in osteoporosis (87.6% of osteoporosis cases occurred in those over 60. Underweight female patients had an increased incidence of osteoporosis ($p < 0.05$), whereas we failed to show a significant correlation between BMI and BMD in males. The study's limitations, including a limited number of blood results and non-random patient selection, which could have affected the generalizability of our findings.

Conclusion:

The study explored the relationship between BMD, biochemical parameters, and demographic factors. Notably, an elevated PTH showed a significant negative correlation with BMD.

Underweight female patients had a higher osteoporosis incidence than those with normal BMI, and aging increased osteoporosis risk. Early detection, considering diverse risk factors, and comprehensive patient evaluations are crucial in the diagnosis of osteoporosis.

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Abbreviations and Symbols

BMC	Bone Mineral Content
BMD	Bone Mineral Density
BMI	Body Mass Index
DXA	Dual Energy X-ray Absorptiometry
PTH	Parathyroid Hormone
25-hydroxyvitamin D	25(OH)D
WHO	World Health Organization

1. Introduction

1.1 Osteoporosis and Osteopenia

1.1.2 Definition, classification, and diagnosis

Osteoporosis is a systemic skeletal disorder, resulting in increased fracture risk due to low bone mass and deteriorated bone tissue structure.[1] The World Health Organization (WHO) defines osteoporosis based on bone mineral content (BMC) / bone mineral density (BMD) and the occurrence of fragility fractures.[1,3,4] (Table 1.1)

Table 1.1: WHO Diagnostic Criteria for Bone Mineral Density and Bone Mineral Content: T-Score Comparison with Young Adult Reference Mean

Diagnostic criteria	**T-Score comparison with young adult reference mean**
Normal	T-score ≥ -1
Osteopenia	T-score between –1. and –2.5
Osteoporosis	T-score ≤ 2.5
Severe Osteoporosis	T-score ≤ 2.5 with fragility fracture

The diagnosis of Osteoporosis in postmenopausal women and men older than 50 is made using the WHO diagnostic criteria using the T-score comparison with young adult reference mean.[1]
Whereas in premenopausal women and men under the age 50, the recommendation is to use the Z-score (age, gender and race corrected values). A Z-score of less than –2 is regarded as abnormal and referred to as low BMD for age.[1]

Osteoporosis often remains asymptomatic until a fracture eventuates.[2,3] The National Osteoporosis Foundation of South Africa (NOFSA) advises BMD screening by Dual Energy X-Ray Absorptiometry (DXA) for men aged ≥70, women aged ≥65, those at risk for secondary osteoporosis, evident vertebral fractures or osteopenia, significant clinical risk factors, or fragility fractures post age 40. [1,2,3]

A clinical osteoporosis diagnosis is possible with a fragility fracture, especially in specific bone areas such as a hip or vertebral fracture in the absence of major trauma.[3,5] Postmenopausal women at high fracture risk may also be clinically diagnosed with osteoporosis. This includes those with a FRAX 10-year fracture probability ≥20% or a hip fracture probability ≥3%. [5] The FRAX score considers factors such as age, sex, BMD, and clinical risk factors to estimate the 10-year probability of major osteoporotic fractures.[1]

1.2 Biochemical markers to assess bone health

In the context of exploring the relationship between various serum markers and bone mineral density (BMD), the literature offers a multitude of insights:

In a cross-sectional study by Liu et al. involving 4595 participants aged ≥50, a gender-based variation was found in the association of serum calcium and 25-hydroxyvitamin D (25(0H)D) with lumbar BMD. Older females exhibited a negative correlation between serum calcium and lumbar BMD, whereas older males showed a U-shaped relationship. 25(0H)D consistently correlated positively with lumbar BMD in the elderly.[6] However, the connection between serum 25(0H)D and BMD remains a topic of debate. An American study assessing 2748 adults did not find a significant association between the two.[7] Conversely, research conducted on Saudi men identified a positive correlation.[8]

The trace element magnesium plays a pivotal role in bone matrix synthesis. Its deficiency, (hypomagnesaemia), impacts BMD in multiple ways: directly, by altering bone cells, and indirectly, by influencing the homeostasis of Parathyroid Hormone (PTH) and 25(0H)D.[9,10] Several studies have identified a link between dietary Mg restriction and osteoporosis.[11] Furthermore, research from 2018 found that postmenopausal osteoporotic women exhibited significantly reduced serum magnesium levels compared to their healthy counterparts.[9] These observations are substantiated by meta-analyses.[12]

Phosphate is an essential component of bone homeostasis and is primarily stored in bones as hydroxyapatite crystals, which are crucial for mineralization.[13] Despite extensive research, the

literature is yet to conclusively determine the relationship between BMD and serum phosphate.[14] A study by Billington et al. discerned a negative correlation between serum phosphate and BMD in female subjects. Interestingly, this association persisted, albeit attenuated, even after adjusting for confounders.[15] In contrast, another research work by Yang et al. documented varied associations, contingent on gender and bone location.[14]

PTH is pivotal for maintaining the equilibrium of calcium and phosphate in the blood. Beyond this, it plays a significant role in bone metabolism by promoting bone resorption, leading to potential decreases in BMD.[16] The literature consistently points towards an inverse relationship between PTH levels and BMD. This inverse association is particularly pronounced in patients diagnosed with osteoporosis.[16,17,18] For instance, research by Qu et al. illustrated that elevated PTH levels were linked to reduced BMD levels at crucial sites such as the hip and spine.[16] This finding is echoed by Kota et al.'s study, further emphasizing the intricate relationship between PTH and BMD.[17]

The literature highlights a complex relationship between different serum markers and BMD, consistently showing associations like PTH with BMD, while the link between serum 25(0H)D and BMD remains a subject of debate.

1.3 Age and Gender in Relation to BMD

BMD is known to be influenced by various factors, amongst which age and gender are considered paramount. In a comprehensive study by Alswat, the disparities in osteoporosis between genders were elucidated.[22] Notably, the report emphasized that women, particularly postmenopausal, are more predisposed to osteoporosis compared to their male counterparts. This vulnerability in women is often attributed to the decline in estrogen levels after menopause, which plays a vital role in maintaining bone strength.

Aging is a significant determinant of BMD reduction. Khosla and Riggs delved into the pathophysiology of age-related bone loss, noting that as individuals age, there's a concomitant

decline in BMD, predisposing older adults to osteoporosis.[23] This observation is consistent with findings by Riggs and Melton, who highlighted osteoporosis as a global concern, particularly among the aging population.[24] Their work underscored the epidemiological insights that affirm age as a significant risk factor for reduced BMD.

Age and gender don't operate in isolation when it comes to influencing BMD. A study by Ngugyen et al. examined risk factors for osteoporotic fractures in elderly men, suggesting that while age universally impacts BMD, gender nuances particularly concerning risk factors and fracture rates, must be considered for a comprehensive understanding.[25]

While aging universally affects BMD, gender disparities, particularly the heightened vulnerability of post-menopausal women to osteoporosis, are crucial for tailoring preventive and therapeutic strategies. Future research must continue to delve into the interplay between these factors and other potential determinants to holistically address the challenges posed by osteoporosis.

1.4 BMI and its Association with BMD

Body mass index (BMI) is another pivotal factor that influences BMD. Given the increasing prevalence of obesity worldwide, understanding the relationship between BMI and BMD becomes ever more pertinent.

Turcotte et al. conducted a systematic review and meta-analysis examining the link between obesity and bone health parameters in adults.[26] Their findings suggested that individuals with obesity generally have a higher BMD compared to those without. Interestingly, the study also indicated a potential protective effect of obesity against fracture risks.

While an elevated BMI might confer some benefits in terms of BMD, it's essential to recognize the broader health implications of increased BMI, such as its metabolic and cardiovascular risks. BMI impacts BMD in varied ways, offering skeletal benefits at higher levels while also presenting significant health risks associated with obesity. Further research is necessary to better understand this relationship.

Low BMI is associated with an increased risk of osteoporosis. A study conducted by Lim et al. on 1767 premenopausal Korean women, found that underweight women exhibited a higher odds ratio for low BMD (OR, 3.41; 95% CI, 2.31–5.05) compared to women with a normal BMI.[29] Another study conducted by Coin et al on 111 elderly subjects also demonstrated that low BMI was associated with an increased risk of osteoporosis.[30] In our study we planned to also analyze the risk of osteoporosis in underweight patients in a South African context.

Our study aimed to clarify the relationship between biochemical markers and BMD, and the impact of BMI and gender on BMD, due to limited research in these areas.

2. Materials and Methods

2.1 Study objectives

2.1.1 Primary objective

A retrospective descriptive study of bone related biochemical parameters and BMD in patients who underwent DXA scans at Helen Joseph Hospital from 1 Jan 2014 to 31 Dec 2021.

2.1.2 Secondary objective

To describe the demographics (age, gender and BMI) of patients that had DXA scans at HJH.

2.2 Study design and setting

A retrospective clinical audit was conducted on patients that had DXA scans done between 1st January 2014 and 31st December 2021 at Helen Joseph Hospital. The study aimed to analyze DXA scan reports obtained from the hospital's Radiology department as well as biochemical data from the National Health Laboratory Services (NHLS). Inclusion criteria included patients who underwent DXA scans during the specified time period and had biochemical testing within a year of their scans. Exclusion criteria consisted of patients without biochemical results within a year of their scans and those lacking complete DXA scan reports. The study was conducted at Helen Joseph Hospital, and the entire population meeting the inclusion criteria were analyzed. The study was approved by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand (HREC ref R14/49 for protocol M220612).

2.3 Data collection

The data collected included demographics (age, gender, BMI) and parameters from DXA scan reports (BMD, T-score, Z-score) as well as various biochemical parameters (calcium, Mg, phosphate, albumin, PTH, and 25(0H)D. Data sheets were assigned study numbers only, without recording patient names or hospital numbers, ensuring data confidentiality. The standardized DXA scan reports were obtained from the same hospital department (Helen Joseph Hospital Department of Radiology), and the blood results were performed by the same laboratory (NHLS). A single researcher collected the data from patient records, ensuring standardization and reliability.

However, limitations included the potential lack of representativeness of the audited sample, the possibility of significant missing data due to the retrospective nature of the study, and the increased risk of statistical error with a small cohort. Non-parametric testing was used to address sampling bias.

2.4 Statistical analyses

Data was captured electronically on a Microsoft Excel spreadsheet for the purpose of data analysis. Basic data analysis was performed using Microsoft Excel, which involved presenting descriptive statistics for continuous variables as mean ± standard deviation (SD) or median and interquartile ranges (IQR) for normal or skewed data, respectively. Categorical data were reported using proportions, and comparisons between groups were made using the $\chi 2$ test for categorical variables. For continuous variables, Student's unpaired t-test was used if the data were normally distributed, while the Mann-Whitney U test was used for skewed data.

3. Results and discussion

A database with 2853 patients was retrieved for analysis. Of those patients, a total of 2267 had complete BMD profiles and we retrieved blood results on 690 patients. (Figure 3.1).

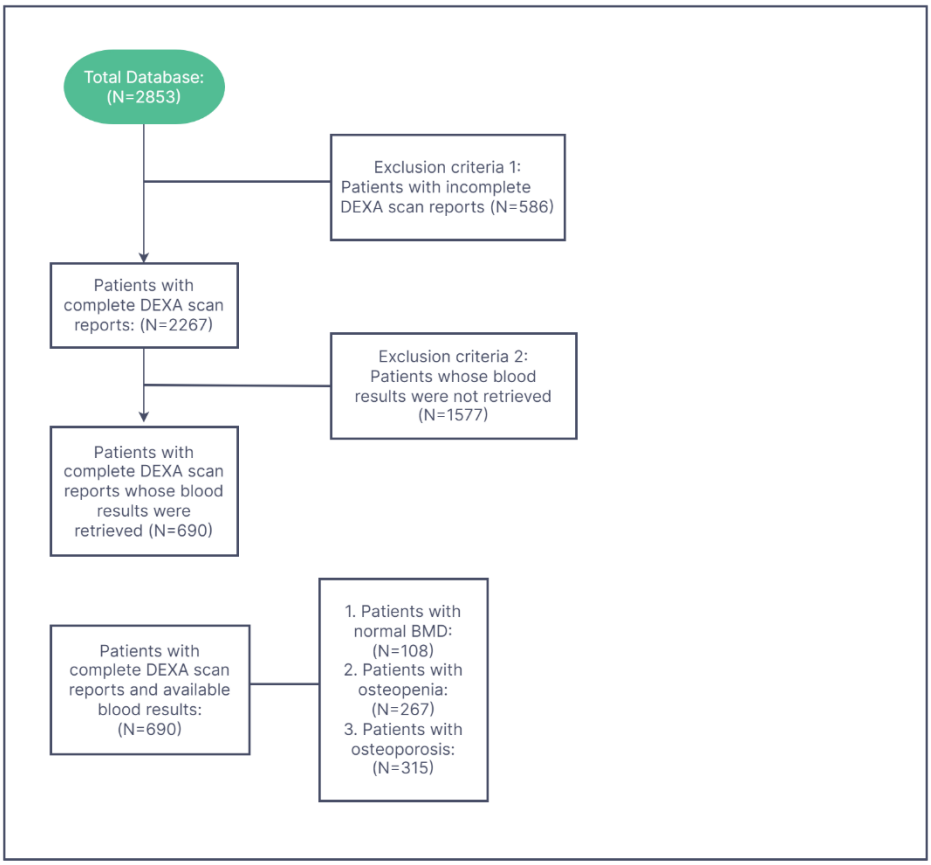

Figure 1: Flow chart of included subjects

Figure 3.1: Flow chart of included subjects

3.1 Results of BMD and demographics

Amongst the completed datasets of 2267 patients, the association between BMD and demographics is summarized below:

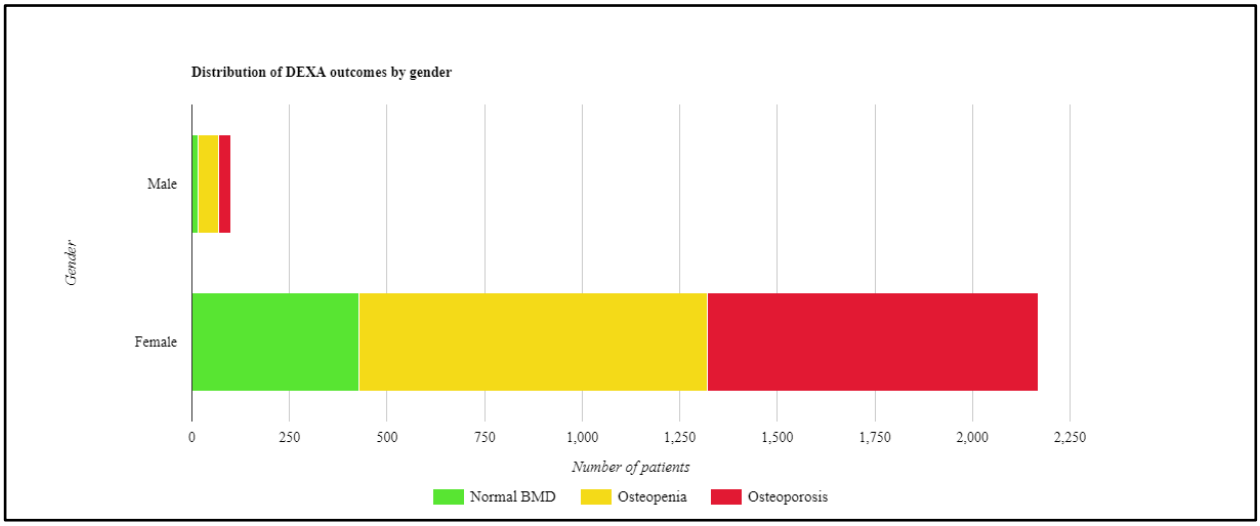

Figure 3.2: Distribution of DXA outcomes by gender

Of the 2267 patients who underwent DXA scans, 2168 (95.6%) were female and 99 (4.4%) were male (p-value 0.078) (figure 3.2). Among the females, 429 had a normal BMD, 892 were osteopenic, and 847 were osteoporotic. Among the males, 15 had a normal BMD, 52 were osteopenic, and 32 were osteoporotic.

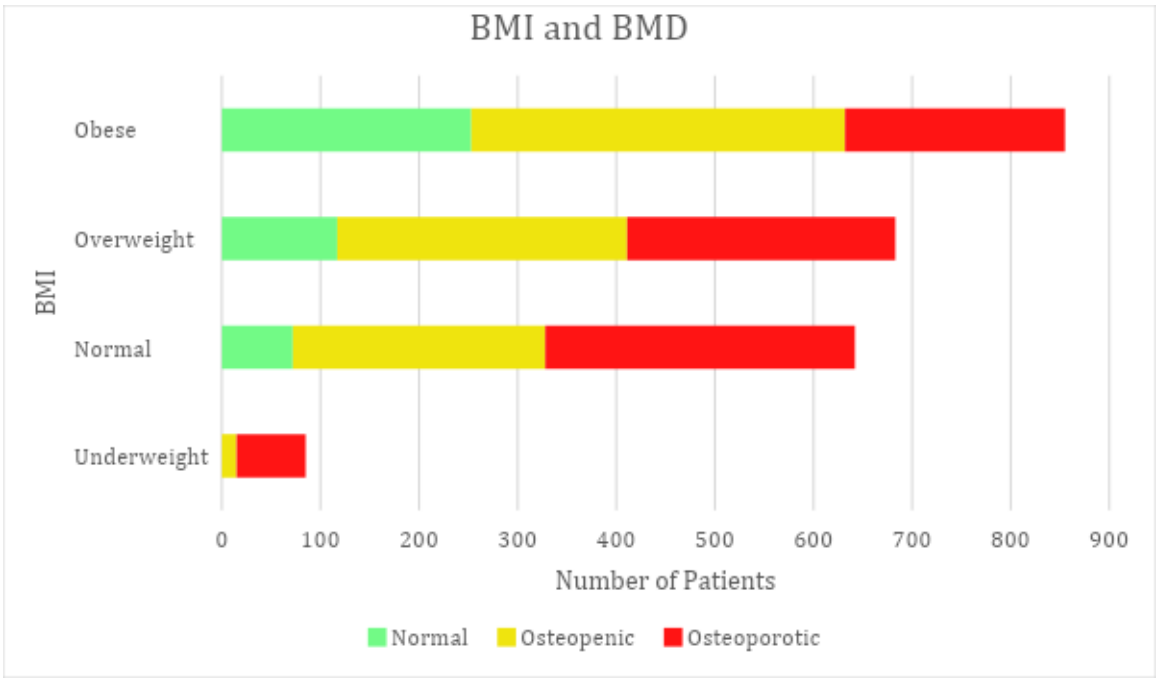

Figure 3.3: BMI and BMD

The relationship between BMI and BMD was examined in 2267 patients (Figure 3.3). The breakdown was as follows: 642 with normal BMI, 85 underweight, 683 overweight, and 855 obese.

Of those with normal BMI, 11.2% had regular BMD, 39.9% had osteopenia, and 48.9% had osteoporosis. Of those who were underweight 82% were osteoporotic and 18% were osteopenic. Among the overweight, 17.1% had normal BMD, 43% had osteopenia, and 39.8% had osteoporosis. For the obese group, 29.6% had normal BMD, 44.3% had osteopenia, and 26.1% had osteoporosis.

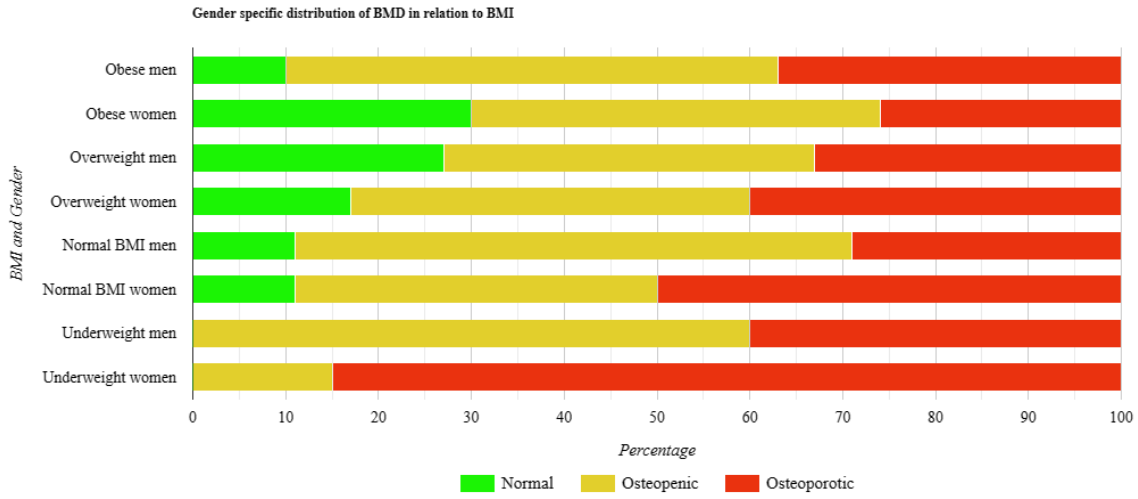

Figure 3.4: Gender specific distribution of BMD

The BMI in relation to BMD was further stratified based on gender (Figure 3.4). The findings were as follows: In the obese male patients 11% had a normal BMD, 52% were osteopenic and 37% were osteoporotic, whereas in the female patients with obesity 30% had a normal BMD, 44% were osteopenic and 26% were osteoporotic. In the overweight male patients 27% had a normal BMD, 40% were osteopenic and 33% were osteoporotic, whereas in the overweight female patients 17% had a normal BMD, 43% were osteopenic and 40% were osteoporotic. In the male patients with a normal BMI 11% had a normal BMD, 60% were osteopenic and 29% were osteoporotic, whereas in the female patients with normal BMI 11% had a normal BMD, 39% were osteopenic and 50% were osteoporotic. In the underweight male patients, none had a normal BMD, 60% were osteopenic and 40% were osteoporotic, whereas in the underweight female patients none of the patients had a normal BMD, 15% were osteopenic and 85% were osteoporotic.

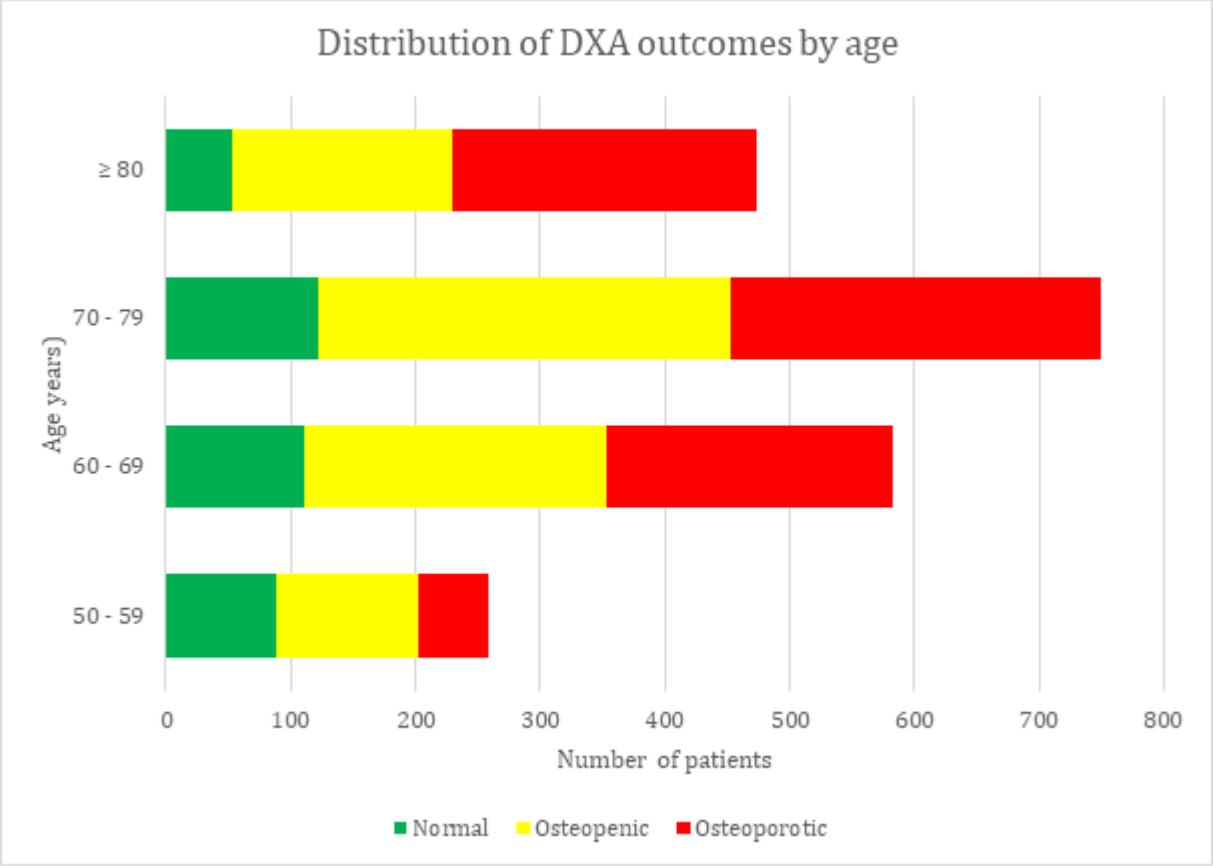

Figure 3.5: Distribution of DXA outcomes by age in patients aged 50 and older

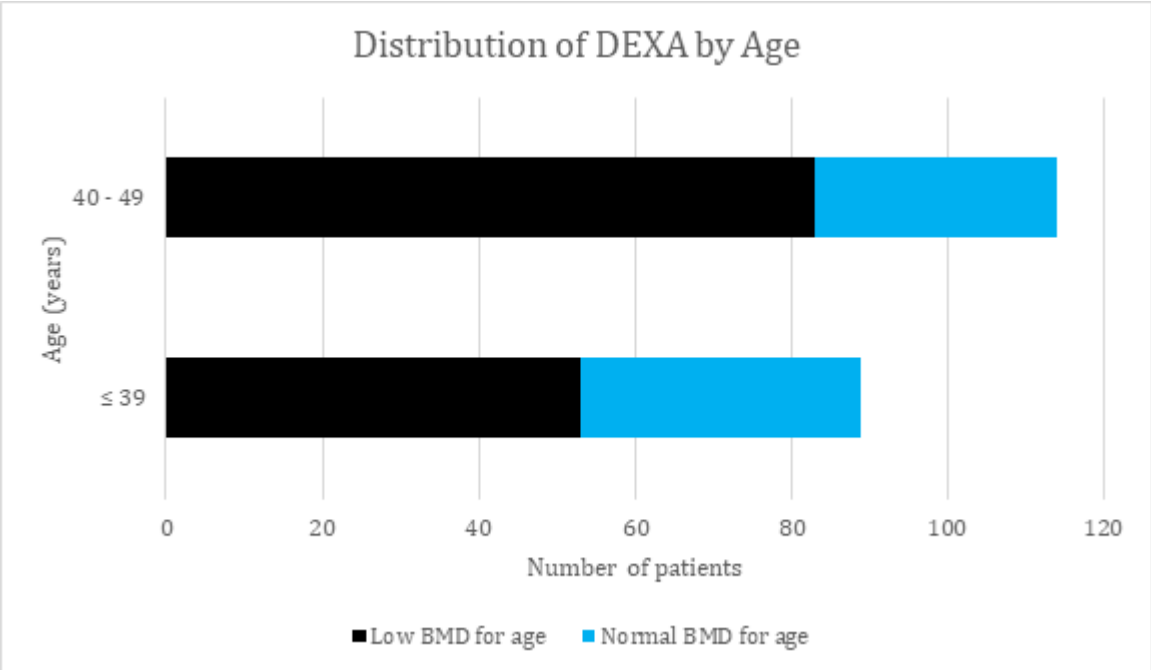

Figure 3.6: Distribution of DXA outcomes by age in patients younger than 50

The study investigated the relationship between age and BMD. (Figure 3.5) In the 50-59 age group, there were 89 with a normal BMD, 114 with osteopenia, and 55 with osteoporosis. Among those aged 60-69, the numbers were 111 with a normal BMD, 242 with osteopenia, and 229 with osteoporosis. Participants aged 70-79 had 122 with a normal BMD, 330 with osteopenia, and 298 with osteoporosis. Finally, in those aged 80 and above, 53 had a normal BMD, 177 osteopenia, and 244 osteoporosis.

In patients younger than 50, Z-scores were used, and patients were either described as low BMD for age vs normal. (Figure 3.6) In patients aged 39 and younger, 53 had low BMD for age and 36 had a normal BMD for age. In the patients aged 40 to 49, 83 had low BMD for age and 41 had normal BMD for age.

3.2 BMD and biochemical results

Amongst the 690 patients with completed DXA scan reports as well as retrieved biochemical parameters, the association between BMD and biochemical parameters is summarized below (Table 3.1):

Table 3.1: Bone mineral density and blood results

		Diagnosis				P-value
		Normal	Osteopenic	Osteoporotic	Total	
Corrected calcium	Have both Calcium and 25(0H)D tested	14	43	65	122	0.275
	Normal (2.15 - 2.55 mmol/L)	70	197	237	504	
	Low (<2.15 mmol/L)	9	21	24	54	
	High (>2.55 mmol/L)	21	30	41	92	
Magnesium	n=	92	211	275	578	
	Normal (0.63 - 1.05 mmol/L)	82	182	224	488	0.140
	Low (<0.63 mmol/L)	8	19	37	64	0.220
	High (>1.05 mmol/L)	2	10	14	26	0.494
Phosphate	n=	100	247	304	651	0.816
	Normal (0.78 - 1.42 mmol/L)	80	205	246	531	
	Low (<0.78 mmol/L)	8	12	21	41	
	High (>1.42 mmol/L)	12	30	37	79	
25(0H)D	n=	16	49	71	136	0.838
	Normal (≥ 50 nmol/L)	14	41	62	117	
	25(0H)D deficiency (<50 nmol/L)	2	8	9	19	
PTH	n=	10	33	53	96	0.044
	Normal (1.5 - 7.6 pmol/L)	6	23	29	58	
	Low (<1.5 pmol/L)	2	1	1	4	
	High (>7.6 pmol/L)	2	9	23	34	

Our study assessed various blood results alongside DXA scan reports in 690 patients. Specifically, data was gathered on 25(0H)D (136 patients), corrected calcium (650 patients), magnesium (578 patients), phosphate (651 patients), and PTH (96 patients). 25(0H)D and calcium were both tested in 122 patients (17.7% of our cohort), as part of their work-up.

In the study examining 25(0H)D levels across different BMD groups, it was observed that in the normal BMD group consisting of 16 patients, 87.5% had normal 25(0H)D levels while 12.5% had low levels. Among the osteopenic group of 49 patients, 84% had normal levels and 16% were low. Similarly, in the osteoporotic group, which included 71 patients, 87% had normal 25(0H)D levels and 13% had low levels, with the differences across the groups yielding a p-value of 0.83.

Corrected Calcium levels showed differences among BMD groups. In the normal BMD group with 100 patients, 70% had normal levels, 9% low levels, and 21% high levels of corrected calcium. For the osteopenic group of 248 patients, 79.4% had normal levels, 8.5% low, and 12.1% high levels of corrected calcium. In the osteoporotic group comprising 302 patients, the distribution was 78.5% normal, 7.9% low, and 13.6% high levels of corrected calcium, with a p-value of 0.275.

Magnesium did not show a statistically significant correlation with BMD (p=0.49). Magnesium levels varied across different BMD groups, with 89.1% of the normal BMD group (92 patients) having normal levels, 8.7% low, and 2.2% high levels of magnesium. Among the osteopenic group (211 patients), 86.3% had normal levels, 9% were low, and 4.7% high levels of magnesium. In the osteoporotic group (275 patients), 81.5% had normal magnesium levels, 13.5% low, and 5.1% high levels of magnesium.

Phosphate levels showed that in the normal BMD group (100 patients), 80% had normal levels, with 8% low and 12% high levels of phosphate. For the osteopenic group (247 patients), the distribution was 83% normal, 4.9% low, and 12.1% high levels of phosphate. In the osteoporotic group (304 patients), 80.9% had normal levels, 6.9% were low, and 12.2% high levels of phosphate, with a p-value of 0.816, indicating no significant difference across the groups.

PTH showed a significant negative correlation with BMD (p=0.044). Among patients with normal BMD (10 patients), PTH levels were normal in 60%, low in 20%, and high in 20%. In the osteopenic group (33 patients), the corresponding figures were 69.7% normal, 3% low, and 27.3% high levels of PTH. For the osteoporotic group (53 patients), 54.7% had normal PTH levels, 1.9% low, and 35.4% high levels of PTH. Additionally in the cohort of patients with high PTH (33 patients), 55% had a normal calcium level, 3% had an abnormally low calcium level and 42% had an abnormally high calcium level.

4. Discussion

The main aim of our study was to investigate the relationship between biochemical parameters and BMD in patients who underwent DXA scans. In addition, we also looked at demographics and BMD.

4.1 Biochemical parameters and BMD

4.1.1 25-Hydroxyvitamin D

We found no significant correlation between 25(0H)D and BMD (P-value 0.838), consistent with prior research.[7] Despite the NOFSA guidelines recommending 25(0H)D testing in specific patient groups, only 17% of our patients with DXA scans and blood results were assessed for both serum calcium and 25(0H)D.[19] Although our sample size was limited (136 patients), our study emphasizes the importance of guideline adherence in 25(0H)D testing for bone diseases.
To fully comprehend the connection between 25(0H)D and BMD in our population, further in-depth research is necessary. It's noteworthy that most patients in the study had sufficient 25(0H)D levels, although it remains uncertain whether this is due to supplementation or natural de novo production.

4.1.2 Corrected Calcium

We found no significant relationship between serum corrected calcium and BMD (P-value 0.275). While Leu et al. observed a negative correlation between serum calcium and BMD,[6] another study on postmenopausal women by Bahtiri et al. reported no significant association.[20] The lack of significant findings in our study may be due potential limitations including a small patient cohort with available calcium results and inability to account for calcium supplementation. The majority of patients across all BMD groups had normal corrected calcium levels. Thus, in our study cohort, serum corrected calcium may not be a primary predictor of osteoporosis, with other factors like age, genetics, and lifestyle playing more substantial roles.

4.1.3 Phosphate and Magnesium

Our findings showed no significant correlation, which might be attributed to the limited patient data, on serum magnesium (P=0.22) and phosphate(P=0.816) with BMD. Previous research also did not find a significant correlation between linear serum phosphate levels and BMD,[14] but a study on type 2 diabetic women noted a non-linear relationship between phosphate and BMD at specific thresholds.[14]

Concerning serum magnesium, while our results showed no significant relationship with BMD, existing studies have presented conflicting findings. A study on premenopausal women in South Korea associated higher serum magnesium levels with lower spinal BMD,[21] whereas another found lower magnesium levels in postmenopausal women with osteoporosis.[9] Magnesium's role in bone metabolism is debated, with suggestions of its involvement in calcium homeostasis, 25(0H)D activation, and osteoblast/osteoclast modulation.[10]

Our study did not establish a significant association between magnesium and phosphate serum levels with BMD, aligning with certain previous studies while contradicting others. The precise impact of magnesium and phosphate on bone health is still uncertain, highlighting the need for additional research in this area.

4.1.4 PTH

Our study showed a significant negative correlation between an elevated PTH and BMD (p=0.044), corroborating prior research emphasizing PTH's pivotal role in bone metabolism and its influence on BMD. PTH, which regulates calcium and phosphate in the blood and prompts bone resorption, is linked to reduced BMD.[16] Several studies have identified an inverse relationship between an elevated PTH levels and BMD, especially in osteoporosis patients.[16, 17, 18]

Our findings reiterate this negative association in our patient cohort. This underscores the significance of PTH levels in bone health assessment and its potential as an osteoporosis risk biomarker. Further studies are essential to clarify the PTH-BMD relationship dynamics and to explore PTH's clinical potential in osteoporosis detection and prevention.

4.1.5 Calcium, PTH and 25(0H)D

The relationship between calcium, 25(0H)D and PTH has been well described. In health, hypocalcemia stimulates the release of PTH and PTH works to increase the serum calcium levels back to normal by increasing bone resorption, converting 25(0H)D to 1.25 dihydroxy vitamin D which increases intestinal absorption of calcium and by decreasing calcium excretion in the urine .[31] PTH secretion is regulated/reduced by an increase in serum calcium as well as an increase in 1.25 dihydroxy vitamin D.[31]

In our cohort of 33 patients with elevated PTH, we could not reliably assess the correlation between primary, secondary and tertiary hyperparathyroidism with BMD due to the small cohort as well as the lack of additional information such as patient medications as well as co-morbidities etc. It would also be useful to conduct study at Helen Joseph Hospital to explore the relationship between BMD and primary vs secondary vs tertiary causes of an elevated PTH.

4.2 Demographics and BMD

4.2.1 Age and Gender

Our study indicates a notable gender disparity in osteopenia and osteoporosis screening via DXA scan, with females comprising 95.6% of the screened patients.[22] This aligns with earlier research linking higher osteoporosis rates in women to estrogen reduction during menopause, resulting in rapid bone loss.[22] The majority of males in the study were either osteopenic (53%) or osteoporotic (32%), this finding is most likely due to a screening bias where males who were at the highest risk for being diagnosed with osteoporosis were screened.

Age was also significantly related to BMD. When analyzing age and BMD we separated those patients younger than 50 from those aged 50 or older and analyzed them using Z-scores. We found that most of our patients were above the age of 50 (2064 patients) in comparison to those younger than 50 (203 patients).

In patients above the age of 50, osteopenia and osteoporosis prevalence increased with increasing age: 21% of patients screened between the ages of 50-59 had osteoporosis whereas 51% of patients screened above the age of 80 had osteoporosis. This concurs with prior findings showing bone density decreases with age, especially in postmenopausal women.[23, 24, 25]

In patients younger than 50 we found that 63% of screened patients had low BMD for age. This result is most likely due to screening bias where patients younger than 50 that were sent for DXA scans were those at highest probability of being diagnosed with low BMD for age.

However, potential selection bias in our study, stemming from primarily analyzing patients with DXA scans and overlooking other osteoporosis risk factors, suggests our findings may not universally apply.[25] The findings highlight the need for early osteoporosis detection, especially in postmenopausal women and seniors, and stress the importance of further research into other risk factors for osteoporosis.

4.2.2 BMI and BMD

Our study, involving 2267 patients, assessed the correlation between BMI and BMD. Participants were categorized as normal BMI, overweight, or obese. We found that obesity was linked to a reduced incidence of osteoporosis: 26.1% of obese patients had osteoporosis, contrasted with 48.9% of the normal BMI group and 39.8% of the overweight group ($p < 0.05$).

However, on further stratifying the data according to gender, our study did not find a statistically significant correlation between BMI and BMD in males; whereas in females we did find a statistically significant correlation between BMD and BMI ($P<0.05$). Underweight female patients were noted to have a higher incidence of osteoporosis compared to other BMI categories and obese female patients were noted to have a higher incidence of osteopenia rather than osteoporosis. ($P<0.05$).

A 2021 systematic review and meta-analysis, reported higher BMDs in obese individuals and a decreased hip fracture risk in both males and female obese patients, suggesting a potential protective effect of higher BMI on bone health.[26] Our Study failed to show a significant correlation between BMD and BMI in males and this could be due to the limited number of males in our study as well the study not further stratifying based on fat mass and lean mass. A twin study conducted by Makovey et al. that showed that lean mass had a stronger relationship with bone measures compared to fat mass.[28] Potential reasons for the increased BMD in obesity include the conversion of adrenal androgens to estrogen in adipose tissue and the mechanical load exerted by adipose tissue.[27] The exact relationship dynamics between obesity and bone health remain to be fully delineated.

Our study confirmed a significant association between underweight patients and osteoporosis, consistent with prior research.[23,30] Among the 85 underweight subjects in our study, none exhibited normal BMD. Specifically, 82% were classified as osteoporotic, while 18% fell into the osteopenic range. Notably, gender stratification revealed an even more pronounced effect: 85% of underweight females were osteoporotic, with 15% classified as osteopenic. These findings likely stem from reduced adipose tissue in underweight individuals, leading to decreased estrogen levels (which play a protective role in bone health) and the gravitational impact of body weight on bone.[29,30]

5. Limitations

Our research faced several limitations. Incomplete biochemical datasets resulted in a small sample size for specific parameters, potentially affecting the generalizability of our findings. Additionally, the absence of indications as well as information regarding ethnicity of patients undergoing DXA scans limited our ability to contextualize BMD results. Furthermore, due to restricted access to patient co-morbidities and medication details, we couldn't analyze BMD in relation to primary, secondary, or tertiary hyperparathyroidism. Lastly, while Z-scores were used for patients under 50 years of age when comparing age and BMD, T-scores were employed when analyzing the overall population in relation to biochemical parameters, BMI and gender.

7. Conclusion

This study investigated various factors impacting BMD, including 25(0H)D, corrected calcium, magnesium, phosphate, and PTH, along with gender, age, and BMI. It reveals complex relationships, such as a significant negative correlation between PTH and BMD. The study also noted a significant increase in the incidence of osteoporosis in underweight female patients compared to female patients with a normal BMI as well as an increased incidence of osteoporosis with aging. These findings emphasize the need for early detection of osteoporosis, considering a broad range of risk factors, and the importance of comprehensive biochemical datasets in patient evaluations. Further research is crucial to enhance our understanding of bone health.

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8. Appendices

8.1 Plagiarism form

DEPARTMENT OF INTERNAL MEDICINE

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Plagiarism declaration for written work

I Sulaymaan Kajee as a postgraduate student registered for a MMed at the University of the Witwatersrand declare the following:

- I am aware that plagiarism is the use of someone else's work without their permission and or without acknowledging the original source.
- I am aware plagiarism is wrong.
- I confirm that this written work is my own work except where I have stated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or if I have failed to acknowledge the ideas or writing of others.

Signature .....

Date 9.08.22

Edit with WPS Office

8.2 Ethics clearance certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R49 Dr S Kajee

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M220612

NAME: (Principal Investigator)	Dr S Kajee
DEPARTMENT:	School of Clinical Medicine Department of Medicine Division of Internal Medicine - Endocrinology and Metabolism Medical School, University
PROJECT TITLE:	*An evaluation of bone-related biochemical parameters in relation to bone mineral density at Helen Joseph Hospital*
DATE CONSIDERED:	2022/06/24
DECISION:	Approved unconditionally
CONDITIONS:	
NOTE:	If contact information regarding student study participants is required, please contact the Registrar's office - <Nicoleen.Potgieter@wits.ac.za>
SUPERVISOR:	Drs R Daya and Z Bayat
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	2022/09/21

This Clearance Certificate is valid for 5 years from the date of approval. An extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office secretariat on the 3rd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to submit details to the Committee. **I agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **June** and therefore reports and re-certification will be due in the month of **June** each year. Unreported changes to the study may invalidate the clearance given by the HREC (Medical).

Signature of Principal Investigator

1/10/2022

Date

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