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Disparity in bone mineral density of males and females with age

Nusrat Aziz *

Department of Physiology, Faculty of Medicine, Umm Al-Qura University, Makkah 24382, Kingdom of Saudi Arabia.

Abstract

Decline in bone mass with aging leads to osteoporosis and fragility fractures. It has profound effect on the morbidity and health quality of the elderly, creating financial burden on the society.

Usually, age related loss in bone mass goes undiagnosed until a fragility fracture occurs. It was observed that the bone mineral density (BMD) was found to be lesser in females compared to males in all age groups.

There were significant BMD differences between males and females from age 41 yrs and above, BMD declined with age in both males and females. The maximum decline was observed in age group of 41 yrs -50 yrs compared to the control group of 20 yrs-30 yrs.

The decrease in BMD was highly noticeable in females, with osteoporosis from age group 51 yrs-60 yrs. It coincides with peri-menopausal and early after menopause period. In males osteoporosis was not observed until the age of 80yrs, though osteopenia have been observed from 41 yrs onwards.

There is a paramount need of awareness about detrimental effects of aging on BMD in order to bring about necessary lifestyle changes and follow therapeutic measures. This enables us to attain higher peak bone mass and maintain higher bone densities.

Keywords: Osteoporosis; Age; Males; Females, BMD

1. Introduction

Age related bone loss largely goes unnoticed until a fracture occurs. It is one of the leading causes of morbidity. The disability adjusted life years with hip and vertebral fracture were 2496 to 3168 [1,2] with significant reduction in health related quality of life (HRQoL) [3]. The economic cost of osteoporotic fracture $20.3 billion in 2005 in United States of America with projection to $25.3 billion per year by 2025.

The major factors effecting age related bone loss are

- Gender- women have 4 times higher rate of osteoporosis and twice rate of osteopenia than men [5,6]
- Age- Bones attain peak bone mass by the age of 20 years which remains relatively stable for about 15 to 20 yrs. The bones start losing minerals by the age 35- 40 yrs of age.
- Race- Osteoporosis was found to be around 20% and osteopenia in >50% in Asians and Hispanic [7]
- Family History- People with family history of more likely to develop osteoporosis [8].
- Body frame- Individuals with smaller body frame size are more likely to develop osteoporosis.
- Nutritional status- deficiency of calcium and vitamin can increase bone loss.

* Corresponding author Dr.Nusrat Aziz
Department of Physiology, Faculty of Medicine, Umm Al-Qura University, Makkah 24382, Kingdom of Saudi Arabia.

1.1. Physiology of aging changes in bones:

About 10% of bone is remodeled every year and every 10 years the whole skeleton has been remodeled. With age shape of the bone changes according to the activity and mechanical stresses to withstand greater stresses and support the body posture and work demands following the Wolff's law[9,10]The fragility of bone increases with age due to changes in bone minerals and bone matrix. Bone matrix provides resilience to bones while the minerals make them stronger. The bone water associated with collagen decreases with age and may contribute to increased fragility [11]. With normal day to day activities the bone undergoes microfractures. The resulted loss of connectivity between osteocytes produces their apoptosis and inducing remodeling [12]. The accumulation of these effects increases with advancing age. Bone remodeling by the bone remodeling unit with bone formation by osteoblasts following a period of resorption by osteoclasts is imbalanced in elderly. The bone resorption is increased with less bone formation causing net bone loss mainly the trabecular bone. The osteoclasts number and lifespan is increased with lesser differentiation of osteoblasts [13]. Increased remodeling at periosteal and endosteal surfaces produces thinning of cortical bone. The trabecular bone loss is higher in females than in males [14, 15]. The precursor stem cells of osteoclasts and osteoblast are also reduced which may be attributed to telomere shortening and decreasing telomerase activity [16]. Thus decreased bone cells differentiation coupled with apoptosis greatly reduces the bone modeling and remodeling. The differentiation of osteoblasts from mesenchymal stem cells is stimulated by the Wnt/β catenin pathway on pairing with low density lipoprotein receptor-related protein 5 (LRP5) thereby increasing the bone mineral density [17]. LRP5 and β catenin are found to significantly reduce in postmenopausal osteoporosis [18]. Increased reactive oxygen species (ROS) with aging process causes osteoblast apoptosis and also decrease osteoblastogenesis by inhibiting β catenin [19]. . ROS increases osteoclast differentiation increasing bone remodeling with but with impaired bone formation. The ROS increase lipid peroxidation causing more expression of peroxysome proliferator-activated receptor γ (PPAR-γ) known to inhibit β catenin [20]. Proinflamatory cytokines like interleukin-1, interleukin-6 and tumor necrosis factor α are increased with ageing [21] and have been implicated in stimulation of osteoclastogenesis and bone resorption.

1.2. Hormonal changes with age causing bone loss:

Aging has different effects on hormones by decreasing some hormones while increasing some others and some may even remain the same level as younger people. The hormonal effect on the receptors and receptor response is also reduced in elderly. The hormones affecting bone mineral densities and producing age related osteoporosis as follows

1.2.1. Growth hormone

Aging shows decrease in growth hormone secretion and insulin like growth factor-1 (GHF-1). Growth hormone either directly or through IGF-1 increases osteoblast differentiation, activity and survival.growth hormone can also increase osteoclastic activity therefore increasing bone remodeling [22, 23]. IGF-1 are lesser in females than males. Higher levels of IGF-1 are positively associated with BMD in women though the effect is not so evident in males [24, 25].

1.2.2. Parathyroid hormone

The parathyroid hormone increased with aging either due to primary hyperparathyroidism or secondary to Vitamin D deficiency and decreasing calcium levels [26]. Parathyroid hormone increases bone resorption by stimulating production of RANKL, inhibiting OPG by osteocytes, enhanced osteoclastogenesis and increased expression of RANK. It stimulates bone formation by positive effect on osteoblasts by binding with PTH-related peptide type 1 receptor (PPR) [27].

1.2.3. Estrogen

Estrogen decrease with menopause shows 10 year cumulative decrease of 9.6% in BMD. A 5pg/ml decrease in estradiol can increase fracture risk by 2.5 times [28]. Estrogens decrease osteocyte and osteoblast apoptosis, release of RANKL and increase osteoclast apoptosis while inhibiting interleukin-6. The net effect is decreased bone resorption. The main source of estrogen in females are the ovaries. In males estrogen is synthesized from testosterone by the action of aromatase. It exerts its beneficial effect on BMD both in males and females. Aromatase deficiency can lead to decreased BMD in males [29, 30].

1.2.4. Testosterone

2-6% of males above 50yeras of age show symptoms of late onset hypogonadism[31]. Hypogonadism with aging is associated with decreased free testosterone and increased sex hormone binding globulin (SHBG) with increased FSH and LH in males. Active free testosterone declines by 2-3% per year [32]. Testosterone also affect GH/IGF-1 positively and thus on bone too [25]. Low testosterone increases RANKL production by osteoblasts and osteocytes [33]. Ovarian

androgens present in females become half after menopause which may also contribute to post-menopausal bone loss apart from estrogens decline [34].

1.2.5. Dehydroepiandrosterone and dehydroepiandrosterone sulphate from adrenal glands

DHEA and DHEAS decline with aging. DHEA replacement has showed significant improvement in BMD specially in females [35]. The beneficial effect DHEA is due to decreased bone resorption and increased bone formation effects. DHEA acts as precursor for estrogens and androgens and also increases IGF-1 levels. [36].

1.2.6. Follicle stimulating hormone (FSH) and luteinizing hormone (LH)

Aging shows decreased gonadal hormones with increasing levels of FSH and luteinizing hormone (LH). FSH increase 3.5% and LH by 1.1% every year with age in males [32]. FSH increases osteoclast differentiation its activity and survival hence enhancing bone resorption associated with increased expression of RANK and production TNF-α[37]. The levels of FSH increased5-6 years before menopause in females and may explain bone loss in perimenopausal period [38]. LH rise is also seen in hypogonadism but its role if any in bone loss has not become clear.

1.2.7. Vitamin D

Decreased in skin vitamin D producing capacity, lower dehydrocholesterol levels impaired kidney function and decrease conversion of 25(OH)D to 1,25(OH)2D3 has been seen in elderly [39]. Vitamin D deficiency decreases intestinal and renal calcium absorption. It has anabolic effect on bone by increasing mineralization of bones and stimulating osteoblast differentiation by increased expression of osteoblast specific element Osf2/Cbfa1 [40,41]. However vitamin D can also cause increased resorption by increasing differentiation and activity of osteoclasts thus stimulating bone remodeling [42].

1.2.8. Cortisol

With aging process the glucocorticoids secretion increases. Glucocorticoids in normal physiological levels increase bone mass by up regulation of Wnt/β-catenin signaling. The glucocorticoids cause osteoblast apoptosis and decreased survival by increasing reactive oxygen species and decreased mitochondrial activity [43]. Glucocorticoids increase Cathepsin k release by autophagic osteoblasts and which can increase bone matrix degradation [44]. It further decreases bone hydration, vascularity and blood flow [45].

1.2.9. Thyroid stimulating hormone (TSH)

Thyroid stimulating hormone decreases bone remodeling by inhibiting osteoblasts differentiation and collagen-1 along with decrease in osteoclast differentiation [46]. Aging is observed to decrease thyroid function with 3-6% people in > 60years age group show subclinical hypothyroidism with elevated TSH [47].its overtreatment or associated iodine deficiency can produce subclinical hyperthyroidism with increased TSH and more risk of fractures [48].

2. Material and methods

A crossectional study was done in adult males and females from 20 to 80 years of age.

Bone mineral densities of 180 male and female participants were checked, during free BMD camps, conducted at Hyderabad India. Gender distribution included 90 males and 90 females. Their age, weight, height, body surface area and Body mass index was recorded. Inclusion criteria were healthy subjects free of any endocrine disorder or bone related chronic disease. Exclusion criteria: subjects suffering from bone disorders or any chronic condition affecting bones such as diabetics mellitus, gout rheumatoid arthritis etc were excluded. Subjects who were on drugs such as corticosteroids, thyroxin and hormone replacement therapy were also excluded. The subjects were divided into groups depending upon their age and sex. Their height, weight, body mass index and BMD were taken and analyzed. The participants were explained about the study and informed consent was taken.

DEXA – The bone mineral density was found with Dual Energy X-ray Absorptiometry (DEXA) .This technique uses two types of X-ray beams, one is absorbed by soft tissue and the other by bone. It has very low levels of radiation. The DEXA test gives result in two variables that is T Score and Z score. The T score is comparison BMD in standard deviation with that of young adult of 30 years of age while the Z score is the comparison of BMD with a healthy adult of same age and sex. The DEXA test can measure BMD with 2-4% precision [49]. The GE Lunar Achilles Express Densitometer Machine was used for the BMD measurement. The T scores values for the BMD interpretation is taken in terms of Standard deviation (SD) from normal young adult mean. The criteria for interpretation of bone loss is given in table 1

Table 1 T score and its interpretation for bone mineral density

T Score	Interpretation
-1 to 1 SD	Normal
-1 to -2.49 SD	Osteopenia
<- 2.5 SD	Osteoporosis

2.1.1. Statistics

The data was analyzed and tabulated according age group and gender. Statistical studies were done to find out the mean with the standard deviation, standard error and 95% confidence intervals of age and BMD. t-tests were done to compare the means between different age groups of same gender and different gender

3. Results

Bone mineral densities declined with age in both the genders as shown in Table 2. The mean BMD was lesser in females compared to males in all age groups. The disparity in BMD among the genders that is the T score for BMD is greater from age group of 41-50yrs with statistical significance. In the younger age groups the decreased BMD in females than males was not statistically significant. The mean BMD in males and females with increasing age is depicted in Bar diagram (fig 1).

Table 2 BMD in different age groups of males and females and comparison between two genders

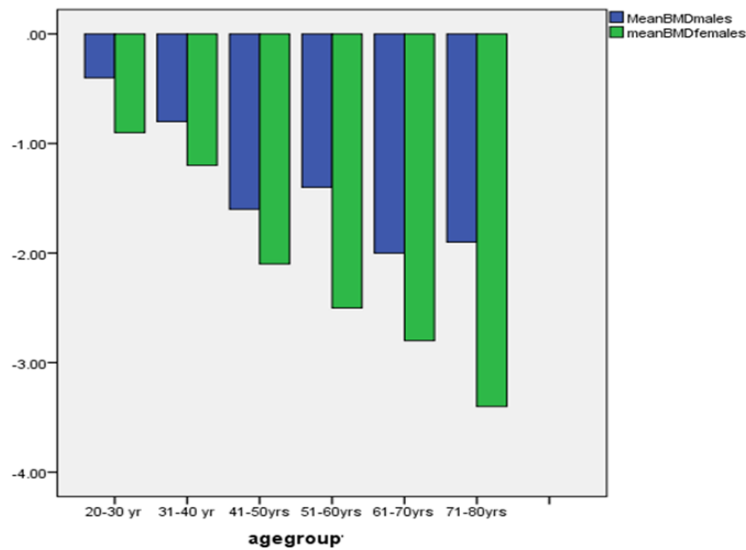| Age group			Mean	SD	SE	95% CI		t-value	p-value
						LL	UL		
20-30 years	Males	Age	25	3	1	23	26	1.7	p>0.05
		BMD	-0.4	0.7	0.2	-0.8	0.05		
	Females	Age	25	2	1	24	26	1.7	p>0.05
		BMD	-0.9	0.9	0.2	-1.4	0.4		
31-40 years	Males	Age	34	2	1	33	3	1.9	p>0.05
		BMD	-0.8	0.7	0.2	-1.2	-0.4		
	Females	Age	35	3	1	33	36	1.9	p>0.05
		BMD	-1.2	0.6	0.2	-1.5	-0.8		
41-50 years	Males	Age	44	3	1	43	48	2	P<0.05
		BMD	-1.6	1.2	0.3	-1.7	-1.5		
	Females	Age	46	3	1	44	48	2	P<0.05
		BMD	-2.1	1	0.3	-2.7	-1.5		
51-60 years	Males	Age	54	3.2	0.8	53	56	3	P=0.001
		BMD	-1.4	0.8	0.2	-1.9	-0.9		
	Females	Age	55	2.7	0.7	53	56	3	P=0.001
		BMD	-2.5	0.7	0.2	-2.8	-2.1		
61-70 years	Males	Age	66	3	0.8	64	67	3.3	P<0.001
		BMD	-2	1.4	0.4	-2.8	-1.2		
	Females	Age	65	3.4	0.9	64	67	3.3	P<0.001
		BMD	-2.8	0.5	0.1	-3.1	-2.6		
71-80 years	Males	Age	74	2.8	0.7	73	76	4	P<0.001
		BMD	-1.9	1	0.3	-2.6	-1.4		
	Females	Age	74	3	0.7	72	75	4	P<0.001
		BMD	-3.4	0.9	0.2	-3.9	-2.9		

Figure 1 Mean BMD in males and females in different age groups

Table 3 Change in BMD with age and its comparison with BMD of control group in females

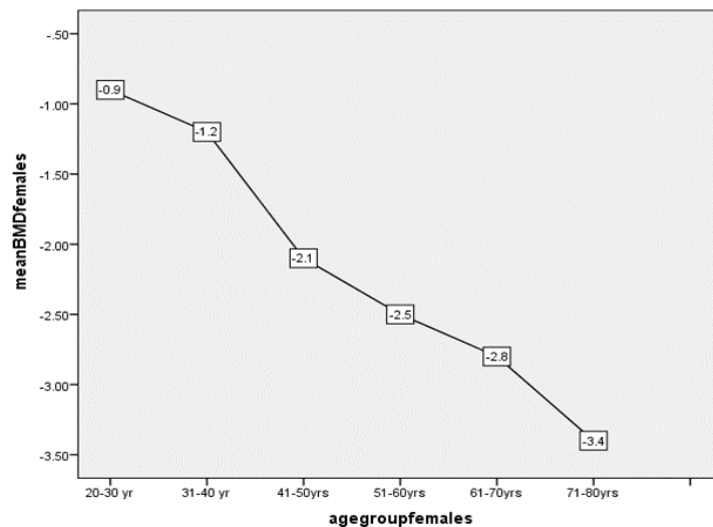| Age Group	Mean Age	Mean BMD	t value	p value
20-30 yrs (control)	25±2	-0.9±0.9		
31-40 yrs	35±3	-1.2±0.6	1.3	p>0.05
41-50yrs	46±3	-2.1±1	3.0	P<0.01
51-60yrs	55±2.7	-2.5±0.7	5.3	P<0.001
61-70yrs	65±3.4	-2.8±0.5	7.5	P<0.001
71-80yrs	74±3	-3.4±0.9	7.7	P<0.001

Figure 2 Mean BMD with different age groups in females

Analysis of BMD within females (Table 3) showed the decline in bone mass to osteoporotic levels from age above 51 years and osteopenia in age groups 31 to 40 and 41-50 years. T tests were done to compare BMD with that of control group that is 20-30 years of age. The decline in BMD compared to y control was statistically significant from 41 years

and above. There was rapid decline in mean BMD from age group 31-40 to 41-50 corresponding perimenopausal period. After which there was decline in BMD of 16-21% with each 10 year increase in age from the age of 41 years. Strong negative correlation was found between mean age and mean BMD in females which was statistically significant. The progressive lowering in BMD with age is depicted in the line diagram (fig 2).

BMD in male participants showed osteopenic changes from ages of 41 and above as shown in Table 4. In males also the maximum decline in BMD was from age group 31-40 to 41-50. There was significant declinein BMD in age group of 41-50 years compered to control. Pearson's correlation showed statistically significant negative correlation between mean age and mean BMD in male participants too. Osteoporosis with a mean BMD of a T score of below -2.5SD was not found even till the age group of 71-80 years in males. The decline in BMD with age in males is shown in line diagram (fig 3) given below.

Table 4 Change in BMD with age and its comparison with BMD of control group in males.

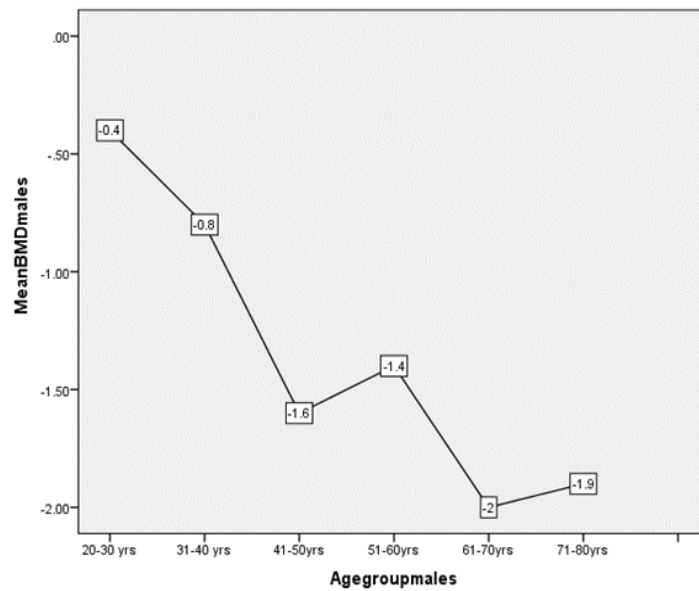| Age Group	Mean Age	Mean BMD	t value	p value
20-30 yrs (control)	25±3	-0.4±0.7		
31-40 yrs	34±2	-0.8±0.7	1.6	p>0.05
41-50yrs	44±3	-1.6±1.2	2.4	P<0.05
51-60yrs	54±3.2	-1.4±0.8	3.7	P=0.001
61-70yrs	66±3	-2 ±1.4	3.9	P<0.001
71-80yrs	74±2	-1.9±1.0	4.9	P<0.001

Figure 3 Mean BMD with different age groups in males

The mean height, mean weight, body surface area(BSA) and body mass index(BMI) were calculated as shown in table 5.The BMI appeared to decrease progressively with age but there was no significant correlation between the BMI and mean age. No significant correlation was found between BMI and mean BMD also.

Table 5 Body surface area and body mass index of males and females of different age groups

Age Group (Yrs)	Males				Females			
	Mean Height	Mean Weight	BSA	BMI	Mean Height	Mean Weight	BSA	BMI
20-30	162.66	59.73	1.62	22.7	154.33	54.66	1.52	23
31-40	164.66	75.6	1.9	28.1	155.73	62.53	1.63	26
41-50	161.73	76.6	1.82	29.55	157.93	60.06	1.62	24.46
51-60	160.93	77.8	1.87	30.03	153.26	60.6	1.62	25.89
61-70	157.33	61.13	1.64	24.8	149.3	57.2	1.52	25.77
71-80	156.2	52.2	1.52	21.45	144	38.71	1.26	18.67

4. Discussion

Bones undergo structural and functional decline with age. Osteoporosis with aging is poses a major problem in society with increased morbidity, mortality and decreased health related quality of life. The propensity for fragility fractures increases tremendously with age related bone loss. The risk of fragility fracture increases by 1.5 2.5% with each 1SD fall in BMD [50].

This study has shown the detrimental effect of age on BMD. The south Asian individuals show relatively lower BMD compared to western standards as has been in our control group attributing to ethnic differences. The peak bone mass as checked by the control group of 20-30 years of age was higher in males than females [51]. The osteopenia changes in males arise 10 years later in males than females. Osteoporotic changes in females were observed from age group of 51-60years similar to study by Lee et al [52]. Osteopenic changes in 31-40 yrs. and osteoporotic by 41- 50 years can be attributed to perimenopausal and early post-menopausal changes [53] as the mean age of menopause in Asians that is 46.2 years in Indian population [54]. The decline in BMD females was rapid between age group 31-40 to 41-50 and thereafter a slower decline of around 19-21% was observed with each 10 year increase in age. Bone loss starts 5-6 years before menopause and continues after, due to increase in FSH from before and loss of estrogens after menopause apart from other physiological changes. Osteoporotic changes were not observed in males even till 80 years of age as also observed by Alswat in his study [5]. The decline in BMD in males was more from age group 31-40 to 41-50 years. After which the decrease in BMD in males was gradual to reach a mean BMD around -1.9 by age 80 near to the similar BMD values by Kruger et al findings [55] with greater fracture risk beyond 80 years.

5. Conclusion

Osteoporotic fractures lead to considerable financial burden on the individual and the society. Despite being so common it has been largely under diagnosed. Postmenopausal women in particular are greatly susceptible to its deleterious effects. Greater knowledge of age related bone loss its prevention and management should be spread among the society. More rigorous screening for BMD with appropriate lifestyle and therapeutic changes in the early stages is the need of the hour.

Compliance with ethical standards

Statement of informed consent

Informed consent was obtained from all Individual participants included in the study.

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