Research Article

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Risk factors for low bone mass in healthy young adults from North India: studies on BMD and bone turnover markers

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ABSTRACT

Background: Despite availability of adequate sunshine, Indian population has the highest prevalence of low bone mass and Bone Mineral Content (BMC). Risk factors for osteoporosis have been extensively studied in the west but poorly investigated in India. We studied BMD and Bone Turnover Markers (BTMs) among healthy young adults.

Methods: Fifty one healthy young adults (28 Males, 23 Females) in the age group of 20-35 years were studied. Morphometric, biochemical parameters and BMD (whole body, spine, hip & wrist) were recorded. Anthropometric measurements included height, weight, BMI and Waist/Hip Ratio (WHR). BTMs studied included - serum Bone-Specific Alkaline Phosphatase (sBAP), serum Collagen cross-linked C-Terminal telopeptide (sCTx), serum Osteocalcin (OC) and human intact parathyroid hormone (hPTH) using standard ELISA kits.

Results: Of 51 healthy volunteers 21.57% had normal BMD, 13.73% were frankly osteoporotic and 64.70% were osteopenic. Age, weight and BMI were the best predictors of total BMD and BMC at all sites. sCTX positively correlated with Total Bone Area (TBA), BMD at Hip and Forearm. Using multiple regressions - age, weight, and BMI were significant predictors of BMD in young adults. Percentage body fat had inverse correlation with BMC, BMD and TBA. Weight and height positively correlated with BMD at femoral neck, inter-trochanter and Ward's triangle. Body weight was best predictor of BMD at femoral neck, Ward's triangle, forearm UD, forearm MID and forearm1/3.

Conclusion: Majority of healthy young Indians have poor bone health as evidenced by bone markers.

Keywords: Indian healthy young adults, BMD, BTMs, Bone health predictors

INTRODUCTION

It is quite disturbing to observe that in developing countries young adults are trying to copy the western lifestyle at an unprecedented speed. Having scant respect for a healthy balanced diet and a lifestyle bereft of outdoor activities and sun bathing, it is not surprising to see less and less healthy and robust younger generation in

India. Despite plenty of sunshine being available, hardly few people go out for sun bathing. Consequently number of osteoporotic patients in India are rising and estimated to reach about 26 million (2003 estimates) a figure likely to shoot up to 36 million after 2013. It has also been estimated that by the year 2020, world population will comprise of about one billion elderly (aged 60 years or above) people of which more than 70% will be living in

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developing countries. Out of these 700 million, about 142 million of this group will reside in India. Thus estimates on elderly population are available for whole of the world and for the developing countries. However, studies on bone health in younger populations are hard to find. Younger people are the main strength of any nation. Since prevention is better than cure, it is quite prudent that these people are made aware about their bone health quite early in their adulthood so that risks for future fractures and other bone diseases can be mitigated well in time.

Osteoporosis is characterized by low bone density and micro architectural deterioration of bone tissue, leading to bone fragility and an increased risk of fracture. It is often known as "the silent thief" because bone loss occurs without symptoms. Since the absolute values of bone mineral density (BMD) measurement vary with different densitometers, BMD is expressed as a T score. T score is the standard deviation (SD) of BMD or bone mineral content (BMC) from the expected BMD for an age and sex matched young normal adult.

WHO definitions of osteoporosis, osteopenia, and normal bone mass

The WHO defines normal bone mass, osteopenia, and osteoporosis as follows:

Normal: Value for BMD or BMC measurement within 1 SD of the young adult. Mean T score is -1.0 or above.

Osteopenia: Value for BMD or BMC of more than one SD but less than 2.5 SD below the young adult mean. Here T score is between -1.0 and -2.5.

Osteoporosis: Value for BMD or BMC of 2.5 SD or more below the young adult mean. Here T score is -2.5 or lower.

Severe osteoporosis/established osteoporosis: Value for BMD or BMC of more than 2.5 SD below the young adult mean in the presence of one or more fragility fractures. T score is -2.5 or lower, or with fragility fracture(s). Current risk assessment for low BMD are based primarily on data for older women, largely ≥65 years of age² which does not directly incorporate risk factors for low peak bone mass or accelerated perimenopausal bone loss. However, risk factors identified for older women may not be appropriate for younger population. Appropriate BMD testing for younger group first requires the identification of risk factors for low BMD in this population. Detection of individuals with significantly reduced BMD will assist in implementation of preventive measures and closer surveillance of those who may benefit from early intervention.

Body Mass Index (BMI): BMI is a measure of body composition, may be associated with risk of

osteoporosis.3 Low BMD is the single best predictor of fracture risk. Estimated by Dual-energy x-ray absorptiometry (DXA) at the hip, spine and whole body is currently considered the "gold standard" for measurement of BMD. Body weight or Body Mass Index (BMI) is known to be positively associated with BMD.⁴ BMI below 19-20 in the elderly is often associated with osteoporosis while individuals with a weight over 70 kg are seldom affected.⁶ Low body weight and low Body Mass Index (BMI) have consistently been shown⁷⁻¹⁰ to be associated with an increased risk of Osteoporosis. Kofi Asomaning et al.¹¹ have shown that women with low BMI are at increased risk of osteoporosis. The change in risk associated with a 1 unit change in BMI (\approx 5-8 lbs.) is of greater magnitude than most other modifiable risk factors. BMI is likely to be more predictive of osteoporosis than weight alone because it adjusts for differences in height and is more reflective of body composition Since Indians have significantly low peak bone mass, increased rate of bone turnover, higher rate of bone mass and one of the highest incidences of osteoporosis in the world.

The aim of this study was to determine the predictors of low BMD and the relationship among bone morphometry, biochemical BTMs and Bone mineral density in young healthy adults aged between 20-35 years.

METHODS

Subjects and methods

The prospective study included 51 (28 Males, 23 Females) healthy subjects in the age group of 20 to 35 years at SGPGIMS, Lucknow, India.

Anthropometric data

Weight (kg) and height (cm) were measured with light indoor clothing without shoes at the time of BMD measurements. Weight was recorded to the nearest tenth of a kilogram using an electronic scale and standing height (cm) was measured to the nearest 0.1cm by a wall-mounted stadiometer. Body Mass Index (BMI) was calculated as body weight in kilograms divided by the height squared in meters.

Total body BMD (g/cm^2)

BMD's of whole body, lumbar spine, femoral neck and wrist was measured by Dual X-ray Absorptiometry (DXA). If a subject was osteoporotic at either the hip or spine was classified as osteoporotic. Subjects were classified as osteopenic if they were not osteoporotic at either site but were osteopenic at least at one site. If they were normal at both sites, they were classified as normal.

A written consent was obtained from all subjects. All subjects were evaluated by a questionnaire proforma

regarding information on their age, race, education, nutrition and other personal details. The exclusion criteria included previous history of any fractures, renal disease, thyroid disorders & adrenal disorders, chronic gastrointestinal disease, liver disease, diabetes and Paget's disease. Subjects with history of medication with glucocorticoids, anticonvulsants, steroids and those with a history of excessive intake of alcohol, cigarette smoking, and use of calcium and vitamin D supplements and consumption of more than six cups of coffee/tea per day were also excluded.

Fasting samples were collected in the morning for the estimation of serum calcium (ca), phosphate (P), creatinine and alkaline phosphatase (ALP) as well as Urinary Creatinine (U Creat), calcium (UCa), inorganic phosphorous (UiP) were assayed by standard laboratory techniques. Serum OC, sBAP, hPTH and sCTx, were determined using commercially available ELISA kits. (Bioline Belgium, Nordic biosciences Denmark). Predictors of lumbar spine and femoral neck BMD were determined using linear regression analysis.

Results of investigations were entered into an Excel worksheet. Statistical analysis was performed using SPSS 11.5 software. Pearson's correlation and T test were calculated.

RESULTS

Epidemiological characteristics

Epidemiological characteristics of the study population are shown in Table 1. Out of fifty-one healthy volunteers, only eleven i.e. 21.57% (7 males & 4 females) had

normal BMD. Seven (4 females & 3 males) i.e.13.73% were frankly osteoporotic while thirty-three (17 males & 16 females) i.e. 64.70% were osteopenic. Bone parameters in different groups are described in Table 2. Predictors of lumbar spine, femoral neck and forearm BMD were determined using multiple linear regression analysis (Figure 1-3).

Collectively, age, weight, and BMI were significant predictors of BMD in young adults.

Statistical analysis

Using Pearson's correlation, age negatively correlated with total BMD and total BMC (r=0.41~&~0.37). Height had a positive correlations with total bone area & lean + BMC (r=0.382~&~0.380). Interestingly percentage body fat had negative correlation with weight, total bone area and lean + BMC (r=0.33,~0.65~&~0.64). Weight had a good correlation with height, total area, total BMC and lean + BMC (r=0.37,~0.80,~0.39~&~0.83). Serum crosslaps negatively correlated with age and BMI (r=0.27,~0.29).

Using Spearman's correlation Weight and BMI positively correlated with BMD at all sites ($r=0.357,\ 0.31$). Percentage body fat had a negative correlation with weight and height ($r=0.35,\ 0.57$). Body Weight positively correlated with BMD at femoral neck, trochanter, intertrochanter and Ward's triangle ($r=0.64,\ 0.6,\ 0.61\ \&\ 0.47$) respectively. Table 2 shows Levels of hPTH and sBAP in the osteoporotic group. Both of these were higher when compared with the normal group as well as the osteopenic group but the difference was not statistically significant.

Table 1: Epidemiological characteristics of the study population.

Parameter	Women (23) (Mean \pm SD)	Men (28) (Mean ± SD)	P value
Age (years)	25.65 ± 3.71	26.33 ± 3.90	NS
Height(cm)	1.55 ± 0.059	$1.69 \pm 0.086**$	< 0.001
Weight(kg)	50.38 ± 7.76	64.21 ± 10.78**	< 0.001
BMI (kg/m ²)	20.77 ± 2.84	22.40 ± 2.76	NS
Waist/hip ratio	0.89 ± 0.062	0.92 ± 0.047	NS
Percent fat	32.74 ± 3.67	21.78 ± 4.50**	< 0.001
Total fat mass (g)	16152.72 ± 3508.68	14630.07 ± 4456.111	NS
Lean body mass (g)	46155.05 ± 70469.13	48979.76 ± 6411.722	NS
Lean body mass + BMC (g)	3397.5636 ± 3872.096	51195.819 ± 6392.07**	< 0.001
BMAD (g/cm ³)	0.028 ± 0.01	0.027 ± 0.009	NS
Total area (cm ²)	1704.895 ± 122.48	2106.674 ± 185.25**	< 0.001
BMD (g/cm ²)			
Whole body	1.176 ± 0.51	1.235 ± 0.44	NS
Lumbar spine	0.92 ± 0.10	0.98 ± 0.09	NS
Forearm	0.538 ± 0.04	$0.633 \pm 0.04**$	< 0.001
Hip	0.799 ± 0.095	$0.951 \pm 0.14**$	< 0.001
Total BMC (g)	2019.779 ± 920.61	2621.238 ± 1058.758**	< 0.001

NS: Not significant (P>0.05); BMAD: Bone mineral apparent density; BMI: Body mass index

Table 2: Group-wise bone parameters in the subject.

Parameter	Normal	Osteopenic	Osteoporotic
Total (51)	21.57% (n=11)	64.70% (n=34)	13.73% (n=6)
Weight (Kg)	65.6 ± 12.6*	57.1 ± 10.4	49.5 ± 11.5*
Hip (cm)	94.5 ± 4.7*	$89.9 \pm 6.7*$	$87.8 \pm 4.9*$
Spine BMC (g)	62.3±9.3**	51.8 ± 9.3**	39.3 ± 6.1**
Spine BMD (g/cm ²)	$1.06 \pm 0.06**$	$0.94 \pm 0.08**$	$0.81 \pm 0.06**$
Hip BMC (g)	$34.3 \pm 9.8**$	$26.9 \pm 7.5*$	$21.9 \pm 6.8**$
Hip BMD (g/cm ²)	$1.01 \pm 0.14**$	$0.86 \pm 0.11**$	$0.72 \pm 0.11**$
Forearm BMC (g)	$13.1 \pm 3.5**$	11.1 ± 2.3	$9.6 \pm 2.1*$
Forearm BMD (g/cm ²)	0.63 ± 0.06 *	0.59 ± 0.06	$0.54 \pm 0.07*$
Total fat (g)	$1735 \pm 4052*$	15318 ± 3537	12884 ± 3882*
Total mass (g)	67172 ± 12642*	59116 ± 11411	50464 ± 11314*
Lean (g)	47098 ± 10432	50119 ± 55835	35016 ± 8365
Lean + BMC (g)	49821 ± 11128*	42161 ± 9443	37579 ± 9686*
hPTH (pg/ml)	22.0 ± 13.5	30.4 ± 20.7	36.5 ± 15.9
sBAP U/L	32.1 ± 5.9	33.5 ± 7.5	39.8 ± 8.4
sOC (ng/ml)	14.5 ± 6.6	15.2 ± 7.9	13.1 ± 2.9
sCTx (ng/ml)	0.53 ± 0.35	0.51 ± 0.21	0.49 ± 0.18

^{**}Correlation is significant at the 0.01 level; *Correlation is significant at the 0.05 level

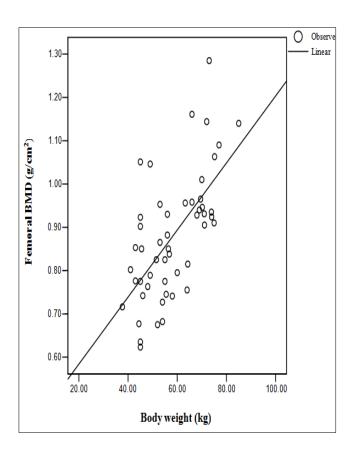


Figure 1: Regression line of spine BMD vs. body weight (Kg) $R^2 = 0.4$; (P < 0.001).

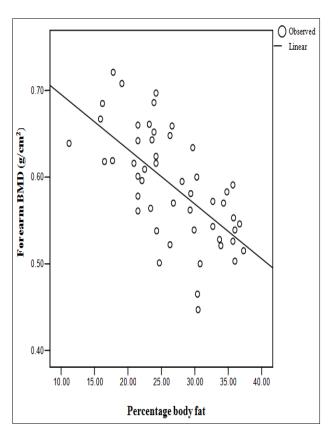


Figure 2: Regression: Forearm BMD vs. percentage body fat $R^2 = 0.4$; (P < 0.001).

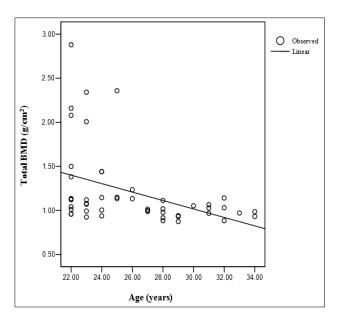


Figure 3: Regression line of total BMD vs. age $R^2 = 0.17$) (P < 0.003).

Regression analysis

Using stepwise linear regression age, weight, height, percentage body fat and serum cross-laps were significant predictors of total bone area (R^2 =0.88). Weight, height and BMI were significant predictors of lean + BMC (R^2 = 0.76). Age, weight, height, waist and waist-hip ratio were significant predictors of BMD (R^2 = 0.57). Body weight was the best predictor of BMD at Hip, Forearm and Spine (R^2 = 0.4 & 0.23 Figure 1). Age negatively correlated with Total BMD (R^2 = 0.17 Figure 2). Percentage body fat had a negative correlation with total BMC, femoral and forearm BMD (R^2 = 0.42, 0.41, 0.27 Figure 3), but not with lumbar spine. Serum hPTH positively correlated with serum OC (R^2 = 0.13 Figure 4).

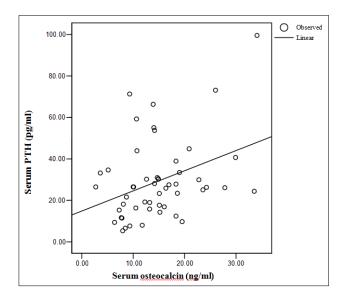


Figure 4: Regression line of Serum PTH vs. serum osteocalcin $R^2 = 0.13$) (P < 0.009).

DISCUSSION

First we tried to identify clinical risk factors for low BMD in young healthy subjects that could be used to discriminately select appropriate candidates for BMD assessment, thereby avoiding unnecessary testing.

Enough evidence is available which indicates that low body weight is associated with lower BMD. Several studies demonstrated a positive association between lower body weight and/or BMI and BMD at one or more skeletal sites. The largest study on 1600 subjects¹² reported that each kilogram increase in weight corresponded to an increase in BMD at the lumbar spine by 0.004 g/cm² and at femoral neck by 0.005 g/cm². In our study, body weight positively correlated with BMD at all the three sites (Hip, Forearm and Lumbar spine) rather than BMI as reported by others. ¹⁹⁻²¹ This implies that while screening healthy subjects low body weight can be safely considered as an important risk factor for low BMD.

Correlation studies showed that age had a negative correlation with BMD as well as total BMC indicating that advancing age was associated with lower total BMD as well as BMC. This observation is in agreement with others who have also documented an annual decrease in BMD by 1% with advancing age.²² This observation has serious implication as the trend of bone loss is observed at a young age as depicted in BMD scan (Figure 5A & B). Skeletal disasters can be foretold for these individuals when they reach the age of 40 years unless the trend gets reversed by appropriate dietary/therapeutic interventions.

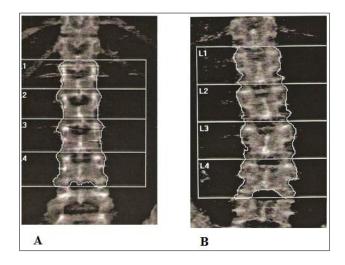


Figure 5: BMD scan of lumbar spine: (A) Twenty one year old female with T score - 2.9 and (B) twenty nine year old male with T score - 3.0.

Positive correlation between PTH and OC (Figure 4) supports the concept that PTH stimulates bone remodeling with age. These findings are in sync with previously described observations made in patients suffering from primary or secondary hyperparathyroidism

in whom increased remodeling was indicated by increased levels of hPTH and serum OC. ^{23,24} Although levels of PTH and sBAP in the osteoporotic group were higher as compared to the normal group as well as the osteopenic group, but the difference was not statistically significant probably due to small sample size.

It is well known that sBAP is an important indicator of osteoid formation and bone mineralization.²⁵ However in our study sBAP did not correlate with bone mineral density observed at any of the 3 regions studied. Same findings have also been reported by Chapurlat et al.²⁶ However, Dresner-Pollak et al. have reported an increase in sBAP with hip bone loss in elderly women (mean age 71).²⁷ Interestingly percentage body fat had strong negative correlation with femoral and forearm BMD, weight, total bone area and Lean + BMC. Other authors have also shown an inverse correlation between BMD and percentage body fat however, a positive correlation was observed between BMD and BMI.²⁸ Percentage body fat was significantly associated with Whole Bone Mineral Content (WBMC) and Whole Bone Area (WBA) yet interestingly was a more prominent contributor to WBMC or WBA than $BMI.^{29}$ Another study also found an inverse relationship between percentage body fat and bone mineral content.³⁰ The authors suggested that percentage body fat may be a proxy for physical activity, and these results may be due to reduced physical activity among those with increasing percentage body fat.

Thus our study indicates that markers of bone metabolism may be associated with loss of BMD at some skeletal sites. However, it was difficult to predict the bone loss thus limiting the utility of studying bone turnover markers alone as predictors of bone loss in these subjects.

CONCLUSIONS

Age, body weight and percentage body fat are important determinants of bone mineral density in younger adults. Within the age group of 20-35 years, only 21% of the population has normal BMD while a majority remains osteopenic. Among urban Indians BMD starts declining around the age of 30 years which is quite early as compared to their western counterparts. Larger studies are necessary to establish or refute these preliminary observations so that the results can then be fruitfully utilized towards development of more effective public health strategies for preventing osteoporosis. Though markers of bone turnover have been advocated to serve as predictors of bone loss in post-menopausal women but extrapolation of this information to predict bone loss in younger population remains largely unknown & elusive.

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Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

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