Original Article

Relationship of lipid parameters with bone mineral density in Indian population

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ABSTRACT

Introduction: Cardiovascular disease and osteoporosis share common risk factors including dyslipidemia. There are conflicting reports of differential relation of various lipid parameters on bone mineral density (BMD). Hence, we studied the correlation between lipid parameters and BMD in healthy adult. **Materials and Methods:** A total of 2347 participants (male 39.4%; female 60.6%) included in this cross-sectional study were divided according to sex and age. Fasting blood samples were drawn for biochemical parameters. BMD at lumbar spine, femur, and forearm were measured by dual energy X-ray absorptiometry (DXA). **Results:** In males, BMD at femur and lumbar spine decreased significantly with increasing quartiles of total cholesterol (TC) ($P < 0.0001$, and 0.004) and low-density lipoprotein cholesterol (LDL-c) ($P = 0.001$, and 0.01). In premenopausal women, BMD at femoral neck ($P = 0.001$) and lumbar spine ($P = 0.029$) showed declining trend with LDL-c ($P = 0.007$). In postmenopausal women, only BMD at total femur decreased significantly with TC ($P = 0.024$) and LDL-c ($P = 0.036$). All above findings were confirmed in correlation studies. In multiple regression analysis after adjusting for age, body mass index, ionized calcium, alkaline phosphatase, 25 hydroxy vitamin D, and parathyroid hormone levels correlation of BMD with TC and LDL-c persisted. TC, LDL-c was higher in subjects with low bone density compared those with normal bone density in both sexes. **Conclusions:** TC and LDL-c had weak but significant negative correlation with BMD at femur and lumbar spine.

Key words: Bone mineral density, dual energy X-ray absorptiometry, high-density lipoprotein-cholesterol, low-density lipoprotein-cholesterol, lipid Profile, total cholesterol, triglycerides

Introduction

Epidemiological studies suggested a relation between cardiovascular diseases and osteoporosis.[1,2] Lipids are strong risk factors for cardiovascular disease. Studies evaluating the relationship between lipid parameters and bone mineral density (BMD) in healthy adults and those with metabolic syndrome have revealed inconsistent results.[3-26]

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While most of the studies have been performed in women, there are a few studies in men[3-8] and adolescents.[5] Since Indians have differences in lipid profiles [higher prevalence of high triglycerides (TGs) and low high density lipoprotein cholesterol] compared with other populations,[27] we assessed the relationship between various lipid parameters with BMD at different sites in previously conducted cross-sectional population in healthy Indian volunteers.[28,29]

Materials and Methods

This study was carried out as part of voluntary general health check-up of all members of Resident Welfare Associations of four residential colonies, one each from North, South, East, and West Delhi.[28,29] The study included all participants > 20 years of age (2347 participants-Male 39.4%; Female 60.6%) excluding those with infectious,

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hepatic, renal, neoplastic, gastrointestinal, dermatological and endocrine disorders, steroid intake or alcoholism and drugs affecting lipid parameters like statins, fibrates, diuretics, and beta-blockers. Demographic, anthropometric, and clinical data were ascertained and a detailed physical examination conducted. Body mass index (BMI) was calculated by weight in kilogram divided by square of height in meters.

Fasting blood samples were drawn for the estimation of serum 25-hydroxy vitamin D [25(OH) D], intact parathyroid hormone (iPTH), total and ionized calcium, inorganic phosphorus, alkaline phosphatase (ALP), total cholesterol (TC), TGs, high-density lipoprotein cholesterol (HDL-c), and low-density lipoprotein cholesterol (LDL-c). Biochemical parameters were carried out using automated analyzer (Hitachi 902 fully automated biochemistry analyzer; Roche, Manheim, Germany) and commercial kits (Roche, Manheim, Germany). Measurements of plasma glucose were done by glucose oxidase-peroxidase method by Trinder (Clonital, Italy). Dyslipidemia was defined by TC >240 mg/dL, serum TG >150 mg/dL, HDL-c <40 mg/dL in males, and <50 mg/dL in females, and LDL-c >160 mg/dL.[30]

All participants were divided according to age with cut-off of 50 years so that pre- and postmenopausal women can be separated. Total population was divided and grouped for analysis into three groups − male (n = 924), female <50 years (premenopausal, n = 788), and females >50 years (postmenopausal, n = 635). All lipid parameters were divided according to quartiles in all three groups separately. Interquartile range for TC was 47.75, 34, and 51 mg/dL; for TG was 59, 26.75, and 58 mg/dL; for HDL was 8, 5, and 8 mg/dL; for LDL 32, 14.75, and 39 mg/dL for three groups, respectively. The study was approved by the ethics committee of the Institute of Nuclear Medicine and Allied Sciences and all participants gave written informed consent.

The normal range for different biochemical parameters are as follows: Serum total calcium (8.5-10.5 mg/dL), ionized calcium (1.12-1.32 mmol/L), inorganic phosphorus (2.5-4.5 mg/dL), ALP were (females: <240 U/L; males: <270 U/L), serum TC (110-230 mg/dL), serum TG (<150 mg/dL), HDL cholesterol (>35 mg/dL), and LDL (<100 mg/dL). The serum concentrations of 25(OH) D (reference range: 10-23 ngl/dL) and PTH (reference range: 10-65 pg/mL) were measured by RIA (Diasorin, Stillwater, MN, USA) and electrochemiluminiscence assay (Roche diagnostics, GmDH-Manheim, Germany), respectively.

BMD at anteroposterior (AP) lumbar spine (L1-L4), femur (total hip, femoral neck), forearm (33% radius), and total body was measured using the Prodigy Oracle (GE Lunar Corp., Madison, WI, USA) according to standard protocol. Low BMD is defined as Z-score <−1.0 in age group <50 years and T-score <−1.0 in age group >50 years in both sexes as also defined by another study,[21] while values higher than these were considered as normal BMD. Quality control procedures were carried out in accordance with the manufacturer's recommendations. Instrument variation was determined regularly using a phantom supplied by the manufacturer and mean coefficient of variation was <0.5%. For *in vivo* measurements, mean coefficients of variation for all sites were <1%.

Statistical analysis was carried out using software SPSS for windows version 20.0 (SPSS, Inc., Chicago, USA). Data were presented as mean ± standard deviation or number (%) unless specified. All parametric data were analysed by independent student's t-test between age groups. All nonparametric data were analyzed by Chi-square test. *P*-for trends were applied to assess significance of differences in BMD among the four quartiles of lipid parameters. Pearson's correlation coefficient was calculated to assess the strength of relationship between lipid parameters and BMD at various sites. Multiple regression analysis was done to ascertain association between lipid parameters with BMD at various sites after adjustment with variables like age, BMI, serum ionized calcium, ALP,25(OH) D, and iPTH levels. A $P < 0.05$ was considered statistically significant.

Results

This study included 2347 participants >20 years of age (male 39.4%; female 60.6%). Mean age and BMI were 49.1 ± 18.2 years (range: 21-90 years) and 25.0 ± 4.7 kg/m^2 (range: 13.0-49.8) respectively. There were 788 (55.4%) premenopausal (≤50 years) and 635 (44.6%) postmenopausal women (>50 years). Male were older than females (54.0 ± 16.7 vs. 45.9 ± 18.5 years; $P < 0.00001$). Basic characteristics of the population are given in Table 1.

Males

BMD at all sites, except radius, decreased significantly from lowest quartile to highest quartile of TC and LDL-c. BMD at femoral neck showed increasing trend with quartiles of TGs, but the relationship was not significant at lumbar spine and radius [Table 2]. BMD at femoral neck, femur total, and lumbar spine were negatively correlated with TC and LDL-c and positively with TG, which further supported the earlier analysis [Table 3]. There was no obvious trend for BMD at any site with quartiles of HDL-c.

Table 1: Basic characteristics of the population

	Male			Female		
	< 50 years	> 50 years	*P* value	<50 years	> 50 years	*P* value
Number (%)	559 (60.5)	365 (39.5)		788 (55.4)	635 (44.6)	
Age (years)	36.1±9.1	65.8±7.5		31.0±8.6	64.5±7.4	
Height (cm)	171.9±7.1	165.8±6.1	< 0.0001	159±5.9	153±6.0	< 0.0001
Weight (kg)	71.2±13.0	70.1±12.3	0.20	57.6±10.2	65.9±12.1	< 0.0001
BMI (kg/m^2)	24.1±4.0	25.5±4.0	< 0.0001	22.8±4.1	28.0±4.9	< 0.0001
Total cholesterol (mg/dL)	153±31	170±36	< 0.0001	147±27	184±37	< 0.0001
Triglycerides (mg/dL)	149±45	137±60	0.001	136±28	136±49	0.850
HDL (mg/dL)	41.8±7.8	42.0±7.1	0.678	43.4±3.9	45.7±7.9	< 0.0001
LDL (mg/dL)	95±20	106±26	< 0.0001	87±12	112±26	< 0.0001
S. calcium (mg/dL)	9.7±0.5	9.7±0.4	0.11	9.7±0.5	9.7±0.4	0.20
Ionized calcium (mmol/L)	1.14±0.07	1.15±0.05	0.0009	1.14±0.03	1.15±0.05	0.0002
S. phosphate (mg/dL)	3.5±0.05	3.5±0.05	0.84	3.8±0.05	3.8±0.05	0.12
ALP* (IU/L)	189±51 (182)	222±88 (205)	< 0.0001	220±80 (206)	244±88 (228)	< 0.0001
serum 25(OH) D* (ng/mL)	9.8±6.5 (8.7)	8.9±6.5 (7.2)	0.041	7.0±4.2 (6.2)	9.1±7.1 (7.0)	0.0001
PTH (pg/mL)	41.1±29.8 (33.4)	60.4±32.6 (55.4)	< 0.0001	49.1±26.5 (44.8)	59.7±35.2 (54.7)	< 0.0001
Femoral neck BMD (g/cm^2)	1.033±0.145	0.906±0.141	< 0.0001	0.987±0.126	0.826±0.146	< 0.0001
Femoral total BMD (g/cm^2)	1.078±0.150	1.000±0.143	< 0.0001	1.016±0.122	0.911±0.148	< 0.0001
Lumbar spine BMD (g/cm^2)	1.120±0.146	1.011±0.185	< 0.0001	1.114±0.128	0.973±0.170	< 0.0001
Radius 33% BMD (g/cm^2)	0.739±0.074	0.718±0.074	< 0.0001	0.659±0.074	0.590±0.100	< 0.0001

*Values are expressed as mean±standard deviation (median). ALP: Alkaline phosphatase, BMD: Bone mineral density, BMI: Body mass index, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, 25(OH) D: 25-Hydroxy vitamin D, PTH: Parathyroid hormone

Table 2: Bone mineral density (g/cm^2) in males with quartiles of lipid parameters

	1st Quartile	2nd Quartile	3rd Quartile	4th Quartile	*P* for trend
Cholesterol	(≤138) (*N*=231)	(>138-157.50) (*N*=231)	(>157.50-186) (*N*=232)	(>186) (*N*=230)	
Femoral neck BMD	1.001±0.161	0.950±0.153	0.948±0.138	0.928±0.160	< 0.0001
Femur total BMD	1.082±0.151	1.026±0.165	1.020±0.136	0.998±0.135	< 0.0001
Spine (L1-L4) BMD	1.146±0.166	1.115±0.176	1.093±0.163	1.090±0.174	0.004
Radius 33% BMD	0.735±0.087	0.726±0.080	0.721±0.073	0.723±0.081	0.088
LDL-cholesterol	(≤86) (*N*=231)	(>86-96) (*N*=231)	(>96-118) (*N*=232)	(>118) (*N*=230)	
Femoral neck BMD	1.001±0.161	0.950±0.153	0.948±0.138	0.928±0.160	0.001
Femur total BMD	1.082±0.151	1.026±0.165	1.020±0.136	0.998±0.135	0.025
Spine (L1-L4) BMD	1.146±0.166	1.115±0.176	1.093±0.163	1.090±0.174	0.01
Radius 33% BMD	0.735±0.087	0.726±0.080	0.721±0.073	0.723±0.081	0.260
Triglycerides	(≤100)(*N*=232)	(>10-134) (*N*=239)	(>134-159) (*N*=235)	(>159) (*N*=218)	
Femoral neck BMD	0.941±0.163	0.939±0.155	0.978±0.144	0.969±0.158	0.008
Femur total BMD	1.019±0.168	1.010±0.138	1.052±0.148	1.048±0.142	0.003
Spine (L1-L4) BMD	1.093±0.181	1.125±0.160	1.110±0.180	1.118±0.180	0.243
Radius 33% BMD	0.724±0.096	0.722±0.074	0.726±0.070	0.733±0.081	0.195
HDL-cholesterol	(≤38) (*N*=232)	(>38-42) (*N*=2390	(>42-46) (*N*=235)	(>46) (*N*=218)	
Femoral neck BMD	0.838±0.150	0.834±0.128	0.823±0.159	0.807±0.145	0.117
Femur total BMD	0.927±0.150	0.921±0.131	0.908±0.140	0.887±0.152	0.760
Spine (L1-L4) BMD	0.975±0.168	0.995±0.173	0.952±0.181	0.968±0.153	0.702
Radius 33% BMD	0.596±0.112	0.587±0.093	0.580±0.095	0.585±0.099	0.184

BMD: Bone mineral density, HDL: High-density lipoprotein, LDL: Low-denisty lipoprotein

In multiple regression analysis, after adjusting for age, BMI, serum ionized calcium, ALP,25(OH) D, and iPTHlevels, the relationship between BMD and TC and LDL persisted, while that with TG became insignificant [Table 4].

Postmenopausal women (females > 50 years)

BMD at total femurdecreased from lowest quartile to highest quartile of TC and LDL-c. No significant trends were observed at any other sites with other lipid parameters [supplementary Table 1]. A significant negative correlation was noticed between BMD at femur total and TC and LDL-c. TG showed a negative correlation with BMD at femur neck; and HDL-c showed positive correlation and BMD lumbar spine [Table 3]. In multiple regression analysis, after adjusting for age, BMI, serum ionized calcium, ALP,25(OH) D, and iPTH levels, the above-observed correlation was maintained except for TG, which became nonsignificant [Table 4].

Premenopausal women (female < 50 years)

BMD at femoral neck decreased from second to highest quartiles of LDL-c, but no significant trend was noticed with TC, TG, and HDL-c. BMD at lumbar spine decreased significantly with quartiles of LDL-c and increased with TG. HDL-c had no effect on BMD at any site [supplementary Table 2].

Table 3: Correlation of lipid parameters with bone mineral density

	Femoral neck *r* value (*P* value)	Femur total *r* value (*P* value)	Spine L1-L4 *r* value (*P* value)	Radius 33% *r* value (*P* value)
Total cholesterol				
Male	−0.136 (< 0.0001)	−0.159 (< 0.0001)	−0.076 (0.021)	−0.017 (0.613)
Female (<50 years)	0.025 (0.481)	0.040 (0.259)	0.023 (0.528)	0.006 (0.856)
Female (>50 years)	−0.069 (0.082)	−0.091 (0.022)	−0.026 (0.512)	0.007 (0.857)
LDL-cholesterol				
Male	−0.116 (< 0.0001)	−0.093 (0.004)	−0.103 (0.002)	0.053 (0.108)
Female (<50 years)	−0.056 (0.114)	−0.017 (0.631)	−0.057 (0.109)	−0.034 (0.345)
Female (>50 years)	−0.047 (0.239)	−0.080 (0.044)	−0.058 (0.142)	0.009 (0.820)
Triglycerides				
Male	0.085 (0.01)	0.084 (0.01)	0.065 (0.047)	0.061 (0.066)
Female (<50 years)	−0.015 (0.669)	0.020 (0.579)	−0.019 (0.591)	−0.003 (0.943)
Female (>50 years)	−0.078 (0.049)	−0.031 (0.431)	−0.025 (0.528)	0.032 (0.416)
HDL-cholesterol				
Male	0.014 (0.674)	−0.020 (0.547)	−0.009 (0.792)	−0.016 (0.609)
Female (<50 years)	0.024 (0.500)	0.016 (0.600)	0.012 (0.747)	−0.029 (0.420)
Female (>50 years)	0.073 (0.065)	−0.019 (0.627)	0.096 (0.015)	0.028 (0.481)

HDL: High-density lipoprotein, LDL: Low-denisty lipoprotein

Table 4: Multiple regression analysis of lipid parameters and bone mineral density (After adjustment for age, body mass index, ionized calcium, alkaline phosphatase, intact parathyroid hormone and serum 25-hydroxy vitamin D)

	Femoral neck beta coefficient (*P* value)	Femur total beta coefficient (*P* value)	Spine L1-L4 beta coefficient (*P* value)	Radius 33% beta coefficient (*P* value)
Total cholesterol				
Male	−0.0001 (0.0009)	−0.0001 (0.0006)	−0.0001 (0.003)	0.000 (0.775)
Female (< 50 years)	0.000 (0.155)	0.000 (0.145)	0.000 (0.661)	0.000 (0.625)
Female (> 50 years)	0.000 (0.272)	−0.0001 (0.036)	0.000 (0.711)	00.000 (0.496)
LDL-cholesterol				
Male	−0.001 (< 0.0001)	−0.0001 (0.005)	−0.001 (< 0.0001)	0.000 (0.064)
Female (< 50 years)	−0.001 (0.019)	−0.001 (0.011)	−0.001 (0.042)	0.000 (0.141)
Female (> 50 years)	0.000 (0.247)	−0.001 (0.028)	0.000 (0.106)	0.000 (0.830)
Triglycerides				
Male	0.000 (0.803)	0.000 (0.849)	0.000 (0.589)	0.000 (0.801)
Female (< 50 years)	0.000 (0.204)	0.000 (0.208)	0.000 (0.703)	0.000 (0.804)
Female (> 50 years)	0.000 (0.062)	0.000 (0.395)	0.000 (0.409)	0.000 (0.271)
HDL-cholesterol				
Male	0.001 (0.077)	0.001 (0.519)	0.001 (0.400)	0.000 (0.317)
Female (< 50 years)	0.000 (0.697)	−0.001 (0.540)	−0.001 (0.401)	−0.001 (0.376)
Female (> 50 years)	0.000 (0.621)	0.000 (0.846)	0.002 (0.010)	0.000 (0.577)

HDL: High-density lipoprotein, LDL: Low-denisty lipoprotein

However, there was no correlation of any lipid parameters with BMD at any site in premenopausal women [Table 3]. In multiple regression analysis, after adjusting for age, BMI, serum ionized calcium, ALP,25(OH) D, and iPTHlevels, LDL-c showed significant but weak negative correlation with BMD at femoral neck, total femur, and lumbar spine, but correlation with TG became nonsignificant [Table 4].

Total population was categorized in to subjects with normal BMD (1239-52.8%) and low BMD (1108-47.2%). In subjects with normal bone density, TC and LDL-c were significantly lower compared with subjects with low bone density in both sexes (Men: TC-159 ± 35 vs. 167 ± 35 mg/dL, $P = 0.001$; LDL-c- 99 ± 24 vs. 105 ± 25 mg/dL, $P < 0.0001$; Women: TC − 153 ± 32 vs. 174 ± 38 mg/dL, $P < 0.0001$; LDL-c: 91 ± 18 vs. 106 ± 25, $P < 0.0001$). There was no significant difference in BMD at any site in any group when study population was categorized according to dyslipidemia (data not shown).

Discussion

In the present large population-based cross-sectional study, we found that femoral BMD was inversely correlated with total cholesterol and LDL-c in both men and women BMD at lumbar spine was negatively correlated with TC and LDL-c in men, and only with LDL-c in pre-menopausal women. There was no correlation of BMD at radius with any lipid parameters.

Similar to our results, a Korean study also found a weak positive correlation of BMD with lipid profile (TC

Supplementary Table 1: Bone mineral density (g/cm²) in postmenopausal women (females>50 years) with quartiles of lipid parameters

	1st Quartile	2nd Quartile	3rd Quartile	4th Quartile	*P* for trend
Cholesterol	(≤158) (*N*=206)	(>158-182) (*N*=202)	(>182-209) (*N*=189)	(>209) (*N*=191)	
Femoral neck BMD	0.838±0.150	0.834±0.128	0.823±0.159	0.807±0.145	0.148
Femur total BMD	0.927±0.150	0.921±0.131	0.908±0.140	0.887±0.152	0.024
Spine (L1-L4) BMD	0.975±0.168	0.995±0.173	0.952±0.181	0.968±0.153	0.146
Radius 33% BMD	0.596±0.112	0.587±0.093	0.580±0.095	0.585±0.099	0.079
LDL-cholesterol	(≤94) (*N*=169)	(>94-110) (*N*=158)	(>110-133) (*N*=151)	(>133) (*N*=157)	
Femoral neck BMD	0.839±0.150	0.834±0.137	0.807±0.148	0.822±0.148	0.128
Femur total BMD	0.933±0.146	0.911±0.128	0.896±0.131	0.903±0.165	0.036
Spine (L1-L4) BMD	0.996±0.191	0.966±0.155	0.955±0.166	0.972±0.161	0.159
Radius 33% BMD	0.590±0.086	0.587±0.119	0.585±0.087	0.596±0.106	0.635
Triglycerides	(≤99) (*N*=163)	(>99-127) (*N*=158)	(>127-157) (*N*=156)	(>157) (*N*=158)	
Femoral neck BMD	0.824±0.149	0.826±0.159	0.839±0.131	0.815±0.144	0.322
Femur total BMD	0.898±0.129	0.907±0.146	0.936±0.142	0.905±0.156	0.582
Spine (L1-L4) BMD	0.978±0.190	0.946±0.141	0.994±0.175	0.972±0.167	0.472
Radius 33% BMD	0.589±0.091	0.573±0.116	0.605±0.089	0.591±0.101	0.337
HDL-cholesterol	(≤41) (*N*=161)	(>41-44) (*N*=158)	(>44-49) (*N*=160)	(>49) (*N*=156)	
Femoral neck BMD	0.825±0.134	0.814±0.151	0.814±0.127	0.851±0.170	0.739
Femur total BMD	0.919±0.148	0.911±0.169	0.902±0.132	0.912±0.122	0.746
Spine (L1-L4) BMD	0.975±0.161	0.945±0.174	0.953±0.163	1.018±0.174	0.619
Radius 33% BMD	0.591±0.084	0.592±0.122	0.584±0.100	0.592±0.094	0.571

BMD: Bone mineral density, HDL: High-density lipoprotein, LDL: Low-density lipoprotein

Supplementary Table 2: Bone mineral density (g/cm²) in premenopausal women (females<50 years) with quartiles of lipid parameters

	1st Quartile	2nd Quartile	3rd Quartile	4th Quartile	*P* for trend
Cholesterol	(≤128) *N*=206	(>128-145) *N*=202	(>145-162) *N*=189	(>162) *N*=191	
Femoral neck BMD	0.989±0.119	0.982±0.118	0.962±0.130	0.966±0.135	0.921
Femur total BMD	1.017±0.117	1.010±0.115	1.014±0.136	1.024±0.120	0.533
Spine (L1-L4) BMD	1.101±0.124	1.120±0.129	1.106±0.131	1.112±0.133	0.460
Radius 33% BMD	0.658±0.056	0.668±0.103	0.652±0.061	0.658±0.067	0.455
LDL-cholesterol	(≤79.25) *N*=197	(>79.25-86) *N*=200	(>86-94) *N*=192	(>94) *N*=199	
Femoral neck BMD	1.001±0.106	1.006±0.120	0.974±0.127	0.956±0.147	0.001
Femur total BMD	1.021±0.112	1.023±0.116	1.014±0.120	1.006±0.140	0.161
Spine (L1-L4) BMD	1.125±0.128	1.119±0.126	1.112±0.131	1.097±0.132	0.029
Radius 33% BMD	0.663±0.058	0.660±0.057	0.668±0.110	0.646±0.063	0.088
Triglycerides	(≤ 121) *N*=205	(>121-132) *N*=201	(>132-147.75) *N*=185	(>147.75) *N*=197	
Femoral neck BMD	0.980±0.127	0.992±0.127	0.988±0.123	0.970±0.127	0.118
Femur total BMD	1.004±0.119	1.018±0.120	1.030±0.114	1.013±0.133	0.060
Spine (L1-L4) BMD	1.108±0.134	1.124±0.133	1.126±0.124	1.097±0.124	0.007
Radius 33% BMD	0.662±0.099	0.658±0.059	0.662±0.062	0.655±0.068	0.086
HDL-cholesterol	(≤41) *N*=195	(>4-143) *N*=203	(>43-46) *N*=180	(> 46) *N*=210	
Femoral neck BMD	0.983±0.115	0.974±0.119	0.986±0.134	0.987±0.135	0.542
Femur total BMD	1.012±0.110	1.010±0.128	1.021±0.125	1.020±0.123	0.361
Spine (L1-L4) BMD	1.118±0.118	1.103±0.128	1.122±0.131	1.113±0.137	0.906
Radius 33% BMD	0.664±0.052	0.659±0.060	0.653±0.065	0.661±0.103	0.662

BMD: Bone mineral density, HDL: High-density lipoprotein, LDL: Low-density lipoprotein

and LDL-c) after adjustment with age, BMI and age at menarche in pre- and postmenopausal women.[20] In contrast, studies from USA (National Health and Nutrition Examination Survey-NHANES)[23] and UK (Framingham Osteoporosis Study-FOS)[7] reported no association of lipid parameters and BMD. Both these studies (NHANES and FOS) have only evaluated women and have not provided data separately for pre- and postmenopausal women. Further, women with associated comorbidities, including alcohol and drug intake, were not excluded in these studies. Many smaller studies have reported stronger but less significant correlation;[10,12,13,15-17] however, larger studies have found weaker but more significant correlation being large sample.[23,24]

Men

There are very few studies which have evaluated the relationship between lipid parameters and BMD in men,[3-8,23] mostly with small sample size.[3-6] Only two large community-based studies have reported the relationship between lipid parameters and BMD in men,[8,23] but are not suitable for comparison because in one instance data for

men was not separately reported,[23] while in the other, BMD was measured only at the wrist.[8] The NHANES-III also reported a similar trend of a negative association between TC and LDL-c with BMD, though it became insignificant after adjusting for multiple variables.[23] Smaller studies among European men reported either absent[5] or positive association[4,6] of TC and LDL-c with BMD at femur and spine. These differences can probably be explained by ethnic differences in BMD[31] and lipid levels.[27] It has been proposed that oxidized LDL increase Receptor activator of nuclear factor kappa-B ligand expression on osteoblast and increase interaction with osteoclast which affect bone remodeling and may cause decrease in BMD.[32] Further, in animal models, the primary cholesterol metabolite, 27-hydroxycholesterol, interacts with estrogen and liver X-receptors, decreases osteoblast differentiation, and increases osteoclastogenesis, thereby resulting in increased bone resorption and decrease in BMD.[33] BMD at femoral neck showed positive correlation with TG, which was lost when adjusted for various factors including age and BMI. A similar positive association of TG with BMD was reported in men[5] and adolescents,[3] which became insignificant when adjusted for body fat[5] or markers of insulin resistance.[3] However, other small studies have reported both absent[4] and positive correlation of TG with BMD which persisted even after adjustment with body fat.[6] Obesity, weight, and BMI are positively correlated with BMD[34] and TG is also positively correlated with obesity.[28] Hence, it is not surprising to find a positive correlation of TG with BMD, which gets neutralized when adjusted for BMI or fat mass.

HDL-c was not correlated with BMD at any site in the present study, which was also reported previously.[4] Other studies in European men found a negative correlation of HDL-c with BMD at femur and spine,[5,6] but the relationship was attenuated after adjustment for body fat content in one study.[5] There was no association of BMD at radius with any lipid parameters. A similar finding was reported in a large population based study.[8] On the contrary, a weak negative association of BMD at radius was observed with TC in one population-based study.[7]

Postmenopausal women

Serum TC and LDL-c had weak negative correlation with only total femur BMD. Several studies, including large population-based studies, have also reported a negative association of TC and LDL-c with femur[10,15], lumbar spine[10,16,17,21], and radius.[8,17] In contrast, a positive correlation of TC with hip BMD[6] and total body BMD[14] has also been reported, though in one of these studies, samples for lipid profiles were drawn in a nonfasting state.[14] Few studies have also shown no relationship between TC and LDL-c with BMD at any site.[5,7,8,16,19] Several of these studies are weakened by either small sample size,[5,11] selection bias,[19] or inclusion of subjects with comorbidities, as well as and consumption of medication known to affect BMD.[5]

BMD at femoral neck was positively related with TG, which became nonsignificant in multivariate regression analysis after adjustment with various factors. A similar positive association was reported in smaller studies[6,14,15] as well large population-based studies.[5] Some studies have reported the association to remain significant even after adjustment for weight.[6,14]

HDL-c revealed a positive correlation with lumbar spine BMD only in this group, which was maintained in multiple regression analysis. This relation was further confirmed by observation that HDL-c was higher in women with normal bone density compared with those women with low bone density. Several large population based studies[20,23,35] and smaller studies[17,35] also reported a positive association between HDL-c and lumbar spine BMD. However, other studies reported either a negative association[5,6] or no association of HDL-c and BMD.[10,15,21,22,36] These differences have been explained by ethnic and racial differences, size of the study population, and inclusion of women on hormone replacement therapy.[37]

Premenopausal women

In the present study, BMD at femoral neck and lumbar spine decreased significantly with increasing quartiles of LDL-c, and this weak negative correlation was maintained in multiple regression analysis. Large population based studies also found a negative association of TC and LDL-c with lumbar spine BMD[15] and whole body mineral content[22], but not with femur in premenopausal women.[15]

After adjustment, no significant correlation was found between TG and BMD at any site. In contrast, a Korean population-based study has reported a negative association of TG with BMD at total hip.[20] However, this study was retrospective and suffers from selection bias.[20]

HDL-c was not correlated with BMD at any site and a similar observation has been reported among Chinese premenopausal women.[22] However, another large population-based study found a positive relation between HDL and BMD at lumbar spine and femur.[10]

The main limitation of the study was absence of longitudinal data. Another limitation was absence of data on dietary habits, smoking, and physical activity, which can adversely affect both BMD and lipid parameters. The strength of

our study was the large sample sizes from healthy Indian population who were free from common morbidities and were not consuming any medication affecting BMD. Further, data on serum 25OHD and iPTH strengthened the study further.

Conclusion

While we report a weak correlation between lipid parameters and BMD at various sites in men, pre- and premenopausal women, its clinical significance needs to be elucidated.

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