Association between metabolic syndrome and bone mineral density among menopausal Saudi women: Case-control study

Essra Al-Dawood[1], Mubashir Zafar*[2] (ID)

Abstract

Background: Metabolic syndrome (MetS) and osteoporosis are two of the world's major healthcare issues. There are several studies which explored the association between MetS and bone mineral density (BMD), but all of them are cross-sectional. These studies cover all populations, including expatriated, which did not determine the actual problem among Saudi women. This is the first case-control study that determines the causal relationship between MetS and BMD. The objective of this study is to determine the relationship between metabolic syndrome and bone mass density among Saudi menopausal women in Eastern Province - Saudi Arabia.

Methods: It's a case-control study and 380 menopausal Saudi women were selected through simple random sampling. They were divided into 190 cases with osteoporosis and 190 without osteoporosis. Bone Mineral Density (BMD) at the total hip was determined using dual-energy X-ray absorptiometry (DEXA). T score was calculated. The association between the risk factors of MetS and bone mineral density was determined by binary logistic regression analysis using SPSS (statistical package of social science) software.

Results: Among women, the prevalence of MetS was substantially higher in those with osteoporosis. The Mets is positively correlated with bone mineral density. (r=0.08, p=0.051). The occurrence of MetS was associated with increased osteoporosis among Saudi women (B=0.004; p=0.005) after adjustment of confounders. The existence of obesity was significantly associated with increased odds of Bone marrow density among women (OR 2.56; 95 % CI, 2.22-3.44; p=0.030) after adjustment of confounders.

Conclusion: The incidence of MetS was associated with osteoporosis in Saudi women.

Keywords: Bone mineral density, Menopausal women, Metabolic syndrome, Osteoporosis

Introduction

The occurrence of metabolic syndrome (MetS) is expanding at a very high rate in developed and developing nations throughout the world (1). MetS is a cluster of risk factors of heart disease such as high blood pressure, high blood cholesterol level, high waist circumference, raised fasting plasma glucose and abdominal obesity (2). Epidemiologic researches indicate that metabolic syndrome is the most important risk factor for various numbers of chronic diseases mainly heart-related diseases and type II diabetes (3). It is estimated that the prevalence of MetS ranges from 20% to 25% of the population in the world. (3) A study found that people with MetS likely to die

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Corresponding author: Dr Mubashir Zafar, researchmubshir@outlook.com

1. Primary Health Care Centre, Ministry of Health, Al-Jubail, KSA
2. Department of Family and Community Medicine, College of Medicine, University of Hail, Hail, KSA

↑What is "already known" in this topic:
There are several studies that determine the relationship between MetS and BMD, but all of them are cross-sectional; These studies cover all populations including expatriated which did not determine the actual problem among Saudi women.

→What this article adds:
This is the first case-control study that determines the causal relationship between MetS and BMD. This study evaluates only Saudi females who were included as survey respondents. The study results found a positive relationship between MetS and BMD and obesity is an important predictor for BMD.

more than twice compared to individuals with no syndrome. (3) A survey published in 2018 shows that in Saudi Arabia, the prevalence of MetS is approximately 39.8%. (4) It is estimated that 8.9 million fractures yearly are reported among 200 million people; it means every 3 seconds, one fracture is reported. (5) A study conducted previously and the findings showed that waist circumference is significantly related to body surface area (BSA) (r=0.186, p<0.01). This result was similar to a cross-sectional study (6) that included 2007 participants (1045 males and 962 females) over 50 years of age to examine the link between MetS and osteoporosis. Another study was conducted in China showed similar results and a positive association of MetS with osteoporosis among elderly populations. (7).

Although MetS and osteoporosis were earlier thought to be two unrelated diseases, studies have shown that both conditions share several genetic, nutritional, and hormonal factors (8). There are different studies that determine the association of MetS with osteoporosis, but the specific association between MetS risk factors never determined. (9-15).

The prevalence of metabolic syndrome has increased in Saudi Arabia, forcing such a need to determine the causal factors leading to MetS among the aged population. Life expectancy also rises, which raises Saudi women's risk of osteoporosis. Only limited studies have focused on explaining the relationship between MetS and BMD in Saudi Arabia. These studies cover all populations including expatriated which did not determine the actual problem among Saudi women. These studies are cross-sectional and did not determine the temporality (causal association). This research will also be the first case-control study undertaken in Saudi Arabia in order to determine a possible causal relationship between the two conditions. Furthermore, only Saudi females will be included as survey respondents estimating the real issue among Saudi women.

The objective of this study is to determine the association between MetS and BMD among Saudi menopausal women in Eastern Province - Saudi Arabia.

Methods
Study setting
This case-control study was performed at Safwa General Hospital, one of the Eastern Province's main government facilities consisting of nearly 30 beds and serving approximately 150-200 patients daily in the outpatient departments (OPD). And also, patients will be included from one of the biggest primary healthcare centers in Qatif that serve about 80-100 patients daily.

Study participants
All menopausal women (age 45-75 years old) who had a BMD scan of Dual-Energy X-ray Absorptiometry (DEXA) (Lunar Prodigy Advance; GE Healthcare, Madison, WI, USA) and were diagnosed as osteoporotic were included as cases and women without osteoporosis were included as controls. The patients were referred by their physicians after visiting the hospital for regular checkups.

Menopausal status was determined based on the history of lack of menstruation for the last one year.

Inclusion criteria for cases: **A**ll menopausal women between the age of 45-75 years and clinically confirmed by their physician using a BMD scan were included. All were diagnosed with MetS.

Exclusion criteria: Peri-menopausal women, participants with other co-morbidity and women under hormonal treatment were excluded.

Inclusion criteria for controls: All menopausal women aged 45 and 75 years old who were free of osteoporosis with MetS were included.

Exclusion criteria: Perimenopausal women, age above 75 years or patients receiving estrogen replacement therapy were excluded. Hormonal replacement therapy was defined as the therapeutic use of hormones typically to increase diminished levels in the body.

Sample size
Sample size was calculated by WHO sample size calculator for health studies. Based on 95% confidence level, a relative precision of 0.25, the probability of the exposure to disease of 0.6, the probability of the exposure to no disease of 0.4, and anticipated odds ratio of 1.5, the sample size of this study was 380. The sample size was equally divided into 190 participants for the cases and 190 for the controls. The participants were selected through simple random sampling.

Data collection tool and technique
Structured questionnaire was used. The questionnaire was divided into four sections, including sociodemographic characteristics, anthropometric measurement, biochemical measurements including FBG, RBG, lipid profile, and DEXA measurement.

Anthropometry, blood sample and analysis
Anthropometric measures were determined through an automatic Anthrop Meter. Body mass index (BMI) was calculated through the formula, weight (Kg) divided by height (m^2); and then classified according to the WHO classes: Normal weight (18.5-24.99 Kg/m^2), Overweight (25-29.99 Kg/m^2), Obese ($\geq$30 Kg/m^2), the waist circumference (WC) was calculated using a tape.

Blood pressure was calculated using a blood pressure apparatus.

Blood samples were collected after 8 to 12 hours of fasting to measure Fasting Blood Sugar (FBS), High Density Lipoprotein (HDL), and Triglyceride (TG).

Criteria for the diagnosis of metabolic syndrome
Participants were diagnosed with MetS using the criteria (at least three components):

1. Waist circumference: (WC) $\geq$ 102 cm (males), $\geq$ 88 cm (females), 2. Hyperglycemia: fasting blood sugar (FBS) $\geq$ 100 mg/dl, 3. Hypertriglyceridemia: serum triglycerides (TG) $\geq$ 150 mg/dl, 4. Serum HDL-cholesterol (HDL-C) <50 mg/dl, 5. Systolic blood pressure (SBP) $\geq$ 130mmHg and/or diastolic blood pressure (DBP)$\geq$ 85 mmHg.

Criteria for diagnosis of osteoporosis

The bone mineral density of the total hip was measured using dual-energy X-ray absorptiometry (DEXA). The T scores were calculated, and the diagnosis of osteoporosis was made according to the World Health Organization criteria: Osteopenia (T score between from -1 to -2.5), Osteoporosis (T score < -2.5) and Normal (T score > -1).

T-Score Tertiles: T score was divided into tertiles (tertile 1: low score, tertile 3: high score).

Ethical consideration

Ethical approval was received from Imam Abdulrahman Bin Faisal University research ethical review board. Permission was taken from the hospital. Informed consent was obtained from all subjects who agreed to participate in the study before the interview. Participation was voluntary, and participants were free to withdraw at any time without any explanation. The confidentiality and privacy of the subjects were maintained and there was no financial benefit to either the subjects or the researcher.

Statistical analysis

All Statistical analysis was performed with SPSS windows version 23. Continuous data were presented as mean ± standard deviation (SD). Statistical significance between the groups was evaluated using Chi-square test. Correlation between MetS and BMD was determined using Pearson's correlation test. A Confident Interval (CI) of 95% and a P-value of less than 0.05 (two-sided) was considered as statistically significant. Binary logistic regression was used to determine the association between MetS and BMD. T-score tertile was used as a dependent variable (with the lowest tertile as a reference) and full MetS or its individual components (present vs. absent) as independent variables.

Results

The mean age of is the participants were 63.8±7.1 years. The data showed a statistically significant difference in age categories between women with MetS and osteoporosis compared to their counterparts, i.e. those with osteoporosis who were older (p=0.000) (Table 1).

Prevalence of osteoporosis was higher among those women who were physically inactive (57.9% vs. 42.1; p=0.016 compared to those without osteoporosis (58.3% vs. 41.7%); p=0.016).

Table 1. Socio-Demographic characteristics of Study Participants (n=380)

Sr. No	Characteristics	Cases =190 N (%)	Control=190 N (%)	p*
1	Age (years) (Mean ±SD)	65.45±7.24	62.15±7.12	
2	Age Categories			
	45-60 years	59 (36.1)	59 (63.9)	
	61-75 years	131 (56.3)	131 (43.7)	0.001
3	Age at Menopause (years) (Mean ±SD)	51.70±4.97	51.35±3.94	
4	Marital status			
	Single	8 (46.7)	8 (53.3)	0.530
	Married	141 (48.6)	141 (51.4)	
	Widowed& Divorced	41 (55.4)	41 (44.6)	
5	Education level			
	Illiterate	76 (53.3)	76 (46.7)	0.423
	Intermediate	67 (50)	67 (50)	
	High School& University	47 (44.7)	47 (55.3)	
6	Occupation			
	Housewife	173 (51)	173 (49)	0.214
	Employed	17 (40)	17 (60)	
7	Exposure to Sunlight per day			
	No	110 (51.6)	110 (48.4)	0.467
	Yes	80 (47.8)	80 (52.2)	
8	Veil Type			
	Covering hair only	20 (53.8)	20 (46.2)	0.873
	Eyes shown only	108 (49.3)	108 (50.7)	
	Full cover	62 (50)	62 (50)	
9	Physical Activity			
	No	85 (57.9)	85 (42.1)	0.016
	Yes , 1-2 times/day	66 (41.7)	66 (58.3)	
	>3 times/ day	39 (46.8)	39 (53.2)	
10	Smoking			
	Never smoke	103 (49.5)	103 (50.5%)	0.837
	Ever smoke	87 (50.6)	87 (49.4%)	
11	Family History of Met			
	Yes	145 (51.4)	145 (48.6)	0.334
	No	45 (45.6)	45 (54.4)	

Data are given as the mean ± SD or as the number of subjects with percentages given in parentheses, as appropriate. Categorical data are compared by χ2 test, BMD: bone mineral density. P-value <0.05 significant.

Table 2 shows the difference in anthropometric and biochemical parameters of all participants. Osteoporosis was significantly less common among women with higher BMI compared to their counterparts (58% vs.42%, p=0.001). In addition, participants with higher Serum TG level had significantly higher number of osteoporosis compared with their counterparts (p=.000). Moreover, women with lower mean levels of HDL-C had significantly less cases of osteoporosis compared to their counterparts (p<0.001)

A low BMD represented a T1-score and a high BMD represented T3-score. Different components of MetS showed no difference among various tertiles in both groups. The data does not show any significant statistical difference in either group (Table 3).

A very weak negative correlation was observed between BMD and SBP (r=-0.072, p=0.320), TG (r=-0.069, p=0.342) and HDL (r=-.065, p=0.375) in women with osteoporosis, and between BMD and WC (r=-0.091, p=0.213), TG (r=-0.025, p=0.729) and HDL (r=-0.061, p=0.406) in their control counterparts. No statistical significance was found in either group (p>0.05) (Table 4).

According to Table 5, all the socio-demographic characteristics were associated with osteoporosis but none of them were statistically significant. As Table 6 depicts, triglyceride is the only component of metabolic syndrome

Table 2. Anthropometric and biochemical characteristics of Study Participants (n=380)

S. no	Characteristics	Cases=190 N (%)	Control =190 n (%)	p
1	Mean Height (cm) (Mean±SD)	153.20±9.57	155.46±7.08	-
2	Mean Weight (kg) (Mean±SD)	69.71±16.76	78.05±16.86	-
3	Mean WC (cm)			
	Normal (WC<88cm)	43 (58.1%)	43 (41.9%)	0.086
	Obese (WC ≥88CM)	147 (47.6%)	147 (52.4%)	
4	BMI (kg/m²) (Mean±SD)	31.26±22.33	32.15±6.37	-
5	BMI class			
	Normal	30 (67.2%)	31 (32.8%)	0.001
	Under weight	2 (100%)	0 (0%)	
	Overweight	61 (52.8%)	62 (47.2%)	
	Obese	97 (42%)	97 (58%)	
6	Mean SBP (mmHg)			
	Normal (<130mmHg)	154 (50.2%)	154 (49.8%)	0.896
	High (≥ 130mmHg)	36 (49.3%)	36 (50.7%)	
7	Mean DBP (mmHg)			
	Normal (<85mmHg)	44 (51.7%)	44 (48.3%)	0.714
	High(≥ 85mmHg)	146 (49.5%)	146 (50.5%)	
8	Level of Triglyceride (TG)			
	Normal (< 90 mg/dl)	78 (41%)	78 (59%)	0.000
	Borderline (90-129 mg/dl)	54 (40.4%)	54 (59.6%)	
	High (>129 mg/dl)	58(71.3%)	58 (28.7%)	
9	Level of High-Density Lipoprotein (HDL)			
	Normal (> 45 mg/dl)	129 (43%)	129 (57%)	0.000
	Borderline (40– 45 mg/dl)	29 (64.9%)	29 (35.1%)	
	Low (< 40 mmol/L)	32 (64.6%)	32 (35.4%)	
10	Fasting blood Sugar			
	Normal (< 100 mg/dl)	41 (50.6%)	41 (49.5%)	0.744
	Borderline (100–125 mg/dl)	79 (51.9%)	79(48.1%)	
	High >125 mg/dl	70 (47.5%)	70 (52.5%)	
11	T-Score			
	T1 (Lowest)	50 (100%)	50 (0%)	0.000
	T2	93 (47.8%)	93 (52.2%)	
	T3 (Highest)	47 (0%)	47 (100%)	

Categorical data are compared byχ2 test. WHO criteria: a T-score between −1 and −2.5 is indicative of osteopenia, while a T-score of −2.5 and below reflects osteoporosis; a T-score of −1 and above is considered normal. P-value <0.05 significant.

Table 3. Prevalence of metabolic syndrome (MetS) components in tertile of T-score (n=380)

S.no	Components of Metabolic Syndrome	Cases (n=190)			Control (n=190)		
		T1	T2	p	T2	T3	p
1	Obesity	50.7%	42.5%	0.340	53.2%	64.8%	0.211
2	Hyperglycemia	52.5%	47.5%	0.675	49.7%	50.3%	0.357
3	Low HDL level	55.3%	44.7%	0.372	54.7%	45.3%	0.403
4	Hypertension						
	SPB	55.2%	44.8%	0.318	47.3%	52.7%	0.052
	DPB	44.4%	55.6%	0.245	48.6%	51.4%	0.744
5	Hypertriglyceridemia	57.5%	46.8%	0.340	54.5%	45.5%	0.727

Categorical data are compared by χ2 test. WHO criteria: a T-score between −1 and −2.5 is indicative of osteopenia, while a T-score of −2.5 and below reflects osteoporosis; a T-score of −1 and above is considered normal. P-value <0.05 significant.

Table 4. Correlation between Bone Mineral Density and features of the metabolic syndrome in 380 postmenopausal women

S.no	Variables	BMD cases	BMD controls
		T score	T score
		r	r
		(p)	(p)
1	WC (cm)	.082	-.091
		(0.050)	(0.213)
2	SBP (mmHg)	-.072	.141
		(0.320)	(0.052)
3	DBP (mmHg)	.084	.024
		(0.247)	(0.746)
4	FBS (mmol/L)	.030	.067
		(0.677)	(0.360)
5	TG (mmol/L)	-.069	-.025
		(0.342)	(0.729)
6	HDL (mmol/L)	-.065	-.061
		(0.375)	(0.406)

r: Pearson correlations. WC: waist circumference, SBP: systolic blood pressure, DBP: diastolic blood pressure, FBG: fasting blood glucose, TG: triglycerides HDL-C: High-density lipoprotein cholesterol. P-value <0.05 significant

Table 5. Associations of Osteoporosis with Metabolic syndrome other risk factors among women in Dammam, KSA

Risk Factors	Cases (n=190) N (%)	Control (n=190) N (%)	Unadjusted risk Estimate OR (95% CI)	P-value	Adjusted Risk Estimate OR (95% CI)	p
Age						
45-60 years	59.5 (36.1%)	76 (40%)	0.439 (0.281-0.686)	0.000	0.128 (0.050-.327)	0.000
61-75 years	130.5 (56.3%)	114 (60%)	0b	0b	0b	0b
BMI						
Normal	44 (23.2%)	20 (10.5%)	0b	0b	0b	0b
Overweight	65 (34.2%)	58 (30.5%)	.509 (0.270-.962)	0.038	1.087 (0.398-2.964)	0.871
Obese	81 (42.6%)	112 (58.9%)	1.329 (1.180-1.600)	0.000	2.569 (2.224-3.445)	0.030
Marital Status						
Single	7 (3.7%)	8 (4.2%)	0.704 (0.234-2.120)	0.532	0.400 (0.059-2.716)	0.348
Married	137 (72.1%)	145 (76.3%)	0.760 (.465-1.243)	0.274	0.797 (0.355-1.789)	0.582
Widowed	46 (24.2%)	37 (19.5%)	0b	0b	0b	0b
Education						
Illiterate	81 (42.6%)	71 (37.4%)	1.412 (0.843-2.368)	0.190	0.702 (0.222-2.227)	0.548
Intermediate	67 (35.3%)	67 (35.3%)	1.238 (0.729-2.102)	0.429	0.865 (0.306-2.447)	0.785
University	42 (22.1%)	52 (27.4%)	0b	0b	0b	0b
Occupation						
Employed	14 (7.4%)	21 (11.1%)	0b	0b	0b	0b
Unemployed	176 (92.6%)	169 (88.9%)	1.562 (0.769-3.172)	0.217	1.686 (0.345-8.228)	0.519
Veil Type						
Hair only	21 (11.1%)	18 (9.5%)	0b	0b	0b	0b
Eyes shown	107 (56.3%)	110 (57.9%)	0.834 (0.421-1.652)	0.602	0.713 (0.214-2.372)	0.581
Full cover	62 (32.6%)	62 (32.6%)	0.857 (0.417-1.763)	0.675	0.348 (0.097-1.248)	0.105
Physical Activity						
< 1time	99 (52.1%)	72 (37.9%)	1.566 (0.912-2.690)	0.104	1.041 (0.358-3.027)	0.941
1-2 times	55 (28.9%)	77 (40.5%)	.813 (0.462-1.432)	0.475	.685 (0.236-1.988)	0.487
>3 times	36 (18.9%)	41 (21.6%)	0b	0b	0b	0b
Smoking						
Ever	88 (46.3%)	86 (45.3%)	1.043 (0.697-1.562)	0.837	0.541 (0.265-1.108)	0.093
Never	102 (53.7%)	104 (54.7%)	0b	0b	0b	0b

Odds ratio with 95% confidence interval, BMI = body mass index; The reference category is: T1. b: This parameter is reference category. P-value <0.05 significant

that was significantly associated with osteoporosis. Every unit change in the level of triglycerides was related to a-0.004 unit decreased in osteoporosis.

Table 6. Multiple Regression Analysis of the effect of risk factors of metabolic syndrome on T-score

Risk Factors	B	SE	β	p
WC	0.000	0.002	0.014	0.781
SBP	0.001	0.005	-0.014	0.056
DBP	0.006	0.008	0.043	0.443
TG	0.004	0.001	-0.194	0.001
HDL	0.002	0.005	0.019	0.729
FBS	0.001	0.002	0.023	0.664

B; unstandardized beta, SE; standard error, β; standardized beta, WC; waist circumference, SBP; systolic blood pressure, DBP; diastolic blood pressure, TG; triglyceride, HDL-C; high density lipoprotein cholesterol, FBS; fasting blood sugar. P-value <0.05 significant.

Discussion

The study revealed that osteoporosis was significantly associated with metabolic syndrome in Saudi women. This association was unbiased of other covariates. This result is consistent with other studies (16–18). It is suggested that low levels of HDL are risk factors for osteoporosis (19–22).

This study found that metabolic syndrome components were more common in osteoporotic patients compared to non-osteoporotic patients. These results were similar to other studies which found that higher blood pressure in osteoporotic patients is associated with an increased chance of bone loss (23). Furthermore, low HDL levels were observed among those who had osteoporosis (24). A previous case-control study found that high blood pressure was a major contributor to bone loss. (25) Another component of MetS is the TG level. Our study found high levels of TG in osteoporotic patients and TG levels increased with age.

Results found that MetS is statistically related to WC and obesity. This result was consistent with other studies. Pathophysiological systems connecting fracture to obesity is not still determined. Growth of fat around the hip joint may lead to an elevated level of emission of pro-inflammatory cytokines that are harmful to bone. (26–28)

Physical activity was also associated with osteoporosis in this study. This result is in contrast with some other studies. A previous study found that those who were more physically active had a less chance of osteoporosis fracture (29).

The study also found that those women who covered their bodies had more osteoporosis. The reason for this association is that sunlight is an important factor for bone mineralization. This result is consistent with other studies (30-31).

The study had several limitations. This was a case-control study and information bias might be present in the result. Second, the subjects were selected from two centers only.

Conclusion

Our findings suggested a strong association between Mets and BMD. Early diagnosis of osteoporosis in those with MetS is important.

Research involving human participants

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This research was approved by the ethical review committee of the hospital. Confidentiality of data has maintained.

Conflict of Interests

The authors declare that they have no competing interests.

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