Original Article

Depressive symptoms and bone mineral density in menopause and postmenopausal women: A still increasing and neglected problem

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Abstract

Background: The association between depression and loss of bone mineral density (BMD) has been reported as controversial. **Objective:** The objective of the current study was to investigate whether an association exists between depression and low BMD during the menopausal and postmenopausal period. **Materials and Methods:** A cross-sectional descriptive study was used to generate menopause symptoms experienced by Arabian women at the Primary Health Care Centers in Qatar. A multi-stage sampling design was used, and a representative sample of 1650 women aged 45–65 years were included during July 2012 and November 2013. This prospective study explored the association between bone density and major depressive disorder in women. Bone mineral densitometry measurements (BMD) (g/m^2) were assessed at the BMD unit using a lunar prodigy DXA system (Lunar Corp., Madison, WI). Data on body mass index (BMI), clinical biochemistry variables including serum 25-hydroxyvitamin D were collected. The Beck Depression Inventory was administered for depression purposes. **Results:** Out of 1650 women 1182 women agreed to participate in the study (71.6%). The mean age and standard deviation (SD) of the menopausal age were 48.71 ± 2.96 with depressed and 50.20 ± 3.22 without depressed ($P < 0.001$). Furthermore, the mean and SD of postmenopausal age were 58.55 ± 3.27 with depression and 57.78 ± 3.20 without depression ($P < 0.001$). There were statistically significant differences between menopausal stages with regards to a number of parity, and place of living. There were statistically significant differences between menopausal stages with regards to BMI, systolic and diastolic blood pressure, Vitamin D deficiency, calcium deficiency and shisha smoking habits. Overall, osteopenia and osteoporosis and bone loss were significantly lower in postmenopausal women than in menopausal women ($P < 0.001$). Similarly, T-score and Z-score were lower with depression menopause and postmenopausal women ($P < 0.001$). The multivariate logistic regression analyses revealed that the depression, the mean serum Vitamin D deficiency, calcium level deficiency, less physical activity, comorbidity, number of parity, systolic and diastolic blood pressure and shisha smoking habits were considered as the main risk factors associated with bone mineral loss after adjusting for age, BMI and other variables. **Conclusion:** Depression is associated with low BMD with a substantially greater BMD decrease in depressed women and cases of clinical depression. Depression should be considered as an important risk factor for osteoporosis.

Keywords: Bone mineral density, depression, depressive disorders, disease, menopause, physical activity, postmenopausal

Introduction

Menopause is the cessation of a woman's reproductive ability, the opposite of menarche and it is usually a natural change; it typically

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occurs in women in midlife, during their late 40 s or early 50 s, signaling the end of the fertile phase of a woman's life.[1-5] The transition from a potentially reproductive to a nonreproductive state is normally not sudden or abrupt, occurs over a number of years, and is a consequence of biological aging.[3-7] Many women are likely to live more than 30 years after menopause, spending about one-third of their lives in a state of estrogen deficiency.[2] Age at natural menopause is an important research issue because of the suspected links between it and risk for certain diseases.[2,5]

In the last decade, researchers have begun studying the relationship of decreased bone mineral density (BMD) to mood variables, such as depression, anxiety, and stress.[8-13] Literature documenting the relationship of anxiety and stress response to osteoporosis is limited.[13] Most of these studies have focused on the psychological effects of coping with the disease, including pain, difficulties in the ability to function and fractures - which may occasionally require surgery and prolonged rehabilitation.[2-4] Several studies have suggested a strong link between depression and low BMD[5-14] and other studies found no such relationship.[15-17] Most recent meta-analyses supported a significant correlation of depression with low BMD or osteoporosis.[5,14] This situation may explain a condition characterized in an increase in an individual's anxiety level. However, there is no information available on depression during menopause and postmenopause in the State of Qatar. The reported association between depression and loss of BMD have been controversial.[5-14,15,17] The objective of this study was conducted to investigate whether an association exists between depression and low BMD during the menopausal and postmenopausal period.

Materials and Methods

This is a cross-sectional Primary Health Care (PHC) Centres based study conducted in the State of Qatar. The survey was conducted among Qatari Nationals and Arab women aged 45–65 years who had ceased menstruation for 2–5 years, who had not had a hysterectomy, and who had not used hormone therapy during the preceding 6 months. Similar to other reported studies,[3,18,19] women were excluded with contraindications to estrogen use and women who had a current unstable medical or social problem.

Questionnaire and interview

Eligibility criteria

The entry criteria for the study were to be: (1) 45–65 years of age; (2) diagnosis of major depression according to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV); (3) moderate to severe depression according to the 21-item Beck Depression Inventory (BDI) (1–63) score; (4) no current use of homeopathic treatment for depression or antidepressants or anxiolytic drugs for 3 months prior to study entry; (5) no use of psychotherapy for at least 3 months before screening; (6) no intake of estrogens or other medications known to affect ovarian function for at least 3 months before screening; (7) early transition to menopause, defined by a change in cycle length of 7 days or longer in either direction from the participant's own baseline for at least two cycles; (8) postmenopausal stage defined by 12 months or more of amenorrhea; and (9) capability and willingness to give informed consent and to comply with the study procedures.

The BDI-II was a 1996 revision of the BDI,[20] developed in response to the American Psychiatric Association's publication of the DSM-IV, which changed many of the diagnostic criteria for major depressive disorder. The BDI is a widely-used, self-evaluation depression scale. The long form of the BDI, used in this study, comprises of 21 questions or items, each with four possible responses. Each response is assigned a score ranging from 0 to 3, indicating the severity of the symptom.[20] Items 1–13 assess symptoms that are psychological in nature while items 14–21 assess more physical symptoms. The sum of all BDI item scores indicates the severity of depression. A score of 21 or above represents depression. Scores from 1 to 10 are considered normal; 11 to 16 considered mild mood disturbance; 17 to 20 considered borderline clinical depression; 21 to 30 considered moderate depression; 31 to 40 considered severe depression; finally, scores over 40 are determined extreme depression.

Bone mineral densitometry measurements

BMD (g/m^2) was assessed at the BMD unit using a lunar prodigy DXA system (Lunar Corp., Madison, WI). The anteroposterior lumbar spine (L2–L4) and the mean of the proximal right and left femur (including total femur, neck, Ward's triangle, and the trochanter) were be measured by two technologists and then reviewed by one radiologist using methods described.[2,3,18,19] Quality control of the DXA scanner included daily calibration and duplicate measures of a sample of the participants.

T-score and Z-score

The T-score is the most significant parameter for the assessment of osteoporosis, which compares BMD of the subject with average BMD of the young normal population. BMD was categorized according to the World Health Organization criteria based on the T-score.[3,18,19] Values between −1.0 and −2.5 were classified as osteopenia, a T-score of −2.5 or below as osteoporosis, and a T-score of −1.0 and above as normal.[3,18,19] T-score lower than −2.5 is osteoporotic which is an indication of the risk of fracture. Z-score compares BMD of the subject with average BMD of a population of the same age. This comparison determines whether the subject deviates from the normal pattern for her age.

Stiffness index

Stiffness index (SI) which represents BMD, combines broadband ultrasound attenuation (BUA) and speed of sound (SOS) into a single clinical measure that has a lower precision error than either variable alone. This index is formulated by normalizing BUA and SOS through subtracting the lowest observable values (50 dB/MHz and 1380 m/s) from each other and then scaling the resultant values. The SI is the sum of the scaled and normalized

BUA and SOS values. The resultant formula is empirically derived such that the index has 50% contribution due to SOS and 50% contribution from BUA.[21]

$$SI = ([0.67 \times BUA] + [0.28 \times SOS]) - 420$$

The SI is scaled in such a way to make the young adult value equal to 100. The normalized and scaled BUA and SOS values contribute about equally to the resulting SI over the adult age range. SI results expressed as T-score and Z-score are used to assist physicians in the diagnosis of osteoporosis.

Data collection took place from July 2012 to November 2013. The sample size was determined on *a priori* presumption that the prevalence rate of postpartum depression in Qatar would be more or less similar to rates found in other countries in the Arab Gulf Counties,[2,3,19] where the reported prevalence of depression to be 25–30%, with the 95% confidence interval for 2% error of estimation, a sample size of 1650 subjects would be required for this study. Of the 22 PHC Centers available, we have selected 12 health centers, of these, 10 were located in urban and 2 in semi-urban areas of Qatar. Finally, subjects were selected systematically 1-in-2 using a sampling procedure. Each participant was provided with brief information about the study and was assured of strict confidentiality. A multi-stage sampling design was used, and a representative sample of 1650 women aged 45–65 years were included. Incomplete questionnaire or nonresponse subjects were excluded from the total required sample size. The survey instrument was initially tested for validation on 75 patients who visited the health centers through face to face interviews, and those women were excluded from the analysis. The Cronbach's alpha score was 0.87 for internet BDI scales respectively, confirming a high level of consistency among the different Likert items in both of these scales.

Statistical test

Data were analyzed using IBM SPSS Inc. Statistical Software Window Version # 21, Chicago, IL 60611, USA. Sum of scores were calculated for BDI. Proportion with percentage was calculated for categorical variables and mean with standard deviation (SD) for continuous scale variables. Student's *t*-test was used to ascertain the significance of differences between mean values of two continuous variables and confirmed by nonparametric Mann–Whitney test. The Chi-square and Fisher's exact tests (two-tailed) were performed to test for differences in proportions of categorical variables between two or more groups. Multivariate regression analysis using the forward inclusion and backward deletion method was used to assess the relationship between dependent and independent variables and to adjust for potential confounders and orders the importance of risk factors (determinants) for BMD loss among menopausal women. The level $P < 0.05$ was considered as the cut-off value for significance.

Results

Of 1650 women, 1182 women agreed to participate (71.6%) and responded to the study. The mean age and SD of the menopausal age were 48.71 ± 2.96 with depression and 50.20 ± 3.22 without depression ($P < 0.001$). The median age of natural menopause in the present study was 49 years. Furthermore, the mean and SD of postmenopausal age were 58.55 ± 3.27 with depression and 57.78 ± 3.20 without depression ($P < 0.001$). Figure 1 shows the distribution of depression in menopausal and postmenopausal women; there were statistically significant differences between menopausal stages with regards to depression.

Table 1 shows the sociodemographic characteristics of the studied subjects by menopausal and postmenopausal status. There were statistically significant differences between menopausal stages with regards to the number of parity and the place of living.

Table 2 shows the lifestyle characters of the studied subjects by menopause and postmenopausal according to depression. There were statistically significant differences between menopausal stages with regards to body mass index (BMI), systolic and diastolic blood pressure, Vitamin D deficiency, calcium deficiency, and sheesha smoking habits.

Table 3 presents BMD loss regarding osteopenia, osteoporosis SI in with depression and without depression in menopause and postmenopausal women. Overall, osteopenia and osteoporosis and bone loss were statistically significant and lower in postmenopausal women than in menopausal women ($P < 0.001$). Similarly, T-score and Z-score were lower among women with menopause and postmenopausal depression ($P < 0.001$).

Table 4 gives multivariate logistic regression analyses with bone mineral densities. The depression, mean serum Vitamin D deficiency, mean calcium deficiency, less physical activity, comorbidity, the number of parity, systolic and diastolic blood pressure and sheesha smoking habits were considered as the main risk factors associated with the bone mineral loss after adjusting for age, BMI and other variables.

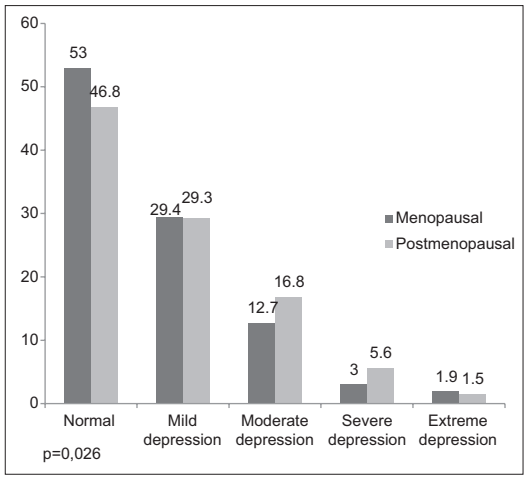

Figure 1: The distribution of depression in menopausal and postmenopausal women

Table 1: The sociodemographic of studied subject by menopause and postmenopausal according to depression (*n*=1182)

Variable	With depression menopause (*n*=101) (%)	Without depression menopause (*n*=474) (%)	*P*	With depression postmenopause (*n*=144) (%)	Without depression postmenopause (*n*=463) (%)	*P*
Age	48.91±2.96	50.25±22	<0.001	58.55±3.27	57.78±3.20	<0.014
Nationality						
Qatari	71 (18.4)	314 (81.6)	0.432	112 (25.1)	335 (74.9)	0.197
Non-Qatari	30 (15.8)	160 (84.2)		32 (20.0)	128 (80.0)	
Level of education						
Illiterate	10 (11.8)	75 (88.2)	0.038	35 (27.3)	93 (72.7)	0.266
Elementary	28 (23.9)	89 (76.1)		32 (26.9)	87 (73.1)	
Intermediate	27 (23.3)	89 (76.7)		25 (18.9)	107 (81.1)	
Secondary	21 (14.3.9)	126 (85.7)		39 (25.5)	114 (74.5)	
University	15 (13.6)	95 (86.4)		13 (17.3)	62 (82.7)	
Occupation						
House wife	51 (16.1)	265 (83.9)	0.21	95 (27.9)	246 (72.1)	0.112
Sedentary and professional	9 (9.8)	83 (90.2)		11 (19.0)	47 (81.0)	
Clerk	26 (25.5)	76 (74.5)		20 (17.4)	95 (82.6)	
Business/private	6 (17.6)	28 (82.4)		9 (18.8)	39 (81.3)	
Arm/police	9 (29)	22 (71)		9 (20.0)	36 (80.0)	
Monthly household income						
<$1500	6 (13.6)	38 (86.4)	0.405	10 (22.2)	35 (77.8)	0.970
$1500-$3499	38 (17.7)	177 (82.3)		55 (23.8)	176 (76.2)	
$3500-$5499	38 (20.9)	144 (79.1)		49 (23.1)	163 (76.9)	
≥$5500	19 (14.2)	115 (85.8)		30 (25.2)	89 (74.8)	
Number of parity (child)						
<3	77 (19.6)	315 (80.4)	0.050	76 (23.3)	250 (76.7)	<0.003
>3	24 (13.1)	59 (86.9)		66 (24.2)	213 (75.8)	
Place of living						
Urban	88 (19.4)	374 (80.5)	0.050	135 (25.9)	386 (74.1)	<0.003
Rural	13 (10.6)	100 (89.4)		9 (10.5)	77 (89.5)	
Consanguinity						
Yes	28 (16.3)	144 (83.7)	0634	44 (23.7	142 (76.3)	0.9799
No	73 (18.1)	330 (81.9)		100 (23.8)	321 (76.2.8)	

Discussion

Menopause produces very complex changes during this stage of life which include other changes such as psychological and social changes.[2,3] More recently, a study in Finland showed that due to postmenopausal depression the predicted bone loss increased.

Depression has been implicated as a possible risk factor for low BMD. However, there is still no solid evidence that could connect these two different illnesses. This research examined the association between depression and low BMD in menopausal and postmenopausal women. The loss of BMD with aging is a result of the complex interactions of hormonal, environmental, nutritional, and genetic factors. In recent years, psychological status has been identified as another factor possibly related to the loss of BMD.[5-14,15,17] In clinics with depression populations, significantly lower BMD has been found compared to without depression controls.[8,11,15,17] Lower BMD in with depression populations could be related to depression itself or to other behavioral disturbances that occur as a result of depression. Factors sometimes associated with depression such as lower levels of physical activity, changes in body weight, lower calcium compliance, or use of antidepressant medications have been postulated as underlying causes of bone loss.[11,14,15,17]

The current study data suggest that there is a strong association between depression symptoms and rates of bone loss in menopause and postmenopausal women: The greater the number of depressive symptoms, the higher the rate of bone loss. These findings are consistent with some previous cross-sectional studies that have reported lower BMD in subjects with depression than in those without depression loss.[5,11,14,22,23]

Furthermore, it is very clear that the depression and osteoporosis share a biological pathway, or one is a consequence of the other, there are some common risk factors such as unhealthy lifestyle[2,3,13-17,24] or co-morbidity.[3,25,26] We, therefore, considered current smoking (only for men), at-risk drinking, regular exercise, and co-morbidity as covariates as well as age, BMD, and current hormone use (only for women).

The current study showed that women with major depression had lower T-scores and Z-scores at the menopause and postmenopause stages. These findings suggest that depressed

Table 2: The lifestyle characters of studied subject by menopause and postmenopausal according to depression (*n*=1182)

Variable	With depression menopause (*n*=101)	Without depression menopause (*n*=474)	*P*	With depression postmenopause (*n*=144)	Without depression postmenopause (*n*=463)	*P*
BMI group (kg/m^2)						
Normal (<25)	29 (28.7)	125 (26.4)	0.562	31 (21.5)	97 (21)	0.907
Overweight (25-30)	44 (43.6)	234 (49.4)		72 (50.0)	241 (52)	
Obese (>30)	28 (27.7)	115 (24.2)		41 (28.5)	125 (27)	
Systolic BP mmHg (mean±SD)	128.7±16.3	126.2±17		128.0±15.7	132.4±16.6	<0.001
Diastolic BP mmHg (mean±SD)	78.4±8.9	76.5±9.1		78.8±8.2	80.1±9.5	<0.001
Vitamin D (ng/ml)	20.98±10.02	26.02±11.06	<0.001	19.46±10.17	24.86±11.3	<0.001
Calcium (mmol/L)	2.13±0.13	2.41±0.12	<0.001	2.10±0.13	2.38±0.14	<0.001
Physical activity						
Yes	23 (22.8)	161 (33.9)	0.028	32 (22.2)	154 (33.3)	0.016
No	78 (77.2)	313 (66.1)		112 (77.8)	309 (66.7)	
Diseases						
Without diseases	56 (55.4)	346 (73.0)	0.140	51 (35.4)	215 (60.5)	0.035
Diabetic	13 (12.9)	48 (10.1)		21 (14.6)	74 (16.0)	
Hypertension	7 (6.9)	29 (6.1)		18 (12.5)	48 (10.4)	
Asthma	7 (6.9)	23 (4.9)		13 (9.0)	35 (7.6)	
Arthritis	4 (4)	12 (2.5)		3 (2.1)	21 (4.5)	
Stroke	2 (2)	4 (0.8)		14 (9.7)	24 (5.2)	
CHD	12 (11.9)	32 (6.8)		24 (16.7)	46 (9.9)	
Cigarette smoking habit						
Yes	13 (12.9)	42 (8.9)	0.284	20 (13.9)	55 (11.9)	0.522
No	88 (87.1	408 (86.1)		124 (86.1)	408 (88.1)	
Sheesha smoking habit						
Yes	21 (20.8)	48 (10.1)	0.003	26 (18.1)	53 (11.4)	0.039
No	80 (79.2)	426 (89.9)		118 (81.9)	410 (88.6)	

SD: Standard deviation; CHD: Coronary heart disease; BMI: Body mass index; BP: Blood pressure

Table 3: Bone mineral density indices in menopause and postmenopause women according to the presence of depression*

Variables	Mean±SD		*P*	Mean±SD		*P*
	With depression menopause (*n*=101)	Without depression menopause (*n*=474)		With depression postmenopause (*n*=144)	Without depression postmenopause (*n*=463)	
Osteopenia						
Stiffness index	82.23±1.60	94.14±1.18	<0.001	80.02±1.58	92.37±1.19	<0.001
BMD	0.875±0.148	0.952±0.126	<0.001	0.823±0.102	0.891±0.115	<0.001
T-score	−1.928±0.922	−1.332±0.423	<0.001	−2.475±0.942	−1.646±0.439	<0.001
Z-score	−0.16±0.43	0.48±0.16	<0.001	−0.12±0.27	0.05±0.12	<0.001
Osteoporosis						
Stiffness index	81.36±1.58	93.51±1.06	<0.001	79.41±1.83	91.84±1.17	<0.001
BMD	0.736±0.109	0.787±0.114	<0.001	0.729±0.128	0.775±0.123	<0.001
T-score	−2.241±0.746	−1.478±0.683	<0.001	−2.615±0.755	−1.835±0.669	<0.001
Z-score	−0.13±0.38	0.53±0.14	<0.001	−0.15±0.17	0.07±0.21	<0.001

*Depression is defined as a score of 21 or more of the Arabic version of BDI. BDI: Beck depression inventory; BMD: Bone mineral density; SD: Standard deviation

patients may be at risk for higher rates of bone loss, and clinicians might consider depression as a factor when deciding when to screen women for low bone density. This is confirmative with the most recent Korean study.[25]

In the present community-based cross-sectional study, menopause and postmenopause women with depression had a lower BMD and a correspondingly 2 times higher probability of having osteoporosis, compared to those without depression. This is consistent with the previously reported studies.[5-11,14,22-27]

In the United Arab Emirates,[28] the study was conducted to identify the prevalence of physical, psychological, and menopause-related symptoms and their association with minor psychiatric disorders in menopause, and postmenopausal women, fatigue was the most frequent complaint in all groups of menopause, and postmenopausal women, respectively. This is consistent with the current and previous reported studies.[5-14] These findings suggest that depressed patients may be at risk for higher rates of bone loss, and clinicians might consider depression as a factor when deciding when to screen women for low bone density.

Table 4: Multivariate logistic regression analyses for predictors of bone mineral loss (*n*=1182)*

Variables	OR	95% CI	*P*
Depression	2.91	1.46-5.65	<0.001
Vitamin D (ng/ml)	2.82	1.74-4.96	<0.001
Calcium (mmol/L)	2.79	1.86-4.52	0.005
Less physical activity	2.65	1.53-4.78	<0.001
Co-morbidity	2.46	1.29-5.07	<0.001
Number of parity	2.35	1.82-3.68	<0.001
Systolic BP mmHg	1.81	1.48-2.24	<0.001
Sheesha smoking habit	1.74	1.45-2.16	<0.035
Diastolic BP mmHg	1.57	1.31-1.89	<0.024

*Adjusted for age and BMI. BP: Blood pressure; BMI: Body mass index; OR: Odds ratio; CI: Confidence interval

Limitations and strengths

There are several limitations of this study. First, this is cross-sectional study and, thereby, subjects might be misclassified in this analysis. Second, the study sample was based on PHC Clinics visits. Third, the majority of the study sample was Arab women and of relatively high socioeconomic and education status; hence, the results are not generalizable to the population of all midlife women. Furthermore, since this is a cross-sectional study, we evaluated the association between factors and quality of life. We were unable to evaluate the impact of these factors on the change in the quality of life over time. Despite these limitations, this study had a number of strengths. This study based on a large representative's sample. The information obtained for the biochemistry variables were based on the latest medical records.

Conclusion

The current study is consistent with previous findings of diminished BMD in people with depression and suggests that depressive symptoms may be a risk factor for reduced BMD in menopause or postmenopause women. A large number of factors were associated with experiencing menopausal symptoms and that had negative effects on the quality of life and BMD among Arabian women. Depression should be considered as an important risk factor for osteoporosis.

AB was involved in data collection, statistical analysis, interpretation of data and writing the manuscript. NMS was involved in data collection, interpretation of data, and editing the manuscript. DB was involved in the interpretation of data, writing and editing the manuscript. All authors approved the final version.

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Conflicts of interest

There is no conflicts of interest.

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