

Majid Malekzadeh Shafaroudi
(PhD) ^{1,2*}

Nourollah Rezaei (PhD) ^{1,2}

Behrooz Mohammadnejad (PhD) ²

Gholamali Usefi (MD) ³

Ali Malekzadeh Shafaroudi ⁴

1. Immunogenetic Research Center (IRC), Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran

2. Department of Anatomy and Cell Biology, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran

3. Vali e Asr Hospital, Ghaemshahr, Iran

4. Student Research Committee, Faculty of Dentistry, Mazandaran University of Medical Sciences, Sari, Iran

* Correspondence: Majid Malekzadeh Shafaroudi, Immunogenetic Research Center (IRC), Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran

E-mail: malek1344@gmail.com

Tel: +98 1133543249

Received: 17 July 2023

Revised: 26 Sep 2023

Accepted: 7 Nov 2023

Published: 30 Aug 2024

Osteoporosis and obesity in the South East of Caspian Seashore and its relationship to osteoporosis prevalence in Iran

Abstract

Background: Osteoporosis is the most common metabolic bone disease that begins with a decrease in bone mass and deterioration in the micro-architecture of the bone tissue, making the bones thinner and susceptible to fragility. A comprehensive estimation of the prevalence of osteoporosis in provinces of Iran seems to be necessary.

Methods: This study was a descriptive-analytical study. The study population included 518 people aged 30-65 years including 297 males and 221 females to measure their bone density. The data collection method was through BMD measurement using Dual-Energy X-ray Absorptiometry (DXA) method. All obtained data stored in the SPSS-16 database and statistically analyzed. The data analyzed using analytical, statistical methods. The significance level of the test was considered to be $P \leq 0.05$.

Results: In the present study, according to BMI status, 45.2% of the patients were obese, 38.2% were overweight. Despite the general belief that increasing in weight can be associated with an increase in bone mass, the present research revealed that nearly 35.9% of the research population, suffered obesity and osteoporosis at the same time. Metaregression analysis of data from different studies have illustrated that changing in frequency of osteoporosis as an oriented change in prevalence of osteoporosis from west to east and south to north ($P \leq 0.05$)

Conclusion: Iran society is under concern to more osteoporosis in the coming years at young and old ages which doubled with severe decline in growth rate of population from 3.7% to 0.63% in 2022. This can increase older people ratio over 30% in 2050.

Keywords: Osteoporosis, Osteopenia, Iran, Obesity, D₃ level, Mazandaran province.

Citation:

Malekzadeh Shafaroudi M, Rezaei N, Mohammadnejad B, Usefi Gh, Malekzadeh Shafaroudi A. Osteoporosis and obesity in the South East of Caspian Seashore and its relationship to osteoporosis prevalence in Iran. Caspian J Intern Med 2024; 15(4): 629-635.

Osteoporosis (OP) is the most common metabolic bone disease that begins with a decrease in bone mass and a deterioration in bone tissue's micro-architecture which led the bones become thin and fragile. Osteoporosis is an age-related disorder revealed clinically by skeletal fractures of the vertebrae, hip, and distal forearm (1, 2). Despite the widespread prevalence of osteoporosis in scattered studies in different regions of Iran, which have reported different forms of osteoporosis in different areas of the human body, according to geological, nutritional, behavioral, and environmental factors like sunlight and wearing culture that affect bone mass from the lumbar region, and femoral neck to the wrists, ankles, and forearms (3, 4). It has been observed and reported statistically significant differences according to gender along with a much higher frequency in the female population, especially postmenopausal women (2, 4, 5). Despite the fact that in 1991, the World Health Organization (WHO) listed osteoporosis as one of the four risk factors of human death. This disease is not included in the medical classifications of the National Health Service (NHS) as a major risk factor for the development of other middle age and old age diseases such as strokes, heart attacks and cancer.



In Iran, various studies have been conducted on osteoporosis that has led to different findings (3, 9-18). A simple review of the supporting documents shows that the reported frequency of osteoporosis in Iran is very different. The location variable can explain part of the difference between the research findings and lead to the formation of stereotyped changes in the south-west and east-west directions of Iran. This study aimed to find part of the osteoporosis prevalence puzzle in Mazandaran, Iran.

Methods

This study was a descriptive-analytical study and cluster sampling was used that is where the whole population is divided into clusters or groups. Subsequently, a random sample is taken from these clusters for example; according to questionnaire, all of which are used in the final sample (Wilson, 2010). Cluster sampling is advantageous for those researchers whose subjects are fragmented over large geographical areas as it saves time and money (Davis, 2005). The stages to cluster sampling can be summarized as follows:

1-Choose cluster grouping for sampling frame, such as geographical region. 2-Number each of the clusters. 3-Select sample using random sampling. The study population included 518 people aged 30-65 years including 297 males and 221 females who were referred to Tooba Clinic in Sari and Valiasr Hospital in Ghaemshahr in 2015-2016 to measure their bone density. In this study, there was no output criterion for people taking certain medications, such as glucocorticoids, calcium supplements, hormones, etc. All people outside the age range or had non-osteoporotic fractures, or were residents of other provinces of Iran were excluded from the study. The data collection tool was a questionnaire and a densitometer device, all scans prepared by an experienced and trained technologist, based on the manufacturer's protocol. The data collection method was through BMD measurement using Dual-Energy X-ray Absorptiometry (DXA) method and a Hologic-discovery-USA device, which was calibrated daily.

The questionnaire collected data such as menopause age, menopause before age 45, number of pregnancies and abortions, history of rheumatic diseases, corticosteroid use, a history of fractures after the age of 50, a history of pelvic fractures in their parents, physical activity, and vitamin D status, etc. (5-7) Afterward, the patients' height and weight were measured and recorded in the questionnaire using a standardized scale and a vertical meter, according to standard instructions and accuracy of respectively 0.5 kg

and 0.5 cm, before densitometry. Based on these numbers, the BMI was determined based on Kg / m^2 . Postmenopause was considered the complete cessation of menstrual cycles over the past 12 months (12-16). After completing the questionnaire, the patient laid on a densitometric bed (supine position), and the BMD of the lumbar spine (L2-L4) and femur (neck and intervertebral region and the entire femur) were measured in gm / Cm^2 .

Before densitometry, the internal rotation of the foot was positioned at 15 degrees. In this standard position, the femoral neck's length reaches its maximum size, and the densitometric values are measured more accurately. To ensure that the position was stable, the legs were fixed with a brace. In 2003, Lekamwasam et al. showed that a 10 degrees external rotation of the foot from its standard position increased the BMD average in the neck, trochanter, and Ward triangles (3).

A person's BMD is compared to the BMD value of the reference population. The reference population is selected from healthy people aged 20-80 who do not have any remarkable disease. Their BMD is measured, and the average BMD is obtained as the normal BMD for that age group. Afterward, using mathematical calculations, the measured BMD of a person is compared with the BMD of the reference population, in which the age group of 28-20 years is in great importance and referred to as the young reference.

This comparison is based on the standard deviation (SD). SD, or standard deviation, is an indicator of how far or close a person is from a young person's bone density. Usually, a 10% reduction in BMD than a young adult's BMD is equivalent to one SD. By reducing each unit of standard deviation in bone density, the femoral fracture risk increases by 2.6 times. Therefore, for a person with OP, $\text{SD} = 2$, the fracture risk is about 4 to 5 times higher.

Assortment of patients based on vitamin D levels:

According to the patient's test results in terms of vitamin D values, the patients were divided into six groups. The sixth group was people whose vitamin D levels were not known (10). Sometimes, in the test results, another unit called nanomoles per liter was used instead of nanograms per milliliter; according to the following method, these units can be converted to each other:

$$1\text{nmol/l}=0.4006\text{ ng/ml} \ \& \ 1\text{ng/ml}=2.496\text{ nmol/l}$$

Statistical analysis: All obtained data were stored in the SPSS-16 database and statistically analyzed. Descriptive analyses were used to calculate the mean, standard deviation, relative and absolute frequency, and 95% confidence interval. The data were analyzed using analytical, statistical methods (regression, t-test, and

ANOVA). Pearson correlation coefficient was used to evaluate the relationship between each risk factor for osteoporosis and BMD of the lumbar and cervical vertebrae. The significance level of the test was considered to be $p \leq 0.05$.

The research data were first extracted and presented in the form of tables and graphs that are added as supplementary files to analyze the findings. All data were then analyzed using SPSS software. Inferential statistics are used to identify the relationships between variables and other components. In the inferential statistics section, the t-test of two communities and linear regression test were used to examine the research hypotheses among correlation tests. The study population included 518 people, with an average age of 52.59 years for women (221) and 50.68 years for men (297). The average menopausal period for women was 9.57 years, and the average age for menopause was 46.12 years. **Determining sample size:** To determine the minimum required sample size, Cochran's formula was used for a limited population:

$$n = \frac{Nz^2 \frac{\alpha}{2} P(1 - P)}{(N - 1)d^2 + Z^2 \frac{\alpha}{2} P(1 - P)}$$

n = minimum sample size required
 N = statistical population size (2500)
 p = attribute distribution ratio in society
 $z\alpha/2$ = The value obtained from the standard normal distribution table (in this study was 1.96).
 d = usually considered in the social sciences equal to 0.05.
 The minimum sample size is 333 people. A larger sample size was considered, equal to 518 people in this study.

Ethical Considerations: Consent was obtained the anonymous use of the patient's personal information. All densitometric measures were performed under the scientific and standard principles of bone density measurement, based on the instructions on how to research human specimens approved by the Ethics Committee of Mazandaran University of Medical Sciences. This study was supported Chancellor of Research and Technology of Mazandaran University of Medical Sciences (Project No: 93-1185) / (Ethical Code: IR.MAZUMS.REC.1393.1185).

Results

Body mass index (BMI): According to BMI status, 45.2% of the patients were obese, 38.2% were overweight, and only 1.5% of patients were underweight (table 1) (figure 1).

Table 1. Classification of Osteoporosis patients of this study is based on body mass index (BMI)

BMI	Frequency	Frequency%
<20	8	1.5
20-25	78	15.1
25-30	198	38.2
>30	234	45.2
Sum	518	100

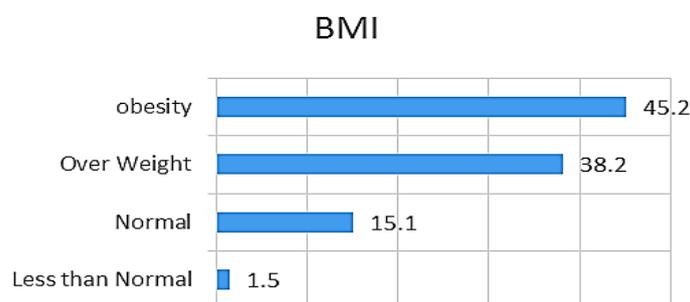


Figure 1. Classification of Osteoporosis patients of this study is based on body mass index (BMI)

Present research revealed that nearly 35.9% of the people under research population who suffered from obesity, had osteoporosis at the same time. If we add the percentage of obese to overweight people, the percentage of people who suffered from low density of bone calcification among over 40-65 ages in this research increases to 76.9%- 98% which can lead to fractures and

disability in their daily life. The results of the correlation test showed a positive and significant relationship between BMI and bone density of the lumbar regions $P < 0.05$, $r = 0.242$) and the femoral neck $P < 0.05$, $r = 0.282$). However, considering that the correlation coefficients is in the range of 0-0.5, this relationship is considered weak. The prevalence of osteoporosis in women less than 58 kg or

BMI <20, was higher than in women over 58 kg. In table 2, the results show that the rate of osteopenia and osteoporosis increased with the increase of age in patients, so that for the age group over 60 years, about 46.1% have osteopenia and 32% have osteoporosis and only 21.9% are within normal limits. While in the age group under 35, this amount has been quite different. As 70% were normal,

10% had osteoporosis and 20% were osteopenia. Table 2 which classified osteoporotic people revealed that 35.9% of population research between 40-55 ages suffers osteoporosis. However, osteoporotic number percentage increased to 57% among people at ages 56-65. However, osteopenia percentage in age groups classification shows nearly the same percentage 41-46% of population research.

Table 2. Prevalence of osteoporosis and osteopenia by age category (the numbers in the table are numerical (%))

Age Groups	Osteopenia%	Osteoporosis%	Normal%
Year≤35	20%	10%	70%
36-40	36.1%	2.8%	61.1%
41-45	41.7%	8.3%	50%
46-50	32.6%	13.5%	53.9%
51-55	42.2%	14.1%	43.8%
56-60	42.2%	25%	32.8%
60-65	46.1%	32%	21.9%

Osteoporosis prevalence: In the present study, the prevalence of osteoporosis and osteopenia for the lumbar region was 15.6% and 36.3%, respectively, and for the femoral neck, 7.7% and 45.6%.

Prevalence of vitamin D deficiency in Iran: Based on the results of vitamin D status, vitamin D levels were normal or higher than normal in only 23.9% of the population. 60.2% of the population had deficient vitamin D levels. Of these, about 2.5 percent had severe vitamin D deficiency (table 3).

Abundance of osteoporosis and osteopenia in the lumbar and femoral neck area: The results of table 4 show that the abundance of osteoporosis and osteopenia were respectively 15.6% and 36.3% in the lumbar region and 7.7% and 45.6% in the cervical region.

The general prevalence of osteoporosis and osteopenia: According to the results of table 5, 19.1% of the population had osteoporosis, 39% had osteopenia and the rest were within normal limits (figure 2).

Table 3. Prevalence of vitamin D deficiency in a population of 518 samples

Vitamin D3 Status	Frequency	Frequency%
Higher than normal (50-70)	10	1.9
Ideal (30-50)	114	22
Good (20-30)	156	30.1
Deficiency (10-20)	143	27.6
Severe Deficiency (5-10)	13	2.5
Unknown	82	15.9
Sum	518	100

Table 4. Percentage of osteoporosis, osteopenia, and normal samples in lumbar and cervical vertebrae

		Frequency	Frequency%
Lumbar	Normal	249	48.1
	Osteopenia	188	36.3
	Osteoporosis	81	15.6
Femur Neck	Normal	242	46.7
	Osteopenia	238	45.6
	Osteoporosis	40	7.7

Table 5. Total prevalence of osteoporosis and osteopenia

Prevalence	Frequency	Frequency%
Normal	217	41.9
Osteopenia	202	39
Osteoporosis	99	19.1
Sum	518	100

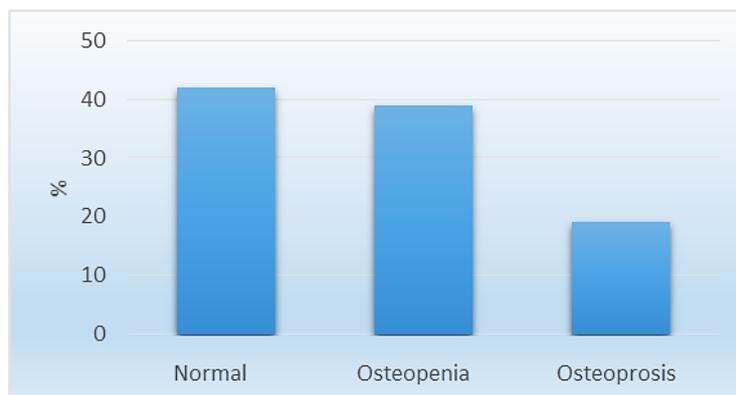


Figure 2. Total prevalence of osteoporosis and osteopenia

Discussion

Despite the general belief that increasing in weight due bone remodeling can be associated with an increase in bone density (bone mass), present research revealed that nearly 35.9% of the research population had osteoporosis and obesity at the same time. Osteoporotic number percentage increased to 57% among people at ages 56-65. However, osteopenia percentage shows nearly the same percentage 41-46% of population research in age groups classification. The percentage of people who suffered from low density of bone calcification among over 40-65 ages in this research are between 76.9% - 98% which can lead to fractures and disability in their daily life. A 2001 survey by Mojibian et al., conducted on 502 women in the central and desert regions of Yazd, Iran, reported 43%, the highest incidence of osteoporosis in the femoral bone. This number was 28.6 times that of a study published in Bushehr in 2004-2003 by Eghbali et al., which included 588 women with a mean age of 60.8%. This study reported 1.5%, the lowest incidence of osteoporosis in the femoral head (14, 15).

However, in 2005, Zamani et al. conducted a study in Kashan, a city located in the south of Alborz line mountains, with a population of 87 women with an average age of 71.6 (17). This study reported the highest incidence of osteoporosis in the spine (51.3%), which was 16.3 times of the frequency of osteoporosis in a study by Eghbali et al. in Bushehr, a city located in the North of

Persian Gulf with a population of 588 women, as this study reported 3.2%, the lowest prevalence of osteoporosis in the spine (16). In a cross-sectional population-based study, Jamshidian et al. estimated the prevalence of osteoporosis in women aged 40-60 years in Tehran at 15.8% in the lumbar region and 2.9% in the femoral region (4) (table 6). In the present study, the prevalence of osteoporosis and osteopenia in the lumbar region was 15.6% and 36.3%, respectively, and 7.7% and 45.6% in the femoral neck. While a cross-sectional population-based study conducted by Jamshidian et al. estimated the prevalence of osteoporosis in women aged 40-60 years in Tehran, 15.8% in the lumbar region, and 2.9% in the femoral region (4).

Metargression Analysis: Metargression analysis in the raw model from different researches took place in Iran showed that the geographic location variable is one of the most important variables that could cause heterogeneity. As the latitude and longitude changes, the prevalence of osteoporosis changes. However, the effect of latitude is far greater than longitude.

Data from different studies have shown that the frequency of osteoporosis in the northern and eastern regions of the country is higher than in the southern and western regions of Iran (11-18). To gather data from other researches and data from this study may illustrate a cline (oriented changes) in the prevalence of osteoporosis pattern in Iran (figure 3).

Table 6. Prevalence of bone region osteoporosis in different provinces in Iran

Province	Femur Prevalence OS	Lumbar Prevalence OS
Mazandaran (North)	7.7	15.6
Golestan (NE)	16.7	23.7
Kurdestan (west)	5.9	32.4
Tehran (Capital-Center)	2.9	15.8
Bushher (SW)	1.5	3.2

**Figure 3. Osteoporotic prevalence cline increased through arrow direction**

Conclusion

A simple review of the documents confirms that the reported frequency of osteoporosis in the Iran is very different. Therefore, a structural review of the documents and their combination with each other can show a more complete picture of the dimensions of this problem in the Iranian society. Differences and similarities between the results of this study and other parts of the country can be attributed to factors such as racial characteristics, nutritional differences, and lifestyle, including the amount of sports activity, geographical differences, air pollution, genetics and hormonal status of individuals. Declining milk consumption from 500 Kg/year in 2000 to less than 70 Kg/year during 2001-2021 period in Iran which declined more to 40 Kg/Year only in one year during 2021-2022 period which is about one fifth of the average per capita consumption of milk in the world, due to milk price increase and economic crisis according to research by the Ministry of Health and Medical Education, that led to decrease in bone density among Iranian people that

occurs in both young and old ages. Iran society is under concern to more osteoporosis in the coming years at young and old ages which doubled with sever decline in growth rate of population according to the Ministry of Health and Medical Education site to 0.63% in 2021.

According to the website of the Ministry of Health and Medical Education, as well as the Iranian Statistics Center, at the end of 2022, due to Covid-19, the growth rate of Iran's population in the four provinces of Gilan, Mazandaran, Golestan and Alborz was negative, and the average population growth of Iran declined from 1.26% to 0.63%. This can increase older people ratio over 30% in 2050. The result of this research is brightly stated, that is the occurrence of high rate of osteoporosis in the population of Mazandaran province despite the increase in obesity rate which could extend all over the county populations according to a report by the Ministry of Health and Medical Education that mentioned more than 44% of students under 12 years old are overweight and more than 23% of Iranian populations are in the risk of obesity. This

article also contains a warning to intensify the growing trend of this metabolic disease due to the higher level impact of nutritional factors and also the steep decline in the population growth rate during the last three decades

Acknowledgments

This study was an extract from the MSc thesis of Behrooz Mohammadnejad under the supervision of Dr. Majid Malekzadeh Shafaroudi.

Funding: This study was supported by the Immunogenetic Research Center (IRC) of Sari Medical Faculty and Chancellery of Research and Technology of Mazandaran University of Medical Sciences (Project No: 93-1185) / (Ethical Code: IR.MAZUMS.REC.1393.1185).

Conflict of Interests: The authors declare no conflict of interest.

Authors' contribution: Concept and design by M.M.Shafaroudi and N. Rezaee. Collecting and obtaining data by B. Mohammadnejad. Using the (DXA) method by a special device by Gh. Usefi. Analyzing statistically and English manuscript editing by M. M. Shafaroudi and A.M. Shafaroudi. All authors approved the final version of manuscript.

References

1. NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. Osteoporosis prevention, diagnosis, and therapy. *JAMA* 2001; 285: 785-95.
2. Kanis JA. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis: synopsis of a WHO report. WHO Study Group. *Osteoporos Int* 1994; 4: 368-81.
3. Lekamwasam S, Lenora RS. Effect of leg rotation on hip bone mineral density measurements. *J Clin Densitom* 2003; 6: 331-6.
4. Jamshidian-Tehrani M, Kalantari N, Azadbakht L, et al. Osteoporosis risk factors in tehrani women aged 40-60 years. *Iranian J Endocrinol Metab* 2004; 6: 139-45. [in Persian]
5. Browner WS, Pressman AR, Nevitt MC, Cummings SR. Mortality following fractures in older women. The study of osteoporotic fractures. *Arch Intern Med* 1996; 156: 1521-5
6. Leibson CL, Tosteson AN, Gabriel SE, Ransom JE, Melton LJ. Mortality, disability, and nursing home use for persons with and without hip fracture: a population-based study. *J Am Geriatr Soc* 2002; 50: 1644-50
7. Cooper C, Atkinson EJ, Jacobsen SJ, O'Fallon WM, Melton LJ 3rd. Population-based study of survival after osteoporotic fractures. *Am J Epidemiol* 1993; 137: 1001-5
8. Keene GS, Parker MJ, Pryor GA. Mortality and morbidity after hip fractures. *BMJ* 1993; 307: 1248-50.
9. Cooper C. The crippling consequences of fractures and their impact on quality of life. *Am J Med* 1997; 103: 12S-7; discussion 17S-9.
10. Fakor M, Mohammad Hosseini P, Shahriyari A, Sabz Alipour E. The effect of calcium and vitamin D intake in controlling the progression of osteoporosis. *Iranian J Orthop Surg* 2020; 18: 70-4. [in Persian]
11. Hashemipour S, Larijani B, Adibi H, et al. Vitamin D deficiency and causative factors in the population of Tehran. *BMC Public Health* 2004; 4: 38.
12. Keramat A, Khalilifard A, Adibi H, et al. Association between demographic factors and osteoporosis in urban Iranian postmenopausal women. *J Reprod Fertil* 2005; 6: 98-106. [in Persian].
13. Ostad Rahimi A, Mahboub S, Kolahi S, et al. The status of nutrition and bone density in monopous women. *J Med SciUni Uromieh* 2006; 1: 48-54. [in Persian]
14. Mojibian M, Owlia MB, Beiki-bandarabadi O, Kochakyazdi L. Osteoporosis in postmenopausal women. *Iranian Surg J* 2006; 14: 35-8. [in Persian]
15. Khani H. The study of bone mineral density in postmenopausal women with rheumatoid arthritis. *J Shahrekord Uni Med Sci* 2013; 15: 53-60.
16. Eghbali SS, Nabipour I, Dehghani Z. Prevalence of osteoporosis in women older than 50 years old in Bushehr port. *Iran South Med J* 2009; 11: 163-9. [in Persian]
17. Zamani B, Ebadi SA, Ahmadvand A, Moosavi GH. The Frequency of Osteoporosis in Hip Fracture Following Minor Trauma and the Resulting Mortality Rate and Direct Treatment Costs in Patients over 45 Years Old in Kashan Naghavi Hospital during 2005-2007. *J Kerman Uni of Med Sci* 2010; 17: 137-44. [in Persian]
18. Saeb M, Beyranvand M, Basiri Z, Haghparast-Bidgoli H. The hospital resource utilization associated with osteoporotic hip fractures in Kermanshah, Iran. *J Inj Violence Res* 2014; 6: 16-20.