

**Original article**

**Change In Bone Mineral Density In Post Menopausal Women With Rheumatoid Arthritis**

Aghaei M<sup>1</sup>, Sedighi S<sup>2</sup>, Pour NB<sup>3</sup>, Khani SH<sup>4</sup>, Shirashiani M<sup>5</sup>, Mohebi EG<sup>6</sup>, Zayeni H<sup>7</sup>, Shojaa M<sup>8</sup>, Jamshir M<sup>9</sup>, Aili A<sup>10</sup>

**Abstract**

**Introduction:** Low bone mass is a serious complication of post menopausal women with rheumatoid arthritis. We determined the Change in Bone Mineral Density in postmenopausal women with rheumatoid arthritis. **Methods:** This retrospective cohort study was carried out on consecutive postmenopausal women with rheumatoid arthritis who were referred to the Azar 5th teaching hospital affiliated to Golestan University of Medical Sciences, North of Iran in 2009. The required data were gathered from the patients' medical records. The data were analyzed using SPSS software and statistical tests. **Results:** We studied 98 postmenopausal women with rheumatoid arthritis. Mean number of years since menopause and mean duration of disease were 9.39 and 5.13 respectively. T Score mean in femoral neck and lumbar spines was  $-1.45 \pm 1.26$  and  $-2.45 \pm 1.44$  respectively. The overall prevalence of osteoporosis at both the lumbar spine and femoral neck was 13.3. We have found a significant correlation between age, duration of disease, duration of menopause and bone mineral density (P-Value < 0.01). **Conclusion:** Our results indicate a negative effect of age, number of years since menopause and duration of disease on bone mineral density. So, BMD should be measured in high risk women prior to the implementation of any treatment or prevention program.

**Key Words:** Bone mineral density, rheumatoid arthritis, osteoporosis, postmenopausal

**Introduction** Osteoporosis is an age-related disorder that is characterized by reduced bone mineral density (BMD) along with bone matrix and microarchitectural deterioration of bony tissue, with a consequent increase in bone fragility and susceptibility to fractures<sup>1,2</sup>. Osteoporosis is a common disease among the elderly, particularly the post-menopausal women<sup>3-7</sup>. BMD values depend on several factors such as age, sex, age at menopause and certain underlying diseases including rheumatoid arthritis<sup>8-10</sup>. Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by symmetrical polyarthritis and local bone erosion<sup>11-</sup>

<sup>15</sup>. Generalized bone loss has been commonly demonstrated in RA patients<sup>15</sup>. The age at onset of RA is usually 50-60 old year and two thirds of the patients are postmenopausal women<sup>16</sup>. It affects 0.5-1% of the world's population and considerably impairs the quality of life<sup>11-13</sup>. Osteoporosis is two times more prevalent in patients with rheumatoid than in the general population and increase with age<sup>10-11,17-18</sup>. The incidence of osteoporosis of the hip and spine is about 15-20% among patients with rheumatoid arthritis<sup>19</sup>. The prevalence of osteoporosis among Iranian women varies from 6 to

1. Mehrdad Aghaei, Bone Joint and Connective Tissue Disease Research Center (BJCRC), Department of Rheumatology, Faculty of Medicine, Golestan University of Medical Sciences
2. Sima Sedighi, Golestan University of Medical Sciences
3. Naser Behnam pour, Golestan University Of Medical Sciences
4. Sharabeh Hezar Khani, Golestan University Of Medical Sciences
5. Mona Shirashiani, Islamic Azad Medical University of Tehran.
6. Elena Gholam Mohebi, Faculty of Veterinary Medicine University of Urmia.
7. Habib Zayeni, Faculty of Gilan University of Medical Sciences.
8. Mahdiah Shojaa, Osteoporosis Research Center, Tehran University Of Medical Sciences
9. Mohsen Jamshir, Golestan University of Medical Sciences
10. Aili Aili, Golestan University of Medical Sciences

**Corresponds to:** Mahdiah Shojaa, Osteoporosis Research Center, Tehran University of Medical Sciences, Tehran, Iran, **E-mail:** Mahdiah.shojaa\_mw@yahoo.com

43.03 percent<sup>20-23</sup>. A study in the south of Iran showed 19.6% of patients with rheumatoid arthritis had osteoporosis at both the lumbar spine and femoral neck<sup>24</sup>.

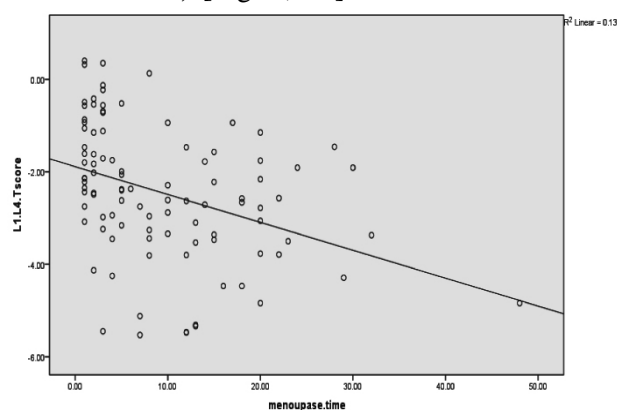
In the present study, we have evaluated the change in bone mineral density in post menopausal women with rheumatoid arthritis.

**MATERIAL & METHODS** This retrospective cohort study was carried out on consecutive postmenopausal women with rheumatoid arthritis who were referred to the Azar 5th teaching hospital affiliated to Gorgan University of Medical Sciences, Gorgan, North of Iran in 2009. The required data, including age, age of menopause, years has passed since the last menses, and duration of the underlying disease, was gathered from the patients' medical records. The BMD assessment was performed both at lumbar spine (L1-L4) and femoral neck using DXA (Hologic, QDR 4500C). The individuals with underlying diseases that may positively or negatively affect bone mineral density values were excluded and bone mineral density was evaluated. Based on WHO classification, individuals with T-score > -1 are classified as normal, with  $-1 > T\text{-score} > -2.5$  as osteopenic, and those with T-score < -2.5 as osteoporotic (25). The data were analyzed using SPSS software version 13.0. The descriptive data were presented as frequency, mean and SD, whereas regression,  $\chi^2$ , ANOVA and T-test were used for further analysis. P-values less than 0.05 were considered statistically significant. The protocol was approved by ethical committee of the institute.

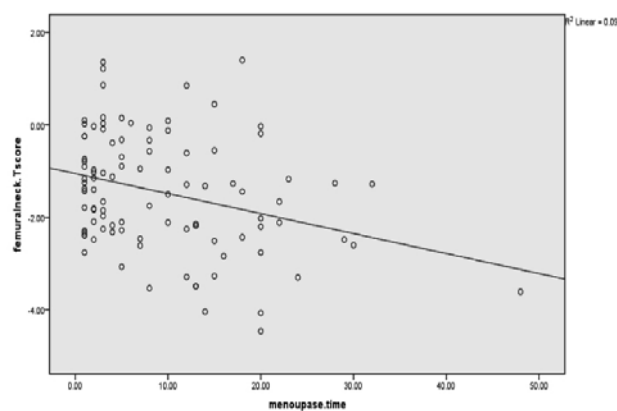
**RESULTS**

Ninety-eight postmenopausal women suffering from rheumatoid arthritis, with a mean age of  $57.88 \pm 9.39$  years (ranging from 44 to 98 years) were studied. 24 patients (24.5%) less than 50 years, 50 patients (51%) 50 to 65 years and 24 patients (24.5%) had more than 65 years old. Mean number of years since menopause was  $9.39 \pm 8.89$  years, ranging from 1 to 48 years. Mean duration of disease was  $5.53 \pm 4.41$  years, ranging from 1 to 20 years. T Score mean in femoral neck and lumbar spines was  $-1.45 \pm 1.26$  (-4.46 to 1.40) and  $-2.45 \pm 1.44$  (-5.53 to 0.40) respectively. According to the lumbar spine T Score, 46 patients (46.9%) had osteoporosis, 34 patients (34.7%) had osteopenia and 18 patients

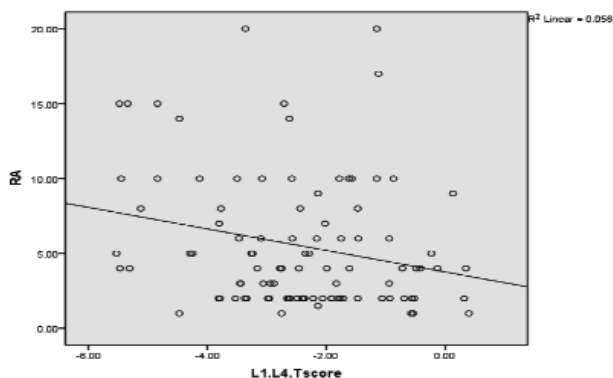
(18.4%) had normal BMD. Furthermore, at the femoral neck region, 17 patients (17.3%) had osteoporosis, 46 patients (46.9%) had osteopenia and 35 patients (35.7%) had normal BMD. The overall prevalence of osteoporosis and osteopenia at both the lumbar spine and femoral neck was 13.3 and 15.3 percent respectively. Only 11.2 % of patients had normal bone mineral density at both the lumbar spine and femoral neck. The more years have passed since menopause the higher would be bone loss at lumbar spine ( $r=0.43$ , P-Value= 0.0001) and femoral neck ( $r= 0.26$ , P-Value= 0.01) [Fig: I, II]. There was a significant correlation between the duration of the disease and bone loss at lumbar spine ( $r=0. 22$ , P-Value=0. 03); such a significant correlation, however, was not reported in the femoral neck region ( $r=0. 15$ , P-Value= 0.12) [Fig III, IV]. There was a positive and significant correlation between age and BMD values at both lumbar spine ( $r= 0.51$ , P-Value ? 0.0001) and femoral neck ( $r= 0.39$ , P-Value? 0.0001) [Fig V, VI].



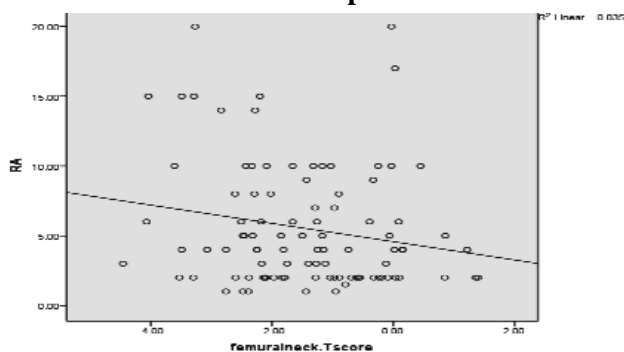
**Fig 1. Correlation between menopause duration and BMD at the lumbar spine**



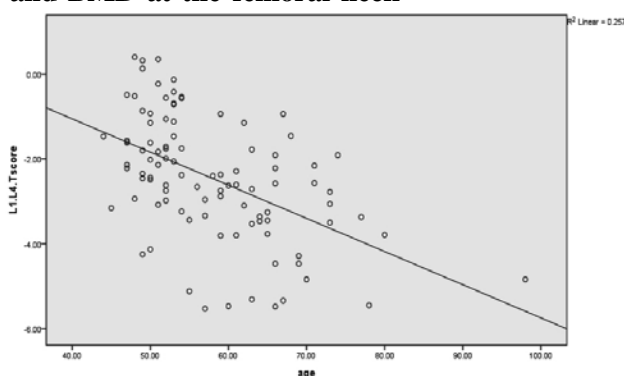
**Fig II. Correlation between menopause duration and BMD at the femoral neck**



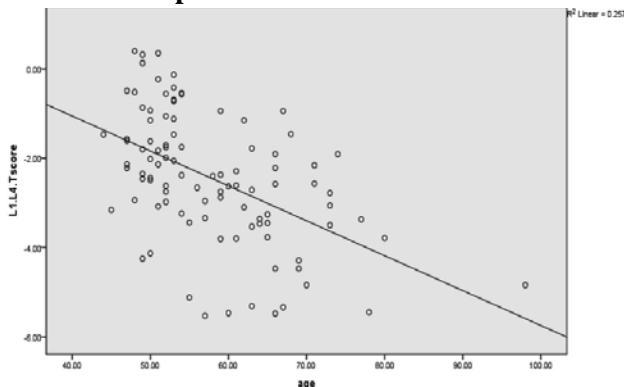
**Fig III: Correlation between duration of disease and BMD at the lumbar spine**



**Fig IV: Correlation between duration of disease and BMD at the femoral neck**



**Fig V: Correlation between age and BMD at the lumbar spine**



**Fig VI: Correlation between age and BMD at the femoral neck**

**TableI: Prevalence of osteoporosis in different places of Iran**

Place	Prevalence of osteoporosis	
	lumbar spine	femoral neck
Booshehr	32	29.6
Khuzestan	5.4	15.3
Kordestan	17	30.8
Yazd	20.5	43
Iran(review)	18.9	18.9

**TableII: Prevalence of osteoporosis in different places of the world**

place	Prevalence of osteoporosis	
	femoral neck	lumbar spine
Japan	11.6	38
Saudi Arabia	6.3	38.3
Canada	7.9	12.1
Japan	27	----

**Discussion**

Our results indicate that 11.2 percent of post-menopausal women with rheumatoid arthritis had normal BMD at the both lumbar spine and femoral neck. This is much lower than that reported in both previous Iranian and international studies<sup>6, 8, 22, 26-31</sup>. “Tables 1, 2” show prevalence of osteoporosis at the lumbar spine and femoral neck in the different places in Iran and world. These discrepancies can be explained based on differences in race, lifestyle and dietary habits of the people of these countries. Several studies in Japan, Brazil<sup>32</sup>, Sweden<sup>33</sup> and Italy<sup>34</sup> have considered the duration of disease as a risk factor for low bone mineral density. Corroborating with our results, some studies have pointed out a significant relation between longer time since menopause and Considering the nature of rheumatoid arthritis, the duration of the disease seems to aggravate the bone loss trend. The present study, however, showed this relation only for the spine, indicating that the duration of disease does not significantly affect bone mineral density values at the FN. Haugeberg et al, on the contrary to our findings, revealed a significant relation between the duration of disease and reduced bone mineral density values at the femoral neck rather than lumbar spine<sup>10</sup>. In line with our study, many

studies have introduced age as an important factor for bone loss<sup>22-23, 35-36, 38, 40-42</sup>. Jang et al showed that the prevalence of osteoporosis in postmenopausal women increases with age from 30.6% in those aged between 45 and 64 to 68.7 percent in those aged 75 and over<sup>43-44</sup>.

### Conclusion

The present research indicated the negative effect of age, number of years since menopause and the duration of rheumatoid arthritis on bone mineral density. So, it is recommended to measure BMD values and implement prevention programs for

high-risk women. In our study, there was no control group and thus we were unable to compare our results between the affected individuals and the general population. Future prospective studies are therefore necessary to gather more accurate information in this regard.

### Acknowledgement

The study was funded by the Department of Research affairs of Golestan University of Medical Sciences. The authors wish to gratefully acknowledge the contribution of all the patients who participated in the study.

### References

1. Ichchou L, Allali F, Rostom S, Bennani L, Hmamouchi I, Abourazzak F Z, Khazzani H, Mansouri L.El, Abouqa R, Hajjaj-Hassouni N. Relationship between spine osteoarthritis, bone mineral density and bone turn over markers in post menopausal women. *BMC Women's Health* 2010; **10**(25):2-7.
2. Raisz LG, Shoukri KG. Pathogenesis of osteoporosis. In: Mundy GR, Martin TJ. *Pharmacology of bone*. New York: Springer-Verlag. 1993: 299-323. [http://dx.doi.org/10.1007/978-3-642-77991-6\\_9](http://dx.doi.org/10.1007/978-3-642-77991-6_9)
3. Kanis JA, Melton LJ, Christiansen C, Johnston CC, Khaltaev N. The diagnosis of osteoporosis. *J Bone Miner Res* 1994; **9**(8):1137-1141. <http://dx.doi.org/10.1002/jbmr.5650090802> PMID:7976495
4. Melton L. J, Chrischilles E. A., Cooper C, Lane A. W, Riggs, B. L. Perspective. How many women have osteoporosis? *Journal of Bone Minerals Research* 1992; **7**(9): 1 0 0 5 - 1 0 1 0 . <http://dx.doi.org/10.1002/jbmr.5650070902> PMID:1414493
5. Baheiraei A, Pocock N A, Eisman J A, Nguyen N D, Nguyen T V, Bone mineral density, body mass index and cigarette smoking among Iranian women: implications for prevention. *BMC Musculoskeletal Disorders* 2005; **6**(34):1-9
6. Bayat N; Haji Amini z, Alishiri Gh, Ebadi A; Hosseini M, Laluee A. Frequency of osteoporosis and osteopenia in Post-Menopausal Military family's women. *JAUMS* 2008;**6**(1): 1-6.
7. Pajoohi M, Hossein Nejad A, Soltani A, Adibi H, Maghbuli G, Larijani B. Changes in bone density and osteoporosis in males 10 to 76 years. *Payesh Journal* 2003; **3**(1): 39-48.
8. Hejazi J, Kolahi S, Mehtadi nia J. The relation between age, weight, BMD and post menopausal age on BMI in post menopausal women. *Journal of Yazd University of Medical Sciences* 2007;**16**(4): 68-74.
9. Momohara Sh, Okamoto H, Yago T, Furuya T, Nanke Y, Kotake Sh and et al. The study of bone mineral density and bone turnover markers in postmenopausal women with active rheumatoid arthritis. *Mod Rheumatol* 2005; **15**:410-414. <http://dx.doi.org/10.1007/s10165-005-0435-5> PMID:17029104
10. Haugeberg G, Uhlig T, Falch JA, Halse JI, Kvien TK. Bone mineral density and frequency of osteoporosis in female patients with RA, results from 394 patients in Oslo County Rheumatoid Arthritis Register. *Arthritis Rheum* 2000; **43**(3):522-530. [http://dx.doi.org/10.1002/1529-0131\(200003\)43:3<522::AID-ANR7>3.0.CO;2-Y](http://dx.doi.org/10.1002/1529-0131(200003)43:3<522::AID-ANR7>3.0.CO;2-Y)
11. Roux C. Osteoporosis in inflammatory joint diseases. *Osteoporos Int* 2011; **22**:421-433. <http://dx.doi.org/10.1007/s00198-010-1319-x> PMID:20552328
12. Brandão L, Ferraz MB, Zerbini CAF. Avaliação da qualidade de vida na artrite reumatóide: revisão atualizada [Evaluation of

- quality of life in rheumatoid arthritis]. *Rev Bras Reumatol* 1997;**37**(5):275-81
13. Pattison DJ, Harrison RA, Symmons DP. The role of diet in susceptibility to rheumatoid arthritis: a systematic review. *J Rheumatol* 2004;**31**(7):1310-9.PMid:15229949
  14. Van Jaarsveld CH, Jacobs JWG, Van Der Veen MJ, Blaauw AAM, Kruize AA, Hofman DM, Brus HLM (2000) Aggressive treatment in early rheumatoid arthritis: a randomised controlled trial. *Ann Rheum Dis*; **59**:468-477. <http://dx.doi.org/10.1136/ard.59.6.468> PMid:10834865 PMCID:1753160
  15. Kroot Eric-Jan J. A, Nieuwenhuizen M.G, Waal Malefijt M.C. de, Riel Piet L. C. M. van, Pieterneel C. M. Pasker-de Jong, and Roland F. J. M. Laan. Change in Bone Mineral Density in Patients With Rheumatoid Arthritis During the First Decade of the Disease. *Arthritis & Rheumatism* 2001; **44**(6): 1254-60. [http://dx.doi.org/10.1002/1529-0131\(200106\)44:6<1254::AID-ART216>3.0.CO;2-G](http://dx.doi.org/10.1002/1529-0131(200106)44:6<1254::AID-ART216>3.0.CO;2-G)
  16. Wijbrandts C A, Klaasen R, W Dijkgraaf M G, Gerlag D M, van Eck-Smit B L F, P P Tak. Bone mineral density in rheumatoid arthritis patients 1 year after adalimumab therapy: arrest of bone loss. *Ann Rheum Dis* 2009;**68**:373-376 <http://dx.doi.org/10.1136/ard.2008.091611> PMid:18408246 PMCID:2945478
  17. Peter E, Lipsky. Rheumatoid Arthritis: Harrison principle of internal medicine. 14th ED: *grow Hill* 2001: 1880-88.
  18. Gabriel SE. The epidemiology of rheumatoid arthritis. *Rheum Dis Clin North Am* 2001; **27**(2): 269-81. [http://dx.doi.org/10.1016/S0889-857X\(05\)70201-5](http://dx.doi.org/10.1016/S0889-857X(05)70201-5)
  19. Lodder MC, Haugeberg G, Lems WF, et al. Radiographic damage associated with low bone mineral density and vertebral deformities in rheumatoid arthritis: the Oslo-Truro-Amsterdam (OSTRA) collaborative study. *Arthritis Rheum* 2003;**49**(2):209-15. <http://dx.doi.org/10.1002/art.10996> PMid:12687512
  20. Larijani B, Resch H, Bonjour JP, Aghai-Meybodi HR, Mohajery-Tehrani MR. Osteoporosis in Iran, Overview and Management. *Iranian J Publ Health* 2007;A supplementary issue on Osteoporosis:1-13.
  21. Bagheri P, Haghdoost A.A, Dortaj Raberi E, Halimi L, Vafaie Zamaneh, Farhangnia M, Shayan L. Meta-analysis of prevalence of osteoporosis in women. *Iranian Journal of Endocrinology and Metabolism* 2011; **13**(3): 315-325
  22. Derakhshan S, Salehi R and Reshadmanesh N. Prevalence of osteoporosis, osteopenia and their related factors in post-menopausal women referring to Kurdistan densitometry center. *Scientific Journal of Kurdistan University of Medical Sciences* 2006; **11**(2):59-67
  23. Mojibian M, Owlia M.B, Beiki Bandarabadi O, Kochak Yazdi L. Osteoporosis in Postmenopausal Women. *Iranian Journal of Surgery* 2006; **14**(1 (36)): 62-70.
  24. Moula K, Esfehiani A.A study of the bone density of Rheumatoid Arthritis patients in Khoozestan province. *Journal of Shaeed Sdoughi University of Medical Sciences Yazd* 2002;**10**(3): 8-12
  25. World Health Organization. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. *Geneva: The organization* 1994. Report no 843.
  26. Jarupanich T. Prevalence and Risk Factors Associated with Osteoporosis in Women Attending Menopause Clinic at Hat Yai Regional Hospital. *J Med Assoc Thai* 2007; **90**(5): 865-9.PMid:17596038
  27. Baig L, Mansuri F.A, Karim S.A. Association of Menopause with Osteopenia and Osteoporosis: Results from Population Based Study Done in Karachi. *Journal of the College of Physicians and Surgeons Pakistan* 2009; **19**(4): 240-244.PMid:19356340
  28. Eghbali S, Nabipour I, Dehghani Z. Prevalence of osteoporosis in women older than 50 years old in Bushehr port. *Iranian South Medical Journal* 2008;**11**(2): 1363-69
  29. Iki M, Kagamimori S, Kagawa Y, Matsuzaki T, Yoneshima H, Marumo F. Bone Mineral Density of the Spine, Hip and Distal Forearm in Representative Samples of the Japanese Female Population: Japanese Population-Based Osteoporosis (JPOS) Study. *Osteoporosis International* 2001; **12**(7): 529-537. <http://dx.doi.org/10.1007/s001980170073> PMid:11527049
  30. Tenenhouse A, Joseph L, Kreiger N, Poliquin

- S, Murray TM, Blondeau L, Berger C, Hanley DA, Prior JC. Estimation of the prevalence of low bone density in Canadian women and men using a population-specific DXA reference standard: the Canadian Multicentre Osteoporosis Study. *Osteoporos Int* 2000; **11**(10): 897-904. <http://dx.doi.org/10.1007/s001980070050> PMID:11199195
31. El-Desouki MI. Osteoporosis in postmenopausal Saudi women using dual X-Ray bone densitometry. *Saudi Med Journal* 2003;**24**:953-956 PMID:12973476
  32. Buttros Dde A, Nahas-Neto J, Nahas EA, Cangussu LM, Barral AB, Kawakami MS. Risk factors for osteoporosis in postmenopausal women from southeast Brazilian. *Rev Bras Ginecol Obstet* 2011;**33**(6):295-302. PMID:21877019
  33. Forsblad d'Elia H, Larsen A, Waltbrand E, Kvist G, Mellström D, Saxne T, Ohlsson C, Nordborg E, Carlsten H. Radiographic joint destruction in postmenopausal rheumatoid arthritis is strongly associated with generalised osteoporosis. *Ann Rheum Dis* 2003; **62**: 617-623. <http://dx.doi.org/10.1136/ard.62.7.617> PMID:12810422 PMCID:1754591
  34. Sinigaglia L, Nervetti A, Mela Q, Bianchi G, Del Puente A, Di Munno O, Frediani B, Cantatore F, Pellerito R, Bartolone S, La Montagna G, Adami S. A multicenter cross sectional study on bone mineral density in rheumatoid arthritis. Italian Study Group on Bone Mass in Rheumatoid Arthritis. *J Rheumatol* 2000; **27**(11):2582-9. PMID:11093437
  35. Namwongprom S, Ekmahachai M, Vilasdechanon N, Klaipetch A, Wongboontan C, Boonyaprapa S. Bone Mineral Density: Correlation between the Lumbar Spine, Proximal Femur and Radius in Northern Thai Women. *J Med Assoc Thai* 2011; **94**(6): 725-31. PMID:21696083
  36. Pinheiro M.M, Reis Neto E.T, Machado F.S, Omura F, Yang J.H K, Szejnfeld I J, Szejnfeld V.L. Risk factors for osteoporotic fractures and low bone density in pre and postmenopausal women. *Rev Saúde Pública* 2010; **44**(3):479-85. <http://dx.doi.org/10.1590/S0034-89102010000300011> PMID:20549019
  37. Szejnfeld VL, Atra E, Baracat EC, Aldrighi JM, Civitelli R. Bone density in white Brazilian women: rapid loss at the time around the menopause. *Calcif Tissue Int* 1995;**56**(3):186-91. <http://dx.doi.org/10.1007/BF00298607> PMID:7750021
  38. Meiyanti. Epidemiology of osteoporosis in postmenopausal women aged 47 to 60 years. *Universa Medicina* 2010; **29**(3): 169-176.
  39. Mamji M. F, Hasan J. A, Sabri. M. S. Risk factors for osteoporosis in postmenopausal women with hip fractures. *Journal of Surgery Pakistan (International)* 2010; **15**(2):82-86.
  40. Jamshidian-Tehrani M, Kalantari N, Azadbakht L, Esmailzadeh A, Rajaie A, Houshiar-rad A, Golestan B and Kamali Z. Osteoporosis risk factors in Tehrani women aged 40-60 years. *Endocrinology and Metabolism* 2004; **6**(2):139-145.
  41. Heidari Z, Zyaie S, Moghassemi S. The relationship between BMI and reproductive histories and bone density in postmenopausal women. *Arak Medical University Journal (AMUJ)* 2010; **13**(3): 53-60.
  42. Zhang HC, Kushida K, Atsumi K, Kin K, Nagano A. Effects of age and menopause on spinal bone mineral density in Japanese women: a ten-year prospective study. *Calcif Tissue Int* 2002; **70**(3):153-7. <http://dx.doi.org/10.1007/s00223-001-1037-7> PMID:11907711
  43. Jang SN, Choi YH, Choi MG, Kang SH, Jeong JY, Choi YJ, Kim DH. Prevalence and associated factors of osteoporosis among postmenopausal women in Chuncheon: Hallym Aging Study (HAS). *J Prev Med Public Health* 2006;**39**(5):389-96.
  44. M Shaheen, R Sharma. Misoprostol - A Wonder Drug. *Bangladesh Journal of Medical Science* 2011; **10**(4): 221-225. <http://dx.doi.org/10.3329/bjms.v10i4.9490>