International Journal of Community Medicine and Public Health
Asadollahi M et al. Int J Community Med Public Health. 2021 Mar;8(3):1099-1103
http://www.ijcmph.com
pISSN 2394-6032 | eISSN 2394-6040

DOI: https://dx.doi.org/10.18203/2394-6040.ijcmph20210787

Original Research Article

Frequency of osteopenia and osteoporosis in patients with multiple sclerosis

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Received: 06 November 2020
Revised: 30 December 2020
Accepted: 02 January 2021

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ABSTRACT

Background: Multiple sclerosis (MS) is one of the most important diseases of the central nervous system and one of the main causes of disability in young and middle age groups. Recent studies show that the risk of osteoporosis and osteopenia in MS patients is higher than the normal population which could be related to many factors. The aim of this study was to determine the frequency of osteopenia and osteoporosis among MS patients.
Methods: This descriptive cross-sectional study was performed on 30 patients with MS. Bone density of patients was assessed by bone mineral density (BMD) method. Necessary demographic and clinical information were collected by a checklist and then analyzed by statistical methods in SPSS version 16.
Results: Of all patients, 36.7% had osteoporosis and osteopenia. According to the results, 86.6% of patients had a decrease in bone density in the pelvic region and 50% in the lumbar spine. 43.3% of patients had osteopenia in the pelvic region and 36.7% in the lumbar spine.
Conclusions: The results showed that BMD was high in MS patients. Due to the problems of walking and lack of balance in these patients and the high probability of falling and fractures among them, paying attention to the problem of osteoporosis by early and repeated performing of BMD.

Keywords: BMD, Interferon, Multiple Sclerosis, Osteopenia, Osteoporosis

INTRODUCTION

MS is a chronic inflammatory disease that effects the brain and spinal cord and causes symptoms such as weakness, imbalance, sensory problems, vision and cognitive problems and gradually limits the patient's performance.[1] The disease has a recurrent or progressive nature and it often involves young people and activists in society and its prevalence is higher in women than men.[2] Patients with MS have several complications during their illness which one of them is osteoporosis. Secondary osteoporosis and mild fractures are more common in MS patients than in the general people.[3,4] Recent studies have shown that some cell types, especially T cells, play a key role in osteoporosis.[5] In inflammatory and autoimmune diseases, T cells are activated and cause bone damage, especially in certain conditions such as estrogen deficiency. Bone regeneration occurs continuously throughout life and bone strength is maintained by removing the damaged bone and replacing it with new bone and this keeps the bone structure stable. This process depends on the production and normal function of osteoclast, osteoblast and osteocyte.[6] MS disease by impact on normal metabolism and bone regeneration cause to reducing bone density and quality and its susceptibility to fracture.[1,7] Imbalance and weakness

caused by the disease, cause to frequent falls of patients and fatigue and muscle weakness also reduce the activity and stimulus of patients.[8] Decreased stimulus and physical activity put mechanical stress on the bone, which causes an imbalance in bone regeneration and destruction of the osteocyte networks.[9] In addition to acquired factors, non-acquired factors such as gender also play a role in the development of osteoporosis in MS patients. Studies have shown that bone density is lower in sick women than in sick men.[10,11] Drugs such as glucocorticoids and other immunomodulatory drugs used to treat MS also play a role in causing osteoporosis.[12,13] Epidemiological studies have shown that the risk of bone fracture after oral treatment with glucocorticoids depending on the dose of the drug, increases the duration of its use.[14] The role of vitamin D in bone homeostasis is well known and the use of vitamin D to prevent and treat osteoporosis is obvious and MS patients have a higher prevalence of vitamin D deficiency than other people.[15,16] Depression is another complication of multiple sclerosis which cause to non-receiving proper treatment and reduces stimulus.[17] The use of antidepressants is common in MS patients due to secondary depression. Serotonin antidepressants are associated with a high risk of fractures in osteoporosis. The degree and duration of disability of MS patients which measured by EDSS are the most important factors determining the rate of osteoporosis in MS patients, which is related to their BMD.[16] BMD is a method of measuring bone density using X-rays. It measures bone density and determines bone fragility before a fracture occurs. In EDSS below 6, the patient has good dynamic function, in EDSS about 5-6, patients can walk a few meters with mutual assistance and in EDSS equal seven, a patient needs a wheelchair. In EDSS above seven, patients should be screened intermittently for BMD.

Decreased physical functioning, pain, excessive fatigue, suboptimal nutrition (particularly low vitamin D), and adverse effects of medications are among the many factors contributing to bone loss in MS.[18]

Despite the fact that MS patients are at high risk of bone fractures and in case of fractures, their problems are added and they enter a vicious cycle that leads to both increased osteoporosis and disability, unfortunately the evaluation of bone health in MS patients is often forgotten and is not part of the treatment protocol of patients, therefore, by conducting this study we decided to estimate the frequency of osteoporosis and osteopenia among patients with MS.

METHODS

This descriptive cross-sectional study was performed on 30 MS patients selected randomly by random sampling method from all patients with MS who referred to the neurology clinic of Loghman Hakim Hospital in Tehran from April 2016 to April 2018.

Inclusion criteria

Inclusion criteria included patients' consent to participate in the study and MS-confirmed disease based on history, examination and MRI results which confirmed by a physician.

Exclusion criteria

Patients with inflammatory and systemic diseases such as autoimmune and endocrine diseases were excluded from the study.

Data collection method

Data collection method through a checklist containing demographic information such as age and sex and clinical information such as duration of disease, disease progression or RR, corticosteroids and interferon intake, BMI (kg/m^2), serum level test results Vitamin D ng/mm and EDSS. Bone mineral density was measured based on the BMD evaluation system at the same center and dynamic function was based on the EDSS scoring system, which was graded from one to 10 depending on the severity of the conflict. T score between -1 and -5 was considered as osteopenia and less than -2.5 was considered as osteoporosis.

Statistical analysis

The collected data were analyzed using SPSS16 and Chi-Square, Mann-Whitney and Kruskal-Wallis statistical tests and $p<0.05$ was considered as significant.

Ethical approval

The result of this study extracted from MD. Fellow thesis in neurology and approved by Shahid Beheshti University of Medical Sciences, Tehran, Iran.

RESULTS

Of 30 patients, 60% were female and the rest were male. 36.7% of all patients had osteoporosis and osteopenia.

The average age of patients was 36.2±9.5 years (range: 21-55). 10% of patients had BMI above 30 that all of whom had osteopenia. The average age of patients with normal BMI was 35.2±9 and high BMI was 10.6±39 years and the difference was not statistically significant. 66.7% of patients were taking interferon and the difference between three healthy, osteoprotic and osteopeniac groups was significant. Glucocorticoids use also showed that 43.4% of patients had 3-5 pulses per day. By measurement of serum vitamin D levels results showed that the majority of patients, especially patients with osteoporosis, had low levels of vitamin D. EDSS was 23.3% of patients from 6-7 that most of whom were generally seen in the osteopenia group (Table 1).

Table 1: Compare the characteristics of patients with osteoporosis and osteopenia.

Parameters	Condition	Total		Osteoporosis		Osteopenia		Normal		P value
		%	N	%	N	%	N	%	N	
Sex	Man	40	12	20	6	16.7	5	3.3	1	0.74
	Woman	60	18	10	3	26.7	8	23.3	7	
BMI	<30	90	27	43.3	13	33.3	10	13.3	4	0.128
	>30	10	3	0	0	10	3	0	0	
EDSS	<6	70	21	30	9	26.7	8	13.3	4	0.12
	06-7	23.3	7	0	0	16.6	5	6.7	2	
	>7	6.7	2	0	0	0	0	6.7	2	
Duration	New case	16.7	5	6.7	2	6.7	2	3.3	1	0.41
	<5 years	20	6	10	3	3.3	1	6.7	2	
	>5 years	60	18	26.7	8	30	9	3.3	1	
Course	Relapsing-remitting	53.3	16	20	6	20	6	13.3	4	0.17
	Progressive	40	12	20	6	20	6	0	0	
Interferon	Users	66.7	20	20	6	36.7	11	10	3	0.047
Use	Non users	30	9	23.3	7	3.3	1	3.3	1	
Glucocorticoid Use	<3 pulse	40	12	20	6	13.3	4	6.7	2	0.84
	3-5 pulse	43.4	13	16.7	5	20	6	6.7	2	
	>5 pulse	10	3	0	0	3.3	1	6.7	2	
	Chronic oral use	3.3	1	0	0	3.3	1	0	0	
Vitamin D Level	Normal	20	6	10	3	6.7	2	3.3	1	0.97
	Low	70	21	33.3	10	26.7	8	10	3	

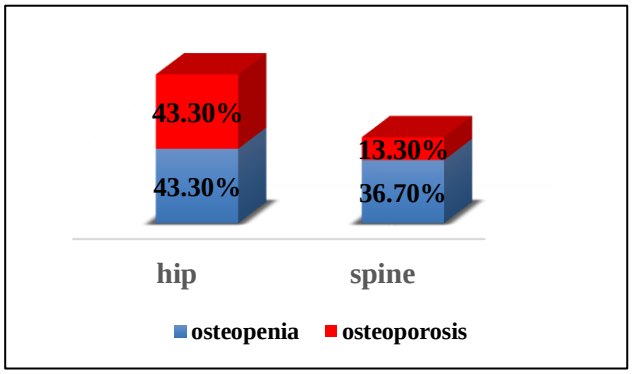

Figure 1. Frequency of osteoporosis and osteopenia by involvement location.

Of 30 patients, 86.6% had osteopenia or osteoporosis that all of whom had a decrease in bone density in the pelvic region and 15 (50%) in the lumbar spine. 43.3% of patients had osteopenia in the pelvic region and 36.7% in the lumbar spine (Figure 1). The average age of patients with normal bone density was 34.8±13.4 years, in osteopenia patients was 35.7±8.2 and in osteoporosis patients was 37.2±10.2 but the difference between them was not statistically significant.

DISCUSSION

In healthy people, bone mass increases up to age of 25-30 and begins to decline after the age of 40.19 This decline occurs in both age dependent sexes. In the present study, 36.7% of all patients in both sexes had a decrease in bone density, osteopenia and osteoporosis but the decrease in BMD was not related to gender. Maximum bone mass per person depends on various causes that about 70% of which depend on hereditary factors and about 30% to environmental factors such as physical activity, hormone status, amount of vitamins and minerals needed for bone metabolism, chronic diseases and effective drugs on bone building.[20] The results of this study showed that 86.6% of people with MS have a decrease in bone density. Agha Ali et al in a study on patients over 60 years of age showed that the prevalence of osteoporosis was 19.9% and osteopenia was 36.2% which was lower than the present study and this statistics confirm that the prevalence of osteoporosis and osteopenia in ms patients is more than normal people over 60 years.[21]

In a study by Sioka et al, found that multiple sclerosis was associated with decreased bone mass and a high incidence of osteoporosis.[22] Another study by Marie et al in 2009 on 9,346 people at the North American Research Center found that 27.2% of MS patients had reduced bone mass and 15% had fractures. They also showed that MS patients often have high risk factors for bone loss and fractures.[12] In this study, all patients in the pelvic region and 15 patients (50%) in the lumbar spine had a decrease in bone density. In a 2011 study on 99 patients and 159 controls, Moen et al found that 50.5% of patients and 37.1% of controls had osteoporosis or osteopenia, which was more common in the lumbar spine and pelvis.[23] The results of the present study showed that the rate of

osteopenia and osteoporosis in the pelvic bones was significantly higher than the bones of the lumbar spine , which is consistent with the results of other studies in this regard.[24,25] In this study, no significant relationship was found between serum vitamin D levels and osteoporosis, but 60% of patients with osteopenia and osteoporosis had low vitamin D levels. According to studies, markers of bone metabolism such as vitamin D and calcium levels are not a reliable and suitable method for diagnosing of osteoporosis in patients.[26] But in a study by Nieves, there was a significant association between low levels of vitamin D and low BMD.[25] In this study similar to Zorzon study on 25 MS patients, there was no relationship between patients' BMD and corticosteroids.[27] In this study the rate of osteoporosis in both the pelvic and lumbar spine was lower in those who took interferon than in those who were not treated with the drug , which was more especially in the pelvis . Interferon beta increases BMD through its inhibitory effect on osteoclasts.[28] Compman et al showed that, the Z score of patients treated and untreated with interferon was not different. The difference in the results of these studies was probably due to differences in the number of patients, the duration of the disease and other factors influencing BMD.[29] According to the results of this study, there was an inverse relationship between EDSS and BMD and by increasing EDSS the patient's BMD decreased, especially in the lumbar spine. More serious motor problems and more severe gait disorders due to inactivity and immobility are likely to reduce bone density in this group of patients. These results show that the lower the patient's dynamic were correlated with the lower the pelvic and lumbar spine BMD.16 But in some studies, there was no significant relationship between EDSS and BMD.[30]

CONCLUSION

The results of the present study showed that the frequency of osteopenia and osteoporosis in MS patients was higher than normal people. Due to the problems of walking and lack of balance in these patients and the high probability of falling and fractures among them, paying attention to the problem of osteoporosis by early and repeated performing of BMD will cause timely diagnosis and treatment of patients with osteoporosis and osteopenia.

Therefore it is suggested that all MS patients should be considered in the high risk group and by considering the risk factors such as vitamin D deficiency and upper EDSS, all patients should be evaluated for osteopenia and osteoporosis. Despite the importance of this issue, there is still no guideline on BMD in MS patients and more studies are needed to develop such a guideline.

Finally, it will propose a strategy for timely assessment and early management of osteoporosis due to all forms of MS, processes which can be initiated during inpatient rehabilitation and continued in either long-term care or in a community setting.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Brouwers JEM, Lambers FM, Rietbergen B, Ito K, Huiskes R. Comparison of bone loss induced by ovariectomy and neurectomy in rats analyzed by in vivo micro-CT. J Orthop Res. 2009;27(11):1521-7.
2. Siva A, Kantarci O. An introduction to the clinical spectrum of inflammatory demyelinating disorders of the central nervous system. Front Mult Scler. 1999;2:1-9.
3. Marrie RA, Cutter G, Tyry T, Vollmer T. A cross-sectional study of bone health in multiple sclerosis. Neurology. AAN Enterprises. 2009;73(17):1394-8.
4. Cosman F, Nieves J, Komar L, Ferrer G, Herbert J, Formica C, et al. Fracture history and bone loss in patients with MS. Neurology. AAN Enterprises. 1998;51(4):1161-5.
5. Yuan FL, Li X, Lu WG, Xu RS, Zhao YQ, Li CW, et al. Regulatory T cells as a potent target for controlling bone loss. Biochem Biophys Res Commun. 2010;402(2):173-6.
6. Seeman E. Bone modeling and remodeling. Crit Rev Eukaryot Gene Expr. 2009;19(3):82-94.
7. Epstein S, Inzerillo AM, Caminis J, Zaidi M. Disorders associated with acute rapid and severe bone loss. J Bone Miner Res. 2003;18(12):2083-94.
8. Krupp LB, Serafin DJ, Christodoulou C. Multiple sclerosis-associated fatigue. Informa Healthcare London; 2010.
9. Hughes JM, Petit M. Biological underpinnings of frost's mechanostat thresholds: the important role of osteocytes. J Musculoskelet Neuronal Interact. 2010;10(2):128-35.
10. Smeltzer SC, Zimmerman V, Capriotti T. Osteoporosis risk and low bone mineral density in women with physical disabilities. Arch Phys Med Rehabil. 2015;86(3):582-6.
11. Garland DE, Adkins RH, Stewart CA, Ashford R, Vigil D. Regional Osteoporosis in Women Who Have a Complete Spinal Cord Injury. J Bone Surg. 2001;83(8):1195-200.
12. Marrie RA, Cutter G, Tyry T, Vollmer T. A cross-sectional study of bone health in multiple sclerosis. Neurology. AAN Enterprises. 2009;73(17):1394-8.
13. Weinstock GB, Gallagher E, Baier M, Green L, Feichter J, Patrick K, et al. Risk of bone loss in men with multiple sclerosis. Mult Scler. 2004;10(2):170-5.
14. Staa TP, Leufkens HGM, Abenhaim L, Zhang B, Cooper C. Oral corticosteroids and fracture risk: relationship to daily and cumulative doses. Rheumatology. Br Soc Rheumatology. 2000;39(12):1383-9.
15. Lips P, Bouillon R, Schoor NM, Vanderschueren D, Verschueren S, Kuchuk N, et al. Reducing fracture

risk with calcium and vitamin D. Clin Endocrinol. 2010;73(3):277-85.
16. Cosman F, Nieves J, Komar L, Ferrer G, Herbert J, Formica C, et al. Fracture history and bone loss in patients with MS. Neurology. AAN Enterprises. 1998;51(4):1161-5.
17. Alajbegovic A, Loga N, Tiro N, Alajbegovic S, Todorovic L. Depression in multiple sclerosis patients. Med Arch. 2011;65(2):115.
18. Oleson CV. Osteoporosis in Multiple Sclerosis. In: Osteoporosis Rehabilitation. Springer, Cham. 2017.
19. Poole KES, Compston JE. Osteoporosis and its management. British Med J. 2006;6:1251-6.
20. Kampman MT, Eriksen EF, Holmøy T. Multiple sclerosis, a cause of secondary osteoporosis? What is the evidence and what are the clinical implications? Acta Neurol Scand. 2011;124:44-9.
21. Agha M, Taheri P, Hossain A, Mosavi M, Reza M, Amini Y, et al. Prevalence of osteoporosis among above 60 years old subjects referred to Ayatollah Taleghani hospital in Tehran and its relationship with age and sex. SJIMU. 2013;20(5):94-102.
22. Sioka C, Kyritsis AP, Fotopoulos A. Multiple sclerosis, osteoporosis, and vitamin D. J Neurol Sci. 2009;287(1-2):1-6.
23. Moen SM, Celius EG, Sandvik L, Nordsletten L, Eriksen EF, Holmøy T. Low bone mass in newly diagnosed multiple sclerosis and clinically isolated syndrome. Neurology. 2011;77(2):151-7.
24. Ozgocmen S, Bulut S, Ilhan N, Gulkesen A, Ardicoglu O, Özkan Y. Vitamin D deficiency and reduced bone mineral density in multiple sclerosis: effect of ambulatory status and functional capacity. J Bone Miner Metab. 2005;23(4):309-13.
25. Nieves J, Cosman F, Herbert J, Shen V, Lindsay R. High prevalence of vitamin D deficiency and reduced bone mass in multiple sclerosis. Neurology. 1994;44(9):1687.
26. Yuan FL, Li X, Lu WG, Xu RS, Zhao YQ, Li CW, et al. Regulatory T cells as a potent target for controlling bone loss. Biochem Biophys Res Commun. 2010;402(2):173-6.
27. Zorzon M, Zivadinov R, Locatelli L, Giuntini D, Toncic M, Bosco A, et al. Long-term effects of intravenous high dose methylprednisolone pulses on bone mineral density in patients with multiple sclerosis. Eur J Neurol. Blackwell Science Ltd. 2005;12(7):550-6.
28. Abraham AK, Ramanathan M, Guttman B, Mager DE. Mechanisms of interferon-β effects on bone homeostasis. Biochem Pharmacol. 2009;77(12):1757-62.
29. Kampman MT, Eriksen EF, Holmøy T. Multiple sclerosis, a cause of secondary osteoporosis? What is the evidence and what are the clinical implications? Acta Neurol Scand. 2011;124:44-9.
30. Schwid SR, Goodman AD, Puzas JE, McDermott MP, Mattson DH. Sporadic corticosteroid pulses and osteoporosis in multiple sclerosis. Arch Neurol. 1996;53(8):753-7.

Cite this article as: Asadollahi M, Hamed Z, Gharagozli K, Atalu A, Nemati B. Frequency of osteopenia and osteoporosis in patients with multiple sclerosis. Int J Community Med Public Health 2021;8:1099-103.