

Is Hypovitaminosis D Associated with Increased Pain in Patients with Knee Osteoarthritis?

MK. Jnyah^{1*}, I. El Mezouar¹, N. Akasbi¹, T. Harzy¹

¹Department of Rheumatology, University Hospital Center Hassan II of Fez, Faculty of Medicine, Dentistry and Pharmacy Sidi Mohamed Ben Abdellah of Fez, Morocco

DOI: [10.36347/sasjm.2024.v10i07.005](https://doi.org/10.36347/sasjm.2024.v10i07.005)

| Received: 25.05.2024 | Accepted: 29.06.2024 | Published: 03.07.2024

*Corresponding author: MK. Jnyah

Department of Rheumatology, University Hospital Center Hassan II of Fez, Faculty of Medicine, Dentistry and Pharmacy Sidi Mohamed Ben Abdellah of Fez, Morocco

Abstract

Original Research Article

Objective: Osteoarthritis is considered the most frequent joint pathology mostly interesting the knee. Hypovitaminosis D, frequent during postmenopausal period, is usually found during osteoarthritis. The aim of this study was to investigate a possible association between hypovitaminosis D in patients followed for knee osteoarthritis and an increase in pain.

Material and Methods: This is a retrospective descriptive and analytical study including 228 patients followed up for knee osteoarthritis in rheumatology consultation between January 2021 and February 2023. Patients who received vitamin D supplementation were excluded. **Results:** Of 385 patients with knee osteoarthritis, 228 had a vitamin D dosage and were subject of our study. The average age was 60.15±11.17 years. 205 of these patients were women (91%) and 23 were men (9%). The mean duration of progression of knee osteoarthritis was 5.61±3.6 years. Vitamin D deficiency (<30ng/L) was observed in 89.5% and only 10.5% had normal vitamin D levels. 94.3% were on analgesic treatment and 54.2% on non-steroidal anti-inflammatory drugs. In univariate analysis, a low vitamin D level was strongly associated with painful knee osteoarthritis with the use of anti-inflammatory drugs and conventional analgesics with an Odds Ratio and a p respectively at OR=2.774(1.05-7.27) - p=0.03 and OR=3.44 (1.41-8.39) - p=0.004. **Conclusion:** According to our study, the association of hypovitaminosis D and knee osteoarthritis could be responsible of an increase in pain in our patients explaining an increased use of analgesics and anti-inflammatory drugs (NSAID).

Keywords: Osteoarthritis, Hypovitaminosis D, knee osteoarthritis.

Copyright © 2024 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

INTRODUCTION

Osteoarthritis is one of the leading causes of physical disability worldwide and affects about 30% of the global population [1]. Pain is a cardinal sign in osteoarthritis, earlier than joint stiffness or functional limitation. In Europe, up to 20% of consultations for chronic pain are related to osteoarthritis. Because of its negative influence on physical mobility, it contributes to the sedentary lifestyle and the development of metabolic diseases, whose socio-economic and psychological impact is major [2]. With the increase in lifespan and increasing overweight, the number of people suffering from osteoarthritis pain is constantly growing.

Osteoarthritis is a heterogeneous disease with a complex pathogenesis, subject to multiple exogenous and endogenous influences. Moreover, each joint may show specific effects of these influences [3]. While mechanical factors play a key role in lower limb joints, they are rather metabolic or genetic factors that

predominate for the joints of the hands or vertebral facets [3].

Hypovitaminosis D, the prerogative of menopausal women, is frequently found during knee osteoarthritis.

A rate greater than 30ng/L is considered a normal rate, the deficit corresponds to a rate between 10 and 30 ng/L, and a deficiency corresponds to a rate less than 10 ng/L.

Vitamin D deficiency is common and underdiagnosed. Globally, it is estimated that one billion people would have such a deficit [4]. In Western countries, more than 40% of the population over the age of 50 would have a deficit. In Europe, a study showed that 80% of the elderly had rates of 25(OH)D below 30 ng/ml [5].

Therefore, the aim of this study was to identify a possible association between hypovitaminosis D in patients followed for knee osteoarthritis and an increase in pain.

MATERIALS AND METHODS

This is a descriptive and analytical retrospective study including 228 patients followed for knee osteoarthritis in rheumatology between January 2021 and February 2023. All patients who received vitamin D supplementation were excluded.

The different parameters analyzed were: age, sex, socioeconomic level, smoking, alcohol, diabetes, arterial hypertension, surgical history, cardiovascular disease, dyslipidemia, rheumatic diseases, digital osteoarthritis, spinal osteoarthritis, neoplasia, dysthyroiditis, osteoporosis, duration of evolution, notion of cracking on examination, use of NSAIDs, analgesics, Anti Arthritis drugs, viscosupplementation, infiltration, rehabilitation.

The data was collected through the Hosix computerized file system.

The data was rated, entered into the Excel 2010 software and analyzed using the Epi info 3.4 version 2007 software.

Initially, qualitative variables were described in terms of proportions and quantitative variables in terms of mean standard deviation.

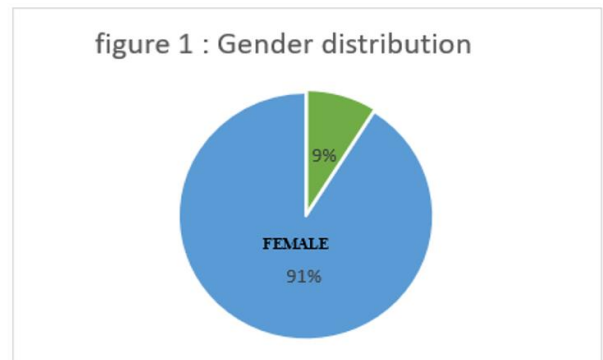
In a second step, a varied uni analysis was carried out to study the association between

hypovitaminosis D and the use of NSAIDs and analgesics and various other parameters (sex, age, ...).

The statistical tests used are khi 2 for percentage comparison and a p value <0.05 was considered statistically significant.

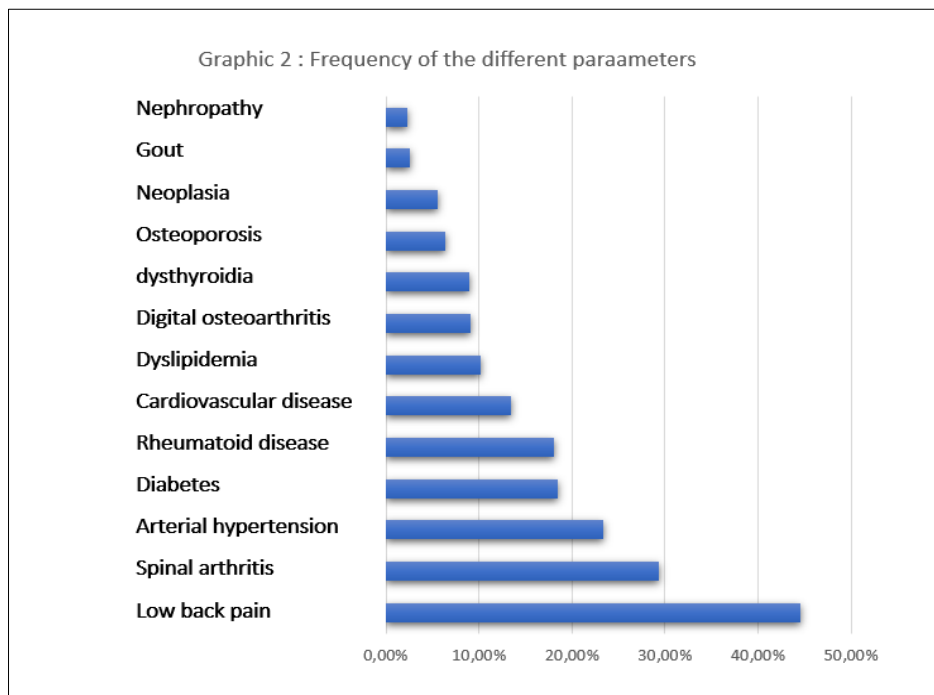
RESULTS

The age of patients collected in our study ranged from 22 to 89 years with an average of 60.15 years +/- 11.17 years. 91% of our sample was female, compared to 9% male as shown in Figure 1.



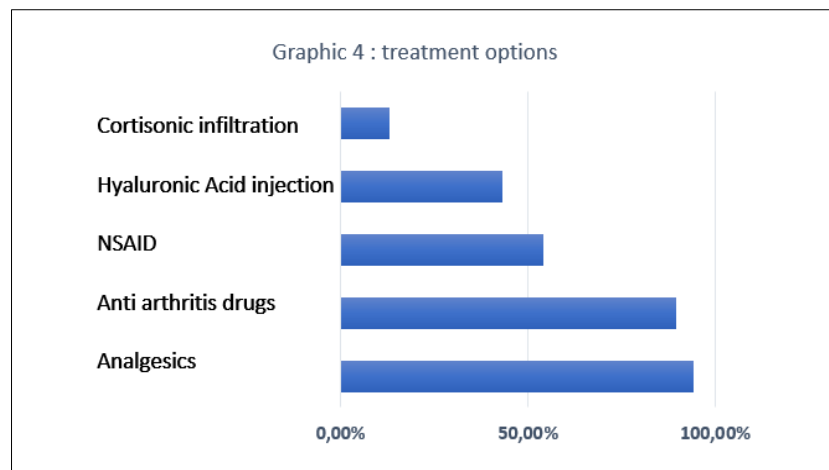
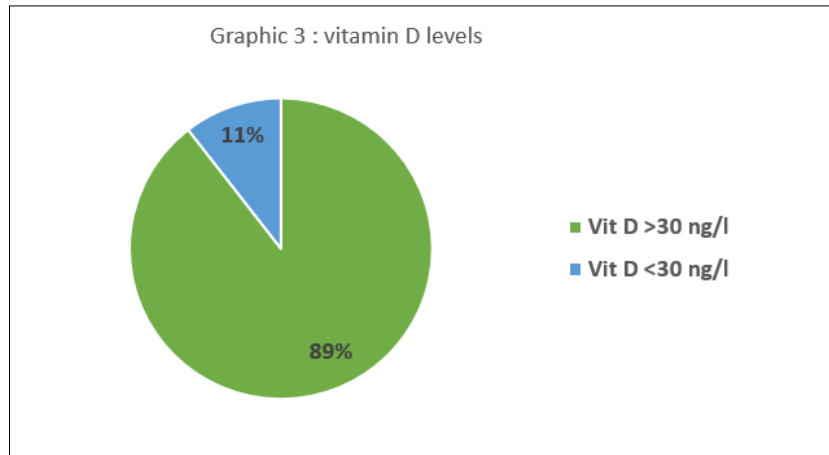
Regarding the socio-economic level 79% of patients had health coverage.

Regarding the history, 23% of our patients were hypertensive, 13.5% had a cardiovascular disease, 10.2% were followed for dyslipidemia, 18% had rheumatism, 9% had digital osteoarthritis, 29.4% spinal arthritis. 43% were sedentary and 53.9% were obese as shown in Figure 2.



About knee osteoarthritis, the average duration of evolution was 5.61years+/-3.6 years. A vitamin D deficiency (<30ng/L) was observed in 89.5% of our patients compared to 10.5% who had a normal vitamin D level (figure 3). 94.3% were under analgesic treatment

and 54.2% under non-steroidal anti-inflammatory drugs. 56.8% had previously benefited from viscosupplementation, 13% from cortisone infiltration and 89.6% were under AASAL as disposed in Figure 4.



On clinical examination, 93.8% of our patients had a positive plane sign, 12% had an effusion, 45.6% had a cracking when mobilizing the knee.

On radiography, 89.1% had internal femorotibial osteoarthritis, 36.7% external femorotibial osteoarthritis, 25.5% femoropatellar osteoarthritis.

A low vitamin D level was strongly associated with a painful knee osteoarthritis with use of anti-inflammatories with a Odds Ratio and a p respectively a OR=2.774 (1.05-7.27), p=0.03. In this sense, a statistically significant association was found between hypovitaminosis D and the use of analgesics with an OR=3.44 (1.41-8.39) p=0.004.

A statistically significant association was also observed between hypovitaminosis D during knee osteoarthritis and: cracking on clinical examination p=0.04.

Nevertheless, no association was found between hypovitaminosis D during knee osteoarthritis and the following parameters: age, comorbidities, sedentary lifestyle, low back pain, duration of evolution, side reached, static disorder, presence of joint effusion.

	p	OR (IC 95%)
NSAIDS	0,030	2,774 (1,05-7,27)
Analgesics	0,004	3,440 (1,41-8,39)
Cracking	0,040	-
Age	0,213	-
Comorbidities	0,569	-
Sedentary lifestyle	0,289	-
Low back pain	0,871	-

DISCUSSION

The aim of this study was to determine whether low levels of vitamin D is associated with an increase in knee osteoarthritis pain.

Our study did demonstrate a statistically significant association between low vitamin D levels and increased pain in these patients explaining an increased use of analgesic and nonsteroidal anti-inflammatory drugs. However, to our knowledge, no studies have investigated the association between hypovitaminosis D and increased pain in patients with knee osteoarthritis.

In this sense, a meta-analysis covering 81 observational studies and no less than 50834 participants was interested in the association between hypovitaminosis D and pain conditions in observational studies. The results suggested that low levels of vitamin D were associated with muscle and osteoarticular diseases including arthritis and muscle pain [6], which was consistent with our results.

Another study aimed to find a possible association between low levels of vitamin D and musculoskeletal pain. Indeed, patients with hypovitaminosis D had a 20% higher risk of suffering from pain [7]. A British study showed that 25-OHD levels were also lower in patients with fibromyalgia than in patients with other rheumatic disorders meaning a direct association between pain and low vitamin D levels [8].

In studies of clinic patients with fibromyalgia, up to half or all participants have been reported to have 'low' (<50 and <20 ng/ml, respectively) serum 25-(OH)D [9-11]. Another study showed low levels of vit D in both patients with osteoarthritis and patients with diffuse pain [12].

In contrast, another study explored the association between vitamin D and risk factors for knee pain in 3,874 participants over the age of 65 [13]. It turned out that vitamin D was not related to an increase in knee pain, which is inconsistent with our results. This discrepancy could be explained by the difference in the study population. Indeed, this study focused mainly on a healthy population not followed for knee osteoarthritis.

What clinical ramifications do these findings have? It has been recommended that all chronic pain patients should undergo screening for low vitamin D levels, although doing so is probably going to be costly [14].

In a small experiment, 25 patients were randomly assigned to receive placebo treatment and 25 patients to receive treatment with 50 000 IU of vitamin D2 (ergocalciferol) once a week. The trial identified patients with fibromyalgia with levels of 25-(OH)D between 9 and 20 ng/ml [12]. Three months later, mean 25-(OH)D levels were significantly higher in the active treatment group (31.2 ng/ml) than in the placebo group (19.3 ng/ml), but there was no change in pain or functional capacity related to pain nor pain-related functional capacity improved. These findings support the

theory that vitamin D deficiency may be a marker for other pain-related variables. However, regardless of the cause of the low vitamin D levels, people with chronic pain face long-term consequences that include reduced bone density and poor general health.

Certainly, our study has some limitations: Indeed, our sample is relatively small focusing on a predominantly female population from a single region which will not allow generalization. But in the other hand, we should not that this study chose an objective way to assess knee pain by looking into the use of NSAID and analgesic.

CONCLUSION

Our study showed that low vitamin D levels are associated with more painful knee osteoarthritis. Therefore, other studies should be interested in this subject given the absence of similar studies and the importance of vitamin D supplementation to allow a better quality of life for patients followed for knee osteoarthritis.

REFERENCES

1. Neogi, T. (2013). The epidemiology and impact of pain in osteoarthritis. *Osteoarthritis Cartilage*, 21, 1145-53. DOI: 10.1016/j.joca.2013.03.018 <https://pubmed.ncbi.nlm.nih.gov/23973124/>
2. Gupta, S., Hawker, G. A., & Laporte, A. (2005). The economic burden of disabling hip and knee osteoarthritis (OA) from the perspective of individuals living with this condition. *Rheumatol(Oxford)*, 44, 1531-37. DOI:10.1093/rheumatology/kei049 <https://pubmed.ncbi.nlm.nih.gov/16091394/>
3. Heim, C. (2018, June 20). Douleurs et arthrose. *Revue Medicale Suisse*. DOI: 10.53738/REVMED.2018.14.612.1287 <https://www.revmed.ch/revue-medicale-suisse/2018/revue-medicale-suisse-612/douleurs-et-arthrose#tab=tab-references>
4. Holick, M. F. (2007). Vitamin D deficiency. *N Engl J Med*, 357, 266-81. DOI: 10.1056/NEJMra070553 <https://pubmed.ncbi.nlm.nih.gov/17634462/>
5. Van der Wielen, R. P., De Groot, L. C. P. G. M., Van Staveren, W. A., Löwik, M. R. H., Van den Berg, H., Haller, J., & Moreiras, O. (1995). Serum vitamin D concentrations among elderly people in Europe. *The Lancet*, 346(8969), 207-210. DOI: 10.1016/s0140-6736(95)91266-5 <https://pubmed.ncbi.nlm.nih.gov/7616799/>
6. Wu, Z., Malihi, Z., Stewart, A. W., Lawes, C. M., & Scragg, R. (2018). The association between vitamin D concentration and pain: a systematic review and meta-analysis. *Public Health Nutrition*, [online] 21(11), pp.2022-2037. DOI: 10.1017/S1368980018000551 <https://pubmed.ncbi.nlm.nih.gov/29559013/>

7. McBeth, J., Pye, S. R., & O'Neill, T. W. (2010). Macfarlane, Musculoskeletal pain is associated with very low levels of vitamin D in men: results from the European Male Ageing Study. *Annals of the Rheumatic Diseases*, 69(8), 1448–1452. doi: 10.1136/ard.2009.116053. <https://pubmed.ncbi.nlm.nih.gov/20498201/>
8. Mouyis, M., Ostor, A. J. K., Crisp, A. J., Ginawi, A., Halsall, D. J., Shenker, N., & Poole, K. E. S. (2008). Hypovitaminosis D among rheumatology outpatients in clinical practice. *Rheumatology*, 47(9), 1348-1351. DOI: 10.1093/rheumatology/ken203 <https://pubmed.ncbi.nlm.nih.gov/18499714/>
9. Huisman, A. M., White, K. P., Algra, A., Harth, M. A. N. F. R. E. D., Vieth, R. E. I. N. H. O. L. D., Jacobs, J. W., ... & Bell, D. A. (2001). Vitamin D levels in women with systemic lupus erythematosus and fibromyalgia. *The Journal of rheumatology*, 28(11), 2535-2539. <https://pubmed.ncbi.nlm.nih.gov/11708429/>
10. Al-Allaf, A. W., Mole, P. A., Paterson, C. R., & Pullar, T. (2003). Bone health in patients with fibromyalgia. *Rheumatology*, 42(10), 1202-1206. doi: 10.1093/rheumatology/keg356. Epub 2003 Jun 16. <https://pubmed.ncbi.nlm.nih.gov/12810939/>
11. Scragg, R., & Camargo, C. A. Jr. (2008). Frequency of leisure-time physical activity and serum 25-hydroxyvitamin D levels in the US population: results from the Third National Health and Nutrition Examination Survey. *Am J Epidemiol*, 168, 577–86; discussion 587–91. DOI: 10.1093/aje/kwn163 <https://pubmed.ncbi.nlm.nih.gov/18579538/>
12. Warner, A. E., & Arnsperger, S. A. (2008). Diffuse musculoskeletal pain is not associated with low vitamin D levels or improved by treatment with vitamin D. *J Clin Rheumatol*, 14, 12–6. doi:10.1097/RHU.0b013e31816356a9 <https://pubmed.ncbi.nlm.nih.gov/18431091/>
13. Lee, A., & Lee, J.-E. (2016). Vitamin D and the characteristics associated with risk for knee pain among Korean older adults: Findings from a nationally representative survey. *Geriatrics & Gerontology International*, 17(9), 1278–1285. DOI: 10.1111/ggi.12857 <https://pubmed.ncbi.nlm.nih.gov/27460443/>
14. Block, S. R. (2004). Vitamin D deficiency is not associated with non-specific musculoskeletal pain syndromes including fibromyalgia. *Mayo Clin Proc*, 79, 1585–6; author reply 1586–7. doi: 10.4065/79.12.1585. <https://pubmed.ncbi.nlm.nih.gov/15595347/>