Vitamin D deficiency in knee osteoarthritis patients and its association with obesity in Saudi Arabia

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Kingdom of Saudi Arabia

Introduction

Vitamin D deficiency is usually defined as serum 25-hydroxyvitamin D (25-(OH)D) levels of less than 20 ng/ml.

It is quite a common problem worldwide.

Adams JS, Hewison M. Update in vitamin D. J Clin Endocrinol Metab. 2010; 95:471–47

Holick MF. High prevalence of vitamin D inadequacy and implications for health. Mayo Clin Proc. 2006; 81:353–3

oduction

It is a highly prevalent condition, present in approximately 30% to 50% of the general population (as a silent epidemic).

In some communities, the rates of vitamin D deficiency range from 50% to 80%.

Cherniack EP, Florez H, Roos BA, et al. *Hypovitaminosis D in the elderly: from bone to brain. J Nutr Health Aging* 2008*; 12:366-7*

Holick MF. *Vitamin D deficiency. N Engl J Med* 2007*; 357:266-8*

Greene-Finestone LS, Berger C, de Groh M, et al. *25-Hydroxyvitamin D in Canadian adults: biological, environmental, and behavioral correlate Osteoporos Int* 2011*; 22:1389-9*

oduction

It is a more prevalent deficiency in the elderly, with 50-60% of the older population in the world having unsatisfactory vitamin D levels.

The main causes of this are:

- Urbanization
- Decreased outdoor activities
- Air pollution and global dimming
- Age-related decreases in cutaneous vitamin D production
- Dietary sources of vitamin D are generally too insignificant

Dobnig H, et al. 2008. Independent association of low serum 25-hydroxyvitamin D and 1, 25-dihydroxyvitamin D levels with all-caus
cardiovascular mortality. *Arch Int Med 268(12)*:139

oduction

In Saudi Arabia, or more specifically in urban areas such as the capital Riyadh, vitamin D deficiency is alarmingly high, despite of plentiful sunlight and vitamin D fortified food products.

Hanan Alfawaz, Hani Tamim, Shmeylan Alharbi, Saleh Aljaser and Waleed Tamimi . Vitamin D status among patients visiting a tertiary care center in Riyadh, Saudi Arabia retrospective review of 3475 cases. *BMC Public Health* 2014, 14:15

Ardawi M, Sibiany A, Bakhsh T, Qari M, Maimani A: High prevalence of vitamin D deficiency among healthy Saudi Arabian men: relationship to bone mineral density, parathyro hormone, bone turnover markers, and lifestyle factors. *Osteoporos Int* 2012, 23:675-68

.Ardawi M, Qari M, Maimani A, Raddadi R: Vitamin D status in relation to obesity, bone mineral density, bone turnover markers and vitamin D receptor genotypes in healthy Sau pre- and postmenopausal women. *Osteoporos Int* 2011, 22:463-4

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According to one study in Saudi Arabia, 65% of participants had adequate exposure to sunlight and more than 90% of participants reported adequate intake of dairy products.

Elsammak M. Y. ; Al Wossaibi A. A.; Al Howeish A. ; Alsaeed J.: High prevalence of vitamin D deficiency in the sunny Eastern region of Sau
Arabia: a hospital – based study. Eastern Mediterranean Health journal (EMHJ) vol. 17 No. 4, 2011

oduction

Vitamin D deficiency is associated with many pathological conditions including osteoarthritis (OA); sufficient levels of serum vitamin D decrease the risk of many chronic illnesses.

Vitamin D deficiency co-exists frequently with OA in older people.

Heidari B, Shokri Shirvani J, Firouzjahi A, Heidari P, Hajian-Tilaki K. Association between nonspecific skeletal pain and vitamin D deficiency. Int J Rheumatol. 2010; 13:340–34

Pérez-López FR. Vitamin D and its implications for musculoskeletal health in women: an update.Maturitas. 2007; 58:117–1

oduction

Osteoarthritis (OA) is the most common chronic arthritis characterized by gradual cartilage loss and also affects other joint structures, causing structural changes and eventually functional failure of synovial joints.

Brand C, Hunter D, Hinman R, et al. *Improving care for people with osteoarthritis of the hip and knee: how has national policy for osteoarthritis bee translated into service models in Australia? Int J Rheum Dis* 2011*; 14:181-9*

oduction

Vitamin D has many biological functions in these structures by acting on vitamin D receptors, and may have beneficial effects on these joint structures in OA.

Holick MF. *High prevalence of vitamin D inadequacy and implications for health. Mayo Clin Proc* 2006*; 81:353-7*

Bischoff-Ferrari HA, Giovannucci E, Willett WC, et al. *Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes. Am J Clin Nu* 2006*; 84:18-2*

Wolff AE, Jones AN, Hansen KE. *Vitamin D and musculoskeletal health. Nat Clin Pract Rheumatol* 2008*; 4:580-*

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- Vitamin D deficiency increases osteoblastic activity and bone turn-over, and may lead to an increased chance of inflammation.

Adams JS, Hewison M. Update in vitamin D. J Clin Endocrinol Metab. 2010; 95:471–47

Miller RR, Hicks GE, Shardell MD, et al. *Association of serum vitamin D levels with inflammatory response following hip fracture: the Baltimore Hip Studies. J Gerontol A Biol S Med Sci* 2007*; 62:1402-*

Wu S, Sun J. *Vitamin D, vitamin D receptor, and macroautophagy in inflammation and infection. Discov Med* 2011*; 11:325-3*

oduction

Raising serum 25-OHD to sufficient levels with supplemental vitamin D will decrease the rate of bone turn-over, suppress the PTH level, increase bone mass density (BMD), and even decrease fracture risk in the elderly population.

Bettica P, Cline G, Hart DJ, Meyer J, Spector TD. Evidence for increased bone resorption in patients with progressive knee osteoarthritis: longitudinal results from the Chingfo
study. Arthritis Rheum.2002; 46:3178–318

Hurst PR, Stonehouse W, Kruger MC, Coad J. Vitamin D supplementation suppresses age-induced bone turnover in older women who are vitamin D deficient. J Steroid Biochem M
Biol. 2010; 121(1–2):293–29

oduction

Vitamin D levels influence the incidence and progression of knee OA.

In one study, OA in serum 25-OHD deficient men was found to be two times more prevalent than those with sufficient levels.

Tsaei KS, Wahner HW, Offord KP, Melton LJ, Kumar R, Rigs BL. Effect of aging on vitamin D stores and bone density in women. Calcif Tissue Int. 1987; 40:241–24

Bergink AP, Uitterlinden AG, Leeuwen JP, Buurman CJ, Hofman A, Verhaar JA, Pols HA. Vitamin D status, bone mineral density, and the development of radiographic osteoarthritis the knee: the Rotterdam Study. J Clin Rheumatol. 2009; 15:230–237. (19-2

Chaganti RK, Parimi N, Cawthon P, Dam TL, Nevitt MC, Lane NE. Association of 25-hydroxyvitamin D with prevalent osteoarthritis of the hip in elderly men: the osteoporotic fractur in men study. Arthritis Rheum. 2010; 62:511–51

oduction

Some studies have concluded that low levels of vitamin D in the serum are associated with worsening radiographic hip and knee osteoarthritis (OA), while other studies' results have not proved so.

Ding C, Cicuttini F, Parameswaran V, Burgess J, Quinn S, Jones G. Serum levels of vitamin D, sunlight exposure, and knee cartilage loss in older adults: the Tasmainan older adu
cohort study. *Arthritis Rheum 2009; 60: 1381-*

ergink AP, Uitterlinden AG, Van Leeuwen JP, Buurman CJ, Hofman A, Verhaar JA, et al. Vitamin D status, bone mineral density, and the development of radiographic osteoarthritis
the knee: the Rotterdam Study. *J Clin Rheumatol 2009; 15: 230–7.* (2

Felson DT, Niu J, Clancy M, Aliabadi P, Sack B, Guermazi A, et al. Low serum levels of vitamin D and worsening of knee osteoarthritis: results of two longitudin

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ystematic review of the evidence for the association between erum 25-hydroxyvitamin D (25-(OH)D) levels and OA has revealed:

- Moderate evidence for the association between low levels of 25-(OH)D and increased progression of radiographic OA as assessed by the Kellgren and Lawrence (KL) score.
- Strong evidence for an association between 25-(OH)D and cartilage loss was apparent when joint space narrowing and changes in cartilage volume were considered collectively as cartilage loss.

Yuelong Cao, Tania Winzenberg, Kay Nguo, Jianhao Lin, Graeme Jones and Changhai Ding. Association between serum levels of 25-hydroxyvitamin D a osteoarthritis

systematic review. *Rheumatology, Volume 52 Issue 7.1323-1334. Jully, 20*

oduction

The authors of the review concluded that 25-(OH)D appears to be implicated in structural changes of knee OA rather than symptoms.

But a study involving patients with knee osteoarthritis (OA) has found that individuals who were vitamin D deficient reported more pain and disability than those with normal levels.

Baker K, Zhang YQ, Goggins J, et al. Hypovitaminosis D and its association with muscle strength, pain and physical function in knee osteoarthritis (OA): a 30-mon
longitudinal, observational study; American College of Rheumatology meeting; San Antonio, TX; Oct 16-21, 2004; abstract 175

oduction

Obesity is defined by the World Health Organization as a body mass index (BMI) of 30 kg/m^2 or more.

It is pandemic, affecting at least five million Australians and substantial numbers in most developed nations.

If the number of those overweight (BMI 25–29.9) is included, then approximately 14 million Australians, and 70% of Americans aged over 60, are obese or overweight

Noncommunicable Diseases Country Profiles; World Health Organisation: Geneva, Switzerland, 2011; p. 20

Pi-Sunyer, F.X. The obesity epidemic: Pathophysiology and consequences of obesity. *Obes. Res.* 2002, *10*, 97S–104

oduction

In Saudi Arabia (KSA), based on the National Nutrition Survey of 2007, 23.6% of women and 14% of men were obese.

If those overweight are to be included, then 30.7% of men were overweight or obese, compared to 28.4% of women.

Al-Othaimeen AI, Al-Nozha M, Osman AK. Obesity: an emerging problem in Saudi Arabia. Analysis of data from the National Nutrition Survey. East Mediterr Health J. 2007 Ma
Apr;13(2):441-

oduction

The association between reduced 25-(OH)D concentrations and obesity is well established, but the mechanisms for the lowered 25-(OH)D concentrations are not fully described.

Simon Vanlint. ***Vitamin D and Obesity.*** *20 March Nutrients* ***2013****, 5, 949-9*

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Possible mechanisms reported by Simon Vanlint, in 2013:

1. Lower dietary intake.
2. Reduced cutaneous synthesis due to:
    A) Altered behavior.
    B) Reduced synthetic capacity.
3. Reduced intestinal absorption.
4. Altered metabolism due to:
    A) Reduced activation and/or increased catabolism.
    B) Sequestration of 25-(OH)D in adipose tissue.

Simon Vanlint. Vitamin D and Obesity. 20 March Nutrients 2013, 5, 949-9

Subjects and Methods

Study population

100 patients with symptomatic knee OA and age-matched 100 controls.

All patients and controls should be either Saudi or non Saudi who lived in Saudi Arabia for at least 5 years.

ects and methods

Control group were selected among subjects who presented to the outpatient clinics over the same period for non-musculoskeletal symptoms, or among subjects without any clinical symptoms who presented for check-up laboratory tests.

The control group had no clinical features of KOA based on history and clinical examination.

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ects and methods

atients were selected consecutively among individuals who complained of knee pain to a rheumatology utpatient clinic located in Salman bin Abdul-aziz niversity Hospital, Al Kharj, Saudi Arabia.

he diagnosis of knee OA was confirmed by ACR iagnostic criteria for classification of knee OA.

ltman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, et al. Development of criteria for the classification and reporting of osteoarthritis: classification of osteoarthritis of the kne
Arthritis Rheum 1986; 29: 1039–4

ects and methods

tudy population exclusion criteria:

- Having rheumatic diseases such as inflammatory arthritis, or connective tissue disease (RA, SLE, AS,…), or hyperuricemia.
- Use of vitamin D supplements.
- Chronic steroid use.
- Intra-articular injections (steroids or hyaluronic acid) in the last three months.

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ects and methods

Clinical evaluation:

- History and clinical examination
- Clinical evaluation of status of KOA :
    - A. Knee pain.
    - B. Physical function evaluation.

Wang, J., Nuite, M., Wheeler, L.M., Badiani, P., Joas, J., Mcadams, E.L., Fletcher, J., Lavalley, M.P., Dawson-Hughes, B., Mcalindon, T.E. 2007. Low Vitamin D levels are associated wi
greater pain and slow walking speed in patients with knee osteoarthritis (KOA). In: American College of Rheumatology Scientific Meeting, 11/6/07-11/11/07, Boston, M
56(9supplement): S12

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ects and methods

Knee pain was evaluated by:

- Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC pain subscale).
- Visual analog pain scales (VAS).

Bellamy N.*WOMAC Osteoarthritis Index User Guide Version V.* Brisbane,. Australia 20

Huskisson EC: Measurement of pain. Lancet 1974. Nov 9;2(7889):1127-31 and J Rheumatol 1982; 9: 768-

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The physical function evaluation:

- Timed (30 second) chair stand test.
- 10-meter walking test.

Gill, S. D., de Morton, N. A., et al. (2012). "An investigation of the validity of six measures of physical function in people awaiting joint replacement surg
of the hip or knee." Clin Rehabil 26(10): 945-

ohannon, R. W. Comfortable and maximum walking speed of adults aged 20-79 years: reference values and determinants." Age Ageing. 1997; 26(1): 1

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Assays

- Serum 25-hydroxy Vitamin D level was assayed for both patients and control.
- Serum 25-hydroxy vitamin D concentrations of less than 20 ng/ml were considered as deficient levels.

ects and methods

For KOA patients we assessed:

- Serum calcium.
- Serum phosphate.
- Serum alkaline phosphatase.
- Serum parathyroid hormone.
- Serum uric acid.

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Radiographs

- Weight-bearing anteroposterior view in full extension, lateral and skyline.
- All radiographs were assessed by two trained observers (DJH, DH), who were blind to the clinical findings.
- The radiological features of KOA were graded on a five-point scale (0–4) for Kellgren and Lawrence classification.

Kellgren JH, Lawrence JS, eds. Atlas of standard radiographs. Oxford: Blackwell Scientific, 196

Results

Patients (100)

- Symptomatic knee OA.
- 70% were women and 30% were men.
- Mean age: 52.47 ± 10.427.
- 66% were of Saudi nationality.

Controls(100)

- 53% were women and 46% were men.
- Mean age: 49.56 ± 9.429.
- 55% were of Saudi nationality.

Comparisons between KOA patients and controls

	Control group (n = 100)	OA Cases (n = 100)	P-va
	46 (46 %) 53 (53 %)	30 (30 %) 70 (70 %)	0.01
ty di	55 (55 %) 45 (45%)	68 (68 %) 32 (32 %)	0.05
SD minimum – maximum)	49.67 ± 9.18 47.5 (33 – 84)	52.47 ± 10.427 51.5 (36 – 82)	0.043
SD minimum – maximum)	19.88 ± 10.34 17.7 (4 – 60) 58 (58 %) 42 (42 %)	19.10 ± 10.99 15.75 (4 – 57) 66 (66 %) 34 (34 %)	0.342 0.24

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- 68% of KOA patients had serum 25-OHD deficiency
- 58% of controls had serum 25-OHD deficiency
- Mean serum 25-OHD level in patients: 18.10 ± 10.99 ng/m
- Mean serum 25-OHD level in controls: 19.88 ± 10.34 ng/m

Difference in mean and proportions of serum 25-OHD deficiency between patients and ontrols were not statistically significant

here was an association between serum 25-OHD deficiency and knee OA which was not tatistically significant [P = 0.244]

ults

KOA patients

72.1% of all KOA patients were obese (BMI ≥30) (mean 33.782 ± 6.107).

80.6% of KOA patients with low 25-OHD level were obese (mean 34.448 ± 5.902) versus 55.0% in patients with normal 25-OHD level (mean 32.563 ± 6.411)

he difference was statistically significant (P= 0.043)

ults

KOA patients

- 74% had radiological evidence of KOA K/L grade 1-2.
- 26% had a K/L grade >=3.

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Clinical evaluation of knee pain and physical function

	Minimum	Maximum	Mean	Std. Deviatio
AGE	36	82	52.47	10.427
BMI	20.3	47.9	33.782	6.1070
WOMAC Score	4	89	46.72	20.792
VAS	1	10	6.04	1.899
Timed Chair	4	17	8.49	2.800
Walk Test Selected	0.258	1.279	0.77206	0.197517
Walk Test Fast	0.359	1.704	1.01660	0.264847
Vitamin D	3.8	57.0	19.103	10.9911

ults

linical evaluation of knee pain

Knee pain scores were high:

WOMAC pain subscale mean: 46.72 ± 20.792

VAS pain score: 6.04 ± 1.899

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Clinical evaluation of physical function

Physical function was low:

Timed chair stand test results were low: mean 8.49 ± 2.80

10-meter walking test velocity results were also low:

Selected walking test: mean 0.77206 ± 0.197 (m/s)

Fast walking test: mean 1.0166 ± 0.264 (m/s)

ults

Clinical evaluation of knee pain and physical function

- The difference in these results from the comparison between KOA patients with low serum 25-OHD levels (<20 ng/ml) and those with normal serum 25-OHD levels (>20 ng/ml) did not reach a statistically significant level.

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Relationship between serum vitamin D levels and clinical/radiological knee OA:

- There was no significant association or correlation between low 25-OHD level and clinical/radiological parameters of KOA.
- 25-OHD level was significantly associated BMI.
- A lower 25-OHD level was significantly associated
- with higher BMI (negative relationship).

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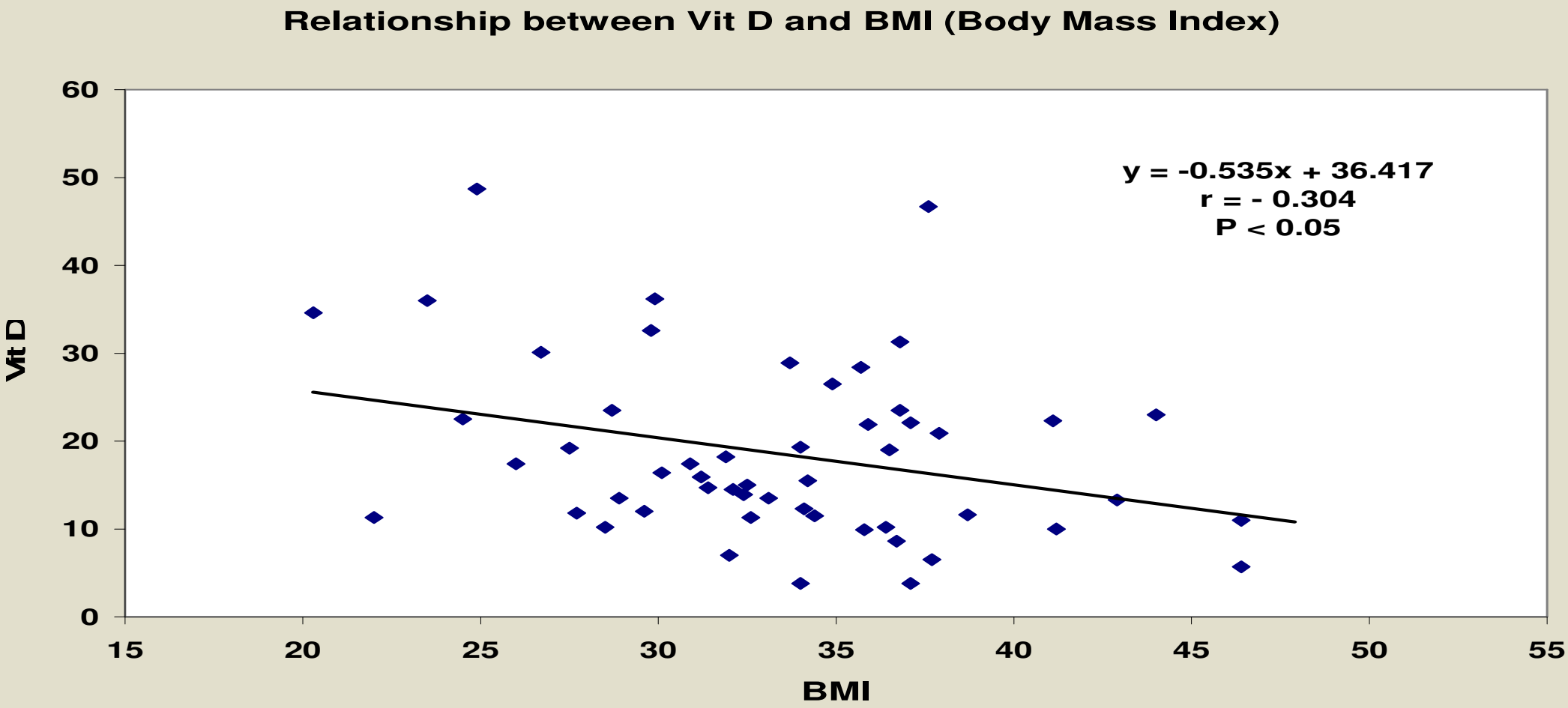
Relationship between vitamin D level and BMI



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High BMI (obesity) was significantly associated with aging, X-ray severity o OA, greater knee pain (high VAS and WOMAC score), and slow walking speed.

Knee pain measures, VAS, and the WOMAC subscale were significantly correlated with each other and with physical function parameters, timed chair stand test, and 10-meter walking tests.

X-ray severity of OA was associated with aging, knee pain measures, and physical function parameters.

Both X-ray severity and aging significantly were associated with greater knee pain, high VAS and WOMAC, slow walking speed, and low timed chair stand results.

Conclusion

Vitamin D deficiency is significantly associated with obesity (BMI), which in turn is associated with greater knee pain, poorer physical function, and severe radiological evidence of KOA.

Recommendation

We recommend measuring and monitoring vitamin D levels in patients with symptomatic knee osteoarthritis, particularly the obese patients.

We recommend further studies for the role of vitamin D supplementation in prevention of obesity and progression of knee OA.

Thank you for your time and attention