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.


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Introduction

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%.


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

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: a retrospective review of 3475 cases. BMC Public Health 2014, 14:159


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.

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.


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.

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.


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Introduction

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


Wu S, Sun J. Vitamin D, vitamin D receptor, and macroautophagy in inflammation and infection. Discov Med 2011; 11:325–332
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.


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.


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.


Introduction

Systematic review of the evidence for the association between serum 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.

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-month longitudinal, observational study; American College of Rheumatology meeting; San Antonio, TX; Oct 16-21, 2004; abstract 1755
Obesity is defined by the World Health Organization as a body mass index (BMI) of 30 kg/m² 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.


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.

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, 949-956
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, 949-956
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.
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Subjects 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.
Patients were selected consecutively among individuals who complained of knee pain to a rheumatology outpatient clinic located in Salman bin Abdul-aziz University Hospital, Al Kharj, Saudi Arabia. The diagnosis of knee OA was confirmed by ACR diagnostic criteria for classification of knee OA.
Study 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.
Clinical evaluation:

History and clinical examination

Clinical evaluation of status of KOA:

A. Knee pain.

B. Physical function evaluation.

Knee pain was evaluated by:
- Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC pain subscale).
- Visual analog pain scales (VAS).

The physical function evaluation:

- Timed (30 second) chair stand test.

- 10-meter walking test.


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

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.
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**Subjects and Methods**

For KOA patients we assessed:
- Serum calcium.
- Serum phosphate.
- Serum alkaline phosphatase.
- Serum parathyroid hormone.
- Serum uric acid.
Subjects and methods

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.

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.
<table>
<thead>
<tr>
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<th>Control group (n = 100)</th>
<th>OA Cases (n = 100)</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Gender</td>
<td></td>
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<tr>
<td>Male</td>
<td>46 (46 %)</td>
<td>30 (30 %)</td>
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<tr>
<td>Female</td>
<td>53 (53 %)</td>
<td>70 (70 %)</td>
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<tr>
<td>Nationality</td>
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<tr>
<td>Saudi</td>
<td>55 (55 %)</td>
<td>68 (68 %)</td>
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<td>Non-Saudi</td>
<td>45 (45 %)</td>
<td>32 (32 %)</td>
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<td>Age (years)</td>
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<td>52.47 ± 10.427</td>
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<tr>
<td>(minimum – maximum)</td>
<td>47.5 (33 – 84)</td>
<td>51.5 (36 – 82)</td>
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<tr>
<td>BMI</td>
<td>19.88 ± 10.34</td>
<td>19.10 ± 10.99</td>
<td>0.342</td>
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<tr>
<td>(minimum – maximum)</td>
<td>17.7 (4 – 60)</td>
<td>15.75 (4 – 57)</td>
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<td></td>
<td>58 (58 %)</td>
<td>66 (66 %)</td>
<td></td>
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<tr>
<td></td>
<td>42 (42 %)</td>
<td>34 (34 %)</td>
<td>0.244</td>
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</tbody>
</table>
Results

68% of KOA patients had serum 25-OHD deficiency

58% of controls had serum 25-OHD deficiency

Mean serum 25-OHD level in patients: $18.10 \pm 10.99$ ng/m

Mean serum 25-OHD level in controls: $19.88 \pm 10.34$ ng/m

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

There was an association between serum 25-OHD deficiency and knee OA which was not statistically significant [$P = 0.244$]
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)

The difference was statistically significant (P= 0.043)
D deficiency in knee osteoarthritis patients and its association with obesity in Arabia

Results

• 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

<table>
<thead>
<tr>
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<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>Std. Deviation</th>
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<td>82</td>
<td>52.47</td>
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<td>BMI</td>
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<td>47.9</td>
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<td>WOMAC Score</td>
<td>4</td>
<td>89</td>
<td>46.72</td>
<td>20.792</td>
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<tr>
<td>VAS</td>
<td>1</td>
<td>10</td>
<td>6.04</td>
<td>1.899</td>
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<tr>
<td>Timed Chair</td>
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<td>17</td>
<td>8.49</td>
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<tr>
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<td>0.197517</td>
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<tr>
<td>Walk Test Fast</td>
<td>0.359</td>
<td>1.704</td>
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<tr>
<td>Vitamin D</td>
<td>3.8</td>
<td>57.0</td>
<td>19.103</td>
<td>10.9911</td>
</tr>
</tbody>
</table>
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Results

Clinical evaluation of knee pain

Knee pain scores were high:
WOMAC pain subscale mean: 46.72 ± 20.792
VAS pain score: 6.04 ± 1.899
D deficiency in knee osteoarthritis patients and its association with obesity in Arabia

Results

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)
Clinical evaluation of knee pain and physical function in 

D deficiency in knee osteoarthritis patients and its association with obesity in

Results

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.
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 with BMI.

A lower 25-OHD level was significantly associated with higher BMI (negative relationship).
Relationship between Vitamin D level and BMI

Results

Relationship between vitamin D level and BMI

\[ y = -0.535x + 36.417 \]

\[ r = -0.304 \]

\[ P < 0.05 \]
High BMI (obesity) was significantly associated with aging, X-ray severity of 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