Prevalence of vitamin D deficiency in Egyptian rheumatoid arthritis patients: correlation with disease activity, functional disability, and bone mineral density
Nashwa T. Allam\textsuperscript{a}, Mohamed M. El-Wakd\textsuperscript{a}, Dina M. El-Abd\textsuperscript{b}, Dalia A. Dorgham\textsuperscript{a}

\textsuperscript{a}Rheumatology and Rehabilitation Department, \textsuperscript{b}Clinical and Chemical Pathology Department, Faculty of Medicine, Cairo University, Cairo, Egypt

Introduction
Rheumatoid arthritis (RA) is a systemic autoimmune disease of unknown etiology [1]. It is characterized by synovitis, cartilage damage, and bone resorption, resulting in structural damage and significant morbidity and mortality [2]. The role of T and B lymphocytes in the disease pathogenesis has been proven [3]. Vitamin D is a steroid hormone synthesized in the skin by the action of ultraviolet irradiation [4]. It plays a major role in the maintenance of proper bone metabolism [5] because it regulates calcium absorption from the gastrointestinal tract [6]. However, the discovery of the vitamin D receptor in nonskeletal tissue, particularly in immune cells, indicated a possible role for vitamin D in maintaining its normal function [7,8]. Interestingly, vitamin D deficiency has been linked to an increased susceptibility to develop autoimmune diseases such as RA [9], systemic lupus erythematosus, multiple sclerosis, and type-1 diabetes in large population studies [10,11]. A low vitamin D level is also linked to increased disease activity in RA patients [12]. However, the exact mechanism for the inverse relationship between low vitamin D level and increased inflammatory disease activity is still under investigation [12–14].

The aim of the present study was to detect the prevalence of 25-hydroxyvitamin D\textsubscript{3} (25(OH)D\textsubscript{3}) deficiency in rheumatoid arthritis (RA) patients and its correlation with disease activity, functional disability and bone mineral density (BMD).

Patients and methods

Patients
A cross-sectional, case–control study was carried out that included 104 RA patients who fulfilled the 2010 American College of Rheumatology/European
League Against Rheumatism (ACR-EULAR) classification criteria for RA [15] in addition to 60 healthy age-matched and sex-matched controls. All participants were recruited from the Rheumatology and Rehabilitation Clinic, Kasr Alainy Hospitals, Cairo University. Full assessment of history and detailed clinical examination were performed for all patients. Demographic data including patients’ age and disease duration were reported. Body weight, height, and BMI (kg/m²) were measured and calculated for all participants. The inclusion criteria were the diagnosis of established RA, age at disease onset above 18 years, and at least 1-year disease duration. Patients or controls on vitamin D supplement or those with endocrine, hepatic, or renal diseases were excluded. Participants provided written informed consent before their inclusion. The current study was approved by the local ethical committees and was carried out in accordance with the ethical standards established in the 1964 Declaration of Helsinki.

**Disease activity assessment**
Modified 28-joints Disease Activity Score (DAS-28) was calculated using three variables: the 28-tender and swollen joints count (TJC-28 and SJC-28) and erythrocyte sedimentation rate (ESR) (mm/h) according to Prevoo and colleagues' formula: DAS-28 = (0.56 × √TJC-28 + 0.28 × √SJC-28 + 0.70 × Ln ESR) × 1.08 + 0.16. Patients were considered to be in remission if DAS-28 is less than 2.6, to have low disease activity if DAS-28 is less than 3.2, moderate disease activity if DAS-28 was between 3.2 and 5.1, and high disease activity if DAS-28 is greater than 5.1 [16].

**Functional disability assessment**
The modified-health assessment questionnaire (M-HAQ) was used. Patients were considered normal if the M-HAQ score was 0.3 or less [17].

**Treatment**
RA-specific treatments were reported for all patients. These drugs were glucocorticoids and disease-modifying antirheumatic drugs.

**Laboratory measurements**
Serum 25(OH)D₃ was measured using an enzyme-linked immunosorbent assay. Its level was considered sufficient if it was greater than 75 nmol/l (>30 ng/ml), insufficient if it was between 50 and 75 nmol/l (20–30 ng/ml), and deficient if it was less than 50 nmol/l (<20 ng/ml) [18,19]. ESR (mm/h) was determined using the Westergren method; rheumatoid factor (considered positive if it is >20 IU/ml) was determined using the nephelometric method; and anticyclic citrullinated polypeptide (considered positive if ≥5 U/ml) was determined using a microparticle enzyme immunoassay for all patients.

**Radiological investigations**
Plain radiography of the hands and wrists, posteroanterior view, was performed for all patients to detect radiological signs of RA.

High-resolution computed tomography of the chest was used to diagnose interstitial pulmonary fibrosis (IPF).

Dual-energy X-ray absorptiometry with advanced fan-beam technology was used to measure BMD according to diagnostic categories proposed by the WHO [20] and modified by the International Osteoporosis Foundation [21]: 1 — normal BMD, hip BMD greater than 1 SD below the young adult female reference mean (T score<−1); 2 — low bone mass (osteopenia), hip BMD greater than 1 SD below the young adult mean, but less than 2.5 SD below this value (T score<−1 and >−2.5); 3 — osteoporosis, hip BMD 2.5 SD or more below the young adult female mean (T score<−2.5); 4 — severe osteoporosis (established osteoporosis), hip BMD 2.5 SD or more below the young adult mean in the presence of one or more fragility fractures.

**Statistical analysis**
The statistical package for social sciences SPSS (Statistical Package for the Social Sciences; SPSS Inc, Chicago, IL, USA) version 15 for Microsoft windows, version 18 was used to analyze data. Continuous variables were summarized as mean ± SD and categorical variables as frequency (percentage). An independent t-test compared two independent groups and the analysis of variance test compared more than two groups. Associations between categorical groups were tested using the χ²-test with Yates correction or Fisher’s exact test as appropriate. The Pearson correlation test was used as a measure of the association of quantitative variables. Two-tailed P values of 0.05 or less were considered to be statistically significant.

**Results**
**Demographic, clinical, radiologic, and laboratory features of RA patients**
Among RA patients, there were 82 (78.8%) women and 22 (21.2%) men. The demographic, clinical, radiologic, and laboratory features of the RA patients at the time of the study are shown in Table 1.
Table 1 Demographic, clinical, radiological, and laboratory features of RA patients

| Patients’ characteristic features | n (%)/mean ± SD |
|----------------------------------|-----------------|
| **Demographic features**         |                 |
| Age (years)                      | 46.39 ± 10.43   |
| Weight (kg)                      | 73.72 ± 12.77   |
| Height (m)                       | 1.59 ± 0.8      |
| BMI (kg/m²)                      | 29.2 ± 5        |
| Disease duration (years)         | 6.61 ± 5.77     |
| **Clinical articular features**  |                 |
| Morning stiffness                | 56 (53.85)      |
| Symmetric arthritis              | 88 (84.61)      |
| SJC-28                           | 2.67 ± 2.63     |
| TJC-28                           | 4.78 ± 4.18     |
| Deformities                      | 19 (18.3)       |
| **Radiological features**        |                 |
| Erosions                         | 83 (79.8)       |
| IPF                              | 7 (6.7)         |
| **Laboratory features**          |                 |
| ESR (mm/h)                       | 37.63 ± 19.89   |
| Positive RF                      | 83 (79.8)       |
| Positive anti-CCP                | 68 (65.4)       |

Anti-CCP, anticyclic citrullinated polypeptide; ESR, erythrocyte sedimentation rate; IPF, interstitial pulmonary fibrosis; RA, rheumatoid arthritis; RF, rheumatoid factor; SJC-28, 28 swollen joint count; TJC-28, 28 tender joint count.

At the time of the study, all patients were on methotrexate at a dose ranging from 12.5 to 20 mg/week, with a mean of 15 ± 2.31 mg/week, 26 (25%) patients were taking leflunomide (20 mg/day), 46 (44.2%) patients were taking hydroxychloroquine (400 mg/day) divided into two doses per day, and 21 (20.2%) patients were on prednisone at a dose ranging from 5 to 10 mg/day, with a mean of 6.5 ± 1.88 mg/day. None of our patients was treated by tumor necrosis factor-α blockers.

Disease activity score and functional disability index

The DAS-28 score ranged from 2.06 to 7.22, with a mean of 4.34 ± 1.03. Nine (8.65%) patients had disease remission, whereas nine (8.65%), 61 (58.65%), and 25 (24.03%) patients had low, moderate, and high disease activity, respectively. SJC-28 ranged from 0 to 12, with a mean of 2.67 ± 2.63. TJC-28 ranged from 0 to 20, with a mean of 4.78 ± 4.18. The M-HAQ score was ranged from 0 to 2.1, with a mean of 0.58 ± 0.59. The M-HAQ score was 0.3 or less in 53 (50.96%) patients and greater than 0.3 in 51 (49.04%) patients.

BMD

BMD was normal, osteopenic, and osteoporotic in 36 (34.6%), 47 (45.2%), and 21 (20.2%) patients, respectively.

Serum 25(OH)D₃ level

The mean serum 25(OH)D₃ level among RA patients was 5.98 ± 6.8 nmol/l, deficient in 103 (99.1%) patients and insufficient in one (0.9%) patient. However, the mean serum 25(OH)D₃ level among the controls was 8.4 ± 9.6 nmol/l and all had 25(OH)D₃ deficiency. Although the mean serum 25(OH)D₃ level was lower in RA patients than in the controls, the difference was statistically insignificant (P = 0.06).

Correlation between serum 25(OH)D₃ level and the disease parameters studied

The correlation between serum 25(OH)D₃ level and the demographic, clinical, radiological, and laboratory features of RA patients is shown in Table 2.

The mean serum 25(OH)D₃ level showed a mild negative correlation with weight and IPF (r = –0.256 and –0.234 with P = 0.009 and 0.017, respectively) and moderate negative correlations with morning stiffness, symmetric arthritis, SJC-28, TJC-28, and ESR (r = 0.398, –0.333, 0.631, –0.559, and –0.39, with P < 0.001 for all, except for arthritis, which was 0.001).

Correlation between serum 25(OH)D₃ level and DAS-28 and M-HAQ

Serum 25(OH)D₃ level showed a strong negative correlation with the DAS-28 score (r = –0.794, P < 0.001) and moderate negative correlations with M-HAQ (r = –0.562, P < 0.001). Although almost all RA patients had 25 (OH)D₃ deficiency, it was found that the mean 25(OH)D₃ level was relatively higher in patients with disease remission and its level was significantly decreased as the disease became more active (P < 0.001; Table 3 and Fig. 1). Also, the mean serum 25(OH)D₃ was significantly higher in patients without functional disability in comparison with those with disability (P < 0.001; Table 3 and Fig. 2).

Correlation between serum 25(OH)D₃ level and treatment

There was an insignificant correlation between serum 25(OH)D₃ and leflunomide (P = 0.57), hydroxychloroquine (P = 0.45), or prednisone (P = 0.16).

Correlation between serum 25(OH)D₃ level and BMD

Also, there was an insignificant correlation between serum 25(OH)D₃ and BMD of the hip (P = 0.11), spine (P = 0.74), or distal radius (P = 0.24).

Discussion

The prevalence and association between vitamin D deficiency and the outcome of various autoimmune diseases are the most evolving topics. The present...
Prevalence of vitamin D deficiency  

Study showed that 25(OH)D3 deficiency was prevalent among RA patients as well as among the controls (99.1% and 100%, respectively), without a significant difference, indicating that vitamin D deficiency might be endemic in our country. Surprisingly, the high prevalence of 25(OH)D3 deficiency that was found in our country, which has abundant sunshine, may be attributed to decreased sun exposure (conservative dressing culture, wearing of veil and muffler, and/or avoidance of exposure to hot sunny weather). Another explanation may be our predisposition as an Arab population for 25(OH)D3 deficiency as a result of certain intrinsic factors related to ethnicity as reported by Braun-Moscovici et al. [22], who found that the prevalence of 25(OH)D3 deficiency was 76.6% in Arab RA patients compared with 35% in Jewish RA patients, with a statistically significant difference ($P < 0.001$). The low socioeconomic status and educational level of our participants, who were recruited from the rural and slums area near Cairo, may be another contributing factor toward 25(OH)D3 deficiency.

Although the mean serum 25(OH)D3 level of our RA patients was lower than that of the controls, there was no statistically significant difference (5.98 ± 6.8 vs. 8.4 ± 9.6 nmol/l, $P = 0.06$), and this is in agreement with the study of Turhanoğlu et al. [23]. However, the prevalence of 25(OH)D3 deficiency in our study was much higher (99.1%) compared with that found by Rossini et al. [18] (52%), Haque and Bartlett [19] (61%), and Braun-Moscovici et al. [22] (42%).

The present study showed an inverse correlation between serum vitamin D level and DAS-28 as well as with its three components: S-28, T-28, and ESR. Our study found a statistically significant moderate inverse correlation between 25(OH)D3 and both

---

**Table 2** Correlation between mean serum 25(OH)D3 level and demographic, clinical, radiologic, and laboratory features of RA patients

| Features of RA patients | $r$   | $P$ value |
|-------------------------|------|-----------|
| Demographic data        |      |           |
| Age                     | −0.162| 0.101     |
| Weight                  | −0.256| 0.009     |
| Height                  | −0.141| 0.153     |
| BMI                     | −0.167| 0.09      |
| Disease duration        | −0.166| 0.091     |
| Clinical features       |      |           |
| Morning stiffness       | −0.398| <0.001    |
| Symmetric arthritis     | −0.333| 0.001     |
| SJC-28                  | −0.631| <0.001    |
| TJC-28                  | −0.559| <0.001    |
| Deformities             | −0.134| 0.176     |
| Radiologic features     |      |           |
| Erosive arthritis       | 0.035 | 0.725     |
| IPF                     | −0.234| 0.017     |
| Laboratory features     |      |           |
| ESR                     | −0.39  | <0.001    |
| RF                      | −0.211 | 0.032    |
| Anti-CCP                | −0.073 | 0.469    |

Anti-CCP, anticyclic citrullinated polypeptide; ESR, erythrocyte sedimentation rate; IPF, interstitial pulmonary fibrosis; 25(OH)D3, 25-hydroxyvitamin D3; RA, rheumatoid arthritis; RF, rheumatoid factor; SJC-28, 28 swollen joint count; TJC-28, 28-tender joint count.

**Table 3** Comparison between the mean serum 25(OH)D3 and DAS-28 and M-HAQ

| Parameters               | 25(OH)D3 (mean ± SD) | $P$ value |
|-------------------------|----------------------|-----------|
| DAS-28<2.6              | 16.31 ± 3.3          |           |
| DAS-28<3.2              | 15.2 ± 4.02          |           |
| DAS-28 3.2-5.1          | 5.2 ± 5.4            | <0.001    |
| DAS-28>5.1              | 0.84 ± 6.78          |           |
| M-HAQ ≤0.3              | 9.7 ± 6.25           | <0.001    |
| M-HAQ>0.3               | 2.12 ± 4.93          |           |

DAS-28, 28-joints disease activity score; M-HAQ, modified-health assessment questionnaire; 25(OH)D3, 25-hydroxyvitamin D3.

---

**Figure 1**

Correlation between the serum 25(OH)D3 level in nmol/l and the DAS-28 score. DAS-28, 28-joints Disease Activity Score; 25(OH)D3, 25-hydroxyvitamin D3.

**Figure 2**

Correlation between the serum 25(OH)D3 level in nmol/l and the M-HAQ score. M-HAQ, modified-health assessment questionnaire; 25(OH)D3, 25-hydroxyvitamin D3.
S-28 and T-28 ($r = -0.631, -0.559$, respectively, with $P < 0.001$ for both), which is in agreement with the study of Zakeri et al. [24], but in contrast to the study of Pakchotanong et al. [25], who found an insignificant correlation between 25(OH)D$_3$ and S-28 and T-28. Also, the present study found a statistically significant mild inverse correlation between 25(OH)D$_3$ and ESR ($r = -0.39, P < 0.001$) that was in agreement with the study of Kostoglou-Athanassiou et al. [13]. Moreover, the current study found a statistically significant strong inverse correlation between 25(OH)D$_3$ and DAS-28 ($r = -0.794, P < 0.001$) and this is in agreement with several previous studies. In a study involving 158 RA patients, Moghimi et al. [10] found an inverse correlation between serum vitamin D and DAS. Kostoglou-Athanassiou et al. [13], Rossini et al. [18], and Haque and Bartlett [19] found the same inverse correlation between vitamin D level and disease activity score in RA patients. Also, Turhanoglu et al. [23], Zakeri et al. [24], and Chen et al. [26] found that vitamin D deficiency was associated with the RA activity score. Welsh et al. [27] and Kerr et al. [28] found a significant correlation between vitamin D deficiency and increased disease activity in RA. However, other studies did not find such a significant correlation between vitamin D level and RA activity [22,25,29–31].

Moreover, there was a statistically significant moderate inverse correlation between 25(OH)D$_3$ and M-HAQ ($r = -0.562, P < 0.001$) that was in agreement with other previous studies [18,23]. In contrast, other studies showed an insignificant correlation between vitamin D and RA functional disability [26,32]. There was a statistically significant mild inverse correlation between 25(OH)D$_3$ and body weight ($r = -0.256, P < 0.009$). Body weight is part of the BMI calculation formula and according to this formula and the WHO classification, the mean BMI of our patients (29.2 kg/m$^2$) was within the overweight range [33]. This significant correlation is in agreement with previous studies that reported an inverse correlation between 25(OH)D$_3$ and obesity [34,35].

Our present study found a statistically significant mild inverse correlation between vitamin D and IPF ($r = -0.234, P=0.017$). In a previous study of 67 patients with interstitial lung disease (ILD) secondary to connective tissue disease including RA and 51 patients with other causes of ILD, significant D deficiency (52 vs. 20%, $P<0.0001$) and insufficiency (79 vs. 31%, $P < 0.0001$) were found among those with connective tissue disease-ILD than those with other forms of ILD [36].

No significant correlation was found between 25(OH)D$_3$ and BMD. In contrast to our results, Chen et al. [26] found a significant positive correlation between 25(OH)D$_3$ and BMD.

No significant correlation was found between 25(OH)D$_3$ and drug intake. This finding is in agreement with the study of Baker et al. [37].

Vitamin D is known to induce immunologic tolerance [32] and its deficiency may increase the risk of development of autoimmune diseases such as RA. Also, vitamin D has immunomodulatory properties [38,39]. It appears to regulate the immune response by decreasing antigen presentation [40], inhibiting the T-helper type-1 (Th-1) cell that is directed against self-antigens [41], and decreases the production of interleukin-2 and interleukin-5 [42]. 1,25(OH)$_2$D$_3$ suppresses proliferation and immunoglobulin production and retards differentiation of B-cell precursors into plasma cells [43]. Varennora et al. [44] reported that vitamin D supplementation may be recommended for RA patients for the prevention and treatment of osteoporosis as well as for its possible effects on disease activity.

Conclusion
Our results showed a high prevalence of vitamin D deficiency among RA patients as well as among the controls, indicating that vitamin D deficiency might be endemic among our population. Although the mean serum level of vitamin D was lower in RA patients, it was insignificantly different from that among the controls. However, there were statistically significant inverse correlations between vitamin D and both RA disease activity and functional disability. Vitamin D deficiency also correlated inversely with IPF, but not with BMD. Our finding justifies the inclusion of vitamin D in the routine RA laboratory workup because of its possible effects on disease activity and disability outcome.

Acknowledgements
Conflicts of interest
There are no conflicts of interest.

References
1 McInnes I, Schett G. The pathogenesis of rheumatoid arthritis. N Engl J Med 2011; 365:2205-2219.
2 Karray EF, Ben Dhifallah I, Ben Abdelghani K, Ben Ghorbel I, Khanfir M, Houman H, et al. Associations of vitamin D receptor gene polymorphisms FokI and BsmI with susceptibility to rheumatoid arthritis and Behçet’s disease in Tunisians. Joint Bone Spine 2012; 79:144–148.
3 Choy E. Understanding the dynamics: pathways involved in the pathogenesis of rheumatoid arthritis. Rheumatology (Oxford) 2012; 51:v3–v11.
4 Mason R, Sequeira V, Gordon-Thomson C. Vitamin D: the light side of sunshine. Eur J Clin Nutr 2011; 65:986–993.
5 Hewison M, Burke F, Evans KN, Lammas DA, Sansom DM, Liu P, et al. Extra-renal 25-hydroxyvitamin D 1α,25-hydroxylase in human health and disease. J Steroid Biochem Mol Biol 2007; 103:316–321.
6 Holick M. Vitamin D: evolutionary, physiological and health perspectives. Curr Drug Targets 2011; 12:4–18.
7 Gopinath K, Danda D. Supplementation of 1,25 dihydroxy vitamin D3 in patients with treatment-naive early rheumatoid arthritis: a randomised controlled trial. Endocrinol Metab Clin North Am 2010; 39:355–379.
8 Biki D. Vitamin D regulation of immune function. Vitam Horm 2011; 86:1–21.
9 Merlino L, Curtis J, Mikuls T, Cerhan J, Criswell L, Saag K. Kowa Women's Health Study. Vitamin D intake is inversely associated with rheumatoid arthritis: results from the Iowa Women's Health Study. Arthritis Rheum 2004; 50:72–77.
10 Moghimi J, Sadeghi A, Malek M, Ghorbani R. Relationship between disease activity and serum levels of vitamin D and parathyroid hormone in rheumatoid arthritis. Endocr Regul 2012; 46:61–66.
11 Jankosky C, Deussing E, Gibson R, Haverkos H. Viruses and vitamin D in the etiology of type 1 diabetes mellitus and multiple sclerosis. Virus Res 2012; 163:424–430.
12 Heidari B, Hajian-Tilaki K, Heidari P. The status of serum vitamin D in patients with rheumatoid arthritis and undifferentiated inflammatory arthritis compared with controls. Rheumatol Int 2011. [Epub ahead of print].
13 Kostoglou-Athanassiou I, Athanassiou P, Lyraki A, Raftaki I, Antoniadis P, Drosatos D, et al. Vitamin D and rheumatoid arthritis. Ther Adv Endocrinol Metab 2012; 3:181–187.
14 Song GG, Ba SC, Lee YH. Association between vitamin D intake and the risk of rheumatoid arthritis: a meta-analysis. Clin Rheumatol 2012;31:1733–1739.
15 Aletaha D, Neogi T, Silman A, Funovits J, Felson D, Bingham C, et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis Rheum 2010; 62:2569–2581.
16 Prevoo MLL, van ’t Hof MA, Kuper HH, van Leeuwen MA, van De Putte LB, van Riel PL. Modified disease activity scores that include twenty-eight-joint disease activity and serum levels of vitamin D and parathyroid hormone in patients with rheumatoid arthritis. Arthritis Rheum 1995; 38:44–48.
17 Pincus T, Summey JA, Soraci SA Jr, Wallston KA, Hummon NP. Assessment of patient satisfaction in activities of daily living using a modified Stanford Health Assessment Questionnaire. Arthritis Rheum 1983; 26:1346–1353.
18 Rossini M, Maddaloni Bongi S, La Montagna G, Minisola G, Malavolta N, Bernini L, et al. Vitamin D deficiency in rheumatoid arthritis: prevalence, determinants and associations with disease activity and disability. Arthritis Res Ther 2010; 12:R216.
19 Haque U, Bartlett S. Relationships among vitamin D, disease activity, pain and disability in rheumatoid arthritis. Clin Exp Rheumatol 2010; 28:745–747.
20 WHO. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis: technical report series 843. Geneva: WHO; 1994.
21 Kanis JA, Gluer CCF or the Committee of Scientific Advisors, International Osteoporosis Foundation. An update on the diagnosis and assessment of osteoporosis with densitometry. Osteoporos Int 2000; 11:192–202.
22 Braun-Moscovici Y, Toledano K, Markovits D, Rozin A, Nahir AM, Balbir-Gurman A. Vitamin D level: is it related to disease activity in inflammatory joint disease? Rheumatol Int 2011; 31:493–499.
23 Turhanoglu AD, Guler H, Yonden Z, Aslan F, Mansuroglu A, Ozer C. The relationship between vitamin D and disease activity and functional health status in rheumatoid arthritis. Rheumatoi Int 2011; 31:911–914.
24 Zakeri Z, Sandoughi M, Mashhadi MA, Raeesi V, Shahbaksh S. Serum vitamin D level and disease activity in patients with recent onset rheumatoid arthritis. Int J Rheum Dis 2013;18. DOI:10.1111/1756-185X.12181. [Epub ahead of print].
25 Pakchantoon R, Chaiyounnuk S, Narongroeknawin P, Asavatanabodee P. The association between serum vitamin D level and disease activity in Thai rheumatoid arthritis patients. Int J Rheum Dis 2013. DOI:10.1111/1756-185X.12222. [Epub ahead of print].
26 Chen J, Liu W, Lin Q, Chen L, Yin J and Huang H. Vitamin D deficiency and low bone mineral density in native Chinese rheumatoid arthritis patients. Int J Rheum Dis 2014; 17:66–70.
27 Welsh P, Peters M, McNines I, Ems W, Lips P, McKellar G, et al. Vitamin D deficiency is common in patients with RA and linked to disease activity, but circulating levels are unaffected by TNFα blockade: results from a prospective cohort study. Ann Rheum Dis 2011; 70:1165–1167.
28 Kerr G, Sabahi I, Richards J, Caplan L, Cannon G, Reimold A, et al. Prevalence of vitamin D insufficiency/deficiency in rheumatoid arthritis and associations with disease severity and activity. J Rheumatol 2011; 38:53–59.
29 Quraishe MK, Badsha H. Rheumatoid arthritis disease activity and vitamin D deficiency in an Asian resident population. Int J Rheum Dis 2010; 13:275–281.
30 Baker J, Baker D, Toedtler G, Shults J, Von Feldt J, Leonard M. Associations between vitamin D, disease activity, and clinical response to therapy in rheumatoid arthritis. Clin Exp Rheumatol 2012; 30:658–664.
31 Weiss S. Bacterial components plus vitamin D: the ultimate solution to the asthma (autoimmune disease) epidemic? J Allergy Clin Immunol 2011; 127:1128–1130.
32 Vanlint S. Vitamin D and obesity. Nutrients 2013; 5:949–956.
33 Parikh SJ, Edelman M, Uwalo GI, Freedman RJ, Semega-Janneh M, Reynolds J, et al. The relationship between obesity and serum 1,25-dihydroxy vitamin D concentrations in healthy adults. J Clin Endocrinol Metab 2004; 89:1199–1203.
34 Laguna Z, Poroncinu A, Lindberg F, Hoxberg S, Moan J. The dependency of vitamin D status on body mass index, gender, age and season. Anticancer Res 2009; 29:3713–3720.
35 Haganam J, Panos R, McCormack F, Thakar C, Wikenheiser-Brock A, Shipley R, et al. Vitamin D deficiency and reduced lung function in connective tissue-associated interstitial lung diseases. Chest 2011; 139:533–536.
36 Baker JF, Baker DG, Toedtler G, Shults J, Von Feldt JM, Leonard MB. Association between vitamin D, disease activity, and clinical response to therapy in rheumatoid arthritis. Clin Exp Rheumatol 2012; 30:658–664.
37 Hewison M. Vitamin D and immune function: autocrine, paracrine or endocrine? Scand J Clin Lab Invest Suppl 2012; 243:92–102.
38 Mora JR, Irwala M, von Andrian UH. Vitamin effects on the immune system: vitamins A and D take centre stage. Nat Rev Immunol 2008; 8:685–698.
39 Bartels L, Hvas C, Agholt J, Dahlerup J, Agger R. Human dendritic cell antigen presentation and chemotaxis are inhibited by intrinsic 25-hydroxy vitamin D activation. Int Immunopharmacol 2010; 10:922–928.
40 Jirapongsanunok O, Melamed I, Leung D. Additive immunosuppressive effects of 1,25-dihydroxyvitamin D3 and corticosteroids on TH1, but not TH2, responses. J Allergy Clin Immunol 2000; 106:981–985.
41 Merlino LA, Curtis J, Mikuls TR, Cerhan JR, Criswell LA, Saag KG. Women's Health Study. Vitamin D intake is inversely associated with rheumatoid arthritis: results from the Iowa Women's Health Study. Arthritis Rheum 2004; 50:72–77.
42 Chen S, Sims G, Chen X, Gu Y, Chen S, Lipsky P. Modulatory effects of 1,25-dihydroxyvitamin D3 on human B cell differentiation. J Immunol 2007; 179:1634–1647.
43 Varennna M, Manara M, Cantatore F, Del Puente A, Di Munno O, Malavolta N, et al. Determinants and effects of vitamin D supplementation on serum 25-hydroxyvitamin D levels in patients with rheumatoid arthritis. Clin Exp Rheumatol 2012; 30:714–719.