

Effects Of Vitamin D3 Supplementation On Lung Function Of Healthy Non-Smoking Young Iraqi Subjects

تأثيرات تناول فيتامين "د" على وظائف الرئتين عند الأشخاص العراقيين الشباب غير المدخنين
الأصحاء

*Basim MH Zwain:

**Ali Abdil Razzaq Aldallal:

الخلاصة

الخلفية: هنالك أدلة متزايدة بأن فيتامين "د3" يحسن وظائف الرئتين عند الأشخاص المرضى بأمراض تنفسية. كما وجد أن تراكيز فيتامين "د3" العالية في بلازما الدم مرتبط بتحسن وظائف الرئتين في عدة مجتمعات.

الأهداف: دراسة تأثيرات تناول جرعة فموية واحدة من فيتامين "د3" (600 وحدة عالمية) على وظائف الرئتين عند الأشخاص العراقيين الشباب غير المدخنين الأصحاء.

المنهجية: أجريت فحوصات وظائف الرئة متمثلة بسعة الزفير القسري (FVC) وحجم الزفير القسري في ثانية واحدة (FEV_1) ونسبة حجم الزفير القسري ($FEV\%$) إلى 82 شاب من طلبة كلية عراقيين أصحاء غير مدخنين (38 ذكر و 44 أنثى) على مرحلتين بينهما شهر واحد (الزيارة الأولى والزيارة الثانية). تم تقسيمهم إلى مجموعتين رئيسيتين: مجموعة السيطرة (CRL) ومجموعة فيتامين "د3" (VTD). احتوت مجموعة CRL على 42 شخص (18 ذكر و 24 أنثى) لم يتناولوا فيتامين "د3" بينما احتوت مجموعة VTD على 40 شخص (20 ذكر و 20 أنثى) الذين تناولوا جرعة فموية واحدة من فيتامين "د3" (600 وحدة عالمية). كانت أعمار جمهرة الدراسة نفسها (20 سنة) ولم تختلف أطوالهم معنوياً داخل مجاميع الذكور والإناث كل على حدة.

النتائج: وجد بأن FVC و FEV_1 (وليس $FEV\%$) كانا أعلى بشكل معنوي (من 80 مل إلى 130 مل) في الزيارة الثانية مما في الزيارة الأولى (كلها $p < 0.05$).

الاستنتاج: اعتماداً على نتائج البحث الحالي يستنتج بأنه عند الأشخاص العراقيين الشباب الأصحاء غير المدخنين لا يبدو أن هناك تأثير إيجابي لفيتامين "د3" على وظائف الرئة أكثر مما لدى أقرانهم في مجموعة السيطرة.

Abstract

Background: There is an increasing evidence that vitamin D3 improves lung function in respiratory diseased subjects. Higher plasma vitamin D3 concentrations are also linked to better lung function in several communities.

Objectives: To study the effects of single oral vitamin D3 supplementation (600 IU) on lung function in healthy non-smoking young Iraqi subjects.

Methodology: Spirometric tests represented by forced vital capacity (FVC), forced expiratory volume in first one second (FEV_1) and forced expiratory volume ratio ($FEV\%$) were done for 82 healthy non-smoking young Iraqi college students (38 males and 44 females) in two occasions one month apart (first and second visits). They were divided into two main groups: Control group (CRL) and Vitamin D3 group (VTD). CRL group contained 42 subjects (18 males and 24 females) who didn't receive oral vitamin D3 supplementation. VTD group contained 40 subjects (20 males and 20 females) who received single oral vitamin D3 supplementation (600 IU). The ages of the study population were the same (20 years) and their heights were not significantly different within each sex.

Results: It was found that FVC and FEV_1 (but not $FEV\%$) were significantly higher (from 80 ml to 130 ml) in the second visit than in the first visit in both groups (VTD and CRL) and in either sex (all $p < 0.05$).

Conclusion: Depending on the results of present research; it is concluded that in healthy non-smoking Iraqi subjects; vitamin D3 doesn't seem to have positive effects on spirometric measurements other than these observed in control subjects.

Keywords: Vitamin D3, forced vital capacity (FVC), forced expiratory volume in first one second (FEV_1), forced expiratory volume ratio ($FEV\%$) and lung function.

*PhD, M.Sc., B.D.S. : Assistant Professor in the Dept. of Basic Sciences, Faculty of Dentistry, University of Kufa.

** M.Sc., B.Sc.Ph. : Lecturer in the Dept. of Basic Sciences, Faculty of Dentistry, University of Kufa.

INTRODUCTION

Pulmonary function tests are still the tools with which pulmonary diseases are identified⁽¹⁾. They remain the most accurate means of quantifying the severity of diffuse lung diseases⁽²⁾. Spirometry is the basic pulmonary function test that is widely used to detect obstructive^(3 and 4) and/or restrictive⁽⁵⁾ lung diseases. Spirometric measurements include forced vital capacity (FVC), forced expiratory volume in first second (FEV₁) and forced expiratory volume ratio (FEV%)⁽²⁾. Interpretation of pulmonary function measurements is complicated by the fact that predicted values from the various published studies vary by as much as 20% for an individual subject. This is due to vast diversity of factors that affect the predicted normal spirometric values including age, height, gender, weight, muscular activity, race, ethnicity, cigarette smoking, occupation, residence, socioeconomic and nutritional status ...⁽⁶⁾ There is also evidence that diet can influence FEV₁ and vital capacity. In keeping with this, both the serum concentrations and the dietary intake of antioxidant nutrients such as vitamin C, vitamin E, beta-carotene, and selenium have been positively associated with lung function. The dietary intake of magnesium is also associated with increased lung function and reduced airway reactivity. Low concentrations of vitamin D₃ have been linked to many diseases including osteoporosis, hypertension, ischemic heart disease, type I diabetes, and cancer⁽⁷⁾. Vitamin D₃ is synthesized in the skin following sunlight exposure, but concentrations of vitamin D₃ can also be influenced by dietary intake. Vitamin D is converted to 25-hydroxy vitamin D through the action of a hydroxylase in the liver, and this, in turn, is converted into 1,25-dihydroxyvitamin D, the active metabolite, in the kidney. 1,25-dihydroxy vitamin D has a number of actions that may be relevant to respiratory disease. It inhibits the formation of matrix

metalloproteinases as well as fibroblast proliferation, and influences collagen synthesis⁽⁸⁾. These actions mean that 1,25-dihydroxy vitamin D could influence tissue remodeling. These observations raise the possibility that vitamin D₃ could influence lung function^(9 and 10) and that vitamin D₃ deficiency could result in decline in lung function⁽¹¹⁾. Recently, evidence is presented that supplementation of high dose of vitamin D₃ reduces exacerbations in chronic obstructive pulmonary disease⁽¹²⁾ but further information are needed to explore the role of vitamin D₃ in healthy lungs.

OBJECTIVES:

To study the effects of single oral vitamin D₃ supplementation (600 IU) on lung function in healthy non-smoking young Iraqi subjects.

SUBJECTS AND METHODS

A total number of 110 subjects (52 males and 58 females) were initially included in the present research. They were, all, second year college students at the age of 20 years. Their heights were ranging from 155 cm to 178 cm. Unhealthy subjects were excluded no matter their diseases were respiratory or not. Subjects with history of respiratory illnesses were also excluded. All of participants claimed not to be smokers. All of the other subjects performed the forced expiratory maneuver during the first visit. Spirometric measurements including FVC, FEV₁ and FEV% were done with the use of a standardized spirometer produced by Vitalograph Medical Instrumentation Co. Ltd, Buckingham, England while measurements of height were done with a well calibrated scale. Spirometric measurements were done in sitting position after a period of resting time in order to achieve the steady state which means that the heart rate in consecutive minutes is changing by less than 3 beats per minute. With a clipped nose, the

subject is instructed to inspire forcefully as much as possible and then to blow out through the fully and tightly encircled mouthpiece of spirometer as forceful and as quick as possible until no more air can be blown from the lungs. This is the right forceful expiratory maneuver which is allowed to be done in three trials with the best result to be recorded ⁽⁶⁾.

For the sake of better adjustments for any other factors that may affect the spirometric outcomes; the results on either far extremes were discarded. The remaining 82 subjects (38 males and 44 females) were divided into two main groups: Control group (CRL) and Vitamin D3 group (VTD). CRL group contained 42 subjects (18 males and 24 females) who didn't receive oral vitamin

D3 supplementation. VTD group contained 40 subjects (20 males and 20 females) who received oral vitamin D3 supplementation which was provided as single dose of 600 IU vitamin D33 (devit3 manufactured by Deva).

Thirty days later, both groups performed the second visit spirometric maneuver as detailed above. Means and standard deviations were calculated for all parameters for the whole study population. Student's t-test was employed to compare the means of paired groups (first versus second visits) and statistical decisions were regarded significant when p values were less than 0.05. Graphs were drawn to clarify the results.

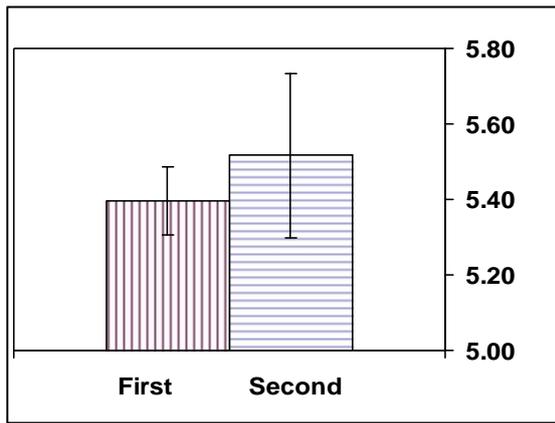
RESULTS

All of the second year college students were 20 years old (SD = 0). Males' average height was 175.18 cm \pm 1.89 cm and females' average height was 162.8 cm \pm 3.99 cm. In either sex; there were no significant differences between the means of heights of VTD and CRL groups.

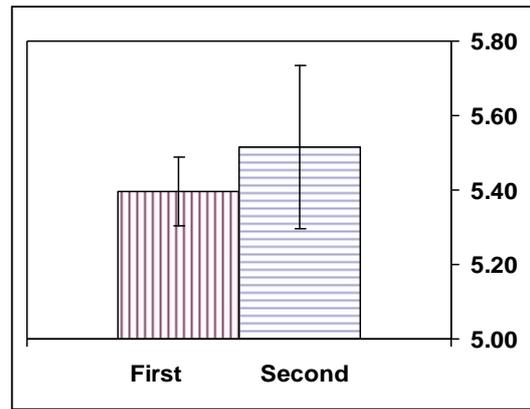
Table 1: Means and standard deviations (SD) of forced vital capacity (FVC), forced expiratory volume (FEV₁) and forced expiratory volume ratio (FEV%) in vitamin D3 (VTD) and control (CRL) groups during the first and second visits in males and females.

		FVC in liters (SD)		FEV ₁ in liters (SD)		FEV% (SD)	
		First visit	Second visit	First visit	Second visit	First visit	Second visit
Males n=38	VTD	5.40 (0.09)	5.52 (0.22)	4.22 (0.31)	4.35 (0.32)	78.24 (5.52)	78.83 (4.58)
	CRL	5.37 (0.11)	5.49 (0.16)	4.09 (0.18)	4.22 (0.15)	76.17 (3.53)	76.90 (3.16)
Females n=44	VTD	3.38 (0.15)	3.46 (0.17)	2.73 (0.20)	2.81 (0.23)	80.81 (5.04)	81.24 (5.42)
	CRL	3.43 (0.14)	3.55 (0.14)	2.81 (0.09)	2.90 (0.12)	81.86 (3.26)	81.85 (3.31)

Table 1 shows the spirometric outcomes for VTD and CRL groups in the two visits and in either sex.



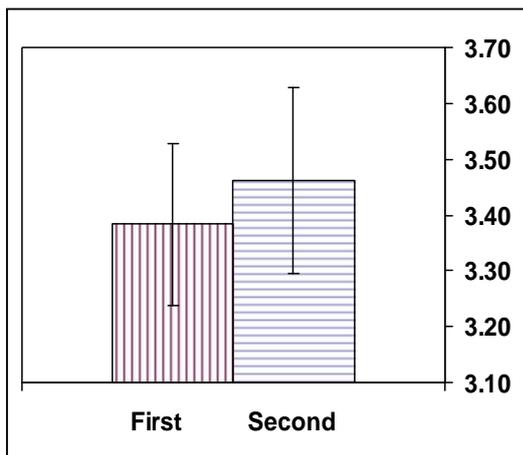
VTD group n=20, p<0.002



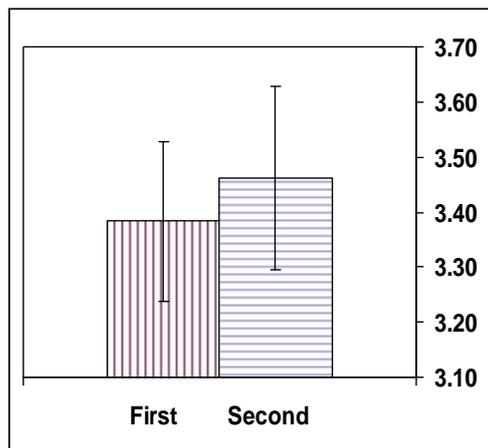
CRL group n=18, p<0.05

Figure 1 : Differences in forced vital capacity (in liters) between first and second visits in CRL and VTD male groups.

Regarding FVC measurements; figure 1 illustrates that they were significantly higher (by about 120 ml) in the second than in the first visits for both VTD and CRL male groups (p<0.002 and p<0.05 respectively).



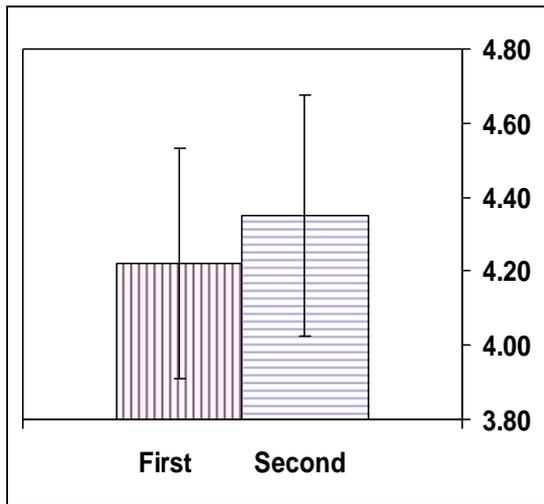
VTD group n=20, p<0.002



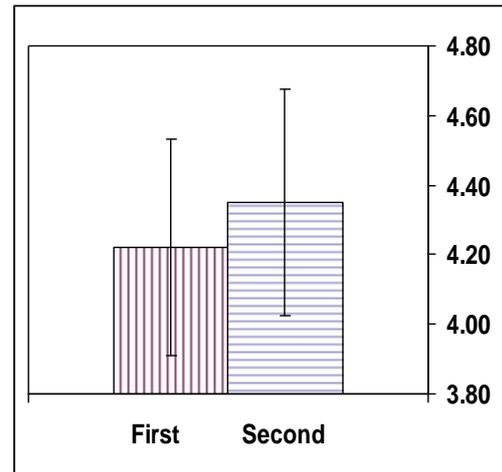
CRL group n=24, p<0.05

Figure 2 : Differences in forced vital capacity (in liters) between first and second visits in CRL and VTD female groups.

Figure 2 illustrates that FVC measurements were also significantly higher in the second than in the first visits for both VTD (by about 80 ml) and CRL (by about 120 ml) female groups (p<0.002 and p<0.05 respectively).



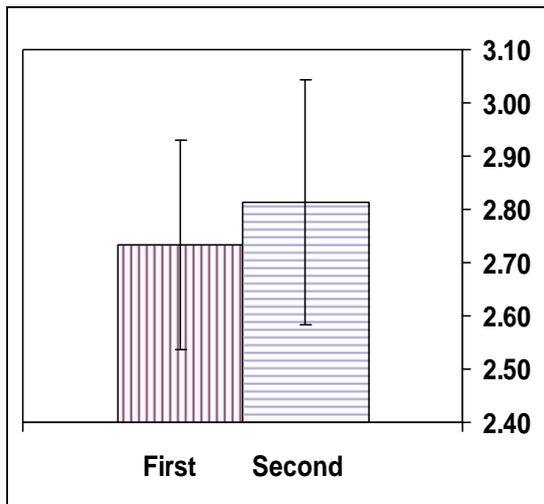
VTD group n=20, p<0.05



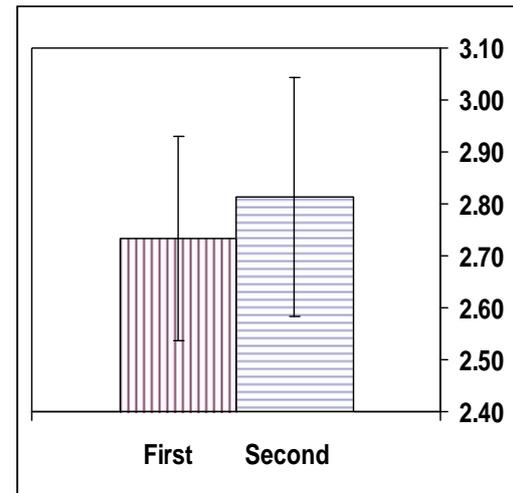
CRL group n=18, p<0.05

Figure 3 : Differences in forced expiratory volume (in liters) between first and second visits in CRL and VTD male groups.

Regarding FEV₁ measurements; figure 3 illustrates that they were significantly higher (by about 130 ml) in the second than in the first visits for both VTD and CRL male groups (p<0.05).



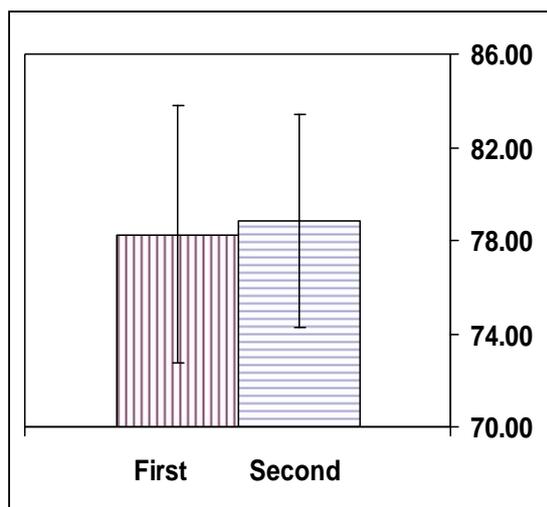
VTD group n=20, p<0.05



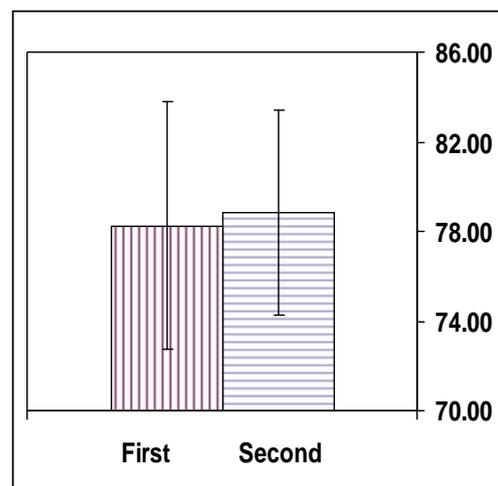
CRL group n=24, p<0.04

Figure 4 : Differences in forced expiratory volume (in liters) between first and second visits in CRL and VTD female groups.

The same results are shown in figure 4 which illustrates that FEV₁ measurements were also significantly higher in the second than in the first visits for both VTD (by about 80 ml) and CRL (by about 90 ml) female groups (p<0.05 and p<0.04 respectively).



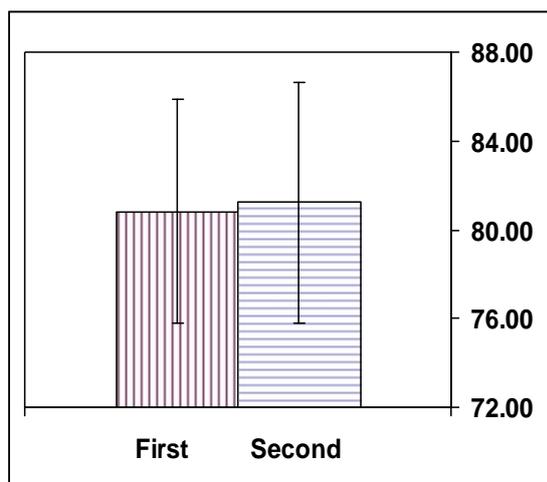
VTD group n=20 , No significance



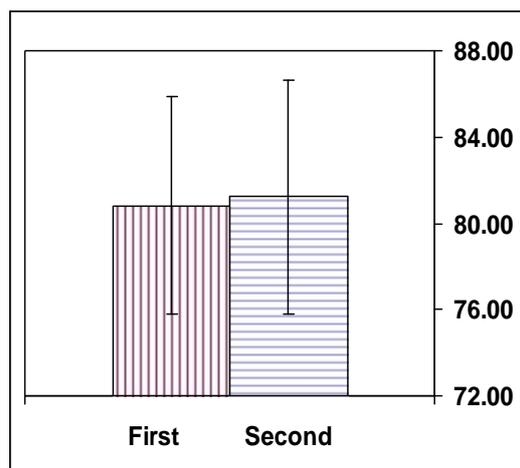
CRL group n=18, No significance

Figure 5 : Differences in forced expiratory volume ratio (as a percentage) between first and second visits in CRL and VTD male groups.

While for FEV%; the results were different as shown in figure 5 which illustrate that there were no significant differences in FEV% between the first and the second visits for both VTD and CRL groups and in males.



VTD group n=20, No significance



CRL group n=24, No significance

Figure 6 : Differences in forced expiratory volume ratio (as a percentage) between first and second visits in CRL and VTD female groups.

Again, figure 6 illustrate that there were no significant differences in FEV% between the first and the second visits for both VTD and CRL groups and in females.

DISCUSSION

Vitamin D3 deficiency was found to be associated with many diseases including osteoporosis, hypertension, ischemic heart disease, type I diabetes, and cancer and declined lung function⁽⁷⁻¹²⁾. High dietary consumption of fruit,

vegetables, oily fish and whole meal cereals was found to be associated with better lung function⁽¹³⁾. Higher prudent diet scores are associated with greater intakes of a range of micronutrients including vitamin D3⁽¹⁴⁾ but the protective effect of the 'prudent' pattern

may not be due to a higher intake of vitamin D3 and is more likely to be explained by antioxidant nutrients in fruit, vegetables and whole grains or nutrients other than vitamin D3 in oily fish such as fatty acids. A higher intake of fruit and whole grains, of various antioxidants including vitamins C and E, beta carotene and selenium, and of fatty acids have all been linked to better lung function⁽¹⁵⁾. Controversy is still present in literature about the relationship between vitamin D3 plasma concentration and lung function. While some researches suggested a positive relationship^(16 and 17); others not^(18 and 19). Present research, however, confirmed that FVC and FEV₁ measurements are increased by 80 - 130 ml after vitamin D3 supplementation, but nearly the same increase was found in control group during the second visit without intake of vitamin D3 (though with lower levels of significance for FVC). This improvement in spirometric measurements may be attributed to the role of vitamin D3 or to other factors like the improved performance of spirometric maneuver by the young students. The mechanisms by which vitamin D3 levels might affect lung function are unclear. Potential explanations in diseased subjects include effects on respiratory infection risk (via both innate and adaptive mechanisms) and lung tissue remodeling (via matrix metalloproteinases and other pathways^(20 and 21)). In apparently healthy subjects, however, there is no induction of tissue remodeling, innate or adaptive mechanisms. Furthermore, there is no vitamin D3 deficiency challenging our temperate climate population to be compensated. It is suggested that the role of vitamin D3 in the improvement of lung function must be comprehensively studied in respiratory diseased subjects.

CONCLUSIONS

In healthy non-smoking Iraqi subjects, vitamin D3 doesn't seem to have positive

effects on spirometric measurements other than these observed in control subjects. An epidemiological study is recommended to elucidate the effects of vitamin D3 supplementation on respiratory compromised Iraqi patients.

REFERENCES

- 1- Otaola M, Quadrelli S, Tabaj G, Aguirre R, Molinari L, Di Boscio V. Pulmonary Function Tests and 5-Year Survival in Patients Systemic Sclerosis and Interstitial Lung Disease (ILD). CHEST 2012 Vol 142, No. 4
- 2- Baughman RP and du Bois MR. Diffuse lung disease a practical approach. Springer Link. 2012, Part 1: Pulmonary Function Testing, pp: 71-84.
- 3- Varkey B. Obstructive, occupational and environmental diseases. Curr Opin Pulm Med. 2012 Vol 18 (2): 95-96.
- 4- Lam, David C.L.; Hui, Christopher K.M.; Ip, Mary S.M. Issues in pulmonary function testing for the screening and diagnosis of chronic obstructive pulmonary disease. Curr Opin Pulm Med. 2012;18(2):104-111.
- 5- Berdal G, Halvorsen S, van der Heijde D, Mowe M and Dagfinrud H. Restrictive pulmonary function is more prevalent in patients with ankylosing spondylitis than in matched population controls and is associated with impaired spinal mobility: a comparative study Gunnhild. Arthritis Research & Therapy 2012; 14:R19.
- 6- Mason R. J. Martin T, King T, Murray J F. and Nadel J A. Murray and Nadel's Textbook of Respiratory Medicine. Chapter 24 : Pulmonary function testing by Matthew J. Hegewald, and Robert O. Crapo. 2010 Elsevier.
- 7- Holick MF. Vitamin D deficiency. N Engl J Med. 2007;357:266-281.

- 8- Kunisaki KM, Niewoehner DE, Singh RJ and Connett JE. Vitamin D status and longitudinal lung function decline in the Lung Health Study. *Eur Respir J*. 2011 February ; 37(2): 238–243.
- 9- Herr C, Greulich T, Kocuzilla RA, Meyer S, Zakharkina T, Branscheidt M, Eschmann R and Bals R. The role of vitamin D in pulmonary disease: COPD, asthma, infection, and cancer . *Respiratory Research* 2011, 12:31.
- 10- Black PN and Scragg R. Relationship between serum 25-Hydroxyvitamin D and pulmonary function in the Third National Health and Nutrition Examination Survey. *CHEST* 2005; 128:3792–3798.
- 11- Li F, Peng M and Jiang L. Vitamin D deficiency is associated with decreased lung function in Chinese adults with asthma. *Respiration* 2011;81:469–75.
- 12- Lehouck A, Mathieu C and Carremans C. High doses of vitamin D to reduce exacerbations in chronic obstructive pulmonary disease. *Ann Intern Med* 2012;156:105-14.
- 13- Shaheen SO, Jameson KA and Syddall HE. The relationship of dietary patterns with adult lung function and COPD. *Eur Respir J* 2010;36:277–84.
- 14- Robinson S, Syddall H, Jameson K, Batelaan S, Martin H , Dennison EM , Cooper C, Sayer AA. Current patterns of diet in community dwelling older men and women: results from the Hertfordshire Cohort Study. *Age and Ageing* 2009;38(5):594–9
- 15- Tricon S, Willers S and Smit HA. Nutrition and allergic disease. *Clin Exp Allergy Rev* 2006;6:117–88.
- 16- Henderson D and Lie D. Vitamin D may slow progression of lung damage in smokers. *Am J Respir Crit Care Med*. Published online July 20, 2012
- 17- Wauters E, Janssens W and Lambrechts D. Accelerated Lung Function Decline in Smokers: Spotlight on Vitamin D Deficiency. *Am. J. Respir. Crit. Care Med*. 2012; 186:579-581.
- 18- Shaheen SO, Jameson KA, Robinson SM, Boucher BJ, Syddall HE, Sayer AA, Cooper C, Holloway JW, Dennison EM. Relationship of vitamin D status to adult lung function and COPD. *Thorax* (online) 2010.
- 19- Brehm JM, Celedon JC and Soto-Quiros ME. Serum vitamin D levels and markers of severity of childhood asthma in Costa Rica. *Am J Respir Crit Care Med* 2009;179:765–71.
- 20- Janssens W, Lehouck A and Carremans C. Vitamin D beyond bones in chronic obstructive pulmonary disease: Time to act. *Am J Respir Crit Care Med*. 2009;179:630–636.
- 21- Bao BY, Yeh SD, Lee YF. Alpha,25-dihydroxyvitamin D3 inhibits prostate cancer cell invasion via modulation of selective proteases. *Carcinogenesis*. 2006;27:32–42..